21ST INTERNATIONAL VASCULITIS WORKSHOP

BARCELONA

7 - 10 APRIL **2024**

ABSTRACTS BOOK

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INTRODUCTION

The 21st International Vasculitis Workshop takes place in the friendly and lively city of Barcelona (Spain) in April 7- 10, 2024.

The conference name has changed indicating our willingness to expand the scope of interest beyond ANCA-associated vasculitis. The workshop focus on all kind of vasculitis and related disorders from a holistic and multidisciplinary approach and is addressed to clinicians as well as clinical and translational researchers working in this area and to trainees interested in this field.

The vasculitis landscape is rapidly evolving with continuous advances in understanding mechanisms of disease, refinement of diagnostic tools and assessment methods, and improving and increasing treatment options.

Important therapeutic advances have been achieved over the past years widening the therapeutic horizon for patients who previously had limited opportunities mostly relying on treatments with marked toxicity. Emerging new concepts and approaches arise from collaboration and joint efforts among basic, clinical, and translational investigators working in academic or industry settings, as well as patient associations and advocacies.

After the difficult constrictions of the Covid 19 pandemic we expect this fully face-to-face meeting to provide a long-desired opportunity to discuss state of the art management (diagnosis, assessment, treatment) of vasculitis and to share new information on biomarkers and mechanisms of disease in order to improve global patient care. Interchanging ideas and experiences, expanding networks and collaboration, as well as fostering inspiration and motivation for established and young investigators as well as trainees are also among the most important goals of this meeting.

We are fully aware that we, along with the International and local organizing committees, are providing an essential framework but that the content and success of the Workshop relies not only on the selected speakers, moderators, and presenters but on the enthusiastic participation and contributions of the attendants.

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VASCULITIS

WORKSHOP

BARCELONA

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PLENARY SESSION: CELLULAR AND MOLECULAR MECHANISMS OF DISEASE (I)

O-001

Regulatory T Cells Contribute to Downregulation of the Autoimmune Anti-MPO Response

Peiqi Hu, Hong Xiao, Sandra Elmore, Christian Agosto-Burgos, Dominic Ciavatta, Ronald Falk, Charles Jennette, Meghan Free.
UNC-Chapel Hill, Chapel Hill, United States.

Background/ Objectives: Anti-neutrophil cytoplasmic autoantibody (ANCA) vasculitis ultimately stems from a break in tolerance against autoantigen. A better understanding of the cell population(s) required for downregulation of the autoimmune response in ANCA vasculitis is necessary for future cellular-based therapies. Using a mouse model of myeloperoxidase (MPO)-ANCA glomerulonephritis (GN), we interrogated the key immune cells necessary to downregulate the anti-MPO response.

Methods: MPO-/- mice were immunized with native mouse MPO to induce an anti-MPO immune response. Anti-MPO splenocytes were transferred to either Rag2-/- or wildtype (WT) B6 mice to induce the disease model. Flow cytometry was used to phenotype and track immune cells from donor and recipient mice.

Results: Rag2-/- mice that receive anti-MPO splenocytes exhibit elevated anti-MPO titers and develop GN by day 14. Conversely, WT B6 mice that receive anti-MPO splenocytes are able to downregulate the anti-MPO immune response and exhibit no anti-MPO titers or kidney involvement. Reconstitution of WT B6 splenocytes into Rag2-/- mice prior to anti-MPO splenocyte transfer was able to prevent anti-MPO titers and kidney disease. Upon phenotyping which immune cells were reconstituted, T cells were the majority of immune cells repopulated in Rag2-/- recipient mice. Furthermore, regulatory T cells (Tregs) were restored to levels similar to WT B6 mice. Therefore, additional experiments purified only WT Tregs to transfer to Rag2-/- prior to disease induction to test the efficacy of Tregs alone in controlling the autoimmune anti-MPO response. Treg transfer alone was able to suppress anti-MPO antibody production by up to 30% in recipient mice.

Conclusions: Through a series of splenocyte transfer, antibody depletion, and purified Treg cell transfer experiments, we determined that Tregs are capable of downregulating and controlling the anti-MPO autoimmune response. These studies are foundational to use this model as a pre-clinical animal model for future Treg studies in humans.

References: None.

Disclosures: None.

O-002

Manipulation of the gut microbiome protects from kidney inflammation and injury in experimental myeloperoxidase anti neutrophil cytoplasmic antibody vasculitis

Diana Tan, Matthew Snelson, Anne Cao Le, Stephanie (U-Shane) Huang, Jenny Nguyen, Melinda Coughlan, Kim O'Sullivan.
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Background/ Objectives: The characteristic pathological feature of anti-neutrophil cytoplasmic antibody vasculitis (AAV) is severe inflammation induced by neutrophils which causes damage to the small blood vessels of the kidney. Neutrophil activity is influenced by microbial metabolites, including short chain fatty acids (SCFAs), produced from fermentation of non-digestible carbohydrates by gut microbiota. Gut bacteria that produce anti-inflammatory SCFAs promote gut barrier health but are notably depleted in inflammatory kidney diseases. We hypothesised that either a diet high in resistant starch or oral administration of SCFAs would promote the growth of SCFA producing bacteria and restore the imbalance of gut microbiota, and reduce systemic and kidney inflammation.

Methods: We utilised a well-established mouse model of AAV. Mice were randomised to receive either a control diet or a diet supplemented with 15% resistant starch (RS) (*n*=8 per group). In an additional experiment SCFAs acetate, propionate and butyrate were administered orally (*n*=8 per group). At day 20, mice were culled, cecal contents were collected and kidneys removed to assess injury. Glomerular neutrophil, macrophage and T cell infiltration were assessed by immunohistochemistry. Cecal contents were collected, DNA extracted and the V1-V2 hypervariable region amplified using 27F and 338R universal primers to assess the gut microbiota via 16s rRNA analysis. Targeted Liquid chromatography-mass spectrometry (LC-MS) was used to measure SCFAs in the cecal contents.

Results: The resistant starch intervention significantly reduced albuminuria and segmental necrosis in glomeruli and reduced glomerular neutrophil, macrophage and T cell accumulation when compared to the control group (Fig.1 all, $p < 0.0001$). The RS diet significantly altered the gut microbial consortium and was associated with a substantial expansion of *Bacteroidaceae* and *Muribaculaceae* both SCFA producing bacteria. Measurement of the cecal contents showed a significant increase in the production of acetate in the RS group when compared to the control group ($p<0.05$). Dendritic cell (DC) activation markers MHCII and CD80 were both reduced in the RS treated group ($p<0.001$). Kidney mRNA results showed a significant increase in IL-4 production with a decrease in CCL2 mRNA expression ($p<0.001$). Oral administration of the SCFA acetate reduced segmental necrosis, glomerular leukocyte recruitment, and the production of MPO-ANCA (all, $p<0.05$).

Conclusions: A high RS starch diet was able to reduce DC activation, leukocyte accumulation and renal injury suggesting the production of gut SCFAs is anti-inflammatory. Similar effects were seen with the administration of the SCFA acetate. This is the first report of the therapeutic efficacy of either a RS diet or a SCFA supplemented diet in experimental AAV. This data represents a promising therapeutic avenue to limit autoimmune kidney injury in AAV.

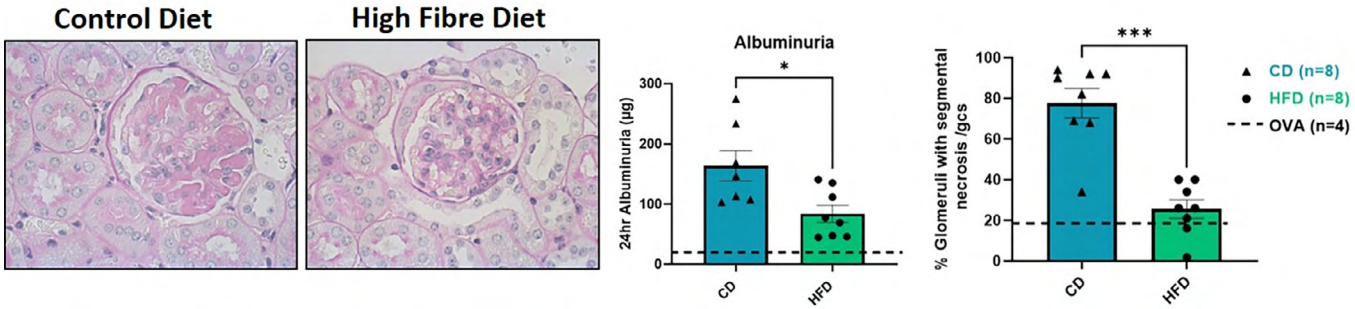

Fig.1. Prophylactic administration of a resistant starch diet reduces glomerular injury and albuminuria in experimental AAV.

O-003

Myeloperoxidase-specific IgM B cells in anti-neutrophil cytoplasmic antibody-associated vasculitis

Corrie Wortel[1], Renee Van De Wetering[1], Helena Keek[1], Eva Maria Stork[1], Theresa Kissel[1], Sanne Reijm[1], Karin A. Van Schie[1], Leendert A. Trouw[1], Onno Teng[1], Abraham Rutgers[2], Peter Heeringa[2], Reinhard E. Voll[3], Marta Rizzi[4], Nils Venhoff[3], Rene E.M. Toes[1], Diane Van Der Woude[1], Hans Ulrich Scherer[1].

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Background/Objectives: Autoantibodies against myeloperoxidase (MPO) or proteinase 3 (PR3) hallmark anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). ANCA-levels in serum fluctuate, and increases in ANCA-IgG levels can predict flare. Here, we focused on the MPO-specific B-cell response and investigated the immunological mechanisms that contribute to disease pathology.

Methods: We developed a flow cytometry-based approach to identify MPO-specific B cells in the circulation of MPO-AAV patients using fluorochrome-conjugated neutrophil-derived MPO. Single cell-sorted, MPO-reactive B cells were cultured and analyzed by ELISA, followed by B cell receptor (BCR) analysis using PCR and Sanger sequencing. In addition, bulk B cell populations from MPO-positive AAV patients and healthy controls (HCs) were isolated, cultured and Ig production measured by ELISA. Serum antibody responses were assessed in three European cohorts.

Results: Our antigen labelling approach identified MPO-specific B cells in the circulation of MPO+ AAV patients, in a frequency of up to 1:1000 B cells. Intriguingly, the MPO-specific B-cell response was dominated by CD27+IgM+ B cells, while IgG+ MPO-specific cells were infrequent. ~65% of single cell-derived BCR sequences contained at least 1 somatic mutation. IgM monoclonal antibodies produced from these sequences (n=5) confirmed MPO-specificity and readily activated complement. Depletion experiments with patient plasma showed a prominent role for anti-MPO IgM rather than IgG in complement activation. Stimulated B cells obtained from peripheral blood of patients and HCs both produced MPO-IgM in culture. Separate cultures of CD27-IgD+, CD27+IgD- and CD27++CD38+++ populations revealed that MPO-IgM B cells were mainly present in the naive compartment in HCs. In patients, they could also be detected in the memory and plasmablast compartments. In plasma, circulating anti-MPO IgM was only present in patients and not in HCs.

Conclusions: We demonstrate the direct ex-vivo identification, isolation and characterization of MPO-specific B cells in human AAV. Our data indicate a defect in early B-cell tolerance to MPO in the human repertoire, highlight activated IgM+ anti-MPO B cells in disease and a dominant role for anti-MPO IgM in complement activation. Together, these results provide a mechanistic basis for treatments targeting complement and B cells in MPO+ AAV.

Disclosures: None.

O-004

CD19 CAR T cells mediate nephroprotective effects in a murine model of ANCA-induced crescentic glomerulonephritis

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Objectives: Anti-neutrophil cytoplasmatic antibody (ANCA)-associated vasculitides (AAV) are life-threatening systemic autoimmune diseases manifesting in the kidneys as necrotizing crescentic glomerulonephritis (NCGN). The main ANCA antigens are myeloperoxidase (MPO) and proteinase 3, both expressed by neutrophils and monocytes (Kitching AR et al. Nat Rev Dis Primers. 2020;6:71). Current treatment options consist of steroids, cytotoxic drugs, and B cell-depleting antibodies (Stone JH et al. N Engl J Med. 2010;363:221–32.). Chimeric antigen receptor (CAR) T cells are modified T cells harboring a receptor with intracellular activating domains and an extracellular antigen-binding domain. They are already used in different B cell malignancies (Brentjens RJ et al. Sci Transl Med. 2013;5:177ra38.; Rhodes JM, Schuster SJ. Cancer J. 2019;25:436–41.), and their application in autoimmune diseases is a promising new therapeutic approach (Mackensen A et al. Nat Med. 2022;28:2124–32.). We tested the hypothesis that CAR T cells targeting CD19 deplete B cells, including MPO-ANCA-producing B cells, thus protecting from ANCA-induced NCGN.

Methods: We used a murine MPO-AAV model where NCGN was established by immunization of $MPO^{-/-}$ mice with murine MPO to induce antibody production against MPO. Afterwards, mice were irradiated and given hematopoietic cells from wild-type mice alone or together with either CD19-targeting CAR T cells or control SP6 CAR T cells. Treatment effects on disease development were evaluated after two, five and eight weeks. For that purpose, histological staining of kidney sections and flow cytometric analyses of spleen, kidney, bone marrow, lymph node and blood samples were done.

Results: CD19 CAR T cells efficiently migrated to and persisted in bone marrow, spleen, peripheral blood, and kidneys for up to eight weeks. CD19 CAR T cells, but not control CAR T cells, depleted B cells and plasmablasts. The anti-MPO-ANCA titer declined faster, and the proportion of damaged glomeruli was reduced in CD19 CAR T cell-treated mice. Therefore, the application of CD19 CAR T cells protected from the development of NCGN.

Conclusion: Our proof-of-principle study shows that depleting CD19-expressing B cells by administration of CD19-targeting CAR T cells is an effective treatment option in murine anti-MPO induced NCGN. It may promote exploration of CAR T cells as a treatment for ANCA-vasculitis patients with the aim of drug-free remission.

Disclosures: None.

O-005

Effect of interleukin-17 in giant cell arteritis

Hélène Greigert[1], André Ramon[2], Baptiste Lamarthée[3], Corentin Richard[4], Claudie Cladière[5], Marion Ciudad[5], Catherine Creuzot-Garcher[6], Laurent Martin[7], Sylvain Audia[1], Romain Boidot[4], Bernard Bonnotte[1], Maxime Samson[1].

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Purpose: Th17 cells have been identified in excess in the blood and affected arteries of giant cell arteritis (GCA) patients. Although the efficacy of secukinumab (SCK) was recently reported in a randomized phase II trial, the role of interleukin-17 (IL-17) in the pathophysiology of GCA is not clearly understood. The aim of this study was to investigate the effect of IL-17 in GCA.

Methods: Fresh fragments of temporal artery biopsies (TAB) were cultured for 5 days in MATRIGEL® as previously described (1,2) in the presence of IL-17, SCK or control IgG. Arterial sections were then harvested, homogenized and analyzed by RNA sequencing and RT-PCR. Vascular myofibroblasts (MF) were obtained from cultures of healthy arteries in MATRIGEL as previously described (1,2). MF were treated *in vitro* with IL-17, interferon-gamma (IFN-γ), SCK or the combination of IL-17 and IFN-γ or IL-17 and SCK for 24 hours. mRNA expression was analysed by RNA sequencing and RT-PCR. Proliferation and migration were measured by impedancemetry and wound-healing assays, respectively.

Results: *Ex-vivo* cultures of TAB from GCA patients with SCK induced major changes in the TAB transcriptome, characterized by decreased expression of genes involved in Th17 polarization and vascular inflammation (*IL1B, IL6, CSF3*), T-cell recruitment (*CCL20*) and fibroblast proliferation (*FGF2*). RT-PCR analysis of *ex-vivo* TAB cultures confirmed that SCK treatment decreased mRNA encoding IL-1β, IL-6 and CCL20 in TAB from GCA patients (n=10; P<0.05), while IL-17 treatment increased the expression of mRNA encoding IL-6, GM-CSF, G-CSF, CCL2, CCL20, FGF2 and VEGF-A in healthy TAB (n=8; P<0.05).

In addition, MF transcriptome was significantly altered when IL-17 was added to the culture, with increased expression of genes involved in vascular inflammation (*CCL2*, *ICAM1*, *IL6*), NFkB pathway activation (*TNFAIP6*, *TNFAIP3*), leukocyte adhesion (*ICAM1*) and MF proliferation (*FGF2*). These changes were reversed in the presence of SCK (Figure 1).

In the presence of IL-17, the mRNA expression of the genes encoding IL-1β, IL-6, IL-12p35, VEGF-A, GM-CSF, G-CSF, CCL2, CCL20 and FGF2 increased in MFs (n=8; P<0.01). There was no significant effect on the mRNA expression of IL-23p19, IL-12p40, collagen alpha chains 1 and 3, PDGFA, PDGFB, CXCL9 and CXCL10. Addition of IFN-γ to the culture increased the expression level of both IL-17 receptor chains (IL17RA and IL17RC) resulting in a synergistic effect with that of IL-17, leading to a sharp rise in the expression of genes encoding IL-1β, IL-6, IL-12p35, GM-CSF, G-CSF, CCL2 and CCL20.

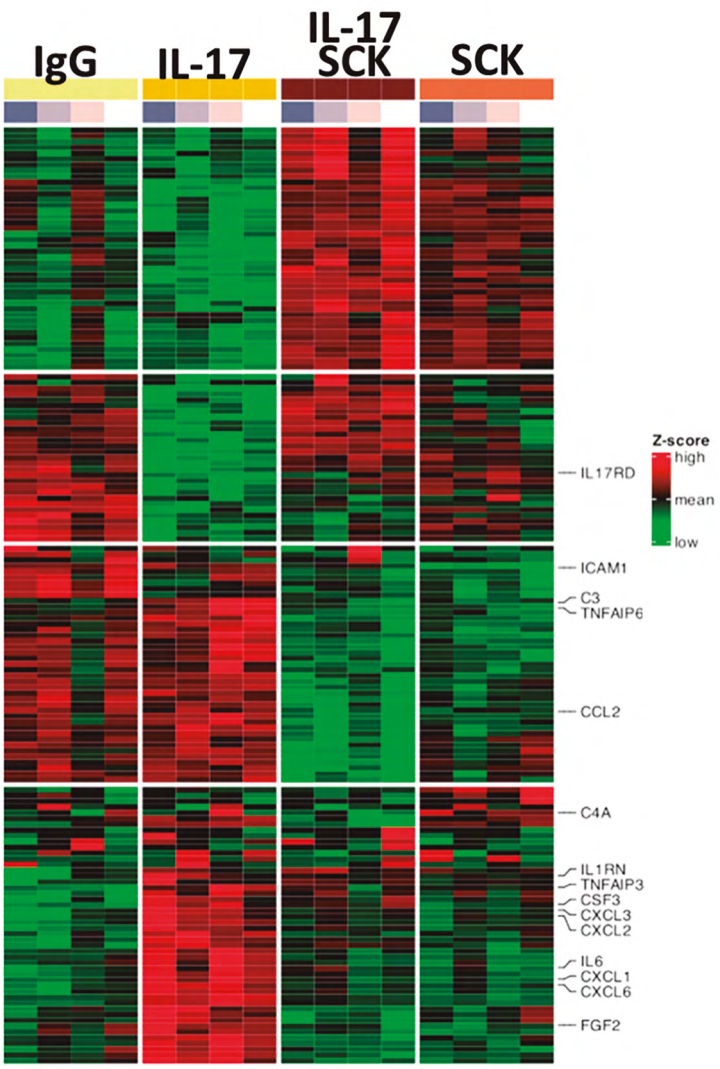

Figure 1. Transcriptomic analysis (RNA sequencing) of MF cultured for 24 hours with IL-17, secukinumab (SCK), IL-17 and SCK or IgG control.

The study of MFs migration and proliferation revealed that IL-17 had no direct effect on these MF functions.

Conclusion: IL-17 increases vascular inflammation and has a direct effect on MFs, with synergy with IFN-γ, which increases the production of pro-inflammatory cytokines (IL-1β, IL-6, GM-CSF, G-CSF), chemokines leading to the recruitment of T cells (CCL20) and monocytes (CCL2) and growth factors involved in neoangiogenesis (VEGF). In contrast, IL-17 does not appear to have a direct effect on MFs proliferation and migration. These data explain why blocking the IL-17 signalling pathway could be useful in the treatment of GCA.

Disclosures: This study was supported by a grant from NOVARTIS.

References:

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O-006

Type I interferon pathway is upregulated in microscopic polyangiitis (vs granulomatosis with polyangiitis)

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Background/ Objectives: The two main types of ANCA-associated vasculitis (AAV), microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA), share common characteristics but also differ on many aspects (epidemiological, genetic, clinical, outcomes). These differences did not justify, to date, different patient management. To identify more specific targetable pathways, we characterized the kidney transcriptome of MPA vs. GPA patients with AAV-glomerulonephritis (AAV-GN).

Methods: This retrospective study included adult patients with AAV-GN from the French Maine-Anjou Registry. Immune gene transcript analysis was performed on RNA extracted from 97 kidney biopsies using NanoString technology. Significant transcripts were examined to identify immune pathways of interest. We then used a publicly available dataset to explore these identified pathways (qPCR / ELISA).

Results: We compared kidney biopsies from GPA (n = 33) and MPA (n = 64) patients. There was no difference in eGFR between both groups at diagnosis. Of the 750 evaluated immune transcripts, 8 genes were found differentially expressed between MPA and GPA patients, all being upregulated in MPA ($log_2FC > 1$, q-value < 0.05) (**Figure 1A**). Seven (out of 8) genes belonged to the type I interferon (IFN-I) signaling pathway.

A personal analysis of unpublished, publicly available, data[1] identified a significantly more pronounced IFN-I signature in the peripheral blood mononuclear cells of patients with MPO-AAV when compared to those with PR3-AAV (**Figure 1B**). Serum levels or CXCL10, a cytokine that mediates immune responses through the recruitment and activation of numerous immune cells under the regulation of IFN-I, were found higher in MPO-AAV patients (**Figure 1C**).

Conclusions: We identified a type I interferon signature, both in kidneys and in blood, in patients with MPA (or MPO-AAV) in comparison to GPA (or PR3-AAV). This is in line with previous lines of evidence brough by Kessenbrock et al.[2] and Kessler et al.[3] suggesting a role for IFN-I in AAV and especially in MPO-AAV. This signature may help gain a deeper understanding of the AAV-GN pathogenesis and provide insights for developing new therapeutic options.

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Disclosures: None.

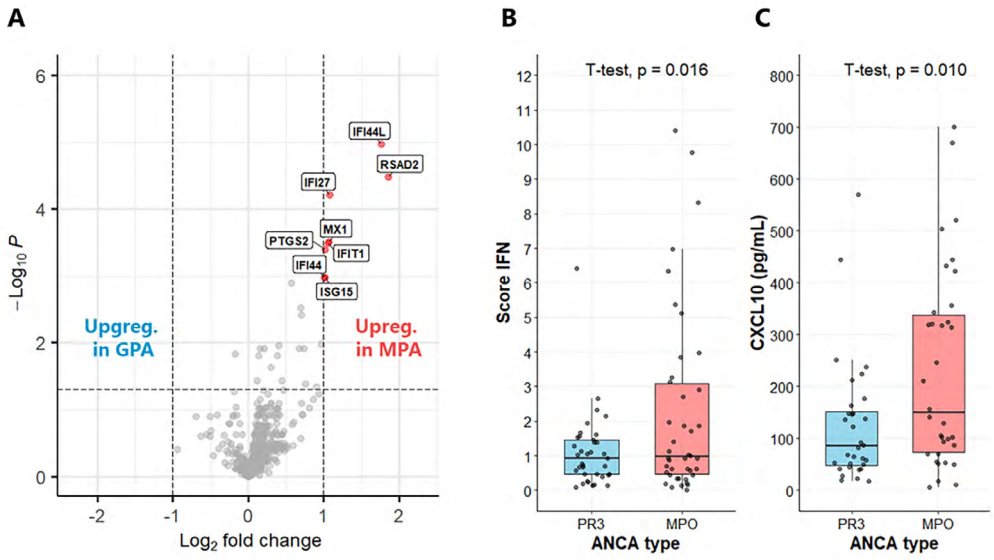

Figure 1. A: differentially expressed genes in kidneys from MPA vs GPA.
B: Type I interferon score in PBMC from MPO-AAV vs PR3-AAV.
C: CXCL10 levels in serum from PR3-AAV and MPO-AAV.

O-007

DNA repair antibody Deoxy Mab 1 inhibits neutrophil extracellular traps (NETs) and attenuates inflammation and kidney injury in experimental anti neutrophil cytoplasmic antibody vasculitis

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Background/Objectives: Neutrophil extracellular Traps (NETs) are a prominent feature in glomeruli of patients with Anti Neutrophil Cytoplasmic Antibody vasculitis (AAV). We hypothesised that a DNA repair antibody (humanized deoxy Mab 1, DX-1) would inhibit NET formation by interfering with DNA damage responses in the neutrophil that results in the release of DNA. DX-1 penetrates live cell nuclei by binding to DNA fragments outside the cell which are transported into the cell through a unique nucleoside transporter. The aim of this study was to investigate the potential of DX-1 to prevent NET formation in human neutrophils and test the therapeutic potential to prevent the development of glomerulonephritis in a well-established experimental model of AAV.

Methods: *In vitro* NET assays were performed from isolated neutrophils from whole blood from healthy donors (*n*=20). We used a well-established 20-day model of anti-myeloperoxidase (MPO) glomerulonephritis (GN). Mice were randomised to receive either vehicle control (*n*=8) or intravenous DX-1 (*n*=8) after establishment of autoimmunity to MPO on day 16. Kidney injury was assessed via albuminuria and histology. Glomerular neutrophil, macrophage and T cell infiltration was assessed by immunohistochemistry. Glomerular NETs were assessed by immunofluorescence and confocal microscopy.

Results: DX-1 inhibited NET formation in stimulated human neutrophils, regardless of stimulus (all P<0.05 compared to non-treated, Fig, 1). Neutrophil phagocytosis assays demonstrated that DX-1 had no impact on phagocytosis, nor did it trigger apoptosis or necrosis. DX-1 treated neutrophils had no significant release of neutrophil elastase (NE) or MPO compared to the vehicle control. In the experimental model, DX- 1 treated mice had significantly reduced MPO specific IFNγ and IL17a splenocytes when compared to the vehicle treated group (both P<0.05). Kidney injury was significantly reduced in the DX-1 treated group as evidenced by a reduction in segmental necrosis (P<0.001, compared to vehicle control), and a reduction in protein and leukocytes in the urine. Glomerular NETs and deposition of the autoantigen MPO were significantly reduced.

Conclusions: DX-1 had no detrimental effect on human neutrophils ability to phagocytose, nor did it cause apoptosis or necrosis of neutrophils. This provides proof of concept that using DX-1 will not compromise host defence. Therapeutic targeting of NETs with DX-1 in the experimental model reduced inflammation and kidney injury suggesting it may be of potential benefit as treatment for AAV.

Disclosures: Consulting Fees for Patrys Ltd.

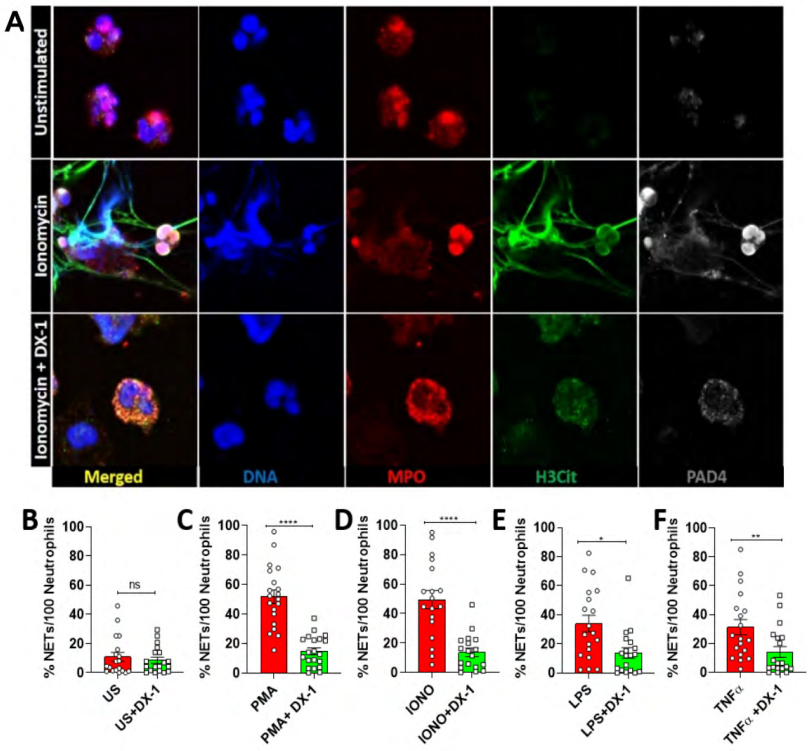

Fig.1. A) Confocal microscopy of human neutrophils stimulated with Ionomycin and treated with DX-1, B) Enumeration of percentage of NETs reduced with DX-1 treatment, *n*=20 human healthy donors.

PLENARY SESSION: ADVANCES IN TREATMENT (I)

O-008

A Randomized, Double-Blind, Placebo-Controlled Trial of Abatacept for the Treatment of Relapsing, Non-Severe, Granulomatosis with Polyangiitis

Carol Langford[1], Nader Khalidi[2], Jason Springer[3], Marcia Friedman[4], Bernhard Hellmich[5], Christian Pagnoux[6], Natasha Dehghan[7], Ora Gewurz-Singer[8], Curry Koening[9], Yih Chang Lin[10], Paul Monach[11], Larry Moreland[12], Aurore Fifi-Mah[13], Oliver Flossmann[14], Lindsy Forbess[15], Peter Lanyon[16], Eamonn Molloy[17], Ulrich Specks[18], Robert Spiera[19], Elaine Yacyshyn[20], Carol McAlear[21], Cristina Burroughs[10], Rachel Jones[22], Rennie Rhee[21], Rula Hajj-Ali[1], David Cuthbertson[10], Jeffrey Krischer[10], David Jayne[22], Peter Merkel[21].

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Background: Granulomatosis with polyangiitis (GPA) is associated with frequent relapses. A Phase III trial was conducted at 22 sites to examine the efficacy and safety of abatacept for the treatment of GPA.

Methods: Patients with relapsing, non-severe GPA were randomized to abatacept 125 mg SC once a week or placebo both combined with prednisone 30 mg/day tapered and discontinued at week 12. Patients receiving methotrexate, azathioprine, mycophenolate, or leflunomide continued this medication at a stable dose. Patients achieving remission remained on their randomized assignment until relapse, early termination, or 12 months after enrollment of the last patient. The primary endpoint was rate of treatment failure, defined as a relapse, disease worsening, or failure to achieve BVAS/WG = 0 or 1.

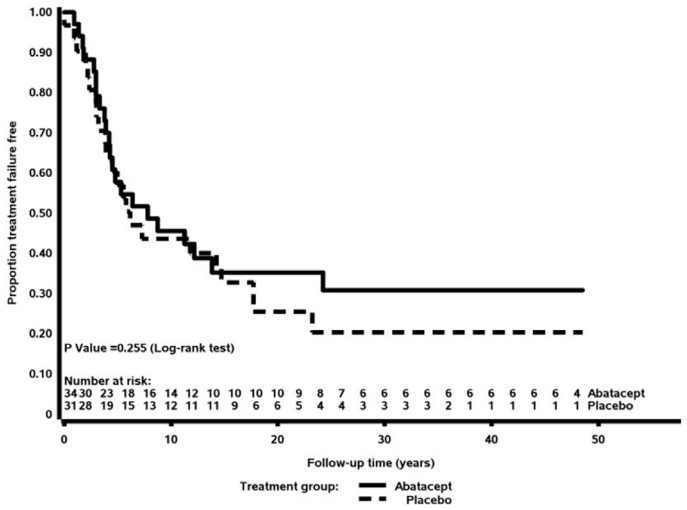
Results: 65 patients were randomized, 34 received abatacept and 31 received placebo. There was no difference in baseline demographic and disease characteristics between arms. The study population consisted of patients with longstanding, relapsing disease who had received a range of immunosuppressive agents, including 28 (43%) patients previously treated with rituximab.

Relapse or disease worsening occurred in 21 (62%) patients randomized to abatacept and 21 (68%) patients randomized to placebo, including episodes of severe disease in 3 patients receiving abatacept and 5 receiving placebo. No statistical difference in the treatment failure rate was found between those who received abatacept compared to placebo (P = 0.255), **Figure**. Treatment with abatacept did not demonstrate statistical differences from placebo in key secondary endpoints, including time to full remission (BVAS/WG=0), duration of glucocorticoid-free remission, relapse severity, prevention of damage, or patient-reported quality of life outcomes. 112 adverse events occurred in 48 patients, including 54 serious adverse events in 33 patients with no difference between treatment arms, including for infections.

Conclusions: In patients with relapsing, non-severe GPA the addition of abatacept to glucocorticoids did not reduce the risk of relapse, severe worsening, or failure to achieve remission. This represents a unique population with challenging unmet needs to better control disease activity. Further research is needed to understand pathophysiologic mechanisms and investigate novel treatment approaches for this subset of patients with GPA.

Disclosures: AbbVie: CL, NK, BH, LF, EM, RS, PM; Alpine: MF; Amgen: JS, CK, LF, US, RS, RH, PM; ArGenx: US, PM; Aurinia: DJ; AZ: CL, BH, CP, US, RS, DJ, PM; Behring: PM; BMS: all authors; BI: BH, US, RS, PM; Cabaletta: PM; Celltrion: AF; Chinook: DJ; Corbus: RS; Eicos: PM; Electra: PM; FK: AF; Formation: RS; Genentech: US; GSK: CL, NK, BH, CP, US, RS, RJ, RH, DJ, PM; HI-Bio: PM, PM; InflaRx: BH, RS, PM; Janssen: BH, PM; Jubilant: PM; Kadmon: RS; Kyverna: PM; Mallinckrodt: NK; Medac: BH; Merck: BH; MiroBio: PM; Neutrolis: PM; Northstar: US; Novartis: BH, AF, LF, RS, PM; NSPharma: PM; Organon: AF; Otsuka: NK, CP, AF; Pfizer: BH, CP, AF, PL; Principia: RS; Q32: PM; Regeneron: PM; Roche: NK, RJ, DJ; Sanofi: AF, RS; Sparrow: PM; Takeda: DJ, PM; Travere: DJ; Vifor: BH, OF, PL, RJ, DJ; Visterra: PM.

Figure. Rate of treatment failure (relapse, disease worsening, or failure to achieve BVAS/WG = 0 or 1) comparing treatment with abatacept to placebo in patients with relapsing, non-severe, granulomatosis with polyangiitis.



O-009

A multicenter, randomized, controlled trial evaluating the effects of low-dose glucocorticoids compared to stopping glucocorticoids to maintain remission of granulomatosis with polyangiitis: The TAPIR trial

Peter Merkel[1], Christian Pagnoux[2], Nader Khalidi[3], Ulrich Specks[4], Curry Koening[5], Carol Langford[6], Larry Moreland[7], Paul Monach[8], Jason Springer[9], Shubhasree Banerjee[1], Simon Carette[2], Rennie Rhee[1], Medha Soowamber[2], Kenneth Warrington[4], Renee Borchin[10], Cristina Burroughs[10], Carol McAlear[1], David Cuthbertson[10], Jeffrey Krischer[10].

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Background: The utility and safety of use of low-dose glucocorticoids to maintain remission among patients with granulomatosis with polyangiitis (GPA) remains controversial. Additionally, there is no consensus approach to the last phases of tapering of glucocorticoids in clinical trials of GPA making comparison of remission and relapse rates across trials problematic. The Assessment of Prednisone In Remission (TAPIR) trial was designed to address this issue.

Methods: Patients with GPA were eligible for TAPIR if they were i) within one year of receiving treatment to induce remission; ii) in remission (BVAS/WG=0); and iii) receiving treatment with prednisone at a daily dose of 5-20 mg. Patients were enrolled when they were down to a dose of prednisone of 5 mg/day at which point they were randomized to either remain on prednisone 5 mg/day for 6 months or taper off prednisone to 0 mg/day in 4 weeks and remain off of glucocorticoids until month 6 (**Figure**). Other immunosuppressive therapy, including azathioprine, methotrexate, mycophenolate mofetil, or rituximab, was continued for the duration of the trial without any dose changes. The primary outcome was measured at month 6 as the rate of relapse, defined as a decision to increase the dose of glucocorticoids to treat active GPA. Secondary outcomes included safety, patient-reported outcomes, duration of remission, and severity of relapses. Patients were enrolled at any of 10 sites in the US or Canada, or through a novel online system of self-enrollment.

Results: 159 patients with GPA were randomized to the 5 mg/day prednisone group (N=77) or the 0 mg/day prednisone group (N=82). The TAPIR study completed enrollment with the last study visit scheduled for January 2024.

Conclusions: The TAPIR study, an international, multicenter, randomized clinical trial with a large sample size for a rare disease, addresses an area of clinical uncertainty with important implications for both clinical care of patients with GPA and clinical trial design in ANCA-associated vasculitis. Complete results will be available at the time of the 2024 International Vasculitis Workshop.

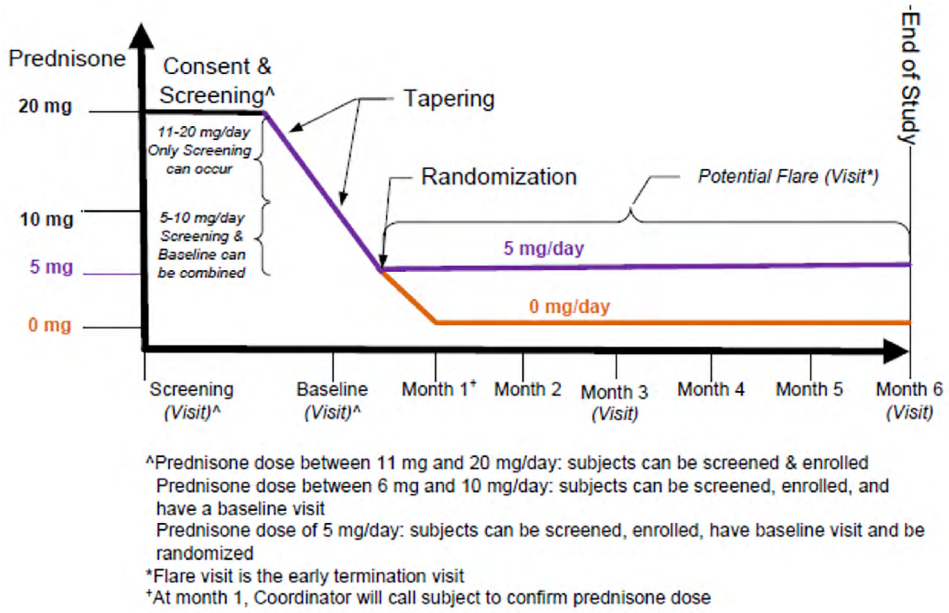

Figure 1. Study schema for the TAPIR clinical trial.

Disclosures: AbbVie PAM, NK **Amgen** CK, KW **Argenx** US **AZ** PAM, CP **Boeringher-Ingelheim** PAM **BMS** PAM, NK, CAL **ChemoCentryx** PAM, JS **CSL Behring** PAM **CSL Vifor** US **Dynacure** PAM **EMDSerono** PAM **Forbius** PAM **Genentech/Roche** PAM, CP, NK, **Genzyme/Sanofi** PAM **GSK** PAM **GSK** PAM, CP, NK **InflaRx** PAM **Janssen** PAM **Kiniksa** PAM **Kyverna** PAM **Magenta** PAM **MiroBio** PAM **Neutrolis** PAM **Northstar Medical Radioisotopes** US **Novartis** PAM **Otsuka** PAM, CP, NK **Pfizer** PAM, CP **Sparrow** PAM **Takeda** PAM US **Talaris** PAM **UpToDate** PAM.

O-010

The effect of plasma exchange on early renal improvement in patients with ANCA-associated vasculitis: a post-hoc analysis of the PEXIVAS trial

Balazs Odler[1], Regina Riedl[1], Geetha Duvuru[2], Wladimir M. Szpirt[3], Carmel Hawley[4], Lisa Uchida[5], Zachary S. Wallace[6], Giles Walters[7], Eri Muso[8], Vladimir Tesar[9], Charles D. Pusey[10], Mark A. Little[11], Peter A. Merkel[12], Michael Walsh[13], David R.W. Jayne[14], Andreas Kronbichler[15].

[1]Medical University of Graz, Graz, Austria; [2]Johns Hopkins University, Baltimore, Maryland, United States; [3]University of Copenhagen, Copenhagen, Denmark; [4]University of Queensland, Brisbane, Australia; [5]University of Cambridge, Cambridge, United Kingdom; [6]Harvard Medical School, Boston, Massachusetts, United States; [7]Canberra Hospital, Canberra, Australia; [8]Medical Research Institute Kitano Hospital, Osaka, Japan; [9]Charles University, Prague, Czech Republic; [10]Imperial College London, London, United Kingdom; [11]Trinity College Dublin, Dublin, Republic of Ireland; [12]University of Pennsylvania, Philadelphia, United States; [13]McMaster University, Hamilton, Ontario, Canada; [14]University of Cambridge, Cambridge, Austria; [15]Medical University of Innsbruck, Innsbruck, Austria.

Background/objectives: Therapeutic plasma exchange (PLEX) is an adjunctive treatment for patients with ANCA-associated vasculitis (AAV) and kidney involvement. The degree to which early changes in kidney function predict recovery of kidney function is uncertain. This study examined the effect of PLEX on early changes in kidney function.

Methods: Post-hoc analysis of an international, randomised, controlled trial of 704 participants with AAV of which 691 had glomerulonephritis: 349 allocated to PLEX and 342 to no PLEX. The primary outcomes of this analysis were change in eGFR from baseline and improvement of eGFR ³15ml/min/1.73m^2. Secondary outcomes were sustained low eGFR (defined as a low eGFR [<15 ml/min per 1.73 m^2] at baseline sustained over at least 4 weeks, evidenced by two consecutive measurements) and decline in eGFR of at least 5 ml/min per 1.73 m^2 from baseline within 4 weeks after randomization. Treatment effects were estimated using general estimating equation models adjusted for glucocorticoid group, age, baseline kidney function, ANCA serotype, immunosuppressive treatment, and degree of alveolar hemorrhage.

Results: eGFR at weeks 2, 4, and 8 improved more in the PLEX than the no PLEX group without notable differences thereafter. At week 4, participants in the PLEX group increased eGFR by at least 15 ml/min/1.73m^2 to a greater extent than the no PLEX group (relative risk [RR] 1.45; 95% confidence interval [CI] 1.13-1.88; p=0.004). Improved early kidney outcomes were consistent with a reduced risk of sustained low eGFR over at least 4 weeks (RR: 0.76; 95%CI: 0.57 to 1.01; p=0.058), and lack of decline in eGFR (RR: 0.53; 95%CI: 0.26 to 1.06; p=0.072). Improvements in kidney function within 4 weeks were associated with a lower risk of kidney failure within 1 year (RR: 0.96; 95%CI: 0.95-0.97 per 1 ml/min/1.73 m^2 eGFR; and RR: 0.29; 95%CI: 0.16-0.52 for an improvement of at least 15 ml/min/1.73 m^2).

Conclusion: PLEX improved early recovery of kidney function in patients with AAV and glomerulonephritis. Regardless of treatment group assignment, early improvements in kidney function were associated a lower risk of kidney failure.

References:

- Walsh M et al. Plasma exchange and glucocorticoids in ANCA-associated vasculitis. N Engl J Med. 2020; 382(7): 622-631.

Disclosures: None.

O-011

Innovative anti-pneumococcal vaccine strategies versus standard vaccination regimen in patients with ANCA-associated vasculitides receiving rituximab therapy: A Multicenter Randomized Controlled Trial (PNEUMOVAS)

Benjamin Terrier[1], Laura Richert[2], Grégory Pugnet[3], Olivier Aumaitre[4], Olivier Moranne[5], Elisabeth Diot[6], Alexandre Karras[7], Fabrice Bonnet[2], Claire De Moreuil[8], Eric Hachulla[9], Maxime Samson[10], Jean-Francois Augusto[11], Thomas Quemeneur[12], Xavier Puéchal[13], Loic Guillevin[13], Noémie Huchet[2], Hendy Abdoul[13], Carine Bellara[2], Frédéric Batteux[13], Odile Launay[13].

[1]Cochin Hospital, Paris, France; [2]CHU Bordeaux, Bordeaux, France; [3]CHU Toulouse, Toulouse, France; [4]CHU Clermont-Ferrand, Clermont-Ferrand, France; [5]CHU Nimes, Nimes, France; [6]CHU Tours, Tours, France; [7]HEGP, Paris, France; [8]CHU Brest, Brest, France; [9]CHRU Lille, Lille, France; [10]CHU Dijon, Dijon, France; [11]CHU Angers, Angers, France; [12]CH Valenciennes, Valenciennes, France; [13]CHU Cochin, Paris, France.

Background/Purpose: Patients receiving glucocorticoids plus rituximab (RTX) show an increased risk of infection, especially invasive pneumococcal infections. Vaccine responses to influenza, *Streptococcus pneumoniae* and SARS-CoV-2 under RTX therapy are strongly impaired. In patients with autoimmune diseases receiving such treatments, especially those with ANCA-associated vasculitides (AAV), there is thus a need to develop enhanced anti-pneumococcal vaccine strategies to increase immune response and protection.

Methods: This multicenter randomized, open label, phase 2 trial, compared two innovative "reinforced" anti-pneumococcal vaccine strategies to the standard regimen in patients with AAV receiving RTX therapy. Adult patients with newly diagnosed or relapsing AAV, with an active disease (BVAS ≥3) and planned to receive RTX as induction therapy were randomized in a 1:1:1 ratio to three parallel arms: standard regimen combining a dose of PCV13 at day 0 followed by a dose of PPV23 at month 5 (M5) (arm 1); double dose of PCV13 at day 0 and day 7 followed by a dose of PPV23 at M5 (arm 2); or 4 doses of PCV13 at day 0 followed by a dose of PPV23 at M5 (arm 3). The primary endpoint was the immune response at M6 against the 12 pneumococcal serotypes common to the PCV13 and PPV23 vaccines, according to four ordered categories of ELISA response: positive antibody response to 0-3, 4-6, 7-9, or 10-12 serotypes. The primary endpoint was analyzed in a proportional odds logistic regression model with a Bonferroni correction for the 2 innovative arms. Secondary end points were local and systemic solicited reactions 7 days following each vaccination and any adverse event related or possibly related to vaccine immunization.

Results: A total of 95 participants were analyzed in the modified intention-to-treat population, with 30 assigned in arm 1, 32 in arm 2 and 33 in arm 3.

At M6, immune response to 0-3, 4-6, 7-9, or 10-12 serotypes was observed in 83.3%, 13.3%, 3.3% and 0% in arm 1; 56.3%, 28.1%, 15.6% and 0% in arm 2; and 60.6%, 33.3%, 6.1% and 0% in arm 3. Patients in arm 2 were significantly more likely to be in any higher response categories compared to the standard regimen after adjustment on age, with a proportional odds ratio (pOR) of 4.1 (97.5% CI 1.1-15.9, p=0.018), while the second innovative regimen only tended to improve vaccine responses (pOR 3.1, 97.5% CI 0.8-11.9, p=0.062).

Local and/or systemic solicited reactions 7 days following each vaccination and any adverse event related or possibly related to vaccine immunization during the first 6 months occurred at higher numbers after the reinforced first vaccinations but were mainly grade 1 or 2 local reactions. No severe adverse events related to vaccination was observed.

During follow-up, 8 vasculitis flares occurred in 6 patients, in median 87 days after the last vaccination: one patient in arm 1, 2 in arm 2, and 3 in arm 3.

Conclusion: In patients with AAV receiving RTX therapy, an innovative reinforced anti-pneumococcal vaccine strategy based on double dose of PCV13 at day 0 and day 7 followed by a single dose of PPV23 at M5 significantly improved the antibody responses against *Streptococcus pneumoniae* compared to the standard regimen (Funded by the French Ministry of Health; PNEUMOVAS ClinicalTrials.gov number, NCT03069703).

O-012

Safety of Avacopan in ANCA-Associated Vasculitis: Combined Data from Three Clinical Trials

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Background/ Objectives: Avacopan is approved as an adjunctive treatment in adults with severe active granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA), two types of antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (AAV). This study aimed to combine and report on data of the safety of avacopan from two phase 2 and one phase 3 studies in 439 patients with GPA/MPA.

Methods: In the three randomized, double-blind trials, all groups received background therapy of cyclophosphamide (followed by azathioprine), or rituximab; control groups received a full prednisone regimen (60 mg tapered to 0 mg over 20 weeks) plus placebo. The phase 2 CLEAR trial had three groups: control (n=23), avacopan 30 mg twice daily (BID)+low dose prednisone (20 mg tapered to 0 mg) (n=22), and avacopan BID+no prednisone (n=22).[1] The phase 2 CLASSIC trial had three groups: control (n=13), avacopan 10 mg BID+prednisone (n=13), and avacopan 30 mg BID+prednisone (n=16).[2] The phase 3 ADVOCATE trial had a control group (n=164) and a 30 mg BID avacopan group with no protocol-prescribed oral glucocorticoid taper (n=166).[3] The treatment period was 12 weeks in the phase 2 trials and 52 weeks in the phase 3 trial. Rates of exposure-adjusted total adverse event (AEs), serious AEs, withdrawal of study medication due to AEs, and pre-specified AEs of interest were calculated based on the integrated data from all three trials.

Exposure-adjusted rate/100 patient-years	Prednisone Control Groups (N=200)	Avacopan Groups (N=239)	Difference (95% Confidence Interval)
Total exposure (patient-years)*	195.7	212.3	
AE patient first incidence rate†	1,626	1,328	-298 (-583.0, -13.0)
AE rate††	1,251.7	1,099.8	-151.9 (-218.6, -85.3)
SAE patient first incidence rate	60.1	61.6	1.5 (-16.5, 19.6)
SAE rate	91.5	70.7	-20.8 (-38.3, -3.3)
Discontinuation of blinded study medication due to AEs: Patient first incidence rate	18.0	18.2	0.2 (-8.4, 8.9)
Discontinuation of blinded study medication event rate	21.5	21.7	0.2 (-8.8, 9.2)
Infections§: Patient first incidence rate	148.5	139.1	-9.4 (-42.6, 23.7)
Infections event rate	166.6	142.2	-24.3 (-48.5, -0.1)
Liver function AEs§: Patient first incidence rate	12.3	14.7	2.3 (-5.2, 9.8)
Liver function AE rate	17.4	18.4	1.0 (-7.2, 9.2)
WBC decrease AEs§: Patient first incidence rate	25.0	18.9	-6.1 (-16.0, 3.8)
WBC decrease event rate	34.2	22.6	-11.6 (-22.2, -1.2)
Hypersensitivity AEs§: Patient first incidence rate	58.0	57.7	-0.3 (-18.1, 17.5)
Hypersensitivity AE rate	61.8	68.8	6.9 (-8.7, 22.6)

AE=adverse event; SAE=serious adverse event; WBC=white blood cell
*Exposure calculated as follow-up time for all patients in the treatment group (irrespective of whether an event occurred).
†Patient first incidence calculated as number of patients with at least 1 event divided by total follow-up time per 100 patient-years.
Follow-up time = total time at risk (in years), defined as the sum of:
(1) follow-up time in patients who did not have a treatment-emergent adverse event, and
(2) time to first occurrence of the event in patients who had a treatment-emergent adverse event.
††Rate calculated as total number of events divided by total follow-up time per 100 patient-years.
§Pre-specified AEs of interest; AE preferred terms identified before unblinding.
Refer to Warnings in full prescribing information that lists hepatotoxicity, hypersensitivity reactions, hepatitis B reactivation, and serious infections

Table 1: Exposure-Adjusted Adverse Event Rates by Treatment Group Across Three Trials of Avacopan for the Treatment of ANCA-Associated Vasculitis.

Results: Across the three trials, 439 patients with GPA/MPA were treated: 200 in the control groups and 239 in the avacopan groups. Results are presented in **Table 1**. The rates of AE patient first incidence and AEs, serious AEs, infection events, and decrease in white blood cell count AEs were statistically fewer in the avacopan group compared with the prednisone group.

Conclusion: In the context of the demonstrated efficacy profile of avacopan, these integrated safety results provide support for use of avacopan in the treatment of patients with GPA/MPA.

References:

1. Jayne et al. *J Am Soc Nephrol* 2017;28:2756-2767.
2. Merkel et al. *ACR Open Rheumatol* 2020;2:662-671.
3. Jayne et al. *N Engl J Med* 2021;384:599-609.

Disclosures: AbbVie/Abbott, Amgen, Argenx, AstraZeneca, Aurinia, Boehringer Ingelheim, Bristol Myers Squibb, Cabaletta, ChemoCentryx, Chinook, CSL Behring, CSL Vifor, Eicos, Electra, Genentech, GSK, HiBio, InflaRx, Janssen, Jubilant, Kyverna, MiroBio, Neutrolis, Novartis, NS Pharma, Q32, Regeneron, Roche, Sanofi, Sparrow, Takeda, UpToDate, Visterra.

O-013

Report on Twelve Patients with Diffuse Alveolar Hemorrhage in the Phase 3 Trial of Avacopan for the Treatment of ANCA-Associated Vasculitis

Ulrich Specks[1], David R.W. Jayne[2], Peter A. Merkel[3].

[1]Mayo Clinic, Rochester, United States; [2]University of Cambridge, Cambridge, United Kingdom; [3]University of Pennsylvania, Philadelphia, United States.

Background/ Objectives: Although respiratory tract involvement in antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (AAV) is frequent and associated with increased mortality, studies focusing on diffuse alveolar hemorrhage (DAH) in AAV are uncommon. The phase 3 ADVOCATE trial compared avacopan to a prednisone taper.[1] The objective of this study was to report on the 12 patients (5 in the avacopan group, 7 in the prednisone taper group) with DAH based on Birmingham Vasculitis Activity Score (BVAS) enrolled in the trial.

Methods: Patients requiring invasive pulmonary ventilation support at screening were excluded from enrollment. Remission at week 4 was defined as BVAS=0. Remission at week 26 was defined as BVAS=0 and no glucocorticoid (GC) use in the previous 4 weeks. Sustained remission at week 52 was defined as BVAS=0 and no GC use in the previous 4 weeks, remission at week 26, and no relapse (return of vasculitis activity on BVAS) between weeks 26 and 52.

Case	Study Treatment/ Background Therapy	Age, Sex, Type of AAV, Race, ANCA status, AAV disease status	Cumulative GC Dose (mg)		Pulmonary Manifestations of AAV			Remission (weeks 4 and 26) Sustained remission (week 52)			Relapse
			Days -1 to -14	Days 1 to 29	Baseline	Week 4	Week 26	Week 4	Week 26	Week 52	
1	Avacopan/ Rituximab	54, M, White, GPA, PR3+, Newly diagnosed	1,758	763	DAH	None	None	Yes	Yes	Yes	No
2	Avacopan/ Rituximab	68, M, White, GPA, PR3+, Newly diagnosed	140	625	DAH	None	None	Yes	Yes	Yes	No
3	Avacopan/ Rituximab	50, M, White, GPA, PR3+, Relapsed	0	500	DAH, Wheeze, Nodules/Cavities	None	None	Yes	Yes	Yes	No
4	Avacopan/ Rituximab	57, M, White, GPA, PR3+, Newly diagnosed	300	0	DAH, Respiratory failure	Nodules/ Cavities	None	No	No	No	No
5	Avacopan/ Rituximab	81, F, Asian, GPA, MPO+, Relapsed	728	650	DAH, Infiltrate, Nodules/Cavities	None	None	Yes	Yes	Yes	No
6	Prednisone/ Rituximab	35, F, Black, GPA, PR3+, Newly diagnosed	2,377	3,019	DAH, Infiltrate, Wheeze	None	None	Yes	Yes	Yes	No
7	Prednisone/ Rituximab	88, M, White, GPA, MPO+, Relapsed	60	1,627	DAH	None	None	Yes	Yes	Yes	No
8	Prednisone/ Rituximab	61, F, White, GPA, MPO+, Relapsed	240	1,779	DAH	None	None	Yes	Yes	Yes	No
9	Prednisone/ Rituximab	81, F, White, MPA, MPO+, Newly diagnosed	4,465	2,112	DAH	None	None	Yes	No	No	No
10	Prednisone/ Rituximab	55, M, White, GPA, PR3+, Relapsed	0	1,558	DAH, Infiltrate	None	None	No	Yes	No	Yes
11	Prednisone/ IV CYC	52, M, White, GPA, PR3+, Newly diagnosed	1,945	1,368	DAH, Infiltrate	None	None	Yes	Yes	Yes	No
12	Prednisone/ IV CYC	48, M, White, GPA, PR3+, Relapsed	2,225	1,597	DAH, Infiltrate, Endobronchial disease	Infiltrate, Endobronchial disease	None	No	No	No	Yes

AAV, ANCA-associated vasculitis; ANCA, antineutrophil cytoplasmic autoantibody; CYC, cyclophosphamide; DAH, diffuse alveolar hemorrhage; GC, glucocorticoid; GPA, granulomatosis with polyangiitis; IV, intravenous; MPA, microscopic polyangiitis; MPO, myeloperoxidase; PR3, proteinase 3

Table 1: Baseline Characteristics and Outcomes for Patients with Diffuse Alveolar Hemorrhage at Baseline in the ADVOCATE trial of Avacopan for ANCA-Associated Vasculitis.

Results: Of the 12 patients, 11 (92%) had granulomatosis with polyangiitis, 10 (83%) received rituximab background therapy, 8 (67%) were male, 8 (67%) had proteinase 3-ANCA, and 6 (50%) were newly diagnosed (**Table 1**). BVAS was 19.5±5.4 (mean±SD) at baseline. The total all-source GC doses (median / mean) for the avacopan and prednisone taper groups, respectively, were 300 / 585 mg vs 1945 / 1616 mg during screening (day -14 to -1) and 625 / 508 mg vs 1627 / 1866 mg during day 1 to 29. DAH was no longer active by week 4 for all patients (**Table 1**). Remission rates in the avacopan and prednisone taper groups, respectively, were 80.0% (4/5) and 71.4% (5/7) at week 4, 80.0% (4/5) and 71.4% (5/7) at week 26, and 80.0% (4/5) and 57.1% (4/7) at week 52. No patients in the avacopan group and 2 in the prednisone taper group relapsed. One patient in the avacopan group (case 3) and 2 in the prednisone taper group (case 9 and 12) were hospitalized. Prednisone taper treatment was not completed in case 9 due to a serious adverse event (day 33). No patients required mechanical ventilation during the study.

Conclusions: In the ADVOCATE trial, the outcomes of patients with DAH were similar for those treated with avacopan vs a prednisone taper. All pulmonary manifestations were resolved in all patients by week 26. None of the patients in the avacopan group progressed to respiratory failure, despite receiving minimal GC doses. In this small number of patients, overall remission rates were higher in the avacopan group than the prednisone taper group at weeks 4, 26, and 52. These data provide support for the treatment of DAH in AAV using avacopan with lower GC doses.

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Disclosures: AbbVie/Abbott, Amgen, Argenx, AstraZeneca, Aurinia, Boehringer Ingelheim, Bristol Myers Squibb, Cabaletta, Chinook, CSL Behring, CSL Vifor, Eicos, Electra, Genentech, GSK, HiBio, InflaRx, Janssen, Jubilant, Kyverna, MiroBio, Neutrolis, North Star Radioisotopes, Novartis, NS Pharma, Q32, Regeneron, Roche, Sanofi, Sparrow, Syneos, Takeda, UpToDate, Visterra.

BREAKOUT SESSION: GENETIC AND ENVIRONMENT CONDITIONINGS OF VASCULITIS

O-014

Association between infections and the onset of giant cell arteritis and polymyalgia rheumatica: a nested case control study from the French E3N-EPIC cohort study

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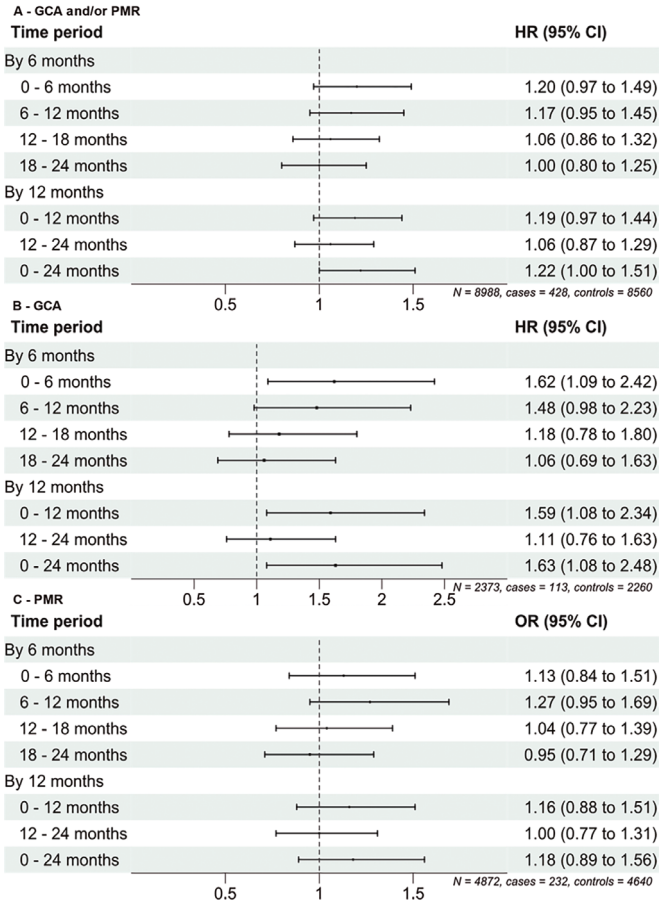
Background/ Objectives: Giant cell arteritis (GCA), the leading cause of large vessel vasculitis, is frequently associated with polymyalgia rheumatica (PMR). Their etiological mechanism remains unclear. In relation to predisposing genetic background (HLA DR4), several elements suggest an infectious mechanism as an etiological or triggering factor. Epidemiological studies (retrospective cohorts or case-control studies (1)), based mainly on coding data, have attempted to assess this association. However, the definition and periods of exposure varied. The aim of our study was to assess the association between infections, assessed by antibiotic reimbursement, and the risk of GCA and/or PMR through a nested case-control study from a large prospective cohort.

Methods: We conducted a nested case-control study within the French cohort E3N (*Etude Epidémiologique auprès des femmes de la mutuelle générale de l'Education Nationale*), which has been following 98,995 women since 1990. Cases, defined as patients who developed GCA and/or PMR during the follow-up period, were matched with 20 controls based on age and vital status. Infections prior to index date (diagnosis date for cases and the same date for their matched controls) were defined by ≥1 antibiotic reimbursement in the medication claims reimbursement database. These infections were compared between the cases and controls using conditional logistic regression models, adjusted for potential confounders. Different time frames before the index date, and different classes of antibiotics were compared.

Results: A total of 428 GCA/PMR cases (113 GCA, 232 PMR alone, 83 undefined) were compared to 8,560 matched controls. Compared to controls, GCA/PMR cases had higher odds to have any infection in the 0-24 months prior to index date (aOR [95%CI] 1.22 [1.00 – 1.51]). The association was notably stronger when the infection occurred closer to the index date (1.20 [0.97–1.49]; 1.00 [0.80 – 1.25] for 0–6 and 18–24 months, respectively). This association was only observed among GCA cases (1.62 [1.09–2.42]; 1.59 (1.08–2.34), for 0-6 and 0-12 months, respectively), but not among PMR cases (1.13 [0.84–1.51] for 0-6 months) (fig. 1). Regarding antibiotic classes, quinolone reimbursements displayed the strongest association with subsequent GCA (2.21 [1.12–4.09] for 0-6 months).

Conclusions: This case-control study, based on a large cohort of French women, showed an increased risk of GCA/PMR after an infectious episode in a two-year period. The risk was mainly at the expense of GCA cases, and was higher when infections occurred close to the diagnosis, supporting the idea of an infectious antigenic "trigger". Nevertheless, a reverse causality bias cannot be ruled out. Quinolone use was strongly associated with the risk of GCA, raising the hypothesis of an altered microbiota in its pathogenesis.



Analyses were made by the use of a conditional logistic regression, adjusted on educational level, socio-professional category, BMI, smoking status, history of type 2 diabetes and history of cancer. OR= odds ratio; 95% CI=95% confidence interval; GCA=giant cell arteritis; PMR=polymyalgia rheumatica.

Figure 1. Association between any antibiotic reimbursement and incident (A) GCA and/or PMR (B) GCA (C) PMR alone by period.

References:

1. Pacoureau L, Barde F, Seror R, Nguyen Y. Association between infection and the onset of giant cell arteritis and polymyalgia rheumatica: a systematic review and meta-analysis. *RMD Open*. 2023;9(4).

Disclosures: None.

O-015

Genetic susceptibility to patterns of arterial involvement in Takayasu arteritis

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Background/Objectives: Takayasu arteritis is a large-vessel vasculitis involving the aorta and its major branches. Specific clusters of the distribution of angiographic involvement in Takayasu arteritis have been identified and confirmed in multiple cohorts. The goal of this study was to determine the role of genetics in influencing the pattern of arterial involvement in Takayasu arteritis.

Methods: Two independent cohorts of patients with Takayasu arteritis were studied, including 282 patients from Turkey and 115 European-American patients from North America. Data obtained from angiography were used to classify patients into one of three previously-identified clusters based on the involvement patterns of the aorta and branch vessels (1). All patients were genotyped using an Illumina genotyping platform. Following imputation and quality control measures, approximately 6.5 million SNPs were evaluated in a meta-analysis that included both cohorts. Logistic regressions were performed to identify genetic associations with angiographic clusters. A p-value threshold of $1X10^{-5}$ was considered suggestive for genetic association.

Results: A genetic locus in the solute carrier family gene *SLC24A2* was associated with the angiographic patient cluster characterized by involvement of the abdominal aorta, renal arteries, and mesenteric arteries (rs2891138, OR= 3.34, P= $2.32X10^{-7}$). Several genetic loci were associated with the angiographic pattern characterized by bilateral carotid and subclavian artery involvement. These include a locus in *LGALSL* (rs883021, OR= 0.43, P= $1.00X10^{-5}$), *AK4P3* (rs1072778, OR= 0.39, P= $4.07X10^{-6}$), and *TMEM132B* (rs4765045, OR= 3.05, P= $6.18X10^{-6}$). The most significant locus associated with the development of asymmetric disease with fewer involved arteries is located in *FRMD6* (rs55692665, OR= 2.79, P= $1.11X10^{-7}$). All these genetic effects were consistent between the Turkish and European-American patient cohorts (**Table 1**). Furthermore, several loci were associated with changes in mRNA expression levels of multiple genes in arterial tissues, including the aorta.

ANGIOGRAPHIC CLUSTER	GENETIC ASSOCIATION				META-ANALYSIS			TURKISH COHORT			EUROPEAN-AMERICAN COHORT		
	CHR	SNP	Effect allele	Closest gene	OR	95 % CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*
Cluster 1	9	rs2891138	C	*SLC24A2*	3.34	2.12-5.28	2.32E-07	3.02	1.85-4.94	9.74E-06	6.56	1.84-23.33	3.70E-03
	8	rs11775954	A	*LRRCC1*	0.38	0.25-0.57	3.83E-06	0.37	0.24-0.59	1.57E-05	0.42	0.15-1.17	9.80E-02
Cluster 2	2	rs2080296	C	*THUMPD2*	2.39	1.63-3.50	7.45E-06	2.77	1.76-4.36	1.08E-05	1.68	0.83-3.39	1.49E-01
	2	rs883021	G	*LGALSL*	0.43	0.30-0.62	1.00E-05	0.47	0.30-0.72	5.52E-04	0.33	0.16-0.71	4.26E-03
	4	rs2465578	G	*NSUN7*	0.35	0.22-0.55	6.96E-06	0.33	0.20-0.56	2.79E-05	0.41	0.15-1.17	9.52E-02
	12	rs1072778	C	*AK4P3*	0.39	0.26-0.58	4.07E-06	0.43	0.27-0.69	4.78E-04	0.30	0.14-0.65	1.95E-03
	12	rs4765045	G	*TMEM132B*	3.05	1.88-4.95	6.18E-06	2.96	1.74-5.04	6.55E-05	3.52	1.11-11.18	3.27E-02
	17	rs8069231	T	*RCVRN*	2.33	1.60-3.38	8.80E-06	2.47	1.61-3.77	3.32E-05	1.93	0.90-4.17	9.35E-02
	18	rs11877439	A	*MRO*	2.80	1.78-4.41	8.36E-06	2.79	1.71-4.57	4.35E-05	2.84	0.90-8.99	7.65E-02
Cluster 3	14	rs55692665	C	*FRMD6*	2.79	1.91-4.08	1.11E-07	2.60	1.71-3.96	8.78E-06	3.83	1.60-9.21	2.66E-03
	20	rs6014830	A	*TFAP2C*	2.30	1.62-3.27	3.09E-06	2.13	1.42-3.18	2.35E-04	2.98	1.45-6.12	2.89E-03
	21	rs8127771	A	*TMPRSS15*	2.99	1.86-4.81	6.48E-06	2.97	1.71-5.15	1.07E-04	3.05	1.18-7.85	2.09E-02

Table 1: Genetic associations with angiographic clusters in Takayasu arteritis.

Conclusions: Genetic susceptibility might predispose to specific patterns of arterial involvement in Takayasu arteritis.

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1. Goel R, et al. Derivation of an angiographically based classification system in Takayasu's arteritis: an observational study from India and North America. Rheumatology (Oxford). 2020 May 1; 59(5):1118-1127.

O-016

A large-scale genome-wide association study of polymyalgia rheumatica to identify disease-specific loci

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Background: Polymyalgia Rheumatica (PMR) is an inflammatory, autoimmune condition that presents with systemic myalgic symptoms as well as fatigue and fever [1]. Diagnosis of PMR is complicated and often results in misdiagnosis, commonly as giant cell arteritis (GCA) or rheumatoid arthritis (RA) [1]. PMR has been associated with the HLA-II locus, but there is limited evidence for the involvement of further genetic loci [2]. This project aimed to identify novel PMR susceptibility loci and investigate the overlap between GCA and PMR, by conducting a large-scale PMR Genome Wide Association Study (GWAS), incorporating results from additional datasets by meta-analysis, and comparing significant loci between PMR and GCA.

Methods: The primary PMR cohort used for the GWAS consisted of 2,140 cases and 10,990 controls acquired from the UK Biobank (UKB). For the meta-analysis, summary statistics were used from the Michigan Genomics Initiative (cases *N=252* and controls *N=51,303*) and FinnGen (cases *N=725* and controls *N=309,154*); GCA data were sourced from the UKGCA Consortium and the Spanish GCA group (cases *N=2,134* and controls *N=9,125)* [3]. The Michigan Imputation Server was used for HLA imputation of the UKB PMR data.

Results: Results showed a genome-wide significant peak on chromosome 6, specifically in *HLA-DRB1* (rs36096565, *p-value* = 2.8×10^{-69}), further amplified in the meta-analysis. Secondary loci of interest were associated with *DPP4, UBE2H, USP20* and *SCG2,* but did not reach genome-wide significance (*p-value* = 2.3×10^{-7}, 2.4×10^{-7}, 4.4×10^{-7}, 3.8×10^{-7}). Comparing with results from the GCA GWAS, PMR associations, both on chromosome 6 and at secondary loci of interest, were different. Previously associated GCA loci in *P4HA2* and *PLG* showed no significance in the PMR cohort, despite adequate power. HLA imputation showed association with *HLA-DRB1*, specifically in positions 11, 34 and 52 (*p-value* = 3.23×10^{-42}, *p-value* = 1.74×10^{-45}, and *p-value* = 2.89×10^{-46}) for PMR. Significant positions in *HLA-DQB1*, which is the most significantly associated gene in GCA, differed between PMR and GCA.

Conclusions: This work indicates that while both PMR and GCA share the HLA region, as autoimmune conditions, secondary loci of susceptibility are different, making these two discrete conditions. HLA analysis showed that the most significant HLA loci and positions differ between PMR and GCA. Further case-case analysis could support novel findings differentiating between these two conditions.

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3. Carmona FD, Vaglio A, Mackie SL, et al. A Genome-wide Association Study Identifies Risk Alleles in Plasminogen and P4HA2 Associated with Giant Cell Arteritis. *Am J Hum Genet*. 2017;**100**(1):64-74.

Disclosures: None.

O-017

HLA in ANCA-associated vasculitis: thorough characterization of genetic associations in a Scandinavian cohort

Christian Lundtoft[1], Ann Knight[1], Jennifer Meadows[1], Åsa Karlsson[1], Solbritt Rantapää-Dahlqvist[2], Ewa Berglin[2], Øyvind Palm[3], Hilde Haukeland[4], Iva Gunnarsson[5], Annette Bruchfeld[6], Mårten Segelmark[7], Sophie Ohlsson[7], Aladdin Mohammad[7], Per Eriksson[6], Peter Söderkvist[6], Lars Rönnblom[1], Roald Omdal[8], Roland Jonsson[9], Kerstin Lindblad-Toh[1], Johanna Dahlqvist[1].

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Background / Objective: Previous genome-wide association analyses have identified differential genetic susceptibility in the HLA region for antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) with PR3-ANCA and MPO-ANCA, respectively. Whilst the association between PR3-ANCA positive (+) AAV and the HLA-DP region has been fairly well studied, less is known about MPO-ANCA+ AAV and the association to the HLA-DQ region, in cases of European descent. The aim of this study was to thoroughly map the genetic associations to the HLA region in cases with PR3-ANCA+ and MPO-ANCA+ AAV in Scandinavia.

Methods: SNPs spanning the HLA region were extracted from a targeted exome sequencing dataset of Scandinavian AAV cases and controls. Moreover, aligned sequence reads were used to call classical HLA alleles with xHLA. Association analyses of a joint SNP/classical HLA allele dataset were performed for PR3-ANCA+ (n = 411) and MPO-ANCA+ (n = 162) AAV, separately, versus controls (n=1595). Identified AAV-associated genetic variants were analyzed for association with age at diagnosis and relapse, respectively.

Results: For PR3-ANCA+ AAV, there was a significant association with HLA-DPB1*04:01, and, additionally, an independent significant association with SNP rs1042335 at the *HLA-DPB1* locus. In contrast, MPO-ANCA+ AAV was significantly associated with an HLA-DRB1 classical allele; the allele was linked with the strongest associated SNP located at the *HLA-DQA1* locus. There were no significant associations between the lead genetic variants for PR3-ANCA+ AAV or MPO-ANCA+ AAV and age at diagnosis or risk of relapse, respectively.

Conclusions: HLA risk alleles for MPO-ANCA+ AAV differ between cases of Scandinavian descent and cases of East Asian descent. The two independent associations with the *HLA-DPB1* locus in PR3-ANCA+ AAV may represent distinct functional mechanisms.

Disclosures: None.

BREAKOUT SESSION: TRANSCRIPTOMIC APPROACHES TO THE STUDY OF SYSTEMIC VASCULITIS

O-018

Multi-level transcriptomic profiling of temporal artery tissue reveals novel pathways involved in the immune process and vascular remodelling in giant cell arteritis

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Background / Objectives: Giant cell arteritis (GCA) is a systemic vasculitis whose pathogenic mechanism has not yet been elucidated. Aberrant responses of both the innate and adaptive immune systems have been shown to be driving the inflammation in the arterial wall [1]. This study integrates bulk, single-cell and spatially resolved transcriptomic data to identify layer-specific key genes and pathways related to inflammatory infiltrates and vascular remodelling in GCA.

Methods: Bulk RNA-sequencing of temporal artery biopsy (TAB) samples from GCA individuals (n=79), single-cell sequencing of 9 TAB samples (GCA-positive, n=5, GCA-negative, n=4) and spatial profiling (Nanostring GeoMx) of the whole transcriptome and a panel of 150 proteins in TAB tissue from different layers of the arterial wall (n=26; across 5 slides with 6 specimens on each slide) were performed. Computational deconvolution of the bulk dataset with the single-cell dataset as reference was performed using the MuSiC2 software [2] to infer cell-type proportions in each sample. Differential expression analysis between histological phenotypes reflecting molecular events of GCA pathogenesis was performed at each level of data, followed by gene ontology and pathway functional enrichment analysis.

Results: Presence of periarterial lymphocytic infiltration and presence of damage in tunica media were found to have the strongest associations with 1011 and 568 differentially expressed (DE) genes detected, respectively (at the threshold of FDR-corrected p-value < 0.01 and $\log_2$FoldChange > 1 and < -1). Severity of inflammation in the media showed the highest number of DE genes among the three layers of the arterial wall (245 DE genes detected at aforementioned threshold). Deconvolution analysis revealed the highest abundances of macrophages and endothelial cells, with a substantial proportion of vascular smooth muscle cells and myofibroblast showing transitional expression profiles and indicating cell differentiation process. The most enriched KEGG (Kyoto Encyclopedia of Genes and Genomes) pathways associated with the results of differential expression were cytokine-cytokine receptor interaction (hsa04060) and vascular smooth muscle contraction (hsa04270) [FDR-corrected p-value=1.68×10^{-5} and 4.89×10^{-4}, respectively]. Layer-specific genes and enriched pathways related to the immune response and to vascular remodelling were also identified in spatially resolved data.

Conclusions: These results provide a comprehensive, multi-level molecular characterisation of the inflammatory processes in GCA, highlighting the involvement of both immune and stromal cells. Novel pathways and genes driving inflammatory infiltrates in each layer of the wall and implicated in the mechanism of vascular remodelling were revealed and have potential to provide therapeutically amenable candidates for future studies.

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Disclosures: None.

O-019

Single-cell RNA-sequencing exposes biological differences in giant cell arteritis lesions between disease relapse and disease onset

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Background/Objectives: Disease relapse in giant cell arteritis (GCA) poses a major burden affecting >50% of patients. It is assumed that the therapeutic management of disease relapse is akin to disease onset and, indeed, clinical trials routinely group naïve and relapsing patients together when assessing drug efficacy. However, subgroup analyses demonstrate differential outcomes between these states, alluding to biological differences which have yet to be characterised.

Here, we aimed to explore, for the first time, the differences in the cellular composition of temporal arteries (TA) from relapsing GCA patients compared to disease onset and identify the signalling pathways differentially upregulated in relapse.

Methods: Single-cell RNA-sequencing (scRNA-seq) was performed on TA tissue of patients at disease relapse and onset. Samples were loaded on the 10x Genomics Chromium controller, sequenced using Illumina NextSeq500 and aligned to the genome using Cell Ranger. The SoupX package was used to remove ambient RNA, and quality control analysis was applied to each patient sample to remove dying cells and doublets. Data integration and downstream differential gene expression analysis were performed with Seurat v5. Differential abundance analysis between disease states was employed using edgeR, while the pathfindR package was used to investigate signalling pathways. Results represented were statistically significant ($p<0.05$) and corrected for multiple comparisons.

Results: In total n=6 disease onset (mean age 76 [65-87], n=4 female), and n=6 relapse (mean age 72 [62-82], n=3 females) patients were recruited, with a mean disease duration of 19 (5-51) months. ScRNA-seq analysis identified diverse cell clusters, representing the stromal, lymphoid and myeloid compartments within TAs. Differential abundance analysis between disease relapse and onset revealed a significant absence of dendritic cells and an overrepresentation of plasma cells in relapsing tissue. Further, relapse and onset tissues exhibited distinct T-cell, fibroblast and vascular smooth muscle cell signatures. Pathways significantly enriched in disease relapse compared to onset included Th1 and Th2 cell differentiation pathways, the PD-1/PDL-1 checkpoint pathway, JAK-STAT, Notch, TGF-β, and VEGF signalling pathways, as well as pathways related to cellular senescence.

Conclusions: We have identified significant biological differences between relapsing and onset TA tissue in GCA, as evidenced by the presence of distinct cell subsets and differential signalling pathway activity. Our findings indicate that managing GCA relapse may require a distinct therapeutic approach.

Disclosures: None.

O-020

Genes deregulated in giant cell arteritis by high-throughput expression profiling in temporal artery biopsies

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Background/Objectives: Giant Cell Arteritis (GCA) is a systemic inflammatory disease of large and medium-sized arteries. Temporal artery biopsies (TABs) are performed for diagnosis, giving the opportunity to analyse inflamed tissues. Different histological patterns of inflammation can be found in TABs: transmural inflammation (TMI) is the most frequent pattern (78% of the positive TABs), while inflammation limited to adventitia (ILA) can be found in 7% of the positive TABs [1]. High-throughput assays in TABs are still scarce [2-5]. GCA patients are treated with glucocorticoids, irrespective of clinical presentations and inflammation patterns. It is necessary to increase the knowledge on the molecular features of GCA to implement precision medicine. We aimed to identify differentially expressed genes (DEGs) between TABs with TMI, ILA and normal TABs.

Methods: TABs with TMI from 42 patients with GCA, TABs with ILA from 7 patients with GCA, normal TABs from 7 patients without GCA were analysed. TABs with TMI and normal TABs were from patients naïve from therapy while 4/7 TABs with ILA were from patients receiving glucocorticoids. RNA was extracted from formalin-fixed paraffin-embedded TABs. The expression of 770 genes was profiled with the NanoString nCounter PanCancer Immune Profiling Panel. Data were analysed with nSolver software 4.0. DEGs with fold changes >2.0 and Benjamini-Yekutieli adjusted p-values <0.05 were considered significant.

Results: Unsupervised clustering revealed two groups of samples: the first group contained all the normal TABs plus TABs with ILA, while the second group contained 41/42 TABs with TMI. TABs with TMI showed 31 down- and 256 up-regulated genes compared to normal TABs; 26 down- and 187 up-regulated genes compared to TABs with ILA. TABs with ILA revealed a gene expression profile similar to normal TABs: 38 genes reached fold changes >2.0, but p-values did not maintain statistical significance after Benjamini-Yekutieli correction. These genes were also up-regulated in TABs with TMI. CCR7, CXCR3, CXCR6, IL-21R, CD86, SLAMF6, SLAMF7, CD27, OX40R, 4-1BB, CTLA4 were detected in all the TABs with TMI but were not detected in normal TABs. The following pathways resulted enriched by up-regulated DEGs: TLR1/2/4/6/8 cascade, MyD88 cascade, chemokine signaling, PD-1 signaling, cellular response to IL-1β and TNFα.

Conclusions: TABs with TMI had a distinct transcriptome compared to TABs with ILA. Genes deregulated in ILA were also deregulated in TMI, suggesting that ILA might represent early stages of the disease. Gene profiling allowed to deepen the knowledge on GCA pathogenesis.

References: [1] Am J Surg Pathol. 2014;38:1360-70; [2] Ann Rheum Dis. 2016;75:1196-202; [3] Ann Rheum Dis. 2016;75:1527-33; [4] Neurol Neuroimmunol Neuroinflamm. 2021;8:e0178; [5] Front Immunol. 2023;14:1237986.

Disclosures: None.

O-021

Single-cell multi-omics unveils increased activation of the IL-6/STAT3/PIM1 axis in T cell subsets of granulomatosis with polyangiitis patients

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Background/ Objectives: Granulomatosis with polyangiitis (GPA) is an autoimmune disease that involves inflammation of the microvasculature in various organs. Despite significant advancements in understanding GPA, the precise role of various T cell subsets in its pathogenesis remains elusive. In this study, we employed a single-cell multi-omics approach to decipher the transcriptional signatures of T cell subsets associated with active GPA and disease in remission.

Methods: Peripheral blood mononuclear cells (PBMCs) from active GPA patients (n=3) and controls (n=3) were analyzed using single-cell sequencing (scRNA seq, 10X Genomics). Additionally, PBMCs from active and remission GPA patients and controls (n=5 each) were subjected to scRNA and protein quantification (AbSeq, BD Rhapsody). Selected differentially expressed genes (Pim1, SOCS3, STAT3) were validated by qPCR on flow-sorted $CD4^+$ T cell subsets from active and remission GPA patients and controls. Baseline levels of transcription factor pSTAT3 in $CD4^+$ T cells were measured using phospho-flow cytometry. To elucidate Pim kinases' functional role, their inhibitors were employed to assess effects on $CD4^+$ T cell proliferation, activation, and differentiation.

Results: Differential expression analysis of scRNASeq and AbSeq datasets revealed that mRNA expression levels of Pim1 were upregulated in T cell populations from active GPA patients and patients in remission compared to healthy donors. Pim1 mRNA expression was strongly correlated with the T cell-associated surface markers CCR7, IL7R, and CD28, indicating its potential role in T cell activation. qPCR analysis of flow-sorted $CD4^+T_{naive}$, $CD4^+T_{EM}$, and $CD4^+T_{regs}$ of active GPA patients confirmed elevated expression levels of Pim1 in all subsets. Moreover, qPCR analysis of $CD4^+T_{naive}$ and $CD4^+T_{EM}$ from remission patients demonstrated that Pim1 expression was still upregulated suggesting persistent T-cell activation. In patients with active GPA, elevated baseline levels of pSTAT3 in $CD4^+$ T cells were observed and, serum levels of interleukin 6 (IL-6) were increased. Finally, preliminary data of functional studies showed a reduction in anti-CD3/CD28-induced T cell proliferation and activation in the presence of Pim kinase inhibitors.

Conclusions: These data indicate that the IL-6/STAT3/PIM1 pathway is activated in T cells from active GPA patients. Moreover, our study suggests that Pim1 expression is a potential promising marker to monitor T-cell activation during the disease course but requires further validation. Functional studies are warranted to determine whether inhibition of Pim1 or upstream molecules, such as JAK/STAT, is a rational therapeutic approach for GPA.

Reference:

1. Maney, N. J., et al. (2021)
2. Li, H., et al. (2022).

Disclosures: None.

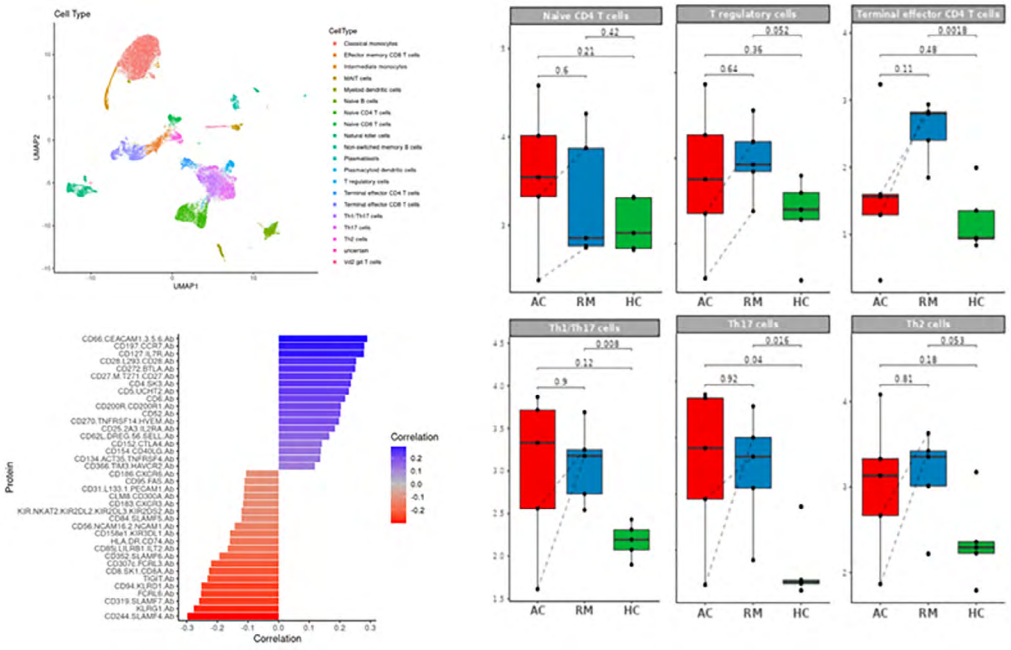

Figure 1 Abseq profiling of PBMCs validates elevated PIM1 expression in T cell subsets in GPA patients.

BREAKOUT SESSION: MANAGEMENT OF SPECIAL SITUATIONS

O-022

Abdominal Surgical Interventions Among Patients with Gastrointestinal Involvement of Behçet Syndrome

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Background/ Objectives: We aimed to investigate the clinical characteristics, treatments, and long-term prognosis of GIBS patients who underwent abdominal surgical interventions.

Methods: We conducted a retrospective chart review of all Behçet syndrome (BS) patients recorded between 1978 and 2022 to identify those with GIBS who had undergone abdominal surgery for GIBS. Relapse was defined as the presence of endoscopic or clinical activity with a positive fecal calprotectin test following bowel resection.

Results: Among our 11,200 BS patients, 119 (1%) had GIBS, and 29 (24%) of these GIBS patients (19 male, mean age: 49 ± 11 years) had undergone abdominal surgery (Table). BS was already diagnosed at the time of gastrointestinal involvement in 19 (65%) patients while 10 were diagnosed with BS with the development of gastrointestinal involvement. All except 1 patient who underwent ileocecal resection due to refractory disease, were diagnosed with GIBS following abdominal surgery. Perforation (n=18, 62%) and massive hematochezia (n=6, 21%) were the main reasons for surgery. The type of surgery was bowel resection in 25 patients, primary closure in 2 and diagnostic laparotomy in 2 patients.

Variable	GIBS patients who underwent abdominal surgery (n=29)
Male, n (%)	19
Mean (SD) current age, years	49 ± 11
Juvenile onset, n (%)	4 (13%)
Mean (SD) age at BS diagnosis, years	28 ± 10
Mean (SD) age at GIBS diagnosis, years	34 ± 11
Patients fulfilling ISG criteria, n (%)	23 (79%)
Major organ involvement, n (%)	15 (51%)
Uveitis	11
Vascular	5
Central nervous system	2
Pathergy positivity , n/N (%)	13/27 (48%)
HLAB51 positivity, n/N (%)	12/18 (66%)
Reasons for surgery	
Perforation	18 (62%)
Massive hematochezia	6 (21%)
Ileus	2
Suspicion of acute abdomen	2
Refractory disease	1
Patients who were receiving immunosuppressive treatment at the time of surgery	3 (10%)

Table. Demographic and characteristics of the patients.

Two patients with refractory GIBS had died due to extensive vascular involvement (n=1) and secondary amyloidosis (n=1). Among the 25 patients who underwent bowel resection, 14 (56%) experienced a relapse during a median follow-up of 24 (IQR: 1.75-36) months. Of these 14 patients, 12 had only one relapse. At the time of relapse, 4 (29%) patients required a reoperation. The remaining 11 patients did not experience any relapses during a median follow-up of 13 (IQR: 10-22) years.

Postoperative azathioprine treatment was initiated in 11 patients, with 3 of them also receiving a TNF inhibitor. Three of these 11 patients experienced a relapse while among the 14 patients who did not receive postoperative immunosuppressive treatment, 11 had a relapse (27% vs 79%; p=0.01). The use of postoperative immunosuppressive treatment was associated with a reduced risk of relapse (OR: 0.10; 95% CI: 0.016-0.644). Moreover, time to relapse was significantly longer in patients who received postoperative immunosuppressive treatment compared to those who did not (p=0.013, log-rank test).

Conclusions: GIBS may presently acutely with perforation or severe bleeding requiring surgery, as the first manifestation. 24% of GIBS patients required abdominal surgery and all except one were diagnosed with GIBS following the surgical procedure. Approximately 50% of the patients experienced a relapse, with most relapses occurring within 3 years. The use of immunosuppressive treatment after surgery showed a significant protective effect, reducing the risk of relapse by 90%.

Disclosures: GH has received research grant, lecture fees and fees for serving on an advisory board from Celgene, receiving consulting fees from UCB Pharma, Bayer, Johnson & Johnson, lecture fees from Novartis, Abbvie, Amgen, and UCB Pharma.

O-023

Reproductive Outcomes for Women with Vasculitis

Catherine Sims[1], Christine Yeung[2], Heather Tam[3], Joyce Kullman[3], Amanda Eudy[1], Renee Borchin[4], Cristina Burroughs[4], Megan E.B. Clowse[1], Peter Merkel[2].

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Objective: There are limited data on the reproductive health of women with vasculitis. This study utilized a large, prospective, international vasculitis pregnancy registry to survey women during and after pregnancy to improve characterization of reproductive outcomes.

Methods: The Vasculitis Pregnancy Registry (VPREG) is imbedded within the online Vasculitis Patient-Powered Research Network (VPPRN). Any pregnant woman with a diagnosis of vasculitis can self-enroll. After enrollment, women are invited to complete online surveys at study entry, once each trimester, and post-partum. Survey questions are organized into three categories: pregnancy outcomes and complications, vasculitis medications, and disease activity. VPREG surveys are currently available in five languages.

Results: Since 2015, 147 women with 149 pregnancies have enrolled in VPREG from 16 countries.

Seventy-one pregnancies were excluded as nine women have ongoing pregnancies and 62 women were lost to follow-up. Seventy-eight pregnancies have known pregnancy outcomes (live or non-live birth) and were included in this analysis. Of these 78 pregnancies, ANCA-associated vasculitis was the most frequently reported diagnosis (n=35, 45%) followed by Takayasu's arteritis (n=15, 19%), Behcet's (n=7, 9%), and other forms (n=21, 26%). During pregnancy, women experienced low pain related to vasculitis (scale 0-10, mean 3.1 ± 3.0) and preserved feelings of wellness (scale 0-10, mean 3.4 ± 3.1). Nineteen women reported experiencing a flare of vasculitis during pregnancy. Of the 15 women requiring hospitalization during pregnancy outside of delivery, four cited vasculitis activity as the indication for inpatient care. Most women (54/73, 74%) were prescribed medications for vasculitis during pregnancy with glucocorticoids (n=36) and azathioprine (n=18) being the most frequently prescribed. Four women were prescribed rituximab. Nineteen (26%) women took no medications to treat vasculitis during pregnancy. Seventy-six (97%) pregnancies resulted in live births. Of these live births, 63% delivered vaginally and 21% experienced a preterm delivery. The median gestational age at delivery was 38 weeks.

Conclusion: These results demonstrate that most women with vasculitis can have successful pregnancies. During pregnancy, a minority of women reported vasculitis flares or the need for hospitalization due to vasculitis. Medications to treat vasculitis are prescribed in most patients for disease control during pregnancy. These data can be used by rheumatologists to inform and facilitate discussions about reproductive health with women with vasculitis.

Disclosures: UCB (Grant/Research Support), Amgen (Consultant), Exagen (Grant/Research Support), GlaxoSmithKlein(GSK) (Grant/Research Support), Immunovant (Grant/Research Support), Pfizer (Grant/Research Support), Exagen (Grant/Research Support), GlaxoSmithKlein(GSK) (Consultant, Grant/Research Support), Immunovant (Grant/Research Support), UCB (Consultant, Grant/Research Support), AbbVie/Abbott (Grant/Research Support), Amgen (Consultant, Grant/Research Support), ArGenx (Consultant), AstraZeneca (Consultant, Grant/Research Support), Boehringer-Ingelheim (Consultant, Grant/Research Support), Bristol-Myers Squibb(BMS) (Consultant, Grant/Research Support), Cabaletta (Consultant), CSL Behring (Consultant), Eicos (Grant/Research Support), Electra (Grant/Research Support), Genentech (Grant/Research Support), GlaxoSmithKlein(GSK) (Consultant, Grant/Research Support), HiBio (Consultant), InflaRx (Consultant, Grant/Research Support), Janssen (Consultant), Jubilant (Consultant), Kyverna (Consultant, Stock options or bond holdings in a for-profit corporation or self-directed pension plan), MiroBio (Consultant), Neutrolis (Grant/Research Support), Novartis (Consultant), NS Pharma (Consultant), Q32 (Consultant), Regeneron (Consultant), Sanofi (Consultant), Sparrow (Consultant), Takeda (Consultant, Grant/Research Support), UpToDate (Royalties), Visterra (Consultant).

O-024

Exploring Reproductive Experiences with Women Enrolled in the Vasculitis Pregnancy Registry

Catherine Sims[1], Christine Yeung[2], Heather Tam[3], Joyce Kullman[3], Amanda Eudy[1], Renee Borchin[4], Cristina Burroughs[4], Megan E.B. Clowse[1], Peter Merkel[2].

[1]Duke University, Durham, United States; [2]University of Pennsylvania, Philadelphia, United States; [3]VPPRN, Kansas City, United States; [4]University of South Florida, Tampa, United States.

Objective: There are limited data on the reproductive health and experiences of women with vasculitis. This study engaged women with vasculitis to understand their perspectives about pregnancy and breastfeeding.

Methods: The Vasculitis Pregnancy Registry (VPREG) is an international, online, prospective, patient-reported registry within the Vasculitis Patient-Powered Research Network (VPPRN). The VPREG team partnered with the Vasculitis Foundation and patient research partners to develop two qualitative interview guides to prompt discussions of reproductive experiences with i) women who had live births; and ii) women who had non-live births. The guides included closed-ended scale items and open-ended prompts to elicit participant experiences. The interviews, performed by a rheumatologist, explored topics including pregnancy, medication choices to treat vasculitis, disease activity levels, patient-physician relationships, experiences with delivery, and breastfeeding. Participant responses were evaluated using thematic analysis.

Results: The 18 participants were located in North America, ranged in age from 25-43 years, and most had more than one pregnancy (n=11) (**Table 1**). Anti-neutrophil cytoplasmic antibody-associated vasculitis was the most common diagnosis (n=10) followed by Takayasu's arteritis (n=4), Behçet's disease (n=2), IgA vasculitis (n=1), and relapsing polychondritis (n=1). Almost all pregnancies ended in a live birth (n=17).

Four major themes emerged from interviews: 1) Women sought information about pregnancy from a range of sources, including their physicians, social media, and online forums; 2) Women cited discussions with family and physicians as important when deciding about treatment of vasculitis during pregnancy; 3) Women with vasculitis developed skills of self-advocacy during pregnancy to optimize communication between medical providers; and 4) Women with vasculitis had positive reproductive experiences with the majority reporting no flares of vasculitis, feeling "very well", and having "no pain" related to their vasculitis. Women who required changes to their medications to pursue their reproductive goals, identified physicians and family members as important participants in these conversations. Women described proactively gathering information about pregnancy and vasculitis from multiple sources, but ultimately decided their physician's perspective was the most influential. All women that used social media and online resources reported it did not impact or determine their reproductive decisions.

Conclusions: Women with vasculitis value the recommendations of their rheumatologists during reproductive healthcare discussions. Self-advocacy was frequently described during pregnancy because women felt they needed to act as liaisons among multiple specialists to ensure proper medical treatment. This study found that patients prioritize their relationships and conversations with physicians when planning for pregnancy.

Disclosures: UCB (Grant/Research Support), Amgen (Consultant), Exagen (Grant/Research Support), GlaxoSmithKlein(GSK) (Grant/Research Support), Immunovant (Grant/Research Support), Pfizer (Grant/Research Support), Exagen (Grant/Research Support), GlaxoSmithKlein(GSK) (Consultant, Grant/Research Support), Immunovant (Grant/Research Support), UCB (Consultant, Grant/Research Support), AbbVie/Abbott (Grant/Research Support), Amgen (Consultant, Grant/Research Support), ArGenx (Consultant), AstraZeneca (Consultant, Grant/Research Support), Boehringer-Ingelheim (Consultant, Grant/Research Support), Bristol-Myers Squibb(BMS) (Consultant, Grant/Research Support), Cabaletta (Consultant), CSL Behring (Consultant), Eicos (Grant/Research Support), Electra (Grant/Research Support), Genentech (Grant/Research Support), GlaxoSmithKlein(GSK) (Consultant, Grant/Research Support), HiBio (Consultant), InflaRx (Consultant, Grant/Research Support), Janssen (Consultant), Jubilant (Consultant), Kyverna (Consultant, Stock options or bond holdings in a for-profit corporation or self-directed pension plan), MiroBio (Consultant), Neutrolis (Grant/Research Support), Novartis (Consultant), NS Pharma (Consultant), Q32 (Consultant), Regeneron (Consultant), Sanofi (Consultant), Sparrow (Consultant), Takeda (Consultant, Grant/Research Support), UpToDate (Royalties), Visterra (Consultant).

Table 1. Patient Characteristics among Women with Vasculitis and a History of Pregnancy.

Mean age at enrollment (range)	33 years (25-43)
Country of origin	United States: 14 Canada: 4
Type of vasculitis	ANCA-associated vasculitis: 10 (55.6%) • *Granulomatosis with polyangiitis: 8* • *Microscopic polyangiitis: 1* • *Eosinophilic granulomatosis with polyangiitis: 1* Takayasu's arteritis: 4 (22.2%) Behçet's disease: 2 (11.1%) IgA vasculitis: 1 (5.6%) Other/suspected: 1 (5.6%)
First pregnancy	No: 11 (61.1%) Yes: 6 (33.3%) No response: 1 (5.5%)

O-025

Evaluating the role of immunosuppression in ANCA+ve and idiopathic subglottic stenosis

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Background: Subglottic stenosis, which is defined as narrowing of the airway below the vocal cords, is a recognised manifestation of ANCA-associated vasculitis (AAV), occurring in ~20% of patients with granulomatosis with polyangiitis (GPA), and often requiring a combination of medical, endoscopic, and surgical treatment approaches. The optimal modality of management of SGS remains unclear and challenging in the absence of standard guidelines.

Idiopathic SGS is a rare fibro-inflammatory disorder of unknown aetiology that shares clinical features with GPA. Whether immunosuppression has a role in treatment of idiopathic SGS is unclear.

The aim of this study was to evaluate the role of immunosuppression, as an adjunct to endoscopic and surgical treatment, in patients with both SGS and positive ANCA serology (SGS-ANCA) and in idiopathic SGS (i-SGS).

Methods: This is a retrospective analysis of patients with SGS managed in a combined airway-vasculitis service. Patients were categorized as:

(i) SGS, ANCA positive (with or with other features of AAV; SGS-ANCA);

(ii) idiopathic SGS (i-SGS) based on distinct demographic and histological criteria, not immunosuppressed; and

(iii) i-SGS, selected for treatment with immunosuppression due to frequent need for airway intervention.

Baseline demographic, histological and serological data were collected for each group. Disease activity and treatment response was measured by analysing the inter-dilatation interval (IDI). In groups (i) and (iii) the IDI was measured before and after systemic immunosuppression to assess its effectiveness.

Results: Sixty-two patients with SGS are included in the current analysis:

Group (i): SGS-ANCA, n=23, 74% female, age at diagnosis 45 (±29)

Median pre-immunosuppression IDI increased from 8.9 (5-12) to 26.0 (12-36) months following immunosuppressive treatment.

Group (ii) i-SGS, n= 33, 100% female, age at diagnosis 42 (±26)

Median IDI during follow up was 21.1 (12 – 28) months.

Group (iii) i-SGS, treated with immunosuppression, n=7, 86% female, age 49 (±21)

Median pre-immunosuppression IDI increased from 7.6 (6-12) months to 27.8 (17-33) months following immunosuppressive treatment (Figure 1).

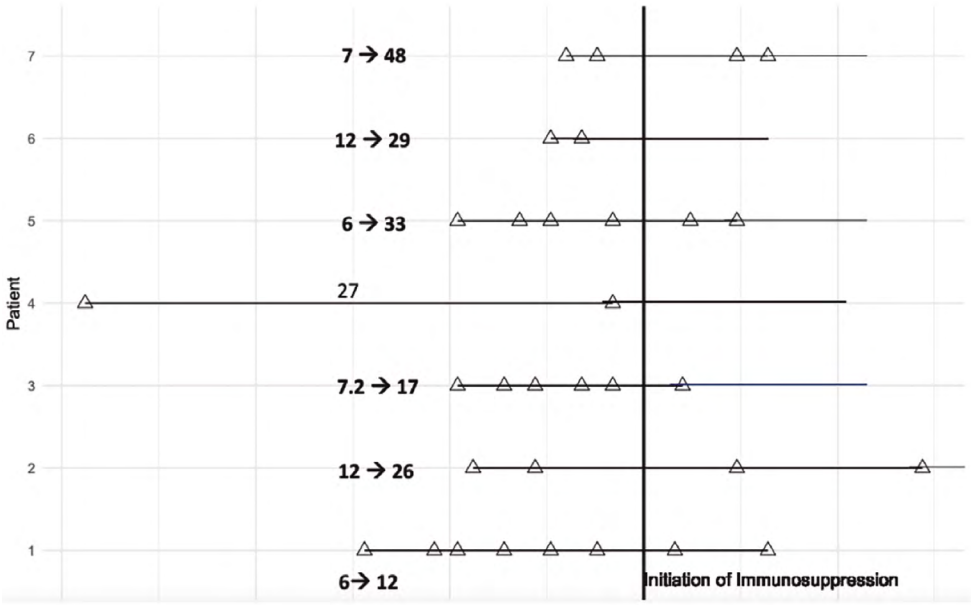

Figure 1: Timeline showing inter-dilatation interval pre- and post-immunosuppression in individual patients with i-SGS.

Conclusion: This study confirms that immunosuppressive treatment has a beneficial role in the treatment of SGS-ANCA and is associated with prolongation of airway inter-dilatation interval. Patients with i-SGS requiring frequent airway intervention experienced an equivalent benefit in IDI prolongation following treatment, suggesting that immunosuppression may have a role in the treatment of i-SGS. Ongoing analyses aim to identify patient characteristics that predict response to treatment and the role of specific immunosuppressive therapies in an extended patient cohort.

References: None.

Disclosures: None.

O-026

Subglottic stenosis in patients with granulomatosis with polyangiitis – the clinical value of an airway biopsy

Louise Linde, Mikkel Faurschou, Sophine Boysen Krintel, Bo Baslund.
Rigshospitalet, Copenhagen, Denmark.

Background/Objectives: Subglottic stenosis (SGS) is a disease manifestation seen in approximately 20 % of patients with granulomatosis with polyangiitis (GPA)[1,2]; Among GPA patients with SGS, the airway stenoses tend to be difficult to treat and to re-occur after treatment. We aimed to 1) review the literature on histopathological findings in SGS, and 2) describe the histopathological findings among GPA patients treated for SGS at our hospital department.

Methods: Using a variety of search terms, we searched Pubmed for articles describing biopsy findings in GPA patients treated for SGS until May 2023. Our local cohort encompassed GPA patients diagnosed with subglottic stenosis following laryngoscopy or bronchoscopy during 1991-2022. For all patients, biopsy findings and number of biopsies were recorded. Granulomatous inflammation with or without necrosis, multinucleated (giant) cells, microabscesses, or vasculitis were considered GPA-characteristic histopathological findings, while all other histological findings were considered non-specific.

Table 1. Studies retrieved from the literature search.

Studies			Patients		Biopsies		
Authors	Year	Design	Number	Number with biopsies / total number, n (%)	Number	Characteristic GPA-findings*, n (%)	Non-specific findings, n (%)
Catano et al	2021	Retrospective	33	18/33 (55%)	18	8 (44%)	10 (56%)
Girard et al	2015	Retrospective	26	17/26 (65%)	26	12 (47%) **	
Pajor et al	2015	Case report	1	1/1 (100%)	1		1 (100%)
Jakez-Ocampo et al	2010	Case report	2	2/2 (100%)	2	2 (100%)	
Solans-Laqué et al	2008	Case series	6	6/6 (100%)	6	6 (100%)	
Gluth et al	2003	Retrospective	27	16/27 (59%)	26	4 (15%)	
Stappaerts et al	2000	Case report	1	1/1 (100%)	1		1 (100%)
Langford et al	1996	Retrospective	43	26/43 (60%)	140	7 (5%)	
Herridge et al	1996	Case series	5	5/5 (100%)	5	1 (20%)	4 (80%)
Daum et al	1995	Retrospective	17	17/17 (100%)	21	12 (57%)	
Gaughan et al	1990	Case report	1	1 (100%)	1		1 (100%)
Devaney et al	1990	Retrospective	Not stated	Not stated	17	4 (23%)	
Hoare et al	1989	Case series	4	4/4 (100 %)	14		14 (100%)
Hellman et al	1987	Case report	1	1 (100%)	1	1 (100%)	
Waxman and Bose	1986	Case report	2	2/2 (100%)	3	1 (33%)	2 (67%)
McDonald et al	1982	Case series	17	3/17 (18%)	3	3 (100%)	
Arauz-fonseca	1982	Case series	10	2/10 (20%)	2	1 (50%)	1 (50%)
Lampman et al	1981	Case report	1	1 (100%)	1	1 (100%)	
Scully et al	1979	Case report	1	1 (100%)	1		1 (100%)
Djalilian et al	1975	Case series	5	4/5 (80%)	4		4 (100%)
Talerman and Wright	1972	Case report	1	1 (100%)	3	1 (33%)	2 (67%)
Total			203	128/203 (63%)	296	64/296 (22%)	

GPA: granulomatosis with polyangiitis. *Granulomatous inflammation with or without necrosis, multinucleated (giant) cells, microabscesses or vasculitis; **granuloma, vasculitis and necrosis is reported in 47%, 12% and 29% of the biopsies, respectively, however the distribution of each finding is not further described.

Results: In the reviewed literature, we identified 128 GPA patients with SGS and data on biopsy findings **(Table 1).** In a total of 296 biopsies, characteristic GPA-findings were described in 64 (22%). Our local cohort comprised 27 patients. Among these, 24 had SGS, 7 had endobronchial stenosis, and 4 had SGS as well as endobronchial stenosis. The median (range) age at GPA diagnosis was 31.9 (14.4-76.9) years, and the follow-up time since GPA diagnosis was 16.7 (0.5-31.2) years. Airway stenosis occurred after a median of 2.5 (-0.4-21.2) years of follow-up. Twenty-three patients underwent a surgical dilation procedure at some point during the disease course. In 18 patients, 2 or more procedures were needed. The median time interval between the procedures in these patients was 23 (2 – 113) months. Twenty-six of the 27 patients had at least one and up to nine available airway biopsies. In total, 67 biopsies had been performed, and characteristic GPA findings was observed in 15 (22%) of the biopsy specimens.

Conclusions: Among GPA patients with SGS, histopathological findings characteristic of GPA was seen in only one fifth of the obtained biopsies. The added clinical value of a biopsy may thus be limited in patients with GPA and SGS.

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2. Del Pero MM, Jayne D, Chaudhry A, Sivasothy P, Jani P. Long-term outcome of airway stenosis in granulomatosis with polyangiitis (Wegener Granulomatosis): An observational study. *JAMA Otolaryngol - Head Neck Surg*. Published online 2014. doi:10.1001/jamaoto.2014.2430

Disclosures: None.

O-027

An Updated Cohort of Diffuse Alveolar Hemorrhage Secondary to Antineutrophil Cytoplasmic Antibody–Associated Vasculitis

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[1]Mayo Clinic, Rochester, United States; [2]Mayo Clinic, Scottsdale, United States.

Background/ Objectives: Despite advances in remission induction therapies for anti-neutrophil associated cytoplasmic antibody (ANCA) associated vasculitis (AAV), diffuse alveolar hemorrhage (DAH) remains a feared pulmonary manifestation of AAV. DAH in AAV progress to respiratory failure with frequencies ranging from 10-60% and mortality >10% in modern case series[1]. Cartin Ceba et. al described a series of patients evaluated at Mayo Clinic presenting with DAH due to AAV from 1997 to 2012 and risk factors associated with respiratory failure[2]. We sought to identify an updated cohort of patients presenting with DAH and AAV at our institution, re-evaluating risk factors for patient morbidity and mortality.

Methods: We performed a retrospective analysis of all consecutive patients with DAH due to AAV presenting at Mayo Clinic sites from January 1st, 2013, to August 31st, 2022. Inclusion criteria were age over 18 years, Chapel Hill and ACR/EULAR consensus definitions for AAV, and DAH. We collected demographic data, clinical data, imaging, and laboratory results. We then compared these clinical characteristics to those described by Cartin-Ceba et. al. in table 1.

Results: 104 patients meeting eligibility criteria were identified. Patients were predominantly female (N=55) with a median age at presentation of 66 years (IQR 51-72). At the time of presentation, 54 (53%) were classified as GPA and 55 (52%) were proteinase 3 (PR3) ANCA . Median Birmingham Vasculitis Activity Scores for Wegener's Granulomatosis (BVAS/WG) was 9 (IQR 5-10). 34 (33%) patients developed respiratory failure, 22 (21%) requiring invasive mechanical ventilation (IMV). Remission induction consisted of IV methylprednisolone and/or oral prednisone in 102 (97%) of patients, rituximab in 86 (82%), and cyclophosphamide in 18 (17%). Median follow up time was 31 (IQR 9-97) months after presentation with DAH. Complete remission was seen in 57 (77%) of patients with follow up at 26 weeks and 20 patients died during follow up.

Conclusion: In this updated series of patients with DAH and AAV at a multi-site single center study, we noted increased trends in the utilization of rituximab for remission induction for DAH with decreasing use of cyclophosphamide and plasma exchange. Rates of progression to respiratory failure appeared comparably lower in this updated cohort.

Table 1: Comparison of demographics, clinical features, treatments, and outcomes of cohorts describing diffuse alveolar hemorrhage at Mayo from Cartin Ceba et. al and our updated cohort.

	Cartin Ceba (N=73)[2]	Current Cohort (N=104)
Sex, no. (%) female	32 (44)	55 (52.8)
Age, median (IQR) years	61.8 (49.3-72.4)	66.0 (51-72)
Smoking Status, no. (%)		
Never smoker	54 (74)	60 (57)
Former smoker	17 (23)	38 (36)
Current Smoker	2 (3)	7 (7)
AAV Subtype		
GPA, no. (%)	44 (60)	54 (53)
MPA, no. (%)	29 (40)	48 (47)
PR3-ANCA, no. (%)	40 (55)	55 (52)
MPO-ANCA, no. (%)	33 (45)	51 (48)
BVAS/WG score, median (IQR)	10 (8-13)	9 (5-10)
Symptom, no. (%)		
Dyspnea	68 (93)	60 (57)
Cough	60 (82)	59 (56)
Hemoptysis	55 (75)	32 (30)
Fever	36 (49)	24 (23)
Laboratory Findings		
Hemoglobin, median (IQR) gm/dL	9 (8-10.4)	8.2 (6.7-10.4)/91
ESR, median (IQR) mm/hr	61 (31-86)	62.5 (28.7-85.5)/70
CRP, median (IQR) mg/L	21.3 (7.4-134.2)	62 (33.2-138.9)/75
Creatinine, median (IQR) mg/dL	1.4 (0.9-3.2)	1.9 (1-3.6)

Bronchoscopy/BAL Findings		
Neutrophils in BAL fluid, median (IQR) %	28 (8-66)	36 (9.5-64)/71
Hemosiderin-laden macrophages, median (IQR) %	56 (27-91)	65 (28-92)/45
Intervention		
Remission induction treatment, no (%)		
Methylprednisolone IV	65 (89)	80 (76)
Prednisone	8 (11)	22 (21)
Rituximab	37 (51)	86 (82)
Cyclophosphamide	31 (42)	18 (17)
Avacopan	0 (0)	13 (12)
None	2 (3)	3 (3%)
Plasma exchange, no. (%)	32 (44)	29 (28)
Plasma exchange sessions, median (IQR) no.	7 (5-7)	5.5 (5-7)
Outcome		
ICU admission, no. (%)	41 (56)	33 (32)
Hospital mortality, no. (%)	8 (11)	7 (8.6)/83
Length of hospital stay, median (IQR) days	10 (5.7-16.6)	9 (7-18)/83
Length of ICU stay, median (IQR) days	6.1 (3.1-9.5)	5 (3-9)/33
Invasive Mechanical Ventilation (IMV), no (%)	26 (36)	22 (21)
Duration of IMV, median (IQR) days	2.4 (1.5-4.4)	4 (2.75-5)
Non-invasive ventilation, without IMV	16 (22)	12 (11)
Complete Remission no. (%)	55 (75)	57 (77)/74

Disclosures: Specks – Consulting/Advisory Boards: Amgen, Argenix, AstraZeneca, Boehringer Ingelheim, CSL Vifor. Research Grant/Support: Amgen, AstraZeneca, Bristol Myers Squibb, Genentech, GSK, Northstar Medical Radioisotopes, Takeda.

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BREAKOUT SESSION: BIOMARKERS OF CLINICAL INTEREST

O-028

Autoantibody profiling to identify novel candidate biomarkers in ANCA associated vasculitis

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Background: ANCA-associated vasculitides (AAV) are a group of rare autoimmune diseases characterized by necrotizing inflammation of small blood vessels requiring prompt initiation of immunosuppressive treatment to limit organ damage. Anti-neutrophil cytoplasmic antibodies (ANCAs) are the hallmark of AAV and play a key role in the disease pathogenesis. However, around 10% of patients with clinico-pathological features of AAV are seronegative for ANCAs. Moreover, ANCA specificity does not fully account for the high heterogeneity in clinical presentation and organ involvement, and does not uniformly predict AAV activity. There is therefore a need for novel autoantibodies associated with AAV per se, disease subgroups and disease activity.

Methods: In-house developed planar and bead-based antigen arrays were generated using the collection of 42,000 protein fragments representing 18,000 unique human proteins from the Human Protein Atlas collection (www.proteinatlas.org). Through a well optimised workflow and data analysis pipeline, we performed a proteome-wide screenings and verification of IgG in serum and plasma samples collected from 450 AAV patients, as well as disease and healthy controls, from the University of Vienna (Austria), the University of Cambridge (UK), the University Medical Centre of Groningen, and the Rare Kidney Disease Registry in Dublin (Ireland).

Result: The analyses evidenced anti-kinesin antibodies at higher prevalence in AAV compared to the controls. Anti-kinesin antibodies showed high prevalence especially in anti-MPO positive patients. The profiling of autoantibodies in samples collected from AAV patients at remission also revealed a preliminary association of specific autoantibodies with future relapses.

Conclusion: The autoantibody profiling allowed the identification of several autoantibodies as possibly associated with AAV, anti-MPO positive AAV, and AAV at risk of relapse. Further studies are currently under development to verify and broaden this selection of targets.

Disclosures: The studies have been funded by the RELapses prevention in chronic autoimmune disease: common mechanisms and co-morbidities (RELENT) consortium, the HEalth data Linkage for ClinicAL benefit (HELICAL) training network, and the PersonAlisation of RelApse risk in autoimmune DISEase (*PARADISE*) consortium.

O-029

Torque teno virus as a potential biomarker for assessment of immunocompetence in patients with ANCA-associated vasculitis

Balazs Odler[1], Regina Riedl[1], Jacinta Lee[2], Laura A. Cooney[3], Peter A. Merkel[4], E William St Clair[5], Fernando C. Fervenza[6], Duvuru Geetha[7], Paul A. Monach[8], David R.w. Jayne[2], Rona M. Smith[2], Paul A. Lyons[2], Mark A. Little[9], Ewan Harrison[2], Salem Almaani[10], Alexander R. Rosenkranz[1], Ulrich Specks[6], John H. Stone[11], Andreas Kronbichler[12].

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Background/objective: ANCA-associated vasculitis (AAV) is a life-threatening disorder characterized by a relapsing-remitting disease course necessitating immunosuppression to control disease activity. Balancing the risks of infection against maintaining good disease control is crucial and yet often challenging. There is a lack of validated biomarkers to tailor immunosuppression to minimize therapy-related complications while maintaining a relapse-free period. The monitoring of Torque teno virus (TTV) has been successfully used in transplant medicine to predict the risk of organ rejection and infectious complications. However, the presence and role of TTV in association with clinical outcomes in AAV has yet to be reported.

Methods: Consecutive plasma samples (N=915) of 81 patients with AAV from the RAVE trial were used for assessment of the TTV load. Participants received either rituximab (RTX, N=40) or cyclophosphamide (CYC, N=41) followed by azathioprine (AZA). The TTV DNA was quantified using a real-time polymerase chain reaction method (TTV R-GENE®, BioMérieux) at multiple study visits. Change in TTV load and differences between non-relapsing and relapsing patients were investigated during a follow-up period of 1080 days.

Results: In total, 915 TTV quantifications were performed. At baseline, 72% (N=58) of patients had detectable TTV in the peripheral blood. The baseline median TTV load of all patients was 3×10^2 c/mL (interquartile range [IQR]: 0 – 3×10^3 c/mL). TTV load increased after initiation of immunosuppression and peaked at day 120 (median 2×10^3 c/mL, IQR: 2×10^2 – 5×10^5) and was detectable in 80% of the patients. Patients receiving RTX as a remission induction therapy showed a non-significant higher TTV load during the first 180 days in comparison to CYC/AZA-treated individuals at any visits. Patients with disease relapse had a lower TTV load at day 120 as compared to those without relapse (median 4×10^2 [IQR: 0 – 3×10^4] c/mL vs median 8×10^3 [IQR: 2×10^2 – 6×10^5] c/mL, p=0.036, respectively). For the 25 severe relapses, the median time to relapse was 339 (IQR: 232-516) days. Six relapses occured before day 120, while 19 after day 120.

Conclusions: Among patients with AAV, TTV load reflects the intensity of immunosuppression and is associated with disease relapses. These results suggest that TTV might be a biomarker for the assessment of immunocompetence and identifying patients with AAV at risk of relapse.

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Disclosures: None.

O-030

A germline genetic biomarker predicts treatment response to tocilizumab in giant cell arteritis

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Background/Objectives: Biomarkers that predict treatment response to tocilizumab (TCZ) in patients with giant cell arteritis (GCA) have not been identified. A common single-nucleotide polymorphism in the IL-6 receptor (Asp358Ala, rs2228145) increases solubilization of membrane bound IL-6R. The study objective was to determine if Asp358Ala predicted treatment response to TCZ and to understand the impact of this variant on IL-6 signalling in leukocytes from patients with GCA.

Methods: Samples and clinical data were obtained from two independent cohorts. Genetic sequencing was performed to identify GCA patients with the Asp358Ala variant. Clinical symptoms, laboratory values, and response to TCZ was compared by variant status. Serum was used to quantify soluble IL-6R (sIL-6R) levels by ELISA. Peripheral blood mononuclear cells (PBMC) from patients and controls were evaluated for expression of the IL-6R and its co-receptor, gp130, using flow cytometry. The same PBMC were stimulated ex vivo with IL-6 and evaluated for downstream targets of IL-6, STAT3 phosphorylation (pSTAT3), and IL-17A expression. $P<0.05$ defined statistical significance.

Results: 100 patients with GCA were included in the study (58 patients in cohort #1 and 42 patients in cohort #2). Clinical response rates to TCZ were 76% and 81% in each cohort respectively. No clinical factor was significantly associated with treatment response to TCZ. In contrast, the Asp358Ala variant predicted treatment response in each cohort. In cohort #1, a gene dose-dependent response was observed with a 36% response rate in the homozygous GCA patients and a response rate of 91% in patients without the variant ($p=0.003$). In cohort #2, TCZ response rates were 50% for homozygotes and 85% for patients without the variant ($p=0.04$). Time to TCZ failure differed significantly by variant ($p<0.0001$). sIL-6R levels were significantly increased in homozygotes. CD4 and CD8 T cells from patients with GCA had signifcantly higher membrane expression of IL-6R and gp130 than healthy controls. pSTAT3 levels were significantly increased in response to IL-6 stimulation in a gene dose-dependent manner in CD4 T cells from patients with GCA, but not in PBMC from healthy controls or patients with other forms of vasculitis. Response to IL-6 correlated with gp130 expression. Moreover, IL-17 producing CD4 T cells were significantly increased in a gene dose-dependent response ($p<0.01$).

Conclusions: The Asp358Ala IL-6R variant is associated with decreased treatment response to TCZ in GCA by enhancing IL-6 signalling in CD4 T cells. Future trials should investigate whether GCA patients with this variant respond more favourably to JAK inhibition or targeting of the IL-17 pathway.

References: None.

Disclosures: None.

O-031

Serial measures of usCD163 predict kidney failure in AAV-GN

Sinead Stoneman[1], Cliona Cowhig[1], Conor Coughlan[1], Niall Conlon[2], Jean Dunne[3], Jennifer Scott[2], Julie Power[4], Darren Dahly[1], Mark Little[2], Michael Clarkson[1], Sarah Moran[1].

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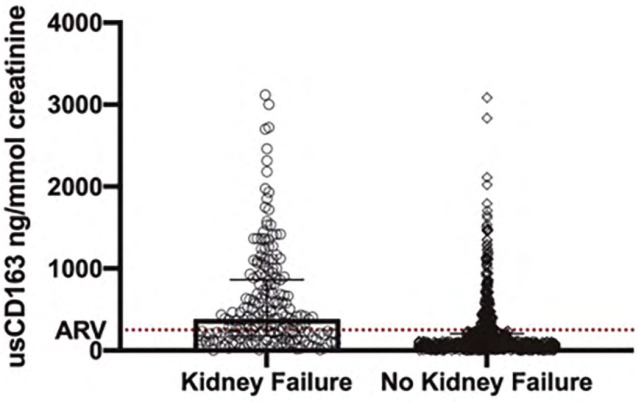
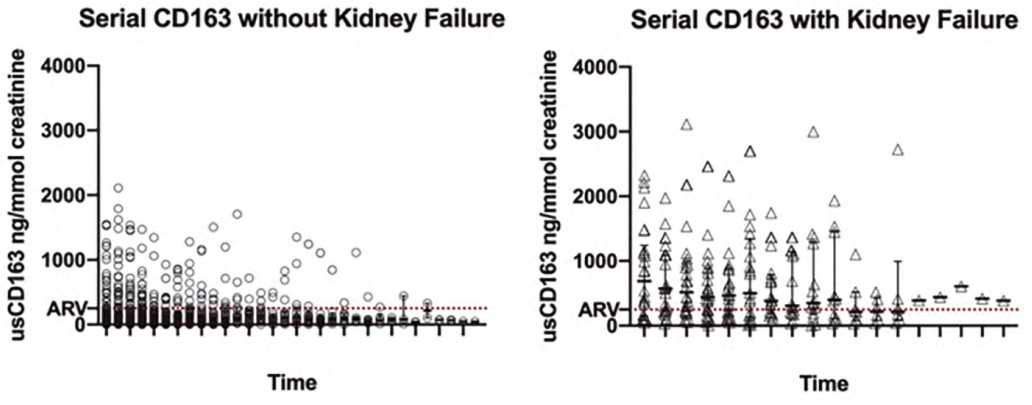
Background: AAV-GN affects 70 – 85% of AAV patients during their disease course. 26% of patients with AAV progress to end-stage kidney disease [ESKD] over a median of 40 months and 43% progress without a recognised disease flare. Identifying those at highest risk of progression to kidney failure is an urgent unmet need. Urine soluble CD163 [usCD163] has excellent biomarker characteristics and has been validated as a clinical biomarker in detecting active AAV-GN at diagnosis and flare. The use of usCD163 to predict ESKD in those considered to be in clinical remission is undefined.

Methods: We utilised longitudinal clinical data and biobank urine samples from a national multicentre rare kidney disease registry to evaluate the utility of serial usCD163 measurements to predict of kidney failure in AAV-GN. Inclusion criteria were 4 or more urine sCD163 measurements and diagnosis of AAV. The primary endpoint was kidney failure defined as death, ESKD or GFR <15mls/min/1.73m^2. Statistical analysis was performed using GraphPad Prism and R.

Results: We identified 113 participants with 4 or more usCD163 measurements over at least a 12-month period. 26 (23%) participants developed kidney failure (death (13), ESKD (17), GFR <15 (16)). Excluding the initial urine sample (generally from a period of clinically apparent disease activity) the median usCD163 level normalized to urine creatinine was higher in those meeting the endpoint (median value of 385ng/mmol vs 89ng/mmol, p<0.0001), see figure 1A. In those with kidney failure 62.6% (128) of values were above the diagnostic threshold for active renal vasculitis of 250ng/mmol, see figure 1B, C. Analysis of this cohort identified the optimal diagnostic threshold for usCD163 for the future development of kidney failure as 160ng/mmol, with a sensitivity of 77.7%, a specificity of 69%, negative predictive value [NPV] of 92.3, and positive predictive value [PPV] 39.4.

Conclusions: A urine sCD163 result less than 160 ng/mmol has a strong NPV for predicting future kidney failure. These results suggest that in addition to detecting active GN, urine sCD163 may provide reassurance that subclinical glomerular injury is not missed in AV. The suppression of usCD163 associates with a significantly lower risk of progression to kidney failure, supporting a key role for undetected disease activity as the major driver of progression to kidney failure.





O-032

Plasma and urine metabolomic profiles reveal potential biomarkers in MPO-ANCA-GN

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Background/ Objectives: The precise mechanism of myeloperoxidase- anti-neutrophil cytoplasmic antibody associated glomerulonephritis (MPO-ANCA-GN) remains elusive. There is a lack of dependable biomarkers for evaluating disease activity, therapeutic resistance and risk of relapse. We seek valuable biomarkers and explore the mechanism of MPO-ANCA-GN by metabolomics.

Methods: Urine and plasma samples from 63 MPO-ANCA-GN, 31 lupus nephritis (LN), 15 IgA nephropathy (IgAN), and 15 minimal change disease (MCD) patients and 30 healthy controls (HC) were collected for metabolomics analysis as a training set. The samples were analyzed using Ultra Performance Liquid Chromatography and Tandem mass spectrometry. Kyoto Encyclopedia of Genes and Genomes annotation and enrichment analysis were performed for key pathways.

Results: Compared with the disease control (DC) and HC, we observed 79 significantly upregulated metabolites and 32 downregulated metabolites in the plasma samples of MPO-ANCA-GN patients. KEGG enrichment analysis suggested that these upregulated metabolites were mainly associated with phenylalanine and galactose metabolism and downregulated metabolites were mainly associated with bile secretion, steroid biosynthesis, and ovarian steroidogenesis. Compared with the DC and HC, we identified a total of 122 differential metabolites in the urine samples of MPO-ANCA-GN patients, 40 of which were significantly upregulated and 68 of which significantly were downregulated. Subsequently, KEGG analysis revealed that these upregulated metabolites were mainly enriched in glycerolipid metabolism, lipid and atherosclerosis, cholesterol metabolism, insulin resistance (Corrected $P<0.05$). Downregulated metabolites were mainly enriched in steroid hormone biosynthesis (Corrected $P < 0.05$).

504 differential metabolites in plasma samples were identified between the active and remission phases of nine MPO-ANCA-GN patients. Of these, 425 metabolites were downregulated, while 79 lipid metabolites were upregulated in the active group. Besides, gluceptate in plasma samples and Trans-Zeatin in urine samples had excellent diagnostic ability in distinguishing treatment-responsive patients from treatment-resistant patients, and the AUC was 0.833 and 0.845, respectively.

Conclusions: We identified many novel potential metabolic biomarkers in urine and plasma samples for evaluating disease activity, therapeutic resistance, and risk of relapse in patients with MPO-ANCA-GN.

References: None.

Disclosures: None.

O-033

Circulating Immune Profile in Granulomatosis with Polyangiitis Reveals Distinct Patterns Related to Disease Activity

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Background/Objectives: Granulomatosis with polyangiitis (GPA) is an autoimmune disorder characterized by recurrent relapses that can cause severe tissue damage and life-threatening organ dysfunction. Multiple immune cells and cytokines/chemokines are involved in the different stages of the disease. Immune profiling of patients may be useful for tracking disease activity. However, reliable immune signatures for GPA activity are lacking. In this study, we examined circulating immune profiles in GPA patients during active and remission disease states to identify potential immune patterns associated with disease activity.

Methods: The distribution and phenotypic characteristics of major circulating immune cells, and the profiles of circulating cytokines/chemokines, were studied on cryopreserved peripheral blood mononuclear cells from GPA patients (active, n=20; remission, n=20) and healthy controls (n=20) leveraging a 40-color optimized multicolor immunofluorescence panel (OMIP-69) and in serum using a 46-plex Luminex multiplex assay, respectively.

Results: Deep phenotyping uncovered a distinct composition of major circulating immune cells in active GPA and GPA in remission, with the most significant findings emerging within the monocyte compartment. Our detailed analysis revealed circulating monocyte diversity beyond the conventional monocyte subsets. We identified eight classical monocyte populations, two intermediate monocyte populations, and one non-classical monocyte population. Notably, active GPA had a higher frequency of $CD45RA^{+}CCR5^{+}CCR6^{-}CCR7^{+/low}CD127^{-}HLA\text{-}DR^{+}CD2^{-}$ classical monocytes and a lower frequency of $CD45RA^{-}CCR5^{-/low}CCR6^{-}CCR7^{-}CD127^{-}HLA\text{-}DR^{+}CD2^{+/-}$ classical monocytes, which both strongly correlated with disease activity. Furthermore, serum levels of CXCL1, CXCL2, and CCL20, all linked to monocyte biology, were elevated in active GPA and correlated strongly with disease activity.

Conclusions: These findings shed light on the circulating immune profile of GPA and may form the foundation for the establishment of immune signature profiles to assess disease activity. Monocytes in particular may be studied further as potential markers for monitoring disease progression in GPA.

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3. Vegting, Y., et al. (2021).

Disclosures: None.

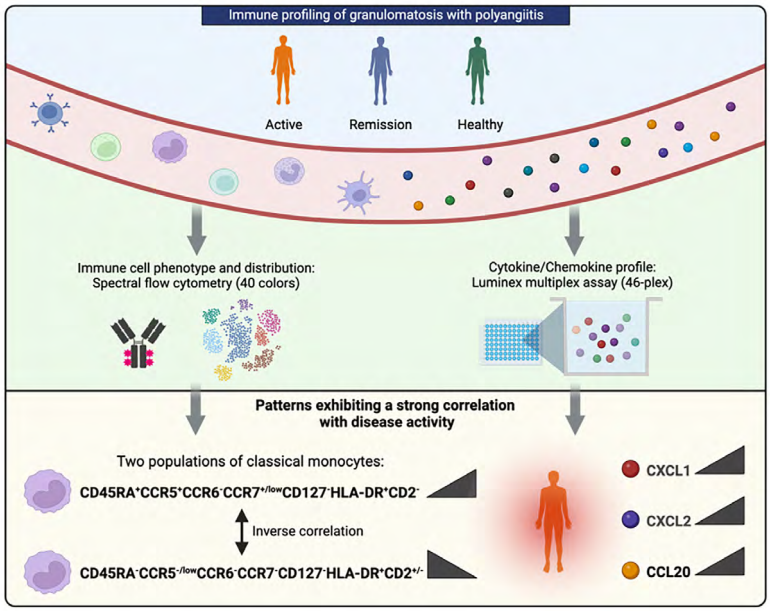

Figure 1 Graphical abstract and highlights. Deep immunophenotyping unveils a higher degree of circulating monocyte heterogeneity beyond the conventional monocyte subsets in granulomatosis with polyangiitis (GPA). Frequencies of circulating CD45RA+CCR5+CCR6-CCR7+/lowCD127-HLA-DR+CD2- and CD45RA-CCR5-/lowCCR6-CCR7-CD127-HLA-DR+CD2+/- within the CD14+CD16- population are associated with disease activity in GPA. Serum levels of both CXCL1, CXCL2, and CCL20 strongly correlate to disease activity in GPA.

BREAKOUT SESSION: OPTIMIZING NEW TREATMENTS

O-034

Avacopan for the Treatment of ANCA-Associated Vasculitis: a Multicenter Prospective Real-Life Study on Efficacy, Safety, and Impact on Quality of Life

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Background/Objectives: The aim was to assess efficacy, safety and impact on quality of life associated with the use of avacopan in a real cohort of Italian patients.

Methods: The prospective collection of clinical data commenced in May 2022, and encompassed patients with either GPA or MPA, including those with newly diagnosed or relapsing diseases, who initiated avacopan therapy.

Results: Twenty-four patients (17 GPA, 7 MPA) were included: median age 60 years (IQR 52-63), 58% women. One-third of the patients initiated avacopan following a new diagnosis of AAV.

At avacopan initiation, BVASv3 and VDI were 9 (IQR 5-20) and 3 (IQR 1-4), respectively. The main disease manifestations included renal involvement (75%) and pulmonary involvement (46%).

Avacopan was administered in combination with RTX in all patients, preceded by CYC IV in 5 patients. Two out of 12 patients with RPGN also underwent plasmapheresis. At baseline, the median corticosteroid (CS) dose was 25 mg/day (IQR 7-41). For patients with renal involvement, the median baseline creatinine and proteinuria values were 1.9 mg/dL (IQR 1.6-2.8) and 1140 mg/24h (IQR 300-2400), respectively. Sixteen out of 18 patients had microhematuria.

At 12 weeks, 75% of patients had achieved clinical remission, with 28% being CS-free. The median CS dose had decreased to 5 mg/day (IQR 2-5) (**p-value<0.001**). The median creatinine and proteinuria values had reduced to 1.6 mg/dL (IQR 1.2-2.1) (**p-value=0.029**) and 300 mg/24h (IQR 100-1223) (**p-value=0.014**), respectively. Only eight out of 18 patients still presented microhematuria (**p-value=0.005**).

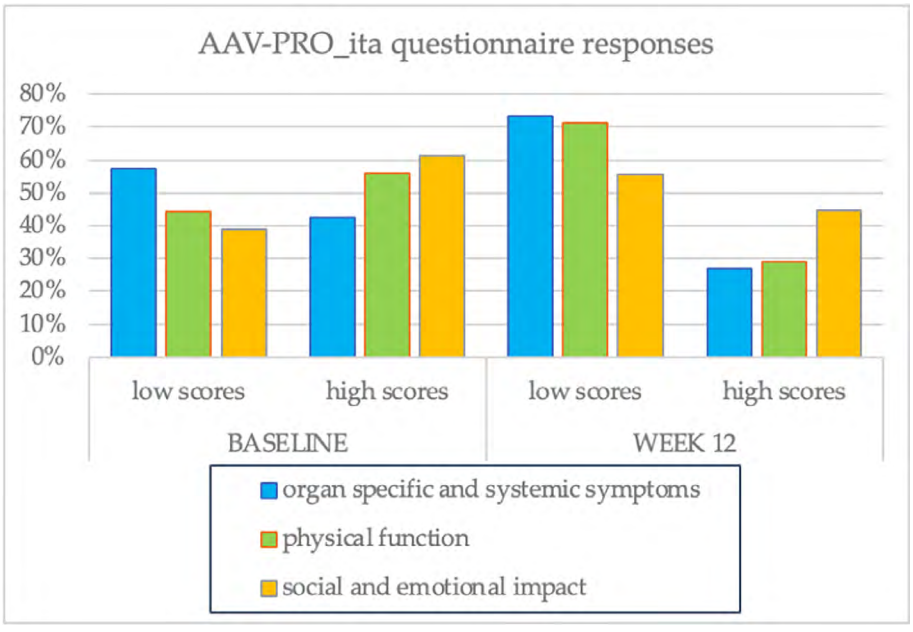
During the observation period (median follow-up: 26 weeks [IQR 22.5-52]), avacopan was suspended 8 times, primarily due to infectious(62.5%). Two clinical relapses were reported at weeks 26 and 52, necessitating the resumption of CS and RTX plus CS, respectively. One death at week 65 due to a fungal infection was registered.

Finally, a progressive reduction in AAV-PRO questionnaire scores was observed from baseline to week 12 (**Fig.1**).

Conclusions: The addition of avacopan to AAV induction therapy allows a significant reduction in CS in the early weeks of treatment, with a good safety profile and positively impacting the perception of patients' quality of life.

References: None.

Disclosures: None.



O-035

A UK parallel cohort study on renal ANCA associated vasculitis outcomes for avacopan exposed and matched unexposed cohorts

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Background/ Objectives: Avacopan was approved in the UK for severe ANCA associated vasculitis (AAV) in December 2022. The ADVOCATE trial found the differential effect of avacopan on kidney function was greatest in patients with the lowest estimated glomerular filtration rate (eGFR), at highest risk of progression to end stage kidney disease (ESKD). Patients with an eGFR <15 ml/min/1.73 m^2, pulmonary haemorrhage requiring invasive ventilation, under 12 months prognosis, use of plasma exchange and dual therapy with cyclophosphamide (CYC) and rituximab (RTX) were excluded from ADVOCATE; all common scenarios in real life practice. We aim to provide further information on these subgroups and evaluate 6 month renal outcome data in the UK.

Methods: Parallel cohort study on renal AAV outcomes for avacopan exposed and matched unexposed cohorts, with severe, active GPA or MPA. 120 patients on avacopan from 7 UK centres have been recruited to date. Controls matched by renal function and age will be presented. Comparisons of ESKD, delta eGFR, eGFR recovery, reduction in proteinuria/haematuria, remission, relapse and mortality will be presented, with subgroup analyses for eGFR<15ml/min/1.73 m^2. Steroid exposure will be presented.

Results: Baseline characteristics of the avacopan cohort are below.

	Number of patients (120)
Demographics	
Median age (IQR)	65 (53-76)
Age >75	13
Female	55 (46%)
Male	65 (54%)
ANCA serotype	
PR3	46 (38%)
MPO	74 (62%)
New presentation	90 (75%)
Relapse	30 (25%)
Pulmonary haemorrhage	21 (18%)
Median eGFR	22ml/min/1.73 m^2 (IQR 10-36)
Berden class if biopsy undertaken (75/120)	
Focal	26 (35%)
Mixed	27 (36%)
Crescentic	15 (20%)
Sclerotic	6 (8%)
Inadequate sample	1 (1%)
Indication	
Steroid sparing	39 (33%)
Refractory disease	1 (1%)
Severe nephritis	19 (16%)
Steroid sparing & refractory disease	1 (1%)
Steroid sparing & severe nephritis	56 (47%)
Refractory disease & severe nephritis	4 (3%)

Table 1. Baseline characteristics.

Most received oral prednisolone at avacopan initiation (89%, n= 107) and 54% received intravenous methylprednisolone (n= 65). The majority received RTX alone (44%, n = 53) or RTX and CYC combination therapy (43%, n=52). Fewer received CYC alone (9%, n=11) and 3% were initiated on alternative immunosuppression (n=4). 26% (n=31) underwent plasma exchange and 13% required haemodialysis (n=16). 3% of patients have died.

Excluding dialysis dependent patients at presentation, median eGFR was 22ml/min/1.73 m^2 (IQR 10-36). eGFR at the time of avacopan initiation was 21ml/min/1.73 m^2 (IQR 11-34).

Conclusions: Avacopan is commonly being used to treat nephritis in patients with a low eGFR, including haemodialysis dependent and elderly patients. Avacopan is frequency used with RTX and CYC combination therapy. 6 month outcome data will provide new data on important patient subgroups excluded from the ADVOCATE trial.

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O-036

Avacopan in combination with rituximab and low-dose cyclophosphamide for treatment of severe ANCA-associated glomerulonephritis

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Background: Avacopan, an oral C5a receptor inhibitor, is a novel treatment for ANCA-associated vasculitis. There are limited data regarding avacopan use in those with severe renal disease, and of 'real-world' experience using avacopan in combination remission-induction regimens.

Objectives: The aim of this study was to evaluate safety, glucocorticoid use and renal recovery in patients treated with avacopan in combination with rituximab and low-dose cyclophosphamide for severe ANCA-associated glomerulonephritis.

Methods: Single-centre prospective observational cohort study of 37 patients with ANCA-associated glomerulonephritis (ANCA-GN) treated with avacopan 30mg twice daily as part of remission-induction therapy. Observation period from December 2022 to October 2023, with median follow-up of 6 months (IQR 4-7). Data reported as median (±IQR) unless otherwise stated.

Results: *Baseline features*: 37 patients have been treated: mean age 59 (SD±18) years; 22/37 (60%) male; 28/37 (76%) new presentations of AAV and 9/37 (23%) relapsing; 25:12 MPO:PR3-ANCA positive. At baseline, BVAS was 16 (14-21), eGFR 23 (12-38) ml/min/1.73m^2 and urinary protein:creatinine ratio (uPCR) 156 (69-253) mg/mmol. Two patients required dialysis and 9/37 (24%) had alveolar haemorrhage.

Treatment: 31/37 patients received combination induction treatment with rituximab (2g) and low-dose IV cyclophosphamide (median dose 3.25g [0.875-3.5]). Five patients were treated with rituximab alone, and one with cyclophosphamide alone. Ten patients (27%) received adjunctive plasmapheresis. The median dose of IV methylprednisolone was 0 mg (0-500) and 32/37 patients received oral prednisolone with median dose and duration of 325mg (210-675) and 8 days (7-26), respectively.

Outcomes: The evolution of disease activity variables at baseline, 3 and 6 months is summarised in Figure 1. At 3 months, eGFR and uPCR had improved to 47 (21-75) ml/min/1.73m^2 and 28 (0-168) mg/mmol, respectively. In those who presented with eGFR ≤20 ml/min/1.73m^2 with minimum 3 months follow-up (n=15), median eGFR increased from 13 (9-18) to 22 (11-43) ml/min/1.73m^2. Six patients (16.2%) had mild infections treated with oral antibiotics and did not require hospitalisation; one patient required intravenous antibiotics for a respiratory infection.

Conclusions: This series suggests that avacopan is well-tolerated and facilitates glucocorticoid minimisation in patients with active ANCA-GN. This is in a non-trial setting, and when used in combination with rituximab and low-dose cyclophosphamide. Renal recovery was favourable in those presenting with eGFR ≤20ml/min/1.73m^2.

References: None.

Disclosures: None.

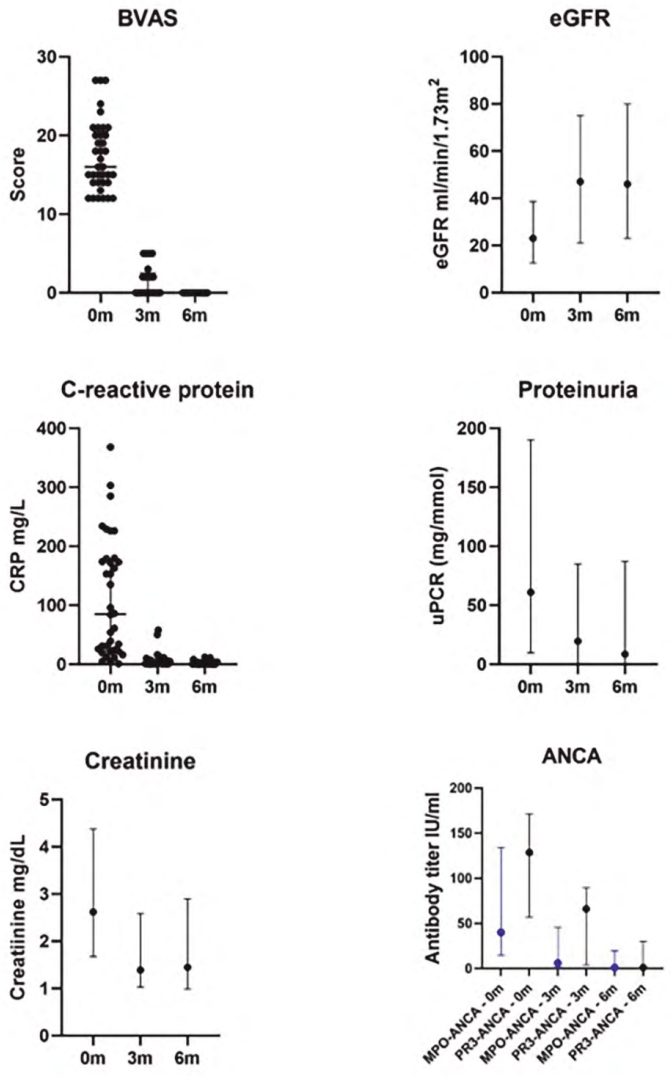

Fig. 1: Evolution of activity variables at baseline, 3 and 6 months – data shown as individual values or median with IQR.

O-037

Safety and Efficacy of Avacopan in Patients 65 Years and Older with ANCA-Associated Vasculitis

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Background/ Objectives: Older adults are at increased risk of glucocorticoid (GC)-related toxicity; minimization of GCs is a major focus for treatment of patients with anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (AAV). Although AAV predominantly affects older adults, many studies have excluded patients >75 years (y). In the phase 3 ADVOCATE trial of avacopan, there was no exclusion criterion for maximum participant age.[1] This post hoc analysis reports safety and efficacy of avacopan compared to a prednisone taper in the subgroups of patients 65-74y (N=109) and ≥75y (N=51).

Methods: Key outcomes were percentage of patients achieving remission at week 26 and sustained remission at week 52. Other outcomes included kidney function, glucocorticoid dose (prednisone-equivalent), the Glucocorticoid Toxicity Index, health-related quality of life (HRQoL; using 36-item Short Form Survey version 2 and EuroQoL Group 5-Dimensions 5-Level instrument), and safety.

Results: In both studied age and treatment groups, a similar proportion of patients (69.4-73.1%) achieved remission at week 26 (**Table 1**). In the 65-74y age group, sustained remission rates at week 52 were 55.1% in the prednisone arm and 65.0% in the avacopan arm. Relapse rates were 18.8% in the prednisone arm and 12.3% in the avacopan arm. The total all-source median GC dose was 5.3 times higher in the prednisone vs avacopan arm. Serious adverse events (SAEs) occurred in 22/49 patients (45%) in the prednisone arm (2 deaths) and 25/60 patients (42%) in the avacopan arm (2 deaths). In the ≥75y age group, sustained remission rates at week 52 were 56.0% in the prednisone arm and 65.4% in the avacopan arm. Relapse rates were 20.8% in the prednisone arm and 3.8% in the avacopan arm. Median GC dose was 4.8 times higher in the prednisone vs avacopan arm. SAEs occurred in 14/25 patients (56%) in the prednisone arm and 17/26 patients (65%) in the avacopan arm. Other results including kidney and quality of life outcomes are in **Table 1**.

Outcome	Age 65-74 (N=109)		Age ≥75 (N=51)	
	Prednisone taper (n=49)	Avacopan (n=60)	Prednisone taper (n=25)	Avacopan (n=26)
Remission at week 26, n (%)	34 (69.4)	43 (71.7)	18 (72.0)	19 (73.1)
Sustained remission at week 52, n (%)	27 (55.1)	39 (65.0)	14 (56.0)	17 (65.4)
Relapse rate*, n (%)	9 (18.8)	7 (12.3)	5 (20.8)	1 (3.8)
eGFR change at week 52†, LSM ± SEM	5.4 ± 1.6	4.6 ± 1.5	7.8 ± 1.7	10.7 ± 1.7
UACR percent change at week 4‡, LSM ± SEM	-19 ± 16.6	-34 ± 15.5	-8 ± 24.7	-33 ± 26.3
SF-36 PCS change at week 52, LSM ± SEM	1.3 ± 1.3	3.0 ± 1.2	0.7 ± 2.5	3.2 ± 2.2
SF-36 MCS change at week 52, LSM ± SEM	5.4 ± 1.6	6.9 ± 1.4	7.4 ± 3.0	7.0 ± 2.6
EQ-5D-5L VAS change at week 52, LSM ± SEM	6.0 ± 2.5	13.0 ± 2.2	2.4 ± 5.5	13.7 ± 4.7
EQ-5D-5L Index change at week 52, LSM ± SEM	0.020 ± 0.03	0.032 ± 0.02	0.021 ± 0.06	0.040 ± 0.05
GTI-CWS at week 26, LSM ± SEM	53.6 ± 7.2	43.4 ± 6.3	51.4 ± 10.1	33.1 ± 8.8
GTI-AIS at week 26, LSM ± SEM	15.1 ± 6.8	13.6 ± 5.9	15.1 ± 9.7	0.4 ± 8.5
Total all-source GC dose, mg (mean / median)	3,579 / 3,055	1,410 / 575	3,382 / 2,840	1,718 / 588
Total AEs, n (%) patients, n events	48 (98.0) 681 events	59 (98.3) 623 events	25 (100.0) 318 events	26 (100.0) 273 events
AEs of Infections, n (%) patients, n events	38 (77.6) 88 events	40 (66.7) 86 events	20 (80.0) 40 events	20 (76.9) 42 events
AEs possibly related to GCs, n (%) patients	41 (83.7)	30 (50.0)	20 (80.0)	24 (92.3)
Total SAEs, n (%) patients, n events	22 (44.9) 51 events	25 (41.7) 43 events	14 (56.0) 34 events	17 (65.4) 22 events
SAEs of Infections, n (%) patients, n events	5 (10.2) 6 events	11 (18.3) 13 events	6 (24.0) 8 events	4 (15.4) 4 events
SAEs possibly related to GCs, n (%) patients	4 (8.2)	7 (11.7)	7 (28.0)	5 (19.2)
Deaths, n (%)	2 (4.1)	2 (3.3)	0 (0.0)	0 (0.0)

* Relapse rates are based on the number of patients who achieved a BVAS of 0 during the 52-week treatment period
† eGFR assessed only in patients with renal involvement (based on BVAS) at baseline
‡ UACR assessed only in patients with renal involvement (based on BVAS) at baseline and baseline UACR≥10 mg/g creatinine
AE, adverse events; AIS, aggregate improvement score; BVAS, Birmingham Vasculitis Activity Score; CWS, cumulative worsening score; eGFR, estimated glomerular filtration rate; GC, glucocorticoid; GTI, glucocorticoid toxicity index; LSM, least squares mean; MCS, mental component summary; PCS, physical component summary; SAE, serious adverse event; SEM, standard error of the mean; SF-36, Short Form-36; UACR, urine albumin:creatinine ratio; VAS, visual analogue scale.

Table 1: Safety and Efficacy Outcomes in Patients with ANCA-Associated Vasculitis Aged 65 to 74 Years and 75 Years and Older in the ADVOCATE Trial of Avacopan.

Conclusions: A subgroup analysis of patients ≥65y demonstrated similar trends of efficacy and safety of avacopan as in the overall ADVOCATE trial, including reductions in GC-related toxicities, supporting a role for avacopan in the treatment of older adults with AAV.

References:

1. Jayne DRW, et al. *New Engl J Med* 2021;384:599-609

Disclosures: AbbVie/Abbott, Amgen, Argenx, AstraZeneca, Aurinia, Boehringer Ingelheim, Bristol Myers Squibb, Bristol Myers Squibb Foundation, Cabaletta, Calliditas, Chinook, CSL Behring, CSL Vifor, Eicos, Electra, Genentech, GlaxoSmithKline, HiBio, InflaRx, Janssen, Jubilant, Kyverna, MiroBio, Neutrolis, Novartis, NS Pharma, Otsuka, Pfizer, Rheumatology Research Foundation, Q32, Regeneron, Roche, Sanofi, Sparrow, Takeda, UpToDate, Visterra.

O-038

Anti-IL5 Receptor therapy with benralizumab in the management of Eosinophilic Granulomatosis with polyangiitis (EGPA)

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Background/ Objectives: In the MIRRA tria[1]l for eosinophilic granulomatosis with polyangiitis (EGPA), 12-month (M) adjuvant therapy with anti-IL5 mAB Mepolizumab, accrued longer times in remission, reduced steroid exposure and reduced relapse rates. The aim of this study is to analyze the outcome of anti-IL5 cytokine receptor blockade with Benralizumab (BRZ) therapy, focusing upon steroid minimization

Methods: In this retrospective descriptive study, 11 refractory EGPA patients received 30mg BRZ every 4 weeks for the first three doses, followed by 8 weekly thereafter. Immunotherapy assessment time points included BRZ commencement (M0), M6, M12, and time to last follow-up (TLF)on BRZ.

Results: In the study, two were (ANCA) anti-myeloperoxidase antibody positive, 9 were negative. All 11 patients commenced on BRZ continued therapy throughout the analysis [median duration 24M (range 18 – 29M)], due to clinical benefit. At T0, the mean prednisolone dose was 12.04mg, at T6 (6.45mg), T12 (4.5mg) and at TLF (3.18mg). Overall, there was a 50% reduction in steroid usage by 6 months. This continued to reduce to 24M (TLF), by which time 2 were off steroids and the remaining 9 were on prednisolone ≤ 5mg. The number on adjuvant conventional immunosuppressants (ACIS), reduced over time. At T0, 3 patients were on mycophenolate mofetil and one on RTX. At 24M (TLF), 2 were on MMF and none on RTX. One patient had 2 cycles of cyclophosphamide for myocarditis, with adjuvant BRZ well tolerated.

Patient	Months	T0	T0	T6	T12	LFU
1	23	1	10	6	3	0
2	22	1	5	5	2.5	2.5
3	26	1	8	4	4	2.5
4	28	1	10	7.5	5	5
5	28	1	10	5	5	5
6	29	1	40	15	10	5
7	22	1	5	3.5	1.5	0
8	24	1	12	9	6.5	3
9	19	1	10	4	4	4
10	18	1	7.5	5	5	5
11	21	1	15	7	3	3
	23.63636	1	12.04545	6.454545	4.5	3.181818

Figure 1: Duration of anti-IL5 Receptor therapy and reduction in glucocorticoids therapy.

Conclusions: The relapsing nature of EGPA places a dependency of therapy on steroids. This study demonstrated a 50% reduction in steroid dosage by 6 months. By 24 months, 2 are steroid free and a further 9 on weaning dose ≤ 5mg. Furthermore, the number on adjuvant conventional immunosuppression reduced over the 24M. This study demonstrates that anti-IL5 receptor therapy serves as a favorable model for steroid and conventional immunosuppressant minimization in EGPA.

References:

1. Wechsler, M. E. *et al.* Mepolizumab or Placebo for Eosinophilic Granulomatosis with Polyangiitis. *N. Engl. J. Med.* **376**, 1921–1932 (2017).

Disclosures: CO has lectured for AZ, GSK, Sanofi, Novartis; course fees from Boehringer. AE study group member for AZ. DJ has received grants from AstraZeneca, GlaxoSmithKline and Roche; consulting fees from Astra-Zeneca, Chemocentryx, GSK, Novartis, Otsuka, Takeda, Roche, Vifor; honoraria from GlaxoSmithKline and Vifor; participation on advisory boards for Chinook, GlaxoSmithKline and Takeda and stock options from Aurinia.

O-039

Comparative efficacy of mepolizumab 100 mg, mepolizumab 300 mg and benralizumab 30 mg in eosinophilic granulomatosis with polyangiitis: a monocentric retrospective study

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Background/ Objectives: Monoclonal antibodies targeting interleukin 5 (IL-5) and IL-5α receptor have proven to be effective in the treatment of eosinophilic granulomatosis with polyangiitis (EGPA). The aim of this study was to compare efficacy of Mepolizumab 300 mg every 4weeks (MEPO300), Mepolizumab 100 mg every 4 weeks (MEPO100) and Benralizumab 30mg every 8 weeks after 3 injections every 4 weeks (BENRA) in EGPA patients.

Methods: Patients with EGPA who were treated with BENRA, MEPO300, and MEPO100 were retrospectively included in this monocentric observational study. Follow-up data, comprising clinical manifestations, pulmonary function tests, and eosinophil count, were collected. Data were compared between the groups at baseline, 3, 6, and 12 months, as well as at the last follow-up (LFU). Complete remission (CR) was defined as Birmingham Vasculitis Activity Score (BVAS) of 0 and prednisone (PDN) dose of 0 mg/day. Partial remission (PR) was defined as BVAS of 0 and prednisone dose ≥ 5 mg/day.

Results: 67 patients (52.2% female, median age of 49 [39-58] years, median disease duration of 30 [9-105] months) were included, 33 treated with BENRA, 22 with MEPO300 and 12 with MEPO100. At LFU, CR was observed in 22/33 (66.7%) patients on BENRA, 15/22 on MEPO300 (68.2%) and 4/12 (33.3%) on MEPO100, p=0.091. PR was reported in 7/33 (21.2%) patients on BENRA, 5/22 on MEPO300 (22.7%) and 5/12 (41.7%) on MEPO100, p=0.356. At LFU 11/33 (33.3%) patients on BENRA shifted to another biologic, while 4/22 (18.2%) on MEPO300 and 5/12 (41.7%) on MEPO100 did so, p=0.238.

A significant reduction in BVAS was observed in the BENRA (p=0.059) and MEPO300 (p=0.021) groups, but not in the MEPO100 (p=0.323), with no significant differences between treatments at each time-point. A significant decrease in blood eosinophils in all group was observed, with BENRA and MEPO300 being the most effective depleting agents. An improvement in FEV1 values was observed in BENRA patients (p<0.001), but not in MEPO300 (p=0.393) and MEPO100 (p=0.178) groups. No significant change was observed in fractional exhaled nitric oxide (FeNO) in all groups (BENRA p=0.367, MEPO300 p=0.993, MEPO100 p=0.868), but those treated with MEPO100 had the highest values.

A significant reduction in PDN dose was observed at LFU in MEPO300 (p=0.013) and MEPO100 (p=0.029) groups, but not in BENRA (p=0.094). Specifically 23/33 (69.7%) patients on BENRA were able to discontinue glucocorticoids, 16/22 (72.7%) on MEPO300, and 5/12 (41.7%) on MEPO100, p=0.150.

The tolerability profile was favourable.

Conclusions: In this real-world monocentric retrospective observational study, BENRA and MEPO300 exhibited a significant steroid-sparing effect, with MEPO300 demonstrating superior drug survival.

Disclosures: None.

CASE REPORT AND PANEL DISCUSSION (I)

O-040

ANCA associated vasculitis (AAV)-phenotype and ANCA positivity in monogenic lupus secondary to *DNASE1L3*mutations: report of a case and review of the literature

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Presentation of Case: A 7-year-old boy with a history of urticaria and arthralgia presented with fever, haemolytic anaemia, lymphadenopathy, hepato-splenomegaly, interstitial lung disease, erythematous-macular and necrotic skin lesions. He also had kidney involvement with acute kidney injury (serum creatinine 5,4 mg/dL), nephrotic-range proteinuria (3,9 g/24h) and microhaematuria.

Diagnostic testing: Immunological tests revealed low C3 and C4, positive anti-nuclear antibodies (ANA) and myeloperoxidase anti-neutrophil cytoplasmic antibodies (MPO-ANCA). Kidney biopsy showed pauci-immune (mesangial C3+ and IgG+) necrotising crescentic glomerulonephritis (GN). The patient proved refractory to standard immunosuppression with cyclophosphamide and steroids. Two years later, due to renal function decline, a new kidney biopsy was performed and showed diffuse necrotising GN with endo- and extra-capillary proliferation; intense mesangial and subendothelial full-house deposits were evident on immunofluorescence. The patient did not respond to other lines of immunosuppression (mycophenolate mofetil, tacrolimus, azathioprine, rituximab), including the JAK inhibitor ruxolitinib. Kidney failure progressed to end stage at the age of 15 years, when the patient began haemodialysis.

Differential and final diagnosis: The kidney presentation, immunological profile and the first kidney biopsy led to a diagnosis of AAV. However, the diagnosis was questioned due to the refractory course, the systemic clinical presentation and the second kidney histology (consistent with lupus nephritis, LN). High interferon signature was detected and in the suspicion of a monogenic systemic lupus erythematous (SLE), Whole Exome Sequencing was performed and revealed homozygous *DNASE1L3* variants (c.290_291delCA p.T97Ifs*2); thus, a final diagnosis of *DNASE1L3*-monogenic SLE was made. DNASE1L3 serum levels were normal but the DNAse enzymatic activity was low.

Conclusions: DNASE1L3 deficiency, either genetic or mediated by anti-DNASE1L3 antibodies, is associated with a broad range of clinical syndromes including SLE and hypocomplementemic urticarial vasculitis syndrome (HUVS) (1) and in some cases can have a mixed SLE-AAV phenotype.

Renal involvement is one of the most frequent manifestations of *DNASE1L3*-related SLE; in the literature 32 cases of *DNASE1L3*-associated LN are described. ANCA are positive in 55% of these cases and are associated with a mixed LN-AAV phenotype. All cases are characterized by resistance to common immunosuppressants and poor renal prognosis. DNASE1L3 regulates neutrophil extracellular trap (NET) clearance and when its function is reduced the permanence of NETs induces endothelial damage and autoantibody formation. This pathogenic pathway is shared by SLE and AAV. There is no association between specific mutations and antibody positivity or clinical manifestations.

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1. Tusseau M et al. DNASE1L3 deficiency, new phenotypes, and evidence for a transient type I IFN signaling. J Clin Immunol. 2022 Aug;42(6):1310-1320.

Disclosures: None.

O-041

When you are told your 34-year old patient with Takayasu's disease has metastases

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Presentation of Case: 34-year old Arab woman with class V Takayasu disease (TD) since she was 25: high blood pressure, asthenia, left carotid pain and bruit, arms BP difference ≥ 10mmHg, stenosis and parietal thickening in common carotids and left subclavian artery, aortic (ao) root dilation, proximal descending ao dissection, and renal and infrarrenal abdominal ao aneurysms (Fig. a/b). On treatment with prednisone and MTX, switched to AZA for pregnancy (preeclampsia) and breastfeeding.

Presented with persistent cough for 2 months, right pleuritic and hypochondrium pain, headache, altered depositional rhythm, diaphoresis, hyporexia and loss of 5-6kg. Chest CT: multiple liver lesions, confirmed in abdominal (abd) CT. Abd MRI: multiple lesions with ring enhancement reported as metastases (Fig c).

Diagnostic Testing: Blood test: high APR, mildly high liver enzymes, normal ACE, eosinophils, calcium, calciuria and vitamin D. +IGRAs (no previous determinations). Negative bacterial and fungal serologies, mycobacterial cultures in blood, urine and feces. No malignancies. Percutaneous liver biopsy: mild chronic inflammatory infiltrate, with a cavitated lesion with granulomatous inflammation due to epitheloid histiocytes (Fig. d). Negative for typical and atypical mycobacteria and spirochetes. Negative M. tuberculosis PCR. No PET-CT –breastfeeding–.

Differential & Final Diagnosis: Differential: metastases, abscesses (typical or atypical microorganisms, bacteria or fungus), TD itself, primary biliary cholangitis, sarcoidosis, granulomatous vasculitis, foreign body-type granulomas and drugs[1].

Final diagnosis: Liver granulomas due to tuberculosis (TB).

Discussion of Management: Initial empirical antibiotic treatment –suspicion of abscesses + fever–, withdrawn due to the absence of germs. We assessed whether the involvement could be in the context of TD, but there is only one old mention of liver granulomas in TD and associated with Crohn's disease[2]. As all the tests were negative and the only evidence we had was +IGRAs empiric TB treatment was initiated with resolution of symptoms, blood alterations and lesions –Fig. e: MRI 2 months after treatment initiation–.

Conclusions: We exemplify the difficulties of the differential diagnosis of infectious complications in patients with TD, which, in our case, were initially described as metastases. Even once we had ruled out metastases, we were not able to confirm microbiologically the presence of TB and had to treat empirically, being the good response to treatment the confirmatory diagnosis.

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1. Lagana, SM, *et al.* Clinics in liver disease 14.4 (2010): 605-617.
2. Orive Calzada, A, *et al*. Gastroenterology and Hepatology 31.08 (2008): 548549.

Disclosures: None.

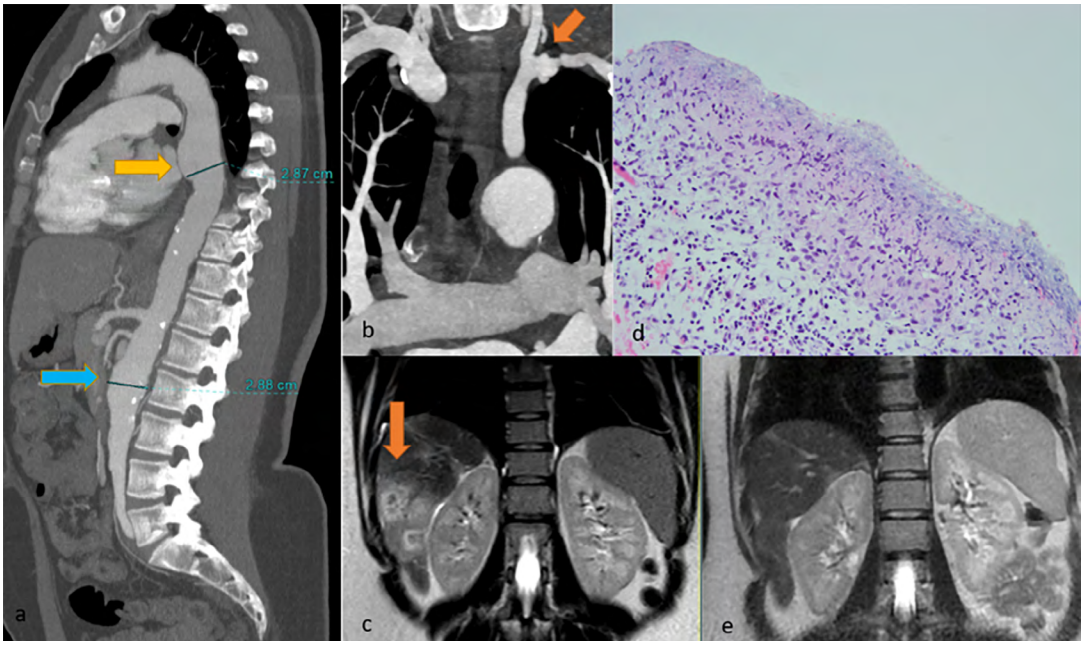

Figure 1. Contrast enhanced CT: aortic root aneurysm (a, yellow), fusiform aortic aneurysm of the infrarenal abdominal aorta (a, blue) and left subclavian artery stenosis (b); Contrast-enhanced (CE) abdominal CT: hepatic confluent oval focal hyperintense lesions with a hypointense center compatible with metastases; Non-necrotizing epithelioid granuloma with inflammatory signs and eosinophilia (d); Follow-up CE abdominal CT: no lesions (e).

O-042

A novel role for obinutuzumab in a patient with relapsing PR3 ANCA-associated vasculitis and anti-GBM disease

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Background and presentation: A 71-year-old female attended a routine Vasculitis Clinic appointment in February 2021 and reported 1 month of increasing fatigue. Her medical history included dual positive proteinase 3 (PR3) anti-neutrophil cytoplasm antibody-associated vasculitis (AAV) and anti-glomerular basement membrane (GBM) disease. This had been diagnosed in Australia in 2009 when she developed a pulmonary-renal syndrome treated with plasma exchange, oral cyclophosphamide, and glucocorticoids. Between 2009 and 2021 she had one major AAV disease relapse (kidney-limited; 2012), treated with intravenous cyclophosphamide, glucocorticoids, and plasma exchange, but persisting low-level lung and sinus disease activity culminating in rituximab re-induction and maintenance (2015-2019; cumulative rituximab dose 6g). PR3 and GBM antibodies were negative at last follow up in August 2020 and serum creatinine was 113mmol/L (estimated glomerular filtration rate (eGFR) 44mL/min/1.73m^2).

Investigations: Bloods tests in February 2021 demonstrated an acute kidney injury (serum creatinine 566mmol/L) and normocytic anaemia (haemoglobin 86g/L). Interestingly, PR3 ANCA ***and*** anti-GBM titres were now elevated at 114iu/mL (normal 0.5-1.9) and 52iu/mL (0-6.9), respectively. There were no clinical or radiological signs of alveolar haemorrhage. A kidney biopsy showed a necrotising, crescentic glomerulonephritis with global linear immunoglobulin G GBM deposition and moderate scarring.

Diagnosis: Kidney-limited relapse of PR3 AAV and anti-GBM disease.

Initial management: The patient received remission induction therapy with plasma exchange, rituximab (1g x 2), intravenous cyclophosphamide (700mg x 2) and oral glucocorticoids. PR3 ANCA and anti-GBM titres rapidly normalised and kidney function improved but remained impaired (serum creatinine 220mmol/L, eGFR 20mL/min/1.73m^2).

Progress: Rituximab (500mg) was administered every 6 months for 18 months for remission maintenance. However, during this time PR3 ANCA titre rose from 1.4iu/mL to 11.0iu/mL despite peripheral B-cell depletion (undetectable circulating CD19 counts), suggesting a tissue-based niche of ANCA generating B-cells unaffected by rituximab. Given this, and the risk of disease relapse resulting in kidney failure, we switched treatment to obinutuzumab, a type II humanised anti-CD20 monoclonal antibody that produces more pronounced peripheral and tissue B-cell depletion compared to rituximab.[1] In response, PR3 ANCA titre fell to within the reference range over 12 months without adverse events. The patient remains in clinical remission with stable kidney function and moderate hypogammaglobulinaemia (5g/L).

Conclusions: Clinicians should be vigilant for relapsing anti-GBM disease in patients with concomitant AAV in whom the diagnosis may be missed. Additionally, obinutuzumab may be a novel strategy to maintain remission in selected high-risk patients who do not respond to rituximab.

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Disclosures: None.

O-043

Bilateral renal infarcts as a manifestation of Granulomatous Eosinophilic Polyangiitis

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Presentation of Case: A 60-year-old Caucasian man, diagnosed of adult-onset eosinophilic asthma, allergic rhinitis and nasal polyposis, treated with bronchodilator, was diagnosed of Eosinophilic Granulomatosis with Polyangiitis (EGPA). He presented with low-grade fever, asthenia and weight loss of 10kg over 6 months, mixed axonal neuropathy, chronic bilateral maxillary and frontal sinusitis, and abnormal kidney function. Eosinophilia and high titer of MPO-ANCA (>1000). Patient exhibited a glomerular filtration rate (GFR) of 69 mL/min, protein to creatinine ratio (PCR) of 400mg/g, and microscopic haematuria. A kidney biopsy was performed, revealing fibrinoid necrosis in 4 out of 14 glomeruli, a 15% eosinophilic infiltrate in the interstitium, and negative immunofluorescence.

He was diagnosed with EGPA and treatment with oral corticosteroids (CTT) (1mg/kg) and rituximab (RTX) was initiated. After a month, he developed abdominal pain, macroscopic hematuria, aggravated asthenia, and acute kidney injury (GFR 21 mL/min). Blood tests revealed leucocytosis (17000 U/L), eosinophilia (>1000 U/L), mild anemia (11.2 g/dL), and elevated C-reactive protein. Furthermore, he maintained high levels of MPO-ANCA, despite a complete depletion of CD20 B-cells. A Contrast-Enhanced CT-SCAN revealed multiple triangular subcapsular hypodense areas consistent with renal infarcts while renal arteries were not compromised.

Exclusion of endocarditis and Thrombophilia, led to the interpretation of renal infarcts as a refractory manifestation of EGPA. Treatment was accordingly modified to cyclophosphamide (CFF) and increased corticosteroid dosage.

After 2 months of CFF therapy and CCT the patient has achieved stabilization in kidney function GFR of 30 mL/min/1.73m², and a reduction of hematuria, proteinuria and decreased anti-MPO. A renal scintigraphy with DMSA revealed no hypoperfused areas.

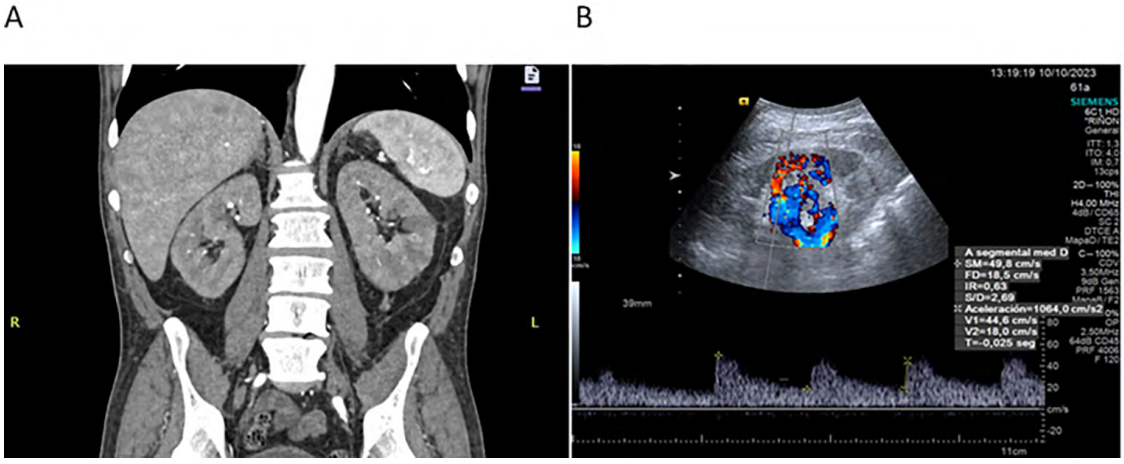

Image 1 :A. Contrast-Enhanced CT-SCAN revealed multiple triangular subcapsular hypodense areas consistent with renal infarcts. B: Renal ultrasound with doppler after 2 months of treatment.

The GFR did not return to its baseline value and patient exhibited persistent eosinophilia. Maintenance therapy with RTX plus mepolizumab (MPL) was prescribed. Currently, the patient has been on MPL for one month, and the efficacy of this treatment is yet to be determined.

Conclusions: We present a rare manifestation of EGPA. Although there is an observed connection between EGPA and an increased of thrombus formation, this is the first report of renal infarction that we are aware of. The association between EGPA and trombophilia is likely rooted in the interplay between inflammation-induced thrombosis, common to all vasculitides and eosinophil specific related factors[1]. Mepolizumab has shown growing evidence of efficacy in managing major organ involvement[2,3].

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Disclosures: None.

O-044

Acrocyanosis After Immunotherapy: Vasculitis or Vasculopathy? A New Iatrogenic Disease

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Background: Immune checkpoint inhibitors (ICI) have revolutionized cancer therapy. Their use is complicated by development of immune-related adverse effects (irAEs). Acral digital ischemia associated with ICIs is a rare and poorly understood toxicity. There are 8 reported cases in the literature, [1-4] with heterogenous management, with mostly poor prognosis.

Methods: We report six cases of acral digital ischemia post ICI from the Canadian Research Group of Rheumatology in Immuno-Oncology (Can-RIO) retrospective cohort between 2017 and 2023 and compared to the existing 8 reported cases. Integrating the findings, we propose a hypothetical pathogenesis and treatment approach.

Results: In comparison to previously reported cases (Table 1), the CanRIO cases had earlier onset after ICI exposure (median 6 weeks vs 9.5 weeks), were mostly seronegative (33% vs 63%) and were treated more aggressively with a combination of immunosuppression, vasodilation and anti-platelet agents (triple therapy). Angiography in all cases did not find evidence of proximal vasculitis; distal imaging uniformly showed small vessel occlusion but no vasculitis. All cases that received triple therapy (from both groups) had either stabilization or resolution of cyanosis. One case in the literature had resolution with immunosuppression alone, where two cases treated with immunosuppression and vasodilation (without anti-platelet) had progression of cyanosis. There were no amputations in the CanRIO group, where 5/8 in the literature required amputation. ICI was stopped in all cases in both groups.

Conclusions: Acral digital necrosis is a rare immune related adverse event associated with ICI therapy, with unknown pathogenesis or optimal treatment. The six cases from CanRIO were identified early and received aggressive “triple therapy” with either resolution or stabilization of cyanosis, contrasting with previously reported cases. We hypothesize that ICI associated acral digital necrosis is a new iatrogenic disease. Based on the lack of vasculitis found on imaging, and response to “triple therapy”, we propose that the underlying mechanism is an inflammatory vasculopathy with distal vessel occlusion leading to ischemia, requiring early initiation of vasodilation and anti-platelet/anticoagulant therapy. Further experience and studies are needed.

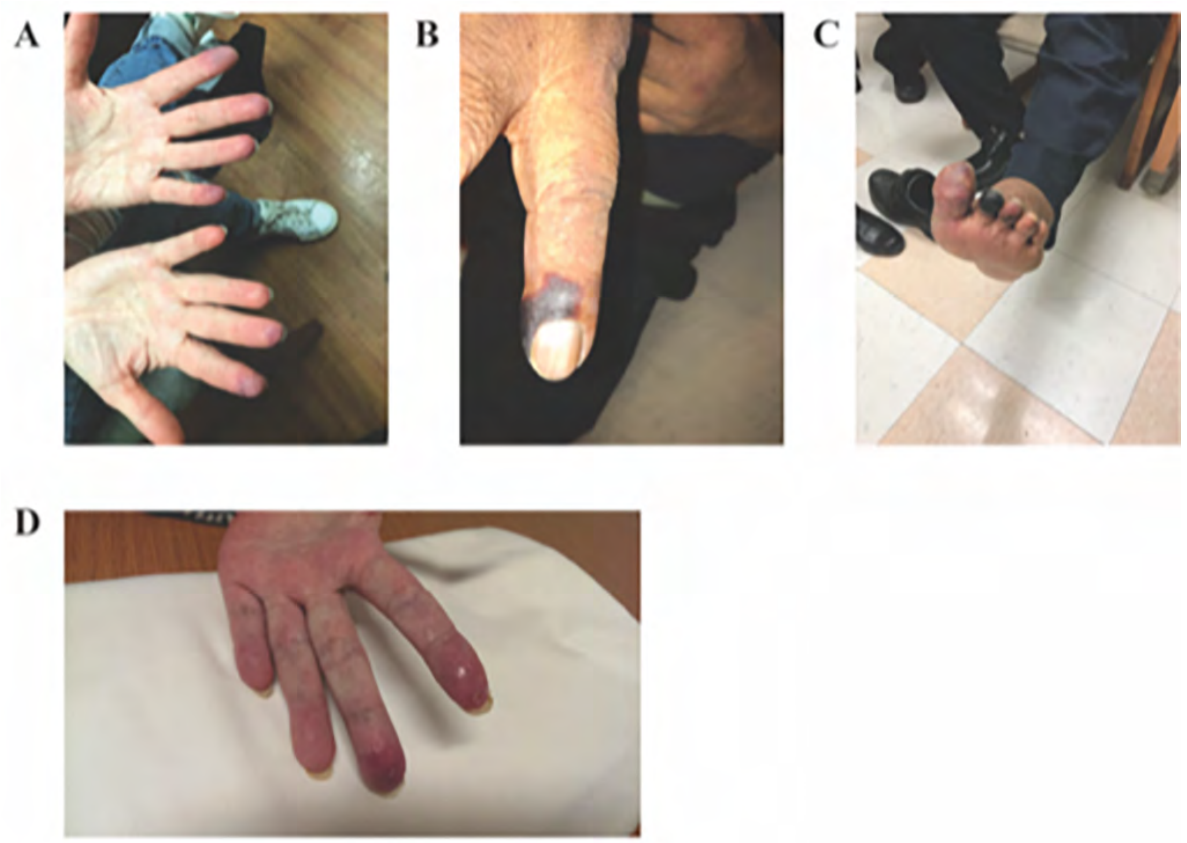

Figure 1. (A) Acral digital ischemia in a 56 year old female after pembrolizumab. Acral digital ischemia **(B)** in fingers and **(C)** toes in a 69 year old male who received nivolumab. **(D)** Acral digital ischemia of fingers in a 63 year old female who received pembrolizumab.

Table 1.			
		Cases In Literature (n=8)	**CanRIO Cases (n=6)**
Onset	**Time post ICI exposure**	9.5 weeks (median)	6 weeks (median)
Serology			
	ANA positive (%)	5/8 (63%)	2/6 (33%)
	In those with positive ANA	• Cryoglobulins in 1/5 • Weakly RNA in 1/5 • No other abn in 3/5	• Cryoglobulins in 1/2 • Jo1 myositis in 1/2
Imaging			
	Angiography	• Small vessel occlusion distally in all three available cases • No proximal occlusion or abn in two available cases • No imaging in other cases	• CT angiogram normal in 6/6 cases with no vasculitis • Digital angiogram in 2 cases – both showed distal small vessel occlusion
	Echo	• Normal in 2/8 available cases; no emboli	• Normal in 2/6 available cases; no emboli
Treatment			
	Embolectomy	1/8	0/6
	Immunosuppression alone	1/8	0/6
	Vasodilation alone	1/8	0/6
	Immunosuppression and Vasodilation	3/8	1/6
	Immunosuppression, Vasodilation & Antiplatelet	2/8	5/6
Cyanosis Outcome			
	Resolved	1/8 with immunosuppression mono and 1/8 with immunosuppression and vasodilation	4/6
	Stabilized	2/8 (triple therapy)	2/6
	Progressed	4/8	0/6
	Amputation	5/8	0/6

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PLENARY SESSION: EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS AND HYPEROESINOPHILIC DISEASES

O-045

Benralizumab vs Mepolizumab in the Treatment of Eosinophilic Granulomatosis with Polyangiitis

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Background: MANDARA compared the efficacy and safety of benralizumab and mepolizumab in patients with eosinophilic granulomatosis with polyangiitis (EGPA) receiving standard of care (SoC).

Methods: MANDARA was a Phase 3, randomised, active-controlled, parallel-group, multicenter, 52-week (wk) double-blind, non-inferiority study (NCT04157348). Adults with EGPA based on asthma and blood eosinophilia plus ≥2 additional features of EGPA, and a history of relapsing/refractory disease requiring stable oral glucocorticoids (OGCs; ≥7.5 mg daily) ± stable immunosuppressive therapy for ≥4 wks before randomisation, were included. Benralizumab 1x30 mg or mepolizumab 3x100 mg were administered subcutaneously every 4 wks for 52 wks, and OGCs could be tapered if disease was controlled. The primary endpoint was remission (defined as BVAS = 0 and OGC dose ≤4 mg/day) at both Wks 36 and 48.

Results: 140 patients were randomised (mean [SD] age 52.3 [14.1] years; 60.0% women) to benralizumab (n=70) or mepolizumab (n=70). Adjusted remission rate at both Wks 36 and 48 was 59.2% for the benralizumab group and 56.5% for the mepolizumab group (difference: 2.71%; 95% CI: –12.54, 17.96; p=0.7278), confirming non-inferiority of benralizumab to mepolizumab (**Figure**). The same proportion of patients relapsed with benralizumab vs mepolizumab (both 30.0%). Benralizumab was associated with greater blood eosinophil depletion than mepolizumab from Week 1 onwards. Mean (SD) OGC dose was 11.02 (5.25) mg/day at baseline. At Wks 48–52, the mean (SD) OGC dose was 2.98 (3.76) mg/day and 3.43 (4.12) mg/day in the benralizumab and mepolizumab groups, respectively; 41.4% and 25.8% of patients were fully tapered off OGC (**Figure**). Changes from baseline in lung function and asthma control were similar between groups. Adverse events were reported in 90.0% of benralizumab and 95.7% of mepolizumab recipients.

Conclusions: MANDARA demonstrated non-inferiority of benralizumab vs mepolizumab over 52 wks in patients with relapsing/ refractory EGPA receiving SoC and provides evidence for the efficacy and utility of benralizumab, with more benralizumab-treated patients being fully tapered off OGC.

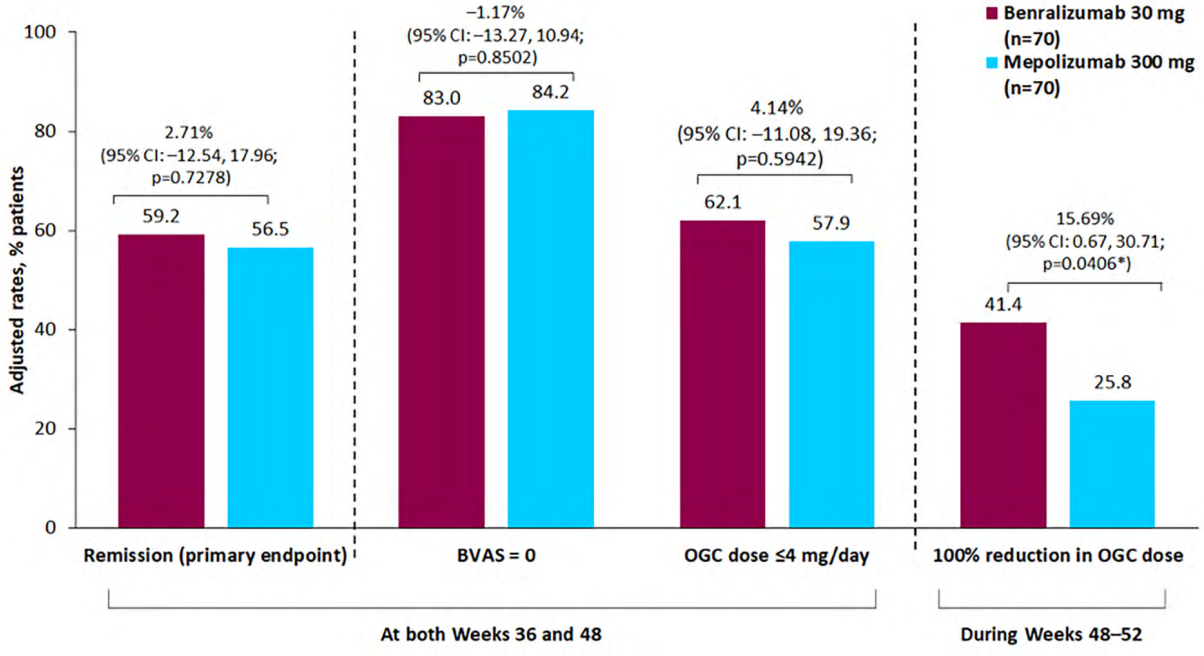

Figure. Efficacy outcomes and between-treatment differences.
*Nominal p-value.

Remission rates and between-treatment differences were estimated using marginal standardisation in a logistic regression model, with treatment arm, baseline dose of OGC, baseline BVAS and region as covariates. The non-inferiority margin was predefined at –25%. P-values are shown for the superiority test.

Disclosures of interest: **MEW** reports receiving consulting fees from AstraZeneca, Boehringer Ingelheim, Cohero Health, Equillium, Genentech, GlaxoSmithKline, Novartis, Regeneron, Sanofi–Genzyme, Sentien Biotechnologies, Teva, and Amgen. **PN** reports that his institution received grant support from AstraZeneca, Cyclomedica, Equillium, Foresee, Genentech, Sanofi, and Teva; he has also received honoraria from Arrowhead, AstraZeneca, CSL Behring, GlaxoSmithKline, and Sanofi. **BT** reports receiving consulting fees from AstraZeneca, GlaxoSmithKline, Vifor, and Pharma. **BW** reports receiving speaker fees and/or consultancies from Amgen, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Janssen, Novartis, Pfizer, Roche; research support from AB2Bio, AbbVie, AstraZeneca, ChemoCentryx, GlaxoSmithKline, Janssen, Novartis, Roche, UCB. **AB** reports receiving consultancy fees and speakers fees from AstraZeneca, Amgen, Boehringer Ingelheim, Novartis, GlaxoSmithKline, Sanofi Regeneron, and Chiesi, and research grants from GlaxoSmithKline, Boehringer Ingelheim and AstraZeneca. **DRWJ** reports receiving speaker fees and/or consultancies from Amgen, AstraZeneca, Bristol-Myers Squibb, Boehringer, Chemocentryx, Chugai, GSK, Novartis, Roche, Takeda and Vifor. **DJJ** consultancy fees and speakers' fees from AstraZeneca, GlaxoSmithKline, Sanofi Regeneron, TEVA, Boehringer Ingelheim, Novartis, Chiesi, and NAPP, and research grants from AstraZeneca. **FR** reports receiving consulting fees from AstraZeneca, GlaxoSmithKline, Merck and Menarini, and royalties from UpToDate. **PAM** reports receiving consulting fees and research support from AbbVie, Amgen, AstraZeneca, Boehringer-Ingelheim, Bristol-Myers Squibb, GlaxoSmithKline, InflaRx, and Takeda; consulting fees only from ArGenx, Cabaletta, CSL Behring, Dynacure, HiBio, Janssen, Novartis, NS Pharma, Regeneron Pharmaceuticals, and Vistera; research support only from Eicos, Electra, Forbius, Genentech/Roche, Genzyme/Sanofi, and Neutrolis; has consulting and stock options in Kyverna, Q32, and Sparrow; and receives royalties from UpToDate. **LBS**, **YF**, **MJ**, **CM**, **SN**, **AS**, and **CW** are employees of AstraZeneca and may own stock/stock options.

O-046

Complete Remission in Eosinophilic Granulomatosis with Polyangiitis (EGPA) in the MANDARA Trial of Benralizumab vs Mepolizumab

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Background/Objectives: In patients with EGPA there is a need to minimise long-term use of oral glucocorticoids (OGCs) to avoid associated adverse outcomes, while sustaining remission and avoiding relapse. MANDARA was a Phase 3, randomised, double-blind, parallel-group, multicenter study (NCT04157348) of benralizumab 1x30 mg versus mepolizumab 3x100 mg, sc Q4W in patients with relapsing/refractory EGPA receiving standard of care. Non-inferiority was demonstrated for remission (Birmingham Vasculitis Activity Score [BVAS]=0 and OGC ≤4 mg/day), at both Weeks 36 and 48 (primary endpoint).

Methods: *Post-hoc* analyses of MANDARA assessed the proportion of patients achieving a more stringent definition of complete remission: BVAS=0 and OGC dose=0 mg/day at both Weeks 36 and 48, and being relapse-free. Remission was considered sustained if criteria were first met by Week 48 and maintained until the end of the 52-week double-blind period. Investigators were encouraged to taper OGCs for patients who reached BVAS=0, according to standard practice and clinical judgement. Proportions of patients achieving remission were calculated using the Kaplan–Meier technique. HR and 95% CIs are estimated using a Cox regression model with Efron method to control for ties, and included treatment arm, baseline dose of prednisone, baseline BVAS, and region as covariates.

Results: 140 patients received benralizumab (n=70) or mepolizumab (n=70). Adjusted rates of remission at both Weeks 36 and 48 (previously published) were 59.2% with benralizumab versus 56.5% with mepolizumab (difference: 2.71 [95% CI: –12.54, 17.96]; p=0.7278). Adjusted rates of complete remission at both Weeks 36 and 48 were 23.5% versus 11.1% (difference: 12.47 [95% CI: 0.46, 24.48]; p=0.0418) in the benralizumab and mepolizumab groups, respectively. Sustained remission was achieved by 65.7% and 64.3% patients (HR: 1.19 [95% CI: 0.78, 1.81]; p=0.7793) in the benralizumab and mepolizumab groups; and sustained complete remission was achieved by 35.7% and 22.9% patients (HR: 1.82 [95% CI: 0.97, 3.50]; p=0.0966), respectively. Time to sustained (complete) remission is shown in the **Figure**.

Conclusions: Patients with EGPA receiving benralizumab and mepolizumab achieve similar remission rates when using a definition of OGC ≤4 mg/day, and numerically higher rates for benralizumab versus mepolizumab using the more stringent definition of complete remission that included OGC=0 mg/day and being relapse-free. These data highlight the possibility of achieving sustained treatment goals for patients with EGPA receiving anti-IL-5/Rα therapy that include full tapering of OGCs and avoiding relapses.

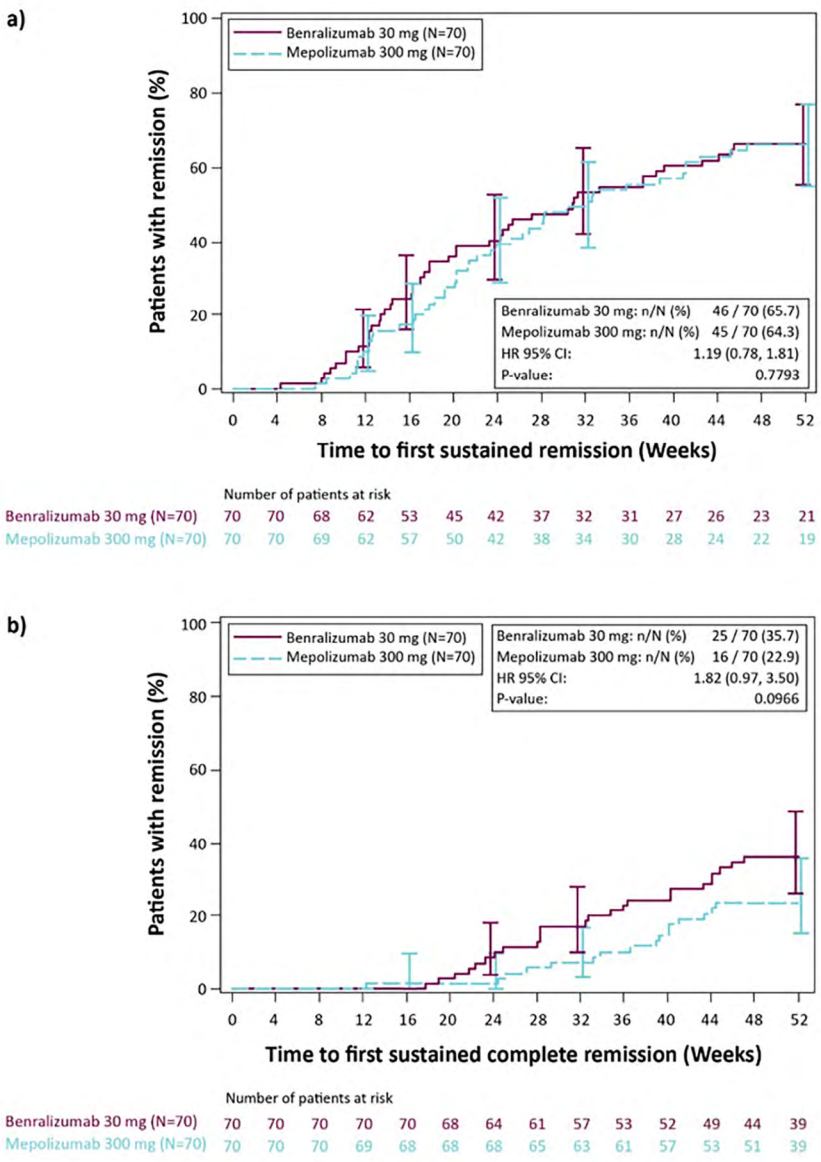

Figure. Time to first a) sustained remission and b) sustained complete remission over the 52-week double-blind period

Funding: AstraZeneca.

Disclosures: **MEW** reports receiving consulting fees from Amgen, AstraZeneca, Boehringer Ingelheim, Cohero Health, Equillium, Genentech, GlaxoSmithKline, Novartis, Regeneron, Sanofi–Genzyme, Sentien Biotechnologies, and Teva; **NA-L** report no conflicts of interest; **DRWJ** reports receiving speaker fees and/or consultancies from Amgen, AstraZeneca, Bristol Myers Squibb, Boehringer, Chemocentryx, Chugai, GlaxoSmithKline, Novartis, Roche, Takeda, and Vifor Pharma; **CP** reports receiving consulting and speaker fees from Roche, GlaxoSmithKline, Otsuka, and Pfizer; grants and personal speakers or advisory board fees from Roche; served on advisory board from AstraZeneca, GlaxoSmithKline, and Otsuka; and received educational grants from GlaxoSmithKline, Otsuka, and Pfizer; **US** reports receiving consulting fees from Amgen, Argenix, AstraZeneca, Boehringer Ingelheim, and CSL Vifor, and research grants from AstraZeneca, Bristol Myers Squibb, Genentech, GlaxoSmithKline, NorthStar Radioisotopes, and Syneos; **PAM** reports receiving consulting fees and research support from AbbVie, Amgen, AstraZeneca, Boehringer-Ingelheim, Bristol-Myers Squibb, GlaxoSmithKline, InflaRx, and Takeda; consulting fees only from ArGenx, Cabaletta, CSL Behring, Dynacure, HiBio, Janssen, Novartis, NS Pharma, Regeneron Pharmaceuticals, and Vistera; research support only from Eicos, Electra, Forbius, Genentech/Roche, Genzyme/Sanofi, and Neutrolis; has consulting and stock options in Kyverna, Q32, and Sparrow; and receives royalties from UpToDate. **LBS**, **EM**, **SN**, **AS** and **CW** are employees of AstraZeneca and may own stock/stock options.

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O-047

Mepolizumab vs Benralizumab: a European real-life retrospective multicentre study

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Background/ Objectives: Eosinophilic granulomatosis with polyangiitis (EGPA) is an anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis characterised by asthma, ear-nose-throat (ENT) involvement, and systemic manifestations. [1] Interleukin (IL)-5 inhibitors are therapies with the potential to control both respiratory and systemic manifestations. [2-5]

This study aimed at comparing the efficacy and safety of mepolizumab to benralizumab in a European cohort of patients with EGPA.

Methods: A retrospective observational cohort study was conducted on EGPA patients treated with mepolizumab (100mg/4 weeks) or benralizumab (30mg/4 weeks for the first three injections, and 30mg/8 weeks thereafter) at 38 centers of the European EGPA Study Group. Patients were matched 1:1 by sex, age, Birmingham Vasculitis Activity Score [BVAS] and oral corticosteroids [OCS] dosage at the time of treatment beginning, and data were then compared after 3, 6, and 12 months. Complete response [CR] was defined as no disease activity (BVAS= 0) and prednisone dose ≤4mg/day. Pulmonary function and safety outcomes were compared over a 12-month follow-up.

Results: 88 EGPA patients were matched for each group (100 [56.8%] females; median age of 54 years [IQR 23-45], median disease duration of 5 years at baseline).

CR was reported in 12/88 (13.6%, 95% CI 7.2-22.6) patients on mepolizumab and 9/88 (10.2%, 95% CI 4.8-18.5) on benralizumab at month 3, 18/83 (21.7%, 95% CI 13.4-32.1) on mepolizumab and 21/66 (31.8%, 95% CI 20.1-44.4) on benralizumab at month 6, and 22/68 (32.4%, 95% CI 21.5-44.8) on mepolizumab and 25/52 (48.1%, 95% CI 34.0-62.4) on benralizumab at month 12.

A reduction of BVAS was observed in both cohorts with no differences between patient subgroups at each timepoint. (Fig 1)

BVAS, median (IQR)	Beginning	3 months	*P-value*	6 months	*P-value*	12 months	*P-value*	
MEPO	4 (2-8)	1 (0-4)	0.094	0 (0-3)	0.102	0 (0-2.5)	0.021	
BENRA	3 (2-8)	0 (0-2.5)		0 (0-2)		0 (0-1)		
CCS, median (IQR)	Beginning	*P-value*	3 months	*P-value*	6 months	*P-value*	12 months	
MEPO	10 (5-12.5)	5 (2.5-8)	0.517	5 (1.5-5)	0.954	4 (0-5)	0.092	
BENRA	10 (7-12.5)	5 (5-8)		5 (1.5-5)		2.5 (0-5)		
FEV1, Δ%	t0-t3	*P-value*	t0-t6	*P-value*	t0-t12	*P-value*		
MEPO	6,6 (2-17,5)	0.039	12,0 (2,1-16-5)	0.669	10.6 (-4.7-25.9)	0.267		
BENRA	13,7 (4,4-22,1)		14,7 (-7,729,3)		13.2 (0.1-43.9)			
FEV1, median (IQR)	Beginning	*P-value*	3 months	*P-value*	6 months	*P-value*	12 months	*P-value*
MEPO	75 (62-83)	0.106	79 (71-89)	0.002*	85 (70-96)	0.204	84 (71-91)	0.005*
BENRA	81 (65-91)		92 (80-98)		94 (77-99)		95 (82-99)	

Fig 1: Clinical results.

An OCS-sparing effect was observed in both groups, the daily prednisone dose decreasing from 10mg (IQR 5–12.5) at baseline to 4mg (0-5.0) at month 12 in mepolizumab cohort and to 2.5mg (0-5) in the benralizumab group.

An improvement in FEV1 was observed in both groups, with a greater improvement as compared to the baseline value in the benralizumab group at month 3 (+6.6% [IQR2-17.5] for mepolizumab and +13.7% [4.4-22.1] for benralizumab), but not at the subsequent timepoints.

Eleven patients reported adverse events during treatment with mepolizumab and fifteen patients during benralizumab. Most events were mild, and only one on mepolizumab and two on benralizumab therapy required hospitalization.

Conclusions: These results suggest that mepolizumab and benralizumab at the dosage approved for eosinophilic asthma showed comparable effectiveness in controlling systemic and respiratory involvement, and both treatments were associated with a good safety profile.

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Disclosures: IM, GL, AB, AE, FF, TN, JWS: None. DJ, MG, RP, GE, VC, AV: consulting fees from GSK and AZ.

O-048

Investigating the impact of Anti-IL5 therapy in eosinophilic granulomatosis with polyangiitis (EGPA); a longitudinal perspective for three years and beyond

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Background/ Objectives: In the randomized, placebo-controlled MIRRA trial for relapsing and refractory eosinophilic granulomatosis with polyangiitis (EGPA), adjuvant therapy with 300mg anti-IL5 mAB Mepolizumab [MEPO] for 12 months (M), accrued longer times in remission, reduced steroid exposure and reduced relapse rates[1]. The aim of this study is to analyze the outcome of 100mg MEPO monthly s/c for a minimum of 36 months. Changes to adjuvant immunosuppression and indications for anti-IL5 class switch from MEPO 100mg s/c to Benralizumab (BRZ) or Reslizumab (Res) were assessed.

Methods: 20 EGPA patients received anti-IL5 therapy for a minimum of 36M (range 49-68M). All commenced on 100mg s/c MEPO every four weeks. Anti-IL5 therapy switched to BRZ or Res due to partial response or intolerance. Assessment time points included MEPO commencement, 6, 12, 18, 24 and 36 months.

Results: Overall, there was a 50% reduction in steroid dose by 12 months. This continued to reduce to 24M, by which time 2 were off steroids and a further 10/20 (50%) on weaning dose ≤ prednisolone 5mg/day. Mean steroid dose continued to decrease to 36 months. The number on adjuvant conventional immunosuppressants (ACIS), reduced over time from 10/20 (50%) at M0 to 4/20 (20%) by M24. Clinical benefits included ANCA serology normalized in all four positive patients by 12 months. Mean eosinophil count reduced from 0.42mg ±0.33 X10^9/L at M0 to 0.04±0.03 X10^9/L at 12 and 24M. BVAS reduced from median 5 [3-7], to 0 [0-1] by 24M. The change in mean FEV1 over 12 months was from (M0) 2.11±0.66 to (M12) 2.39±0.62 and FVC (M0) 3.42±0.87 to (M12) 3.67±0.93/105.60±20.47 respectively.

All 20 EGPA patients receiving anti -IL5 therapy, ranging from 49-68M remain on therapy. At 36M, 9 have remained on 100mg s/c MEPO. 10 (50%) have switched to an altenative anti-IL5 agent - 10 switched to benralizumab, 1 initially on benralizumab to reslizumab. 9/10 had achieved partial response prior to switch (reduction in steroids / relapse rate), 1/10 had no response.. During the duration of the study, 3 patients had a break of therapy, but all resumed anti-IL5 treatment with good response. Hence, all 20 remain on anti-IL5 beyond 24M. After 36M, one patient required cyclophosphamide along with anti-IL5 therapy for myocarditis. A further patient had Rituximab for EGPA/ Rheuamtoid arthritis overlap between anti-IL5 agents.

Conclusions: In this study, there was a 50% reduction in steroid dose by 12 months and steroid requirements continue to decrease to 36M. By 24 months 2 are steroid free and a further 10 on weaning dose ≤ 5mg. The number on adjuvant conventional immunosuppression reduced over the 24M (n=4 at 24M). This study demonstrates that anti-IL5 therapy serves as a favorable model for steroid and conventional immunosuppressant minimization in EGPA.

Response to therapy by 36 months						
M0	**M6**	**M12**	**M18**	**M24**	**M36**	
Prednisolone dose Mean ±SD						
18mg ±10.31	12.26mg ±6.8	9.37mg ± 5.3	9.71mg ±8.1	7.7mg ±7.08	5.95mg ±5.21	
BVAS	**M0**	**M6**	**M12**	**M18**	**M24**	
Median ±IQR	5 [3-7]	1.5 [0-2]	1 [0-2]	0.5 [1.25-0]	0 [0 -1]	
Eosinophil count N=15		**M0**	**M12**	**M24**		
Mean ±SD		0.42mg ±0.33	0.04±0.039	0.04±0.034		
Creatinine n=13		**M0**	**M12**	**M24**		
Mean ±SD		67.53±11.01	67.69±11.98	72.23±15.23		
FEV1/%FEV1 N=15		**M0**	**M12**			
Mean ±SD		2.11±0.66/68.38±22.72	2.39±0.62/82.61±21.79			
FVC /%FVC N=15		**M0**	**M12**			
Mean ±SD		3.42±0.87/94.27±18.57	3.67±0.93/105.60±20.47			
Adjuvant Conventional Immunosuppression (ACIS)						
Time point.	M0	M6	M12	M18.	M24	M30	M36
Participants.	20	20	20	20	20	20	20
No. on ACIS.	10	9	8	7	4	5	4
No. that stopped ACIS	6						
No. that started ACIS.	4 (3 subsequently stopped)						

Table: Response to therapy. Using anti-IL5 therapy supports favorable outcomes including steroid minimization, reduction in adjuvant immunosuppression and reduction in eosinophil count are recorded.

Figure 1: Response to anti-IL5 therapy.

Disclosures: CO lectured for AZ, GSK, Sanofi, Novartis; course fees from Boehringer. AE consultancy for AZ. DJ received grants from AstraZeneca, GlaxoSmithKline, Roche; consulting fees from Astra-Zeneca, Chemocentryx, GSK, Novartis, Otsuka, Takeda, Roche, Vifor; honoraria from GlaxoSmithKline and Vifor.

O-049

Gene expression profile of CD4⁺ T cells is modified in eosinophilic granulomatosis with polyangiitis (EGPA)

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Background: EGPA is a rare autoimmune disorder, included within the AAV. It is characterized by a diverse clinical profile, together with an unsatisfactory response to treatment leading to frequent relapses. Its pathogenesis remains unclear, being supported by experimental studies with limited evidence. However, they all indicate that EGPA pathogenesis is mainly driven by Th2 cells (CD4⁺ T cells), showing oligoclonal expansion in active patients, along with a significant increase in serum levels of chemokines involved in Th2 recruitment and activation. Moreover, some genetic variants associated to Th2 activation have been identified in these patients. In fact, Th2 cells are the main responsible cell type for eosinophil activation, the core effector cells of the disease.

Objectives: To investigate transcriptomic changes of Th2 cells in EGPA patients in order to characterize the molecular basis of EGPA heterogeneity, and to identify pathogenic pathways that could provide clinically useful biomarkers.

Methods: CD4⁺ T cells were isolated from EGPA patients in remission (BVAS = 0, prednisone dose <7.5 mg/day) (n=23) and compared to healthy controls (n=14) and non-EGPA asthmatic patients (n=8). Microarray was used to analyze whole transcriptome signature. Unsupervised hierarchical clustering and PCA were conducted to identify clusters among patients with similar features. Analysis of transcriptomic changes (GSEA) ($p < 0.001$, FC >1.5) among the different groups, and GO enrichment analysis (ShinyGo, KEGG) of the differentially expressed genes (DEGs) were performed. The most interesting DEGs were validated by qPCR. Two-sample permutation T-test was used for statistical analyses through BRB-ARRAY Tools.

Results: 199 DEGs were found between EGPA and control samples, defining two distinct clusters as evidence in the heatmap (fig 1A). PCA of all samples further confirmed these two groups (fig 1B). Pathway enrichment analysis showed significant differences between these two populations regarding Th1, Th2 and Th17 cell differentiation, IL2/STAT5 pathway and IFNα and IFNγ response. qPCR specifically validated IL2/STAT5 pathway through various relevant genes, such as CTLA4, CD81, and LTB, suggesting a potential role in EGPA pathogenesis.

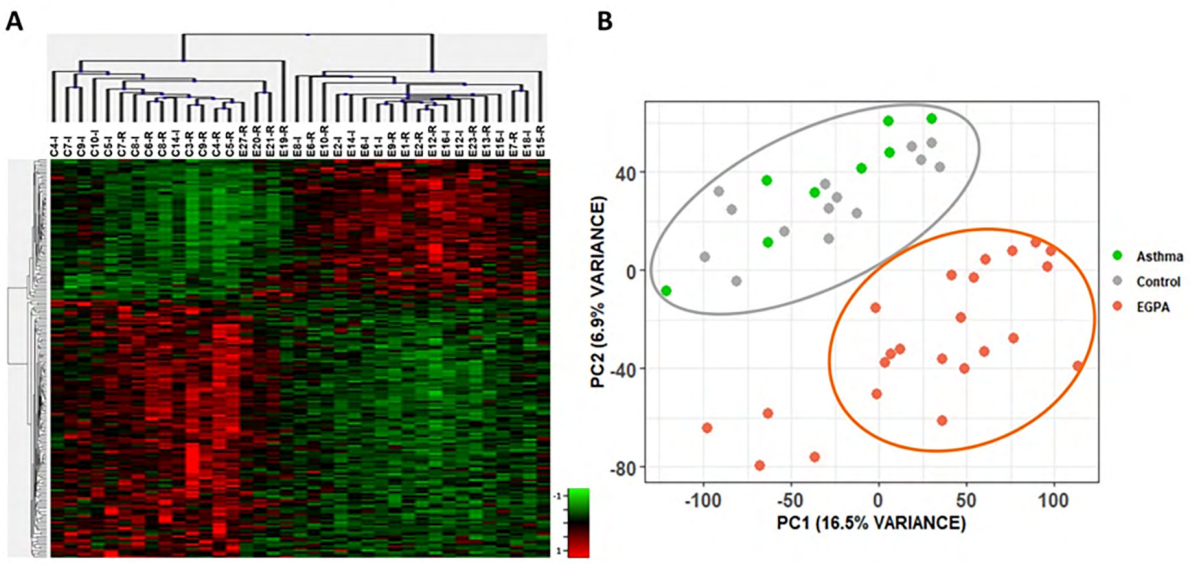

Image 1. Transcriptomic profile of CD4+ T cells reveals separate clusters. **A** Heatmap displaying 199 DEGs between control and EGPA samples. **B** PCA showing two well-defined clusters revealing distinct gene expression signatures between populations.

Conclusions: Our study provides transcriptomic evidence that CD4⁺ T cell expression profile is modified in EGPA patients. GSEA and DEGs show a potential role of different pathways involved in CD4⁺ T cell differentiation and activation, potentially mediated by IL2/STAT5 pathway.

Disclosures: MCC: research grant from Kiniksa, consulting/educational fees from GSK, AstraZeneca, AbbVie and CSL-Vifor; GEF: consultant of Vifor and GSK. This study was supported by AEI (PID2020-114909RB-I00) and GSK.

PLENARY SESSION: CLINICALLY RELEVANT OUTCOMES

O-050

Assessing the predictive role of monitoring creatinine, hematuria, and proteinuria for renal outcomes

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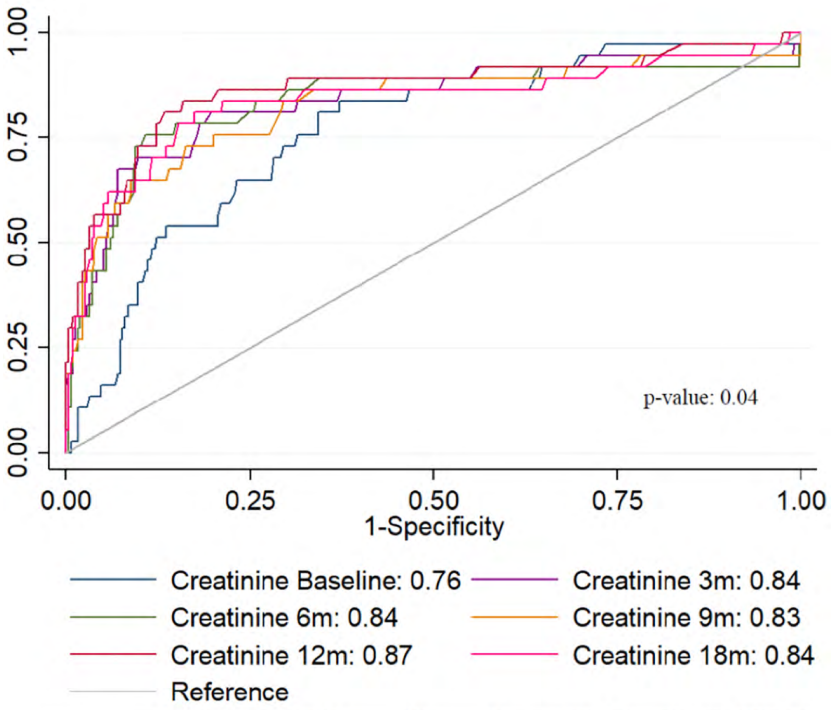
Background: Most prognostic factors in anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV) are derived from baseline clinical–analytical data collected at the time of diagnosis; however, we do not count with prognostic factors throughout the evolution of the disease. The dynamic nature of AAV makes it challenging to establish consistent prognostic factors that hold significance across different stages of the disease. The aim of our study was to determine the prognostic significance of proteinuria, hematuria and serum creatinine monitoring in patients with AAV.

Methods: The dataset included 848 patients with newly diagnosed AAV who participated in 7 RCTs (1995-2012), and median follow-up time was 8 years (IQR: 2.9-13.6). Creatinine, hematuria, and proteinuria was recorded at baseline, 3, 6, 9, 12, and 18 months after randomization. Kidney outcome was defined as permanent dialysis dependency during follow-up or kidney transplantation. ROC curves were calculated and screening performance of cut-off scores was evaluated using the Youden Index. A multivariate Cox regression model was performed to examine the factors associated with the kidney outcome.

Results: Median baseline creatinine was 176 µmol/L (IQR: 97-388.5), 114 µmol/L (IQR: 88-171) at 3 months, 110 µmol/L (IQR: 89-160) at 6 months, 110 µmol/L (IQR: 89-155) at 12 months, and 102 µmol/L (IQR: 84-132.6) at 18 months. Within 12 months, the AUC of creatinine was the highest at 0.87 (95% CI: 0.79-0.95; SE: 0.05; p-value: 0.04) to predict kidney outcome. For the cut-off point of 135 µmol/L, 12-month-creatinine achieved a sensitivity of 83% and specificity of 76% (LR+: 3.35, LR-: 0.23). The lowest AUC corresponded to the baseline creatinine (AUC: 0.76; SE: 0.04; 95% CI: 0.68-0.85).

The ROC curves for hematuria, showed that the highest AUC was found at 9 months (AUC: 0.71; SE: 0.04; 95% CI: 0.64-0.78; p=0.03) (Figure 1). Examination of the ROC curve of proteinuria > 0.5/24h, revealed that the highest AUC corresponded to the baseline determination (AUC: 0.64; SE: 0.08; 95% CI: 0.48-0.80), but there was no statistically significant difference observed among the AUC values of proteinuria across the monitored periods.

In the multivariable Cox regression model, MPA diagnosis, 12-month creatinine, and age > 65 years old were independent prognostic factors for the kidney outcome. The model including creatinine at 12 months was more robust than the model including baseline creatinine (Harrell's C: 0.84 and 0.76, respectively).



	AUC	SE	Lower 95% CI	Upper 95% CI
Baseline Creatinine	0.76	0.04	0.68	0.85
Creatinine 3 months	0.84	0.04	0.75	0.92
Creatinine 6 months	0.84	0.05	0.74	0.93
Creatinine 9 months	0.83	0.04	0.74	0.92
Creatinine 12 months	**0.87**	**0.05**	**0.79**	**0.95**
Creatinine 18 months	0.84	0.04	0.75	0.93

Figure 1. ROC curves for the kidney outcome according to serum creatinine.

Conclusions: The best diagnostic accuracy for ESKD in ROC curves was shown by serum creatinine at 12 months (AUC: 0.87; SE: 0.05; 95% CI 0.79-0.95; p-value: 0.04). Hematuria was a predictor of the kidney outcome of moderate quality (AUC 0.71; SE 0.04; 95% CI: 0.64-0.78), while proteinuria > 0.5g/24h had a modest and non-significant AUC (AUC 0.64; SE 0.08; 95% CI 0.48-0.80). Reevaluation of renal prognosis at 12 months might be useful to reassess treatment in patients with AAV. These findings suggest than incorporating biomarker monitoring into clinical-analytical predictive models can provide a more accurate method for predicting renal outcomes as the disease progresses.

Disclosures: None.

O-051

Prediction of Recovery of Kidney Function in Severe ANCA Glomerulonephritis

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Background/ Objectives: In anti-neutrophil cytoplasmic antibody (ANCA) vasculitis, kidney involvement and particularly kidney failure confer significant morbidity and mortality. Preventing end-stage kidney disease (ESKD) is crucial and an improved prognostication of recovery of kidney function will enable tailoring treatment to patients' needs.

Methods: Unadjusted and adjusted multivariable Cox regression analyses were performed, investigating patients of the ANCA Kidney Risk Score (AKRiS) cohort requiring kidney replacement therapy (KRT) at the time of diagnosis.

Results: Of 1439 patients, 291 patients required KRT at the time of diagnosis and 136 of these recovered kidney function during follow-up (46.7%). The median age was 63.4 years and 58.4% were of male gender. One hundred and twenty-three patients were anti-myeloperoxidase positive (42.3%), 137 patients were anti-proteinase 3 positive (47.1%), and 31 patients were ANCA negative (10.6%). Median creatinine and estimated glomerular filtration rate (eGFR) at time of diagnosis were 615mmol/l and 6.2mls/min. Median AKRiS was 15.0 points and 185 patients developed ESKD (63.2%) during a median follow-up of 3.6 years. Eighty-six patients died during follow-up (29.6%).

Patients recovering kidney function had a median of 22.9% normal and 33.3% crescentic glomeruli, patients remaining KRT-dependent demonstrated a median of 6.7% normal and 29.3% crescentic glomeruli in their biopsies. The percentage of normal glomeruli, interstitial fibrosis and tubular atrophy (IFTA), age, creatinine and eGFR associated with recovery of kidney function but only normal glomeruli percentage and creatinine independently predicted outcome ($p<0.001$, $p<0.001$, respectively).

Conclusions: The percentage of normal glomeruli and the initial kidney function predicted kidney function recovery in patients of the AKRiS cohort who required KRT at the time of diagnosis.

References: None.

Disclosures: None.

O-052

Outcomes after kidney transplantation in anti-Glomerular basement membrane disease

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Background/ Objectives: Anti-glomerular basement membrane antibody disease-associated glomerulonephritis (anti-GBM-GN) can lead to end-stage kidney disease (ESKD), requiring replacement therapy with dialysis or kidney transplant (KT). Few studies evaluated the outcome of these patients after KT. Our aim was to describe, in comparison with a control group, the occurrence of the following events: delayed graft function recovery, graft survival, relapse, acute rejection, overall survival; and to study the risk factors associated with these events.

Methods: This was a retrospective, multicenter (6 French centers), observational study including patients who received a KT between 2005 and 2023 for ESKD secondary to anti-GBM-GN. Each vasculitis case receiving a KT was matched with 2 controls, matched on gender, center, recipient age (± 5 years) and transplant period (± 1 year). Event-free survival and the associated risk factors were analyzed.

Results: 126 patients were included, including 42 with anti-GBM-GN and 84 control patients. The median post-KT follow-up for vasculitis patients was 95 months. There was no difference in the occurrence of DGF between the groups (24 vs 18%, p = 0.5). There was no difference in graft survival when comparing both groups (78% vs 82% at 10 years, p = 0.48) (**Figure 1A**). Only one patient experienced a relapse after KT (being anti-GBM negative at the time of transplantation). There was no difference in the incidence of acute rejection between the groups (p = 0.82). There was no difference in overall survival when comparing both groups (83% vs 89% at 10 years, p = 0.76) (**Figure 1B**).

Conclusions: Kidney transplantation is an interesting option for patients with anti-GBM-GN: outcomes are similar to those of a matched population with similar occurrence of acute rejection, graft loss or death. Moreover, relapse rate is low. Comparison with a matched anti-GBM-GN population remaining on dialysis would be of interest to go further.

References: None.

Disclosures: None.

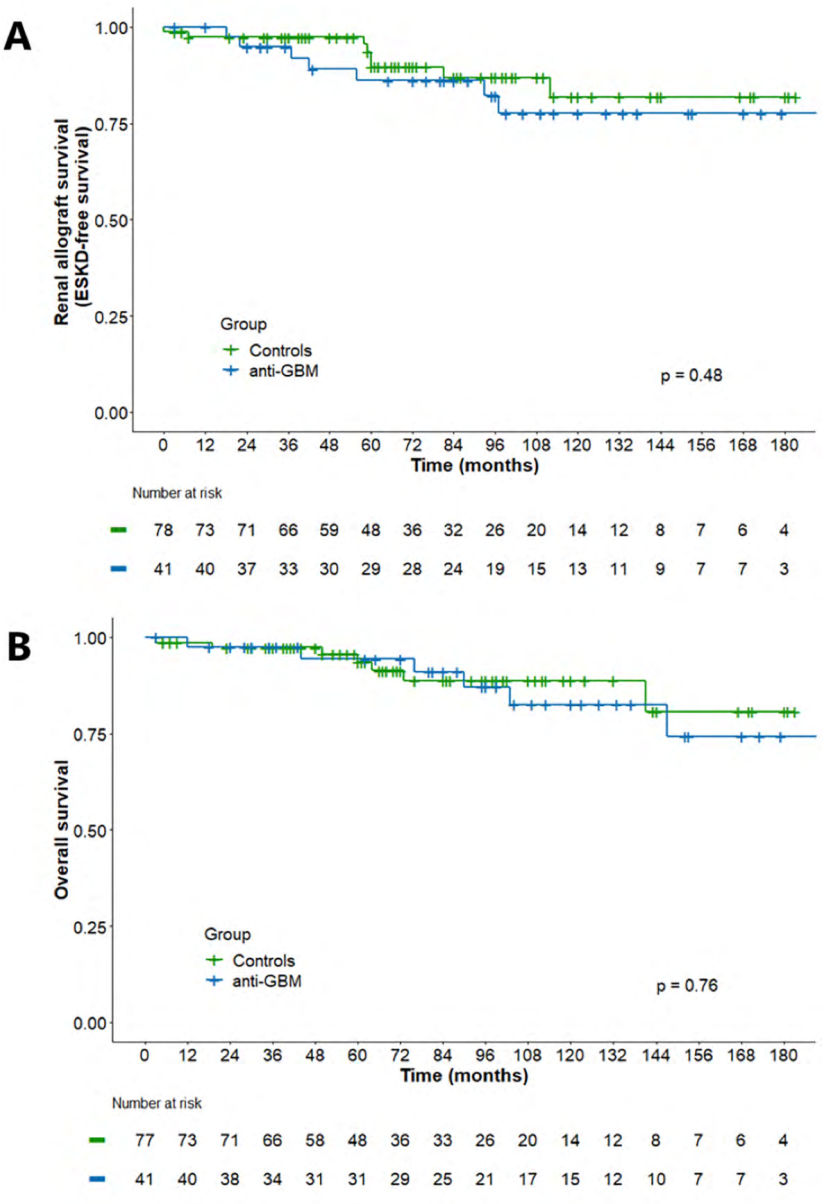

Figure 1. Kidney (A) and overall (B) survival after kidney transplantation. Anti-GBM: anti-glomerular basement membrane disease.

O-053

Agglomerative hierarchical cluster analysis identifies two clusters of Takayasu arteritis based on clinical phenotype which predict angiographic findings and mortality

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Background/ Objectives: Cluster analysis is a data-driven approach to identify natural patterns of disease which may help better understand the phenotype of Takayasu arteritis (TAK), a rare large vessel vasculitis. We evaluated whether clusters based on clinical phenotypes of TAK predict angiographic patterns of disease or mortality.

Methods: From a cohort of TAK, agglomerative hierarchical clustering using Ward method was performed using clinical features. Optimal number of clusters were identified using elbow method and silhouette method. The hitherto identified clusters were compared for differences in clinical features, vascular involvement, and Hata's angiographic subtypes using odds ratios (OR, with 95% confidence intervals), and for survival [crude, using Kaplan-Meier curves; hazard ratios (HR) with 95% condifence intervals (95%CI), adjusted for gender and age of disease onset using Cox regression analyses] using STATA 16.1 I/C.

Results: The optimal number of clusters was two [Ward agglomerative coefficient 0.989; Cluster 1: 111 TAK, mean (SD) age 25.06 (9.97) years, 80.2% females; Cluster 2: 89 TAK, mean (SD) age 25.54 (10.38) years, 65.2% females]. Carotidynia, pulse or BP inequality, pulse loss, vascular bruits, upper or lower limb claudication, and chest pain were more common in cluster 1, whereas, hypertension, renal failure, and stroke/TIA were more common in cluster 2. Intrathoracic arteries were more involved in cluster 1, whereas abdominal vessels were similarly involved in both clusters. Hata's angiographic subtype V was more common in cluster 1 (OR 0.45, 95%CI 0.25 – 0.80), whereas, subtype IV was more common in cluster 2 (OR 6.16, 95%CI 1.70 – 22.35). Over 697 person-years of follow-up (193 patients), cluster 1 had worse survival than cluster 2 (log-rank p value 0.027, **Figure 1**), even after adjustment for gender and age of onset (adjusted HR cluster 2 vs cluster 1 0.09, 95%CI 0.01 – 0.78).

Conclusions: Clinical features corresponded to vascular territories which were more common in cluster 1. Hypertension and renal failure were more common in cluster 2, which correspond to more frequent Hata's subtype IV in this cluster. Clusters based on clinical features could predict well the patterns of vascular involvement. Higher adjusted mortality rate in cluster 1 requires validation in other cohorts of TAK.

References: None.

Disclosures: None.

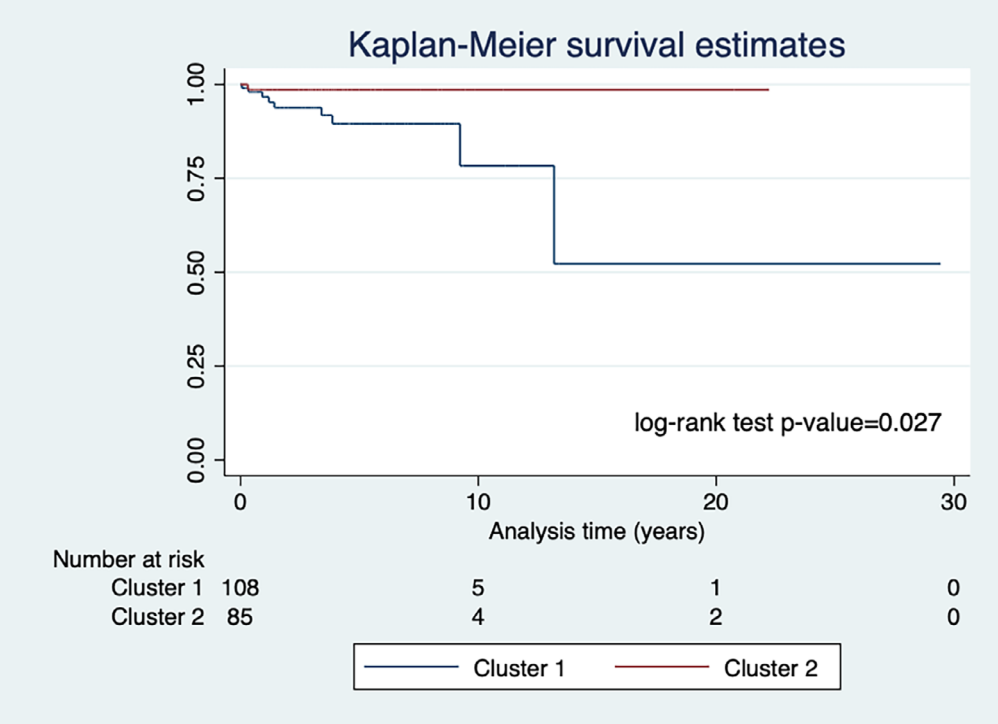

Figure 1: Kaplan-Meier survival curve based on the clusters identified on clinical phenotypes.

O-054

Outcomes of Intensive Care Patients with Acute Small-Vessel Vasculitis: A 23-year Single-Centre Experience

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Background: Patients with acute manifestations of fulminant small-vessel vasculitis (SVV) may require intensive care unit (ICU) admission, which has been associated with mortality and morbidity[1-3]. We report the outcomes and prognostic factors of ICU patients with ANCA-associated vasculitis (AAV) and anti-glomerular basement membrane disease (anti-GBM) over a 23-year period.

Methods: A search of our hospital ICU database between 1999-2022 was performed. Patients with acute manifestations of new or flaring AAV or anti-GBM disease needing ICU admission were included. Those requiring high dependency care were excluded. Primary outcomes were mortality and dialysis dependence at 30 days. A case-control analysis (1:4 ratio) matched for age, gender, APACHE II score and admission year was performed.

Results: 86 cases (81% AAV, 16% anti-GBM) were identified of which 79% were newly diagnosed. The median APACHE II score was 19, with requirement for ventilatory support and continuous venovenous haemodiafiltration in 84% and 67% respectively. Vasculitis treatments were cyclophosphamide (58%), rituximab (43%) and plasma exchange (71%). 30-day and 90-day mortality rates were 15% and 26%, respectively. Mortality rate pre-2008 was higher compared to post-2008 (HR: 5.87, 95% CI: 4.84-6.90, p=0.09), whilst similar improvements were not observed in ICU controls. This coincided with the local introduction of rituximab for AAV on the ICU. New end-stage kidney disease was observed in 20 (31%) of 90-day survivors.

Conclusion: This single-centre study reports ICU outcomes for patients with fulminant SVV over 18 years. 90-day ICU mortality improved over time, and was associated with changes in vasculitis treatment protocols.

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O-055

Frailty and Associated Outcomes in Patients with Vasculitis

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Background/ Objectives: Frailty, a syndrome characterized by an increased vulnerability to stressors, is associated with increased morbidity and mortality. The objective of this study was to report prevalence of self-reported frailty in patients with vasculitis, including associations with patient-reported outcomes (PROs) and health outcomes at 1-year follow-up.

Methods: VascStrong was a longitudinal study using the Vasculitis Patient-Powered Research Network, an internet-based longitudinal cohort. Data elements collected included type of vasculitis, demographics, medications, and PROs, including a patient global assessment (PGA) and several domains of the Patient-Reported Outcomes Measurement Information System (PROMIS).

Frailty was measured by the FRAIL scale, a 5 domain self-report measure. Patients were classified as robust, pre-frail, and frail based on 0, 1-2, or ≥3 criteria, respectively. Frailty was measured at baseline (October 8, 2021 -January 15, 2022) and at 1-year follow-up (October 28, 2022 - January 26, 2023).

At follow-up, participants reported the occurrence over the prior year of hospitalizations, infections, fractures, and disease flares. A multivariable logistic regression was performed to identify factors independently associated with frailty in the entire cohort at baseline.

Results: The baseline survey included 328 responses. The most common diagnoses were granulomatosis with polyangiitis (39.3%), eosinophilic granulomatosis with polyangiitis (12.5%), microscopic polyangiitis (11.9%). Patients had a mean age of 59.5 years and were predominantly female (71.6%) and non-Hispanic white.

Prevalence of robustness, pre-frailty, and frailty was 36.3%, 42.1%, and 21.6%, respectively. Pre-frail and frail patients reported worse PROs at baseline and follow-up (Table 1). In the multivariable logistic regression, frailty was independently associated with female sex (OR 2.78 [95% CI 1.29,5.89]), being overweight (OR 5.02 [95% CI 2.13,11.84]), and obesity (OR 7.34 [95% CI 3.25,16.57]).

At 1-year follow-up, 272/328 participants (82.9%) responded the survey. Prevalence of robustness, pre-frailty, and frailty was 47.1%, 33.8%, and 19.1%, respectively. The majority of participants were classified similarly to their baseline assessment (75%, 50.9%, and 66.1% for robust, pre-frailty, and frailty, respectively). However, transitions in frailty between consecutive states were observed from robust to pre-frail (21.2%), pre-frail to robust (38.9%), pre-frail to frail (10.2%), and frail to pre-frail (25%). Hospitalizations, infections, and flares were most frequent in participants classified as frail at baseline (Table 1).

Table 1. Patient-reported outcomes and adverse health outcomes among patients with vasculitis by frailty classification at 1-year follow-up

Outcome	Robust (N = 128)	Pre-frail (N = 92)	Frail (N = 52)	p-value
Patient Global Assessment	2.0 (0.0, 5.0)	4.5 (1.0, 6.0)	6.0 (5.0, 8.0)	<0.0001
PROMIS domains				
Pain intensity*	1.0 (0, 2.5)	3.0 (1.0, 5.0)	5.5 (4.0, 7.0)	<0.0001
Anxiety**	77.9 (71.2, 81.6)	73.3 (65.3, 81.6)	68.3 (63.4, 71.2)	<0.0001
Fatigue	48.6 (46.0, 53.1)	58.8 (51.0, 66.7)	64.6 (60.7, 69.0)	<0.0001
Depression	49.0 (41.0, 53.9)	52.9 (45.0, 58.9)	57.3 (49.0, 62.2)	<0.0001
Pain Interference	41.6 (41.6, 53.9)	55.6 (41.6, 61.2)	63.8 (58.5, 66.6)	<0.0001
Physical functioning	56.9 (45.3, 56.9)	41.8 (36.7, 48.0)	34.4 (32.1, 36.7)	<0.0001
Adverse health outcomes				
Hospitalizations	13 (12.0%)	20 (18.5%)	18 (32.1%)	0.0075
Infections	48 (44.4%)	55 (50.9%)	35 (62.5%)	0.0134
Severe infections[a]	7 (14.6%)	6 (10.9%)	6 (17.1%)	0.7045
Fractures	6 (5.6%)	9 (8.3%)	6 (10.7%)	0.4911
Flares	17 (15.7%)	26 (24.1%)	23 (41.1%)	0.0005
Flares requiring treatment[b]	9 (52.9%)	20 (76.9%)	16 (69.6%)	0.3698

Data presented as median (interquartile range). *Raw score, scale 0-10. **PROMIS T-score.
[a]Severe infections were defined as infections requiring hospitalization. [b]Flares of disease that required changes in immunosuppressive treatment. PROMIS: Patient-Reported Outcomes Measurement Information System

Conclusions: Self-reported frailty or pre-frailty is prevalent in the majority of patients with multiple forms of vasculitis. Frailty is associated with worse PROs and independently associated with female sex, being overweight, and obesity. At 1-year follow-up, transitions in frailty status were observed in a subset of participants. Frailty and pre-frailty in patients with vasculitis identifies a subset of patients at higher risk for adverse outcomes.

Disclosures: Sattui: Rheumatology Research Foundation RISE Pilot Award, Bristol Myers Squibb Foundation Winn Career Development Award (research funding); AstraZeneca and GlaxoSmithKline (research support, clinical trials); Sanofi and Amgen (consulting and advisory board, funds toward research support).

Merkel: AbbVie, Amgen, AstraZeneca, Boeringher-Ingelheim, Bristol-Myers Squibb, GlaxoSmithKline, InflaRx, Takeda (consulting and research support); ArGenx, Cabaletta, CSL Behring, Dynacure, HiBio, Janssen, Novartis, NS Pharma, Regeneron, Vistera (consulting); Eicos, Electra, Forbius, Genentech/Roche, Genzyme/Sanofi, Neutrolis (research support); Kyverna, Q32, Sparrow (consulting and stock options); UpToDate (Royalties).

Spiera: AbbVie/Abbott, GSK, Novartis (consulting and research support); Amgen, Sanofi (consulting); AstraZeneca, chemocentryx, corbus, Formation Biologics, Inflarx, Kadmon, Principia (research support).

All others none.

O-056

RETRACE-Clustering Creatinine Trajectory and Baseline Features for Predicting End Stage Kidney Disease

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Objectives: Patients with ANCA-associated vasculitis (AAV) may experience end-stage kidney disease (ESKD) and mortality. We aim to investigate the connection between the longitudinal trajectory of creatinine and the occurrence of ESKD and mortality.

Methods: The study included patients with a minimum of two creatinine measurements, encompassing the baseline period (-14 days to +30 days from the date of diagnosis). Creatinine trajectories were formulated using six months of creatinine readings from AAV patients with kidney involvement. In instances where a patient had multiple creatinine values within a given month, the average of those values was employed. Percentage delta creatinine values, representing the percentage difference between a creatinine value and its baseline, were then calculated.

The K-means algorithm for longitudinal data was employed to cluster the creatinine trajectories of AAV patients[1]. Three discernible clusters emerged from these trajectories: Impaired, Stable, and Recovered. The quality of clustering was evaluated using the Calinski-Harabasz Index. Subsequently, we conducted a time-to-event analysis for end-stage kidney disease (ESKD) and mortality, assessing the survival rates of the clusters over a five-year follow-up period through Kaplan-Meier Survival analysis (Figure (b)).

Using 17 baseline features of the patients and a random forest algorithm, we predict at baseline the creatinine trajectory of a patient by predicting the cluster to which their creatinine trajectory belongs.

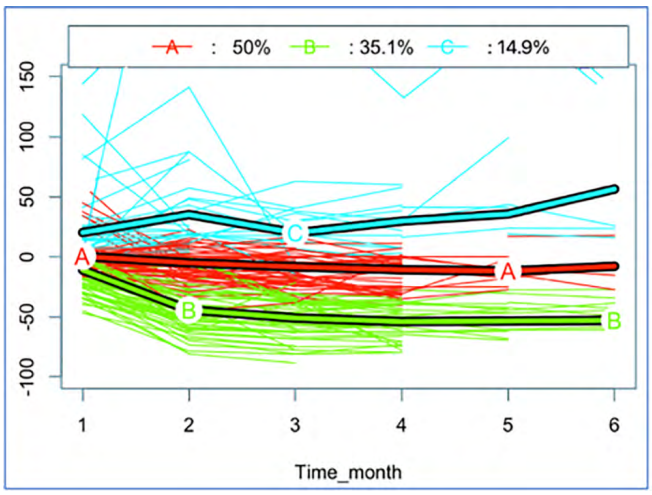
Results: The study incorporates 268 patients with >1 creatinine values, amounting to a total of 2008 creatinine readings. We identified three renal trajectory groups: A-stable(134), B-recovered (N=94), and C- impaired (N=40) (Figure(a)). The baseline features vary across clusters, specifically in terms of creatinine (p<0.001), eGFR (p<0.001), and ENT (p=0.001). The baseline mean creatinine levels differed significantly among the groups, with Group A at 292, Group B at 394, and Group C at 150. Baseline Ear-Nose-Throat involvement was present in 43% of patients in Group A, 16% in Group B, and 53% in Group C. When considering the composite outcome of ESKD and death, substantial variations were noted among the three clusters. Cluster A exhibited a 3-year incidence rate of 23%, Cluster B at 8%, and Cluster C at 28%. Additionally, the 5-year incidence rates were 30%, 19%, and 42% for Clusters A, B, and C, respectively. The random forest model achieves a cluster prediction accuracy of 65%, utilizing a training set of 216 samples and a test dataset comprising 52 samples.

Conclusions: We identified three distinct clusters and developed a prediction model based on these clusters for ESKD and mortality. The features of patients in each group differ, suggesting the potential for personalised care tailored to individuals within different clusters.

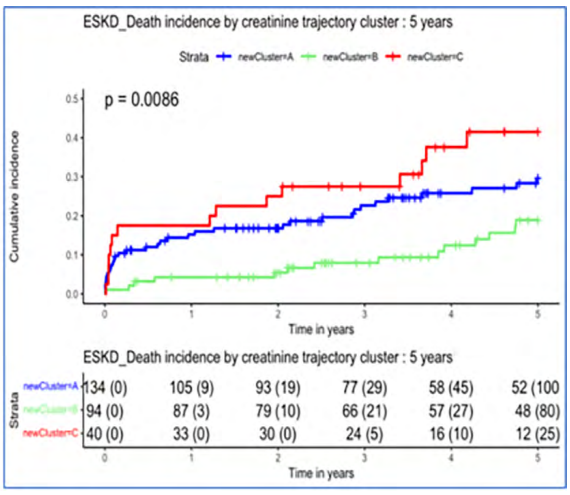
References:

1. Genolini, C., Alacoque, X., Sentenac, M. and Arnaud, C., 2015. kml and kml3d: R packages to cluster longitudinal data. *Journal of statistical software*, *65*, pp.1-34.

Figure-1.



Cluster A, B and C.



Events to time plot: ESKD and Mortality.

Disclosures: MSCA ELITE-S Fellowship.

O-057

Outcomes after kidney transplantation in ANCA-associated vasculitis

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Background/ Objectives: ANCA-associated vasculitis with glomerulonephritis (AAV-GN) can lead to end-stage kidney disease (ESKD), requiring replacement therapy with dialysis or kidney transplant (KT). Few large studies evaluated the outcome of these patients after KT. Our aim was to describe, in comparison with a control group, the occurrence of the following events: delayed graft function recovery, graft survival, relapse, acute rejection, overall survival; and to study the risk factors associated with these events.

Methods: This was a retrospective, multicenter (6 French centers), observational study including patients who received a KT between 2005 and 2023 for ESKD secondary to AAV-GN. Each vasculitis case receiving a KT was matched with 2 controls, matched on gender, center, recipient age (± 5 years) and transplant period (± 1 year). Event-free survival and the associated risk factors were analyzed.

Results: 369 patients were included, including 123 with AAV-GN and 246 control patients. The median post-KT follow-up for all patients was 58 months. There was no difference in the occurrence of DGF between the groups (18 vs 17%, p = 0.9). In univariable analysis, graft survival was lower in the AAV-GN group compared to the controls (76% vs 81% at 10 years, p = 0.017) (**Figure 1A**). 10 patients experienced a relapse after KT. ANCA positivity at the time of transplantation appeared to be correlated with relapse. There was no difference in the incidence of acute rejection between the groups (p = 0.44). In univariable analysis, overall survival tended to be lower in AAV-GN patients compared to controls (62% vs 73% at 10 years, p = 0.084) (**Figure 1B**).

Conclusions: Kidney transplantation is an interesting option for patients with AAV-GN: the relapse rate is low, and the occurrence of acute rejection is comparable to a population of control patients. However, in AAV-GN, graft survival and overall survival appear to be poorer than in control patients. Comparison with a matched AAV-GN population remaining on dialysis would be of interest to go further.

References: None.

Disclosures: None.

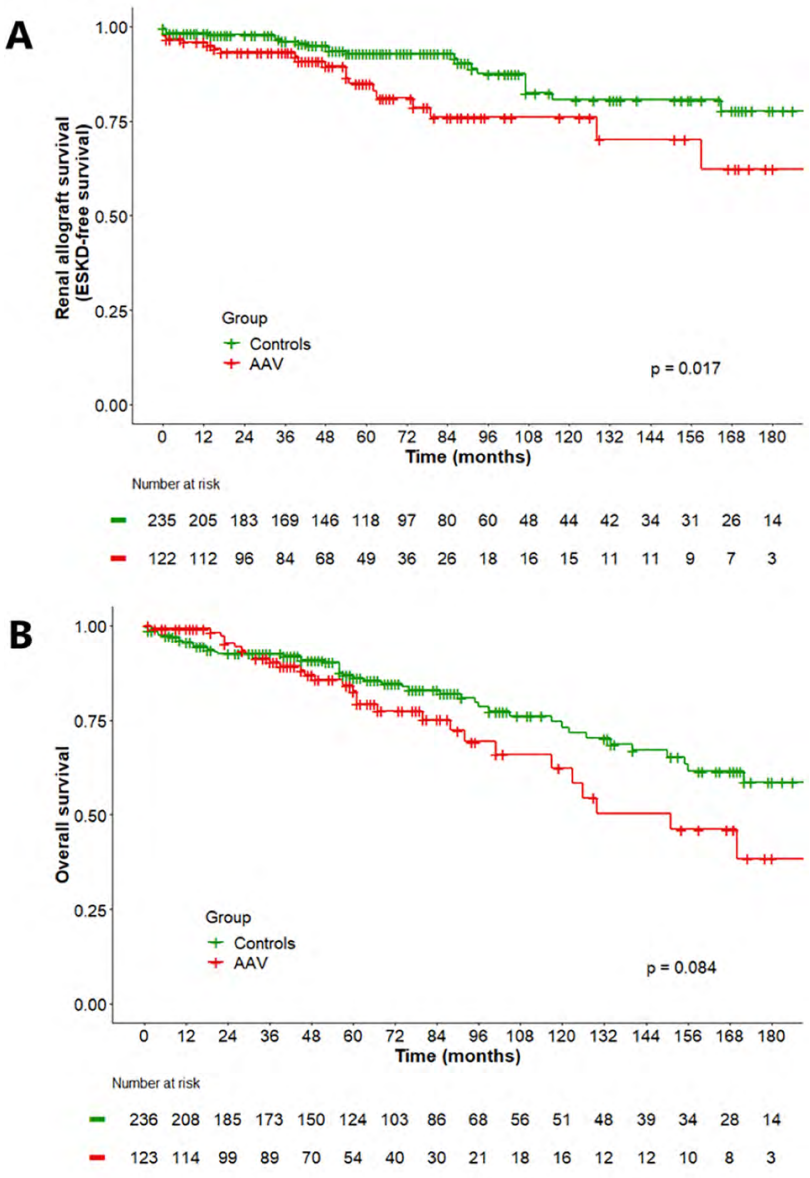

Figure 1. Kidney (A) and overall (B) survival after kidney transplantation. AAV: ANCA-associated vasculitis.

BREAKOUT SESSION: DIAGNOSIS AND CLASSIFICATION OF VASCULITIS

O-058

Application of the EULAR/PRINTO/PRES (Ankara 2008) Classification Criteria for IgA Vasculitis in Adults

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Background/ Objectives: The 1990 American College of Rheumatology Classification Criteria for Henoch Schönlein purpura (HSP), now IgA vasculitis (IgAV), relies on non-specific features and does not address the importance of IgA in diagnosis and pathogenesis of the disease. The 2008 EULAR/Pediatric Rheumatology International Trials Organization/Pediatric Rheumatology European Society validated classification criteria (known as the Ankara criteria) for HSP/ IgAV. The Ankara criteria have a high sensitivity and specificity in children. The aim of this study was to examine the application of the Ankara criteria to adults with possible IgA vasculitis (IgAV).

Methods: This analysis utilized data from the Diagnostic and Classification Criteria for Primary Systemic Vasculitis (DCVAS) study from patients i) with a diagnosis of IgA vasculitis; or ii) a set of comparators with polyarteritis nodosa, ANCA-associated vasculitis, cryoglobulinemic vasculitis, or a different small-vessel vasculitis. Only patients for whom the investigator was either "very confident" or "moderately confident" with the diagnosis were included in the analysis. For this analysis the Ankara 2008 Criteria items were slightly revised as follows: skin involvement or a skin biopsy showing IgA deposition plus one of the following four criteria: abdominal pain, a biopsy showing IgA deposition, arthritis or arthralgia, and renal involvement (any hematuria and/ or proteinuria).

Results: The data set consisted of 258 cases of IgAV and 258 comparators (16 PAN, 215 AAV, 9 cryoglobulinemic vasculitis, and 18 other small-vasculitis vasculitis). When the Ankara criteria were tested in the data set, the sensitivity for classifying patients with IgAV was 90% (95% CI 86% to 93%) and the specificity was 74% (95% CI 68% to 79%).

Conclusions: When applied to adults with IgAV the Ankara 2008 criteria have good sensitivity but only moderate specificity. Use of the Ankara criteria in adult patients could help with harmonization of future clinical research projects. Additional analysis may lead to refinement of the criteria in adults.

References: Ozen S, Pistorio A, Iusan SM, et al. EULAR/PRINTO/PRES criteria for Henoch-Schönlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part II: Final classification criteria. *Ann Rheum Dis*. 2010;69(5):798-806. doi:10.1136/ard.2009.116657

Disclosures: None.

O-059

Data driven subclassification of ANCA associated vasculitis – model-based clustering of the FAIRVASC cohort

Karl Gisslander[1], Arthur White[2], Louis Aslett[3], Zdenka Hrušková[4], Peter Lamprecht[5], Jacek Musiał[6], Jamsheela Nazeer[2], James Ng[2], Xavier Puéchal[7], Matthew Rutherford[8], Mårten Segelmark[1], Benjamin Terrier[7], Vladimir Tesař[4], Augusto Vaglio[9], Krzysztof Wójcik[6], Mark A Little[2], Aladdin J Mohammad[1].

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Background/ Objectives: Subclassification of ANCA-associated vasculitis (AAV) is subject to continued research. Here we develop a data-driven subclassification of AAV, utilising the large, harmonised cohort developed in the FAIRVASC project.

Methods: We performed model-based clustering of 17 mixed type clinical variables using a parsimonious mixture of two latent Gaussian variable models. Missing values were imputed using multiple imputation to obtain 10 complete datasets. The optimal number of clusters and model were decided using Bayesian Information Criterion. Subjects were assigned to the cluster with highest probability when using the optimal model and number of clusters. Adjusted survival analysis and time–to-event analysis for end-stage kidney disease were performed to test whether the clusters had prognostic value, using Cox proportional hazards and Fine-Gray models, respectively. The prognostic value of the cluster affiliations was compared to a classification based on clinical diagnosis and ANCA specificity respectively using the Akaike Information Criterion.

Results: A total of 3868 patients were included, 2434 (62.9%) and 1434 (37.1%) with granulomatosis with polyangiitis and microscopic polyangiitis, respectively. We identified five clusters, with distinct phenotype, biochemical presentation, and disease outcome. Three clusters were characterised by kidney involvement. Cluster 1 (642 [16.6%]), with high C-reactive protein (CRP) and creatinine level, and variable ANCA type, the predominantly anti-MPO-positive cluster 2 (754 [19.5%]) with limited extra-renal disease, and the predominantly anti-PR3-postive cluster 4 (639 [16.5%]) with wide extent extra-renal disease. Two clusters were characterised by relative absence of kidney involvement: the predominantly anti-PR3-positive cluster 3 (1169 [30.2%]) similar to cluster 4, but with limited kidney involvement, and the frequently ANCA negative cluster 5 (664 [17.2%]), with predominantly ear-nose-throat involvement and low CRP, occurring in younger subjects. Compared to models fitted with clinical diagnosis or ANCA status, cluster-assignment models demonstrated improved predictive power with respect to both patient and kidney survival (Table 1).

Conclusions: Our study further reinforces that AAV is not merely a binary construct. Data-driven reclassification of AAV into five distinct subgroups exhibits higher prognostic value than current approaches. This may enhance sample homogeneity in mechanistic studies and clinical trials.

Disclosures: None.

Table 1. Cox Proportional hazards models and Fine-Gray models (adjusted for sex and age) for survival and end-stage kidney disease by cluster assignment, diagnosis and ANCA status.

Survival					
	HR (95% CI)		HR (95% CI)		HR (95% CI)
Cluster 5	REF	GPA	REF	PR3/c	REF
Cluster 1	3.1 (2.1-4.4)	MPA	1.5 (1.3-1.8)	Negative	0.8 (0.6-1.2)
Cluster 2	2.4 (1.7-3.5)			MPO/p	1.0 (0.9-1.2)
Cluster 3	1.8 (1.2-2.6)				
Cluster 4	2.9 (1.8-4.8)				
AIC: 9580		AIC: 9621		AIC: 9645	
End-stage kidney disease					
	HR (95% CI)		HR (95% CI)		HR (95% CI)
Cluster 5	REF	GPA	REF	PR3/c	REF
Cluster 1	17.9 (9.1-35.2)	MPA	2.0 (1.6-2.4)	Negative	1.6 (1.1-2.2)
Cluster 2	12.9 (6.4-26.3)			MPO/p	1.7 (1.4-2.1)
Cluster 3	1.4 (0.6-3.0)				
Cluster 4	7.2 (2.6-20.2)				
AIC: 7110		AIC: 7473		AIC: 7497	

HR: Hazard-ratio, CI: Confidence interval, GPA: granulomatosis with polyangiitis, MPA: microscopic polyangiitis, PR3/c: Proteinase 3 or c-ANCA positive, MPO/p: myeloperoxidase or p-ANCA positive, AIC: Akaike information criterion.

O-060

Application of the 2022 ACR/EULAR classification criteria in a cohort of 152 patients with microscopic polyangiitis and granulomatosis with polyangiitis

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Background/Objectives: The 2022 ACR/EULAR classification criteria for antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) were issued with high sensitivity and specificity.[1,2] Recent studies raised some concerns about its application in populations with high prevalence of myeloperoxidase (MPO)-ANCA.[3,4] This study aimed to reclassify patients diagnosed with microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA) by using 2022 ACR/EULAR criteria in a reference centre.

Methods: Retrospective review of patients previously diagnosed with MPA or GPA according to Chapel Hill Consensus Conference (CHCC) 2012 definitions and European Medicines Agency (EMA) classification algorithm for vasculitides[5] (conventional criteria, MPAcc/GPAcc). All patients were reclassified according to 2022 ACR/EULAR classification criteria (new criteria, MPAnc/GPAnc).

Results: Among 152 patients with AAV, 99 (65.1%) had MPO-ANCA, 35 (23%) proteinase 3 (PR3)-ANCA, and 18 (11.8%) atypical or negative ANCA. 77 (50.7%) patients were diagnosed with MPAcc and 75 (49.3%) as GPAcc. Among GPAcc patients, 33 (44%) had PR3-ANCA, 25 (33.3%) MPO-ANCA, and 17 (22.7%) atypical/negative ANCA. After applying 2022 ACR/EULAR criteria, 88 (57.9%) patients were reclassified as MPAnc, 51 (33.1%) as GPAnc and 15 (9.9%) patients could not be classified in any category (Fig. 1). Two patients with GPAcc, having MPO-ANCA and biopsies depicting granulomatous lesions were reclassified as both MPAnc and GPAnc. Discordant classifications were found in 27 (17.8%) patients, 1 (1.3%) with MPAcc and 26 (17.1%) with GPAcc, which accounted for 34.7% of patients with GPAcc. Among GPAcc, 12 (16%) patients were reclassified as MPAnc (all with MPO-ANCA, 7/12 with paranasal disease, 5/12 lung nodules and 3/12 biopsy confirming granuloma). Of the 15 (20%) unclassifiable patients (5 MPO-ANCA/10 atypical/negative ANCA), 14 were GPAcc, and 11/14 had paranasal disease, 4/14 nasal crusting, 3/14 lung nodules, and biopsies confirming vasculitis (7/14) or granuloma (4/14).

Conclusions: When applying the 2022 ACR/EULAR criteria in our series of MPA and GPA, with a third of GPA patients having MPO-ANCA positivity, 34.7% of patients previously diagnosed with GPA were reclassified as MPA or undefined vasculitis. As suggested by previous studies, 2022 ACR/EULAR criteria for GPA may have lower sensitivity/specificity in populations with a high proportion of patients with MPO-ANCA.

References: 1. Ann Rheum Dis 2022; 81(3):321-326. 2. Ann Rheum Dis. 2022; 81(3):315-320. 3. Rheumatol 2023; 63 (3):1179-1186. 4. Mod Rheumatol. 2023:road017. 5. Ann Rheum Dis. 2007;66(2):222-7.

Disclosures: No disclosures regarding this work.

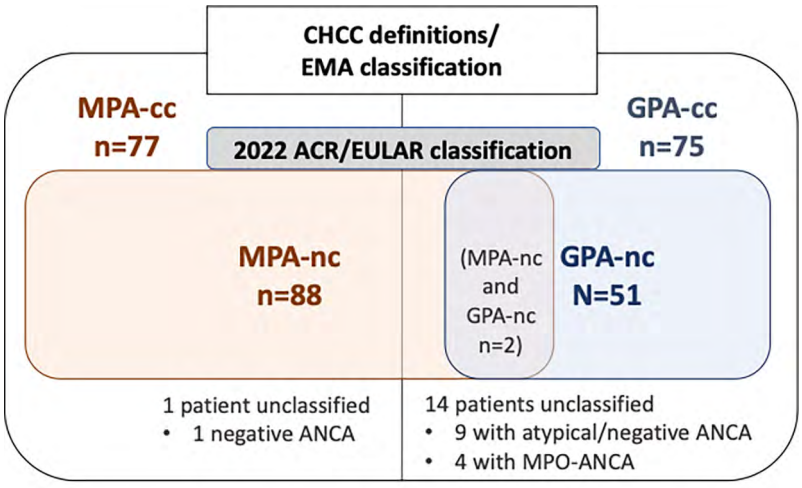

Figure 1. Diagnosis of MPA and GPA according to the definitions of CHCC and the EMA classification algorithm (cc) and classification according to the 2022 ACR/EULAR criteria (nc)

O-061

Using a standardised biopsy evaluation increases the impact of temporal artery biopsy in GCA

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Background: The Diagnostic and Classification Criteria in Vasculitis (DCVAS) study on the place of temporal artery biopsy (TAB) in the diagnosis of Giant Cell Arteritis (GCA) was published in 2022. Mononuclear cell infiltration, presence of giant cells and fragmentation in the internal elastic lamina were defined as histopathological findings associated with definitive vasculitis in biopsy[1]. In this multicenter study, we aimed to re-evaluate the histopathological findings of patients who underwent TAB with suspected GCA.

Method: Patients who were diagnosed with GCA by clinicians and underwent TAB between January 2012 and May 2022 were included in the study. Hospital electronic record systems were reviewed, and two patients diagnosed with ANCA-associated vasculitis were excluded from the study. Available histopathological information in the pathology reports of 90 patients was evaluated by a pathologist (ÖG) and a rheumatologist (GSU). The pathology specimens of 36 (40%) patients whose microscopic findings were not specified in the pathology reports were re-evaluated. The demographic and clinical characteristics of the patients and histopathological findings as a result of TAB were recorded. Patients were divided into definitive vasculitis-GCA and non-definitive-GCA groups, and their clinical and demographic characteristics were compared [1].

Results: The mean age at diagnosis of the 90 patients with GCA was 69.8 (±8.5) years, and 52.2% were female. 80.9% of the patients had at least one cranial symptom or finding. On initial review of pathology reports, 66 (73.3%) patients had definitive vasculitis. The criteria were examined according to independent histopathological findings associated with definitive vasculitis in the DCVAS cohort; definitive vasculitis was present in 76 (84.4%) patients. There was at least one definitive finding of vasculitis in 10 (41.6) of 24 patients whose pathology report was negative. The ROC analysis showed that biopsy length had diagnostic value in predicting the diagnosis of definitive vasculitis (AUC: 0.778, 95% CI: 0.65-0.89, p 0.001). In those with a biopsy length of greater than 1 cm, sensitivity was 76.5%, specificity was 64.3% and PPV was 92%. PPV was increased to 97% in patients with a biopsy length of more than 2 cm. In multivariate analysis, the most significant factor associated with definitive vasculitis was biopsy length (OR: 1.18 (1.06-1.31), p=0.002).

Conclusions: Although temporal artery biopsy is the gold standard for diagnosis, evaluation of histopathological findings is not standardised. Histopathological criteria based on the DCVAS cohort may be useful in defining definitive vasculitis. The length of the biopsy is the major factor in determining definitive vasculitis.

Table. Factors associated with the diagnosis of definitive vasculitis.

Risk factors	OR	RR (%95 CI)	p
Age at the TAB	1.04	(0.96-1.12)	0.26
Gender	1.68	(0.4-7.1)	0.47
CRP	1.44	(0.7-12)	0.81
ESR	0.74	(0.5-9.8)	0.7
Corticosteroid usage before TAB	0.56	(0.13-2.4)	0.4
Biyopsy length,	7.7	(1.8-26)	0.004
Biopsy length, mean (SD)	1.18	(1.06-1.31)	0.002

Abbreviation: CRP, C-reactive protein; ESR, Erythrocyte sedimentation rate; TAB, Temporal artery biopsy; SD: Standard deviation OR: Odds ratio; RR: Relative risk; CI: Confidence interval;

Reference

1. Putman, M.S., et al., *Clinicopathologic Associations in a Large International Cohort of Patients With Giant Cell Arteritis.* Arthritis Care Res (Hoboken), 2022. **74**(6): p. 1013-1018.

O-062

How giant cell arteritis ultrasound diagnostics may profit from phantom research

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Background/Objectives: Giant cell arteritis (GCA) is a vasculitis affecting, among others, the a.axillaris and a.temporalis. Untreated, it can lead to severe complications, such as permanent blindness. Currently, GCA may be diagnosed with ultrasound (US). [1] With a 43-83% sensitivity and a 81-100% specificity [2], diagnostic properties might be improved. US techniques used in other disciplines could improve these properties. However, exploring and implementing new techniques can be challenging. Given the urgency of treating GCA and its low incidence, there is little room for learning by trial and error. A tissue mimicking phantom could aid when testing new techniques. Therefore, we aim to develop a vessel phantom for testing, training and parameter finetuning of US techniques in context of GCA. Feasibility of the phantom will be assessed on the ability to visualize the vessel wall with conventional US.

Method: A tissue mimicking phantom was created using medical gelatin (gel #0, Humimic Medical, Greenville, SC, USA). The acoustic properties are: density: 880.4 kg/m³; speed of sound: 1449 m/s; Young's modulus: 0.57 MPa. We created two vessel geometries (Figure 1). Firstly, a straight pipe phantom with a diameter similar to that of the a.axillaris and a.temporalis. Secondly, a segmented a.axillaris from a computed tomography angiogram, to create realistic curvature, tortuosity, vessel wall and diameter. The vessel was 3D printed with flexible 80A resin (Formlabs Inc., Somerville, MA, USA) and has a 1.0 mm wall (Figure 1c). The gelatin was poured around the vessel. A pulsatile pump was attached to the phantom to mimic blood flow with a.axillaris flow velocities (171 ± 20 mL/min) [3]. B-mode images were made of the phantom.

Results: A clear B-mode image of the phantom's vessel was made, including geometry and wall. The straight pipe phantom shows lumen delineation from surrounding tissue. The wall of the 3D printed vessel phantom was measured at 1.06 mm (Figure 1d), slightly different from the 1.0 mm printed vessel wall. An average flow velocity of 159 mL/min was measured, similar to the a.axillaris.

Conclusion: The phantom provided a visible vessel using B-mode imaging. It measured a similar wall thickness to the printed vessel wall. Such a phantom may help implement novel techniques in context of GCA. In nearby future we will explore contrast enhanced US and 3D tomographic US as novel US techniques for GCA.

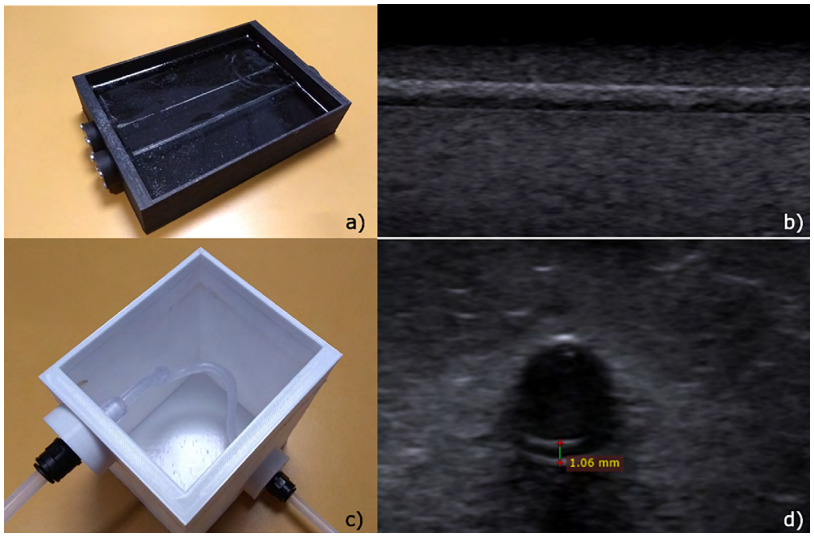

Figure 1 A) Straight pipe phantom with similar diameters to the a.axillaris (ø 6.0 mm) and a. temporalis (ø 1.7 mm) **B)** US image of a straight pipe, similar to the a.temporalis diameter **C)** Phantom with representative a.axillaris geometry. **D)** US image of the phantom with measured vessel wall.

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Disclosures: None.

O-063

Diagnostic performance of short and long [18F]FDG-PET acquisition in giant cell arteritis

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Background/Objectives: In giant cell arteritis (GCA), assessment of the cranial arteries using [18F]fluorodeoxyglucose ([18F]FDG) positron emission tomography (PET) combined with low-dose computed tomography (CT) may be challenging. This study aims to investigate the diagnostic performance of prolonged [18F]FDG PET/CT acquisition time on detectability of GCA compared to short acquisition time.

Methods: Patients with suspected GCA were recruited from the Hospital Group Twente GCA Early in Twente (ZGT GET) cohort in a nested-case control study. Patients who underwent [18F]FDG PET/CT with both short (2 min; SAT) and long acquisition time (5 min; LAT) were included in this study. Two nuclear medicine physicians (NMPs) reported GCA by overall image impression (gestalt) (1) and total vascular score (TVS) of the temporal artery (TA), maxillary artery (MA) and vertebral artery (VA) (2)[1]. Additionally, FDG uptake was assessed semi quantitively by measuring maximum standardized uptake value corrected for lean body mass (SULmax) (3)[2]. The reference standard was clinical diagnosis after six months, blinded for imaging results.

Results: In total, 38 patients were included, of whom 20 had GCA. Sensitivity and specificity for GCA on SAT scans were 80% and 72%, respectively for NMP#1 and 55% and 89% for NMP#2 based on gestalt assessment. On LAT scans this was 65% and 83%, and 75% and 83%. When using TVS, LAT showed similar sensitivity and higher specificity as gestalt (94% for both NMPs). Semi quantitative assessment also resulted in higher specificity in LAT, but sensitivity was lower (Table 1). Inter-observer agreement was higher in LAT scans for both gestalt assessment and TVS (Fleiss Kappa 0.49 to 0.79 for gestalt and 0.79 to 0.89 for TVS). Intra-observer agreement was higher in LAT scans compared to SAT scans.

Conclusions: Inter- and intra-observer agreement were higher using LAT. Specificity of [18F]FDG PET/CT improved on LAT when using TVS or a semi quantitative assessment compared to gestalt. As TVS had similar sensitivities but higher specificities compared to gestalt using LAT, LAT combined with TVS can decrease the number of false positives.

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Disclosures: None.

	Short acquisition time						Long acquisition time					
A Gestalt	NMP #1			NMP #2			NMP #1			NMP#2		
	Pos	Neg		Pos	Neg		Pos	Neg		Pos	Neg	
GCA (n=20)	16	4	Se 80% (58-92)	11	9	Se 55% (34-74)	13	7	Se 65% (43-82)	15	5	Se 75% (53-89)
No GCA (n=18)	5	13	Sp 72% (49-88)	2	16	Sp 89% (67-98)	3	15	Sp 83% (61-94)	3	15	Sp 83% (61-94)
B TVS	NMP #1			NMP #2			NMP #1			NMP#2		
	Pos	Neg		Pos	Neg		Pos	Neg		Pos	Neg	
GCA (n=20)	14	6	Se 70% (48-85)	13	7	Se 65% (43-82)	14	7	Se 70% (48-85)	12	8	Se 60% (39-78)
No GCA (n=18)	3	15	Sp 83% (61-94)	2	16	Sp 89% (67-98)	1	17	Sp 94% (74-100)	1	17	Sp 94% (74-100)
C SULmax	Pos	Neg					Pos	Neg				
GCA (n=20)	18	2	Se 90% (70-98)				12	8	Se 60% (39-78)			
No GCA (n=18)	7	11	Sp 61% (39-80)				1	17	Sp 94% (74-100)			

Table 1 Diagnostic performance in terms of sensitivity and specificity (95% CI) for (1) gestalt assessment (2) total vascular score and (3) highest cranial artery SULmax.

BREAKOUT SESSION: CELLULAR AND MOLECULAR MECHANISMS OF DISEASE (II)

O-064

Lung Granulomas in Murine GPA are Induced by MPO-ANCA and Begin as Microabscesses that Evolve into Granulomas

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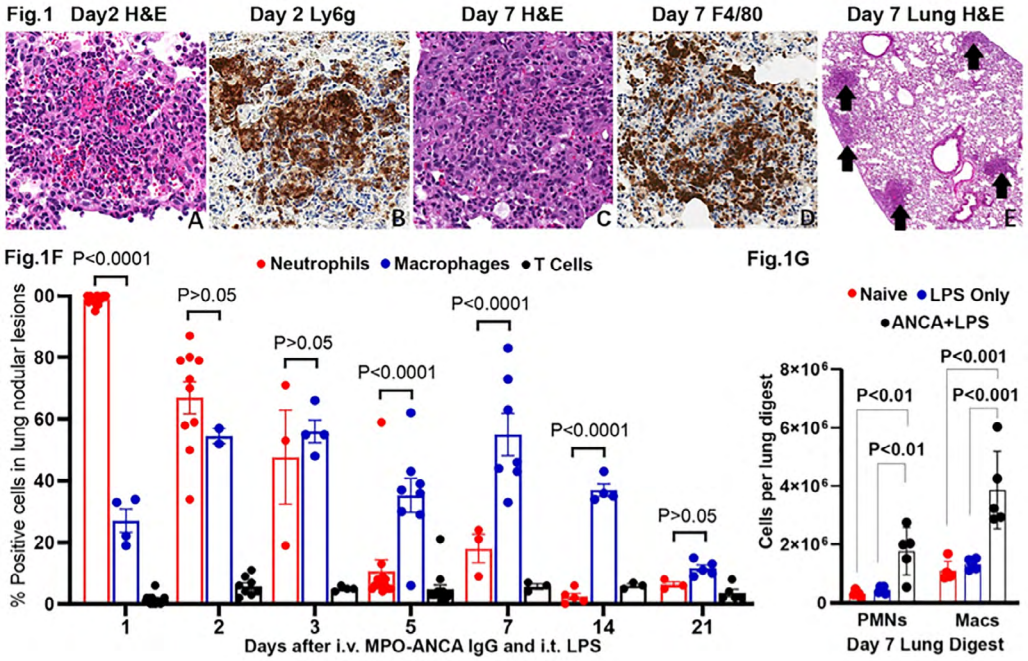
Background/Objectives: The association of ANCA with the pathogenesis of GPA granulomatosis has not been elucidated. Both myeloperoxidase (MPO)-specific autoantibodies and MPO-specific T cells have been incriminated. Our objective was to document that MPO-ANCA IgG (even in the absence of functional T cells) can induce lung granulomatosis, and to understand the pathogenic mechanisms.

Methods: B6 wild type (WT) mice received i.v. ANCA specific for myeloperoxidase (MPO-ANCA) IgG on day 0 and day 1, and intratracheal (i.t.) lipopolysaccharide (LPS) on day 0. Pairs of mice were euthanized on days 1, 2, 3, 5, 7 14 and 21; and lung and kidney tissue obtained for pathologic evaluations. Lung neutrophil, macrophage and T cells in lung lesions were evaluated by light microscopy and immunohistochemistry (IHC) using antibodies for neutrophils (NIMP-R14 and Ly6g), macrophages (F4/80), and T cells (CD3). Quantitative image analysis was performed on discrete lesions using Definiens Architect XD 64. Lungs harvested on day 7 from another group of mice with similarly induced GPA (n=5), LPS only mice (n=5), or naive mice (n=5) were digested to release leukocytes for flow cytometry using markers for lung alveolar, interstitial, and inflammatory macrophages; neutrophils (including Siglec F+ neutrophils), and lymphocytes. Another group of 4 recombination activating gene 2 protein knockout (Rag2 KO) mice received i.v. MPO-ANCA x 2 +i.t. LPS and were evaluated on day 7 for kidney and lung disease.

Results: By day 7, all WT and Rag2 KO mice that received double dose MPO-ANCA IgG and i.t. LPS developed glomerulonephritis (GN) and lung granulomatosis. IHC demonstrates lesion progression from microabscesses to granulomas. Figure 1 shows a day 2 microabscess (A, B), a Day 7 granuloma C&D), and multiple day 7 low magnification granulomas (E, arrows). Fig. 1F shows quantitative IHC data demonstrating that discrete lung lesions at day 1 and 2 contained predominantly neutrophils (C/W microabscesses), with macrophages becoming predominant by day 5 (C/W granulomas). Inflammation (i.e. number of leukocytes) remitted at later time points and replaces with fibrosis as serum MPO-ANCA declined. Flow cytometry of leukocytes from 7 day GPA whole lungs digests confirmed a predominance of macrophages (Fig. 1G), especially inflammatory macrophages versus alveolar or interstitial macrophages (data not shown). Siglec F+ neutrophils were only detected in lungs with late phase granulomas (data not shown). Rag2 KO mice with no functioning T cells developed NCGN and lung granulomatosis no different than WT mice.



Conclusions: A mouse model of GPA shows that lung granulomatosis can be induced by MPO-ANCA IgG, and that the lesions begin as capillaritis and microabscesses, and quickly evolve into granulomas within 7 days. T cells are not required at sites of granuloma formation.

Disclosures: None.

O-065

Neutrophil proteases and free fatty acids mediate giant cell and granuloma formation in GPA: implications for therapy

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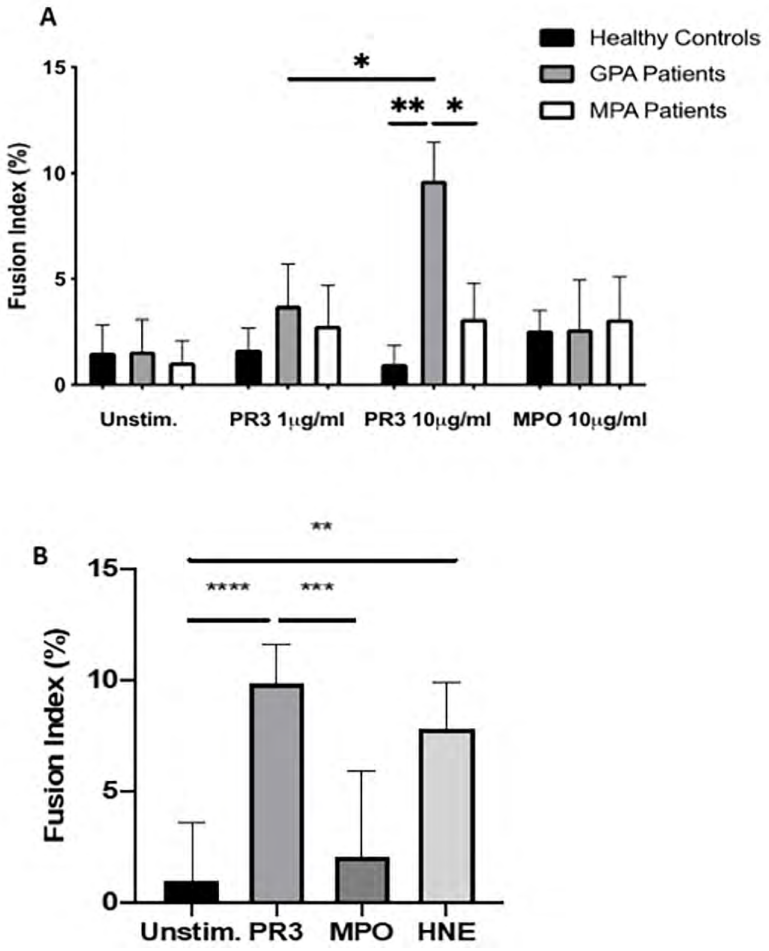
Background: Granulomatosis with Polyangiitis (GPA) and microscopic polyangiitis (MPA) are autoimmune vasculitides associated with anti-neutrophil cytoplasm antibodies (ANCA) that target proteinase-3 (PR3) or myeloperoxidase (MPO) found within neutrophils and monocytes. Granuloma are exclusively found in GPA, and form around multinucleate giant cells (MGC), at sites of microabscesses, containing apoptotic and necrotic neutrophils. Some monocyte proteins and cytokines are known to be fusogenic for MGC. We investigated the role of PR3, elastase and their receptors as well as free fatty acids and CD36 in stimulating giant cell and granuloma formation.

Methods: We stimulated purified monocytes and whole peripheral blood mononuclear cells from patients with GPA, MPA or healthy controls with PR3, elastin, MPO or palmitic acid (a free fatty acid) and visualised multinucleate giant cell and granuloma-like structure formation using light-, confocal- and electron-microscopy, as well as measuring cell cytokine production. We investigated expression of PR3 and free fatty acid binding partners on monocytes and tested the impact of their inhibition. Finally, we injected zebrafish with PR3 and characterised granuloma formation in a novel animal model.



Results: I*n vitro*, PR3 and elastase, but not MPO, promoted monocyte-derived MGC formation using cells from GPA- but not from MPA-patients (Figure), and this was dependent on soluble IL-6, as well as monocyte MAC-1 and protease activated receptor-2 (PAR-2), found to be overexpressed on GPA patients' cells. Additionally, Palmitic acid binding CD36, which was overexpressed on patients monocytes and found at higher levels in the sera of GPA patients, mediated MGC formation but stimulated Macrophage Inhibition Factor production rather than IL-6. PBMCs stimulated by PR3, formed granuloma-like structures with central MGC surrounded by T cells. This effect of PR3 was confirmed *in vivo* using Zebrafish and was inhibited by niclosamide, a STAT3-IL-6 pathway inhibitor.

Conclusions: Neutrophil proteases and fatty acids promote MGC and granuloma formation in GPA patients, who have increased levels of PR3 binding partners and CD36 on their. These data provide a mechanistic understanding of granuloma formation in GPA and a rationale for novel therapeutic approaches targeting IL-6 and MIF.

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Disclosures: None.

O-066

Human MPO-ANCA induces crescentic glomerulonephritis in mice expressing human MPO and FcγRIIa

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Background/Objectives: Polyclonal mouse anti-mouse myeloperoxidase (MPO) ANCA-like antibodies, raised in *Mpo*$^{-/-}$ mice, induce glomerulonephritis when injected into naïve mice. However, *in vivo* experimental evidence for a pathogenic role of human MPO (hMPO) ANCA in ANCA-associated vasculitis (AAV) is lacking. We hypothesized that hMPO-ANCA would induce nephritis in humanized mice knocked in for hMPO and hPR3 and transgenic for human FcγRIIa (with intact mouse FcγRs).

Methods: Immunoglobulin G (IgG) fractions were purified from first plasma exchange effluents of 7 patients with active MPO-AAV and high titres of MPO-ANCA. Neutrophils from healthy individuals were treated with cytochalasin C and tumor necrosis factor, then stimulated with either control human IgG or MPO-AAV patient IgG. Neutrophil reactive oxygen species (ROS) production was assessed by flow cytometry. For *in vivo* experiments, mice were primed with granulocyte-colony stimulating factor (G-CSF, 6 mg daily s.c. for 6 days, beginning 3 days prior to IgG transfer). Female hMPO.hPR3.hFcγRIIa mice (N=9) were injected i.v. with a patient hMPO-ANCA IgG fraction on day 0 (and 1 hour later, lipopolysaccharide [LPS] 0.5mg/g, i.p.), and day 1 (3.2mg IgG/dose). Control mice (N=3) received G-CSF, LPS and the same doses of control human IgG. Experiments ended 6 days after hMPO-ANCA or control IgG injection. A glomerular crescent was defined as two or more layers of cells in Bowman's space.

Results: Primed neutrophils produced more ROS after stimulation with 4 of 7 patient IgG samples (mean fluorescence intensity [MFI] of 4 positive samples 3137), compared with control IgG (MFI 208). The MPO-ANCA IgG fraction inducing the highest ROS production (MFI 7203) was selected for *in vivo* experiments. Six days after MPO-ANCA injection, all hMPO-ANCA treated mice developed crescentic glomerulonephritis, with 15±4% (mean±SD) of glomeruli developing crescents. Control mice did not develop glomerular disease. All hMPO-ANCA treated mice developed (dipstick positive) microscopic hematuria, but no control mouse was urinary dipstick positive for blood. Mice receiving MPO-ANCA developed albuminuria (urine albumin:creatinine ratio 72.7±68.1 vs 6.4±3.1 µg/µmol, $P<0.05$). Serum urea was higher in hMPO-ANCA treated mice (15.6±1.8 vs 12.1±0.9 mmol/L, $P<0.05$).

Conclusions: Human MPO ANCA induces glomerulonephritis in mice expressing hMPO and hFcγRIIa, demonstrating the in vivo pathogenicity of hMPO-ANCA. This humanized MPO-AAV model may be useful in further dissecting the nature of the pathogenicity of hANCA, its associated injury and potential therapeutic targets.

Disclosures: MHD received National Health and Medical Research Council (NHMRC) Scholarship (2022102). ARK has received NHMRC Investigator and EU grants (2008921, 1115805). The work was initiated as part of the EU RELENT Horizon 20/20 consortium (ARK). ARK has received lecture fees from Vifor Pharma and research funding from Vifor Pharma, Visterra, Toleranzia, Variant Bio and CSL Ltd.

O-067

The sequential carbonyl derivatives and hydrazones adduct formation on myeloperoxidase contribute to development of auto-antigenicity

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Background/objectives: Hydralazine exposure, an anti-hypertensive agent and a carbonyl scavenger, is associated with the development of ANCA vasculitis[1]. We propose a pathogenic mechanism for hydralazine associated ANCA vasculitis hinging on formation of hydrazones adduct on myeloperoxidase (MPO), the primary immunogen for MPO ANCA[2].

Methods: *In vitro* hydralazine studies were performed using horse heart metmyoglobin (Mb) and human MPO. Hydralazine modified Mb was digested by trypsin and peptides were analyzed with reverse phase HPLC and electrospray mass spectrometry. In addition, hydralazine modified MPO was separated using PAGE gels and the hydrazones adduct was detected using an anti-hydralazine antibody. Commercially anti-MPO antibodies recognizing different portions of MPO were used to investigate the conformational change of the MPO heavy chain after hydralazine modification. In addition, an immunoprecipitation assay was performed to detect hydrazones adduct on circulating MPO from patients. Furthermore, anti-MPO IgM and IgG antibodies were measured using ELISAs. Purified IgM and IgG from patients and healthy controls' plasma were investigated their ability to recognize control MPO or hydralazine modified MPO.

Results: *In vitro* studies showed that carbonyl derivatives formation on primary amines of a protein in the presence of aldehydic products, such as acrolein, is required for hydralazine to bind a protein. Mass spectrometry data showed that hydralazine bound to a carbonyl group of Mb. Under similar conditions, hydrazones adduct was formed on MPO. Importantly, the hydrazones adduct on MPO could be detected in plasma from hydralazine associated ANCA patients but not from patients with non-hydralazine associated ANCA patients or healthy subjects. Using multiple commercially available anti-MPO antibodies, we demonstrated that hydrazones adduct formation on MPO resulted in conformational changes. In addition, purified IgG and IgM autoantibodies from hydralazine associated ANCA patients were reactive against hydralazine modified MPO.

Conclusions: Under appropriate reactive conditions, hydrazones adduct was able to be formed on MPO in some subjects who were exposed to hydralazine. In addition, hydrazone adduct induced MPO conformational changes. These changes may facilitate autoantibody generation, leading to hydralazine associated ANCA vasculitis.

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Disclosures: None.

O-068

Isolation and profiling of auto-antigen-specific B cells in MPO-ANCA Vasculitis

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Background/ Objectives: Treatments targeting B cells are highly effective in ANCA vasculitis, though we do not know how long or if all B cells need to be eliminated for effective maintenance of remission. Autoantigen specific cells are a small but key subset of lymphocytes in the ANCA immune response. We hypothesized that circulating antigen-specific B cells can be isolated to profile relevant B-cell receptors (BCR) in patients with MPO-ANCA vasculitis. Identifying recurrence of autoantigen specific B cells would allow clinicians to monitor patients at risk for disease relapse and target therapy only with occurrence of pathogenic B cells, thus mitigating risk of infection or off-target effects.

Methods: Peripheral blood mononuclear cells (PMBCs) were isolated from healthy individuals and patients with active MPO-ANCA vasculitis (identified by clinician review and defined by biopsy proven organ involvement or BVAS>0 at time of sample and elevated MPO-ANCA titers). Fluorescent MPO tetramers were validated for specificity to isolate MPO-specific cells. Control tetramers were used to exclude binding to any non-MPO tetramer component. Thawed cryopreserved PBMCs were incubated with tetramers and enriched for fluorophore -binding cells prior to flow cytometry sorting to obtain MPO-tetramer positive (Tpos) cells. Control populations included MPO-tetramer negative cells (Tneg) and B cells recovered from residual fluorophore-negative cells (Aneg). Cells were expanded *in vitro* with antigen stimulation and underwent RNA isolation for library preparation and bulk BCR sequencing (Illumina MiSeq). A sensitive ELISA assay was developed to test MPO-ANCA IgG in culture supernatant.

Results: PBMCs cultured with MPO for 14 days could maintain and increase MPO-specific cells (Fig 1A). Cryopreserved PBMCs from four patients with active disease and three healthy individuals were used to isolate and expand cells *in vitro*. Cell culture supernatants from *in vitro* expanded Tpos cells from patients had higher levels of anti-MPO IgG compared to other cell subsets (Tneg and Aneg) and healthy individuals (Fig 1B). Antigen specific B cells (Tpos) did not share significant sequence overlap with Tneg or Aneg control populations. In the MPO-specific (Tpos) B cell population, patient samples were found to have more sequence (complementarity determining region, CDR3) overlap compared to samples from healthy individuals (Fig 1C) as reflected in higher Morosita-Horn overlap index scores.

Conclusions: MPO tetramers can be used to isolate autoantigen specific B cells in patients with vasculitis. B cell repertoire results are consistent with clonal expansion in MPO-specific B cells (Tpos) cells and CDR3 overlap in MPO patients but not healthy individuals. Additional single cell sequencing from patients during active disease and remission will yield repertoire information to identify shared clonotypes to monitor disease specific B cell activity and guide therapy.

Disclosures: None.

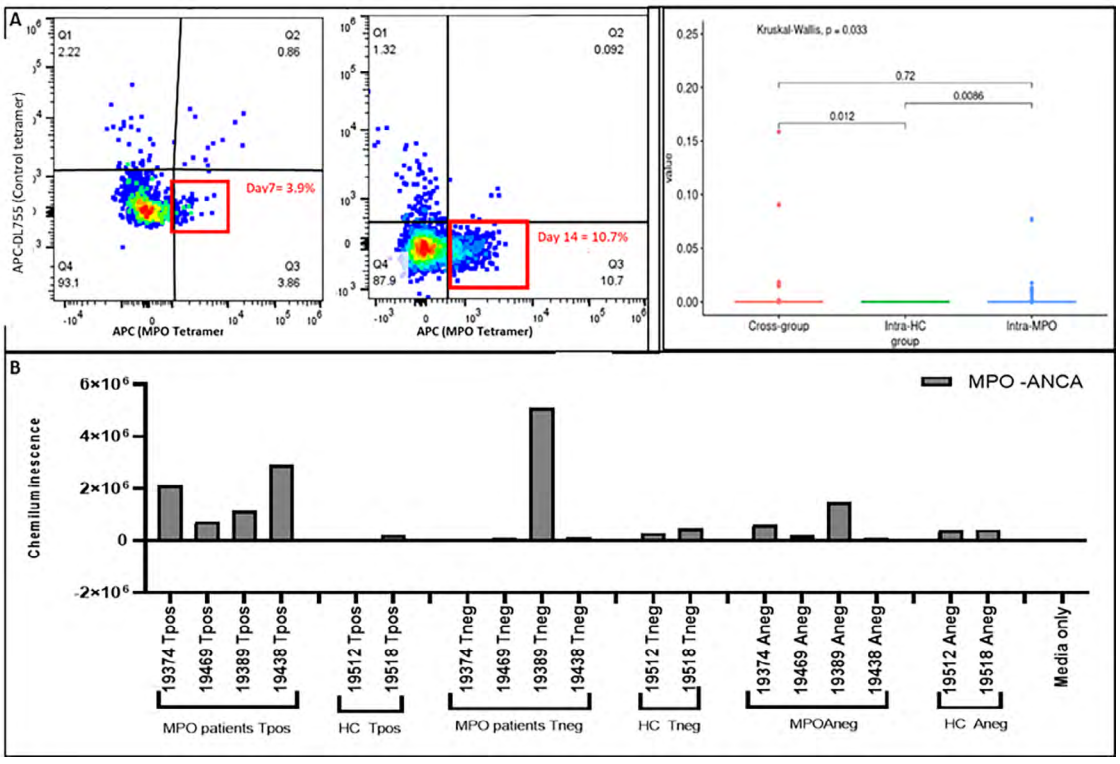

Figure. A) *In vitro* expansion of MPO-positive B cells B) MPO-ANCA in culture supernatant C) CDR3 overlap in healthy controls (HC) and ANCA vasculitis patients (MPO) by Morosita-Horn overlap index.

O-069

Unraveling the Impact of TSST-1 on T and B Cell Responses in Granulomatosis with Polyangiitis: Insights into Disease Pathogenesis and Progression

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Background/ Objectives: Granulomatosis with polyangiitis (GPA) is a systemic relapsing auto-immune vasculitis, associated with anti-neutrophil cytoplasmic autoantibodies (ANCAs) directed against proteinase-3 (PR3). While the cause of the disease and relapse remains elusive, previous studies have demonstrated the association between staphylococcal superantigens, predominantly toxic shock syndrome toxin-1 (TSST-1), and the highest risk of relapse (1, 2). However, the extent to which TSST-1 contributes to GPA pathogenesis is currently unknown. Here, we assessed the impact of TSST-1 on T and B cell responses in GPA patients.

Methods: The frequency and the phenotypic characteristics of TSST-1-reactive Vβ2 Th-cells were analyzed by flowcytometry in peripheral blood mononuclear cells (PBMCs) isolated from 63 GPA patients in remission, of whom 30 S. aureus carriers (SA+) and 33 non-carriers (SA-) patients, along with 24 age- & sex-matched healthy controls (HCs). To evaluate the impact of TSST-1 on Th cell response, patient's PBMCs were stimulated *in vitro* with either TSST-1 or other SA-virulence factors (SEA, SEB, PGN, LTA), and intracellular cytokine production (IL-4, IFN-γ, IL-17, IL-21) was assessed in CD4 Th-cells using fluorescent barcoding assay. For assessing the impact of TSST-1 on B cell response, a fraction of cells was stimulated with TSST-1 in the presence of BAFF for 14 days, and IgG and ANCA production was measured in culture supernatants by ELISA and Phadia EliA, respectively. Additionally, levels of anti-TSST-1 antibodies and total IgG were measured in plasma using ELISA.

Results: Frequencies of circulating TSST-1-reactive Vβ2+ Th-cells were significantly higher in both SA- and SA+ GPA-patients compared to HCs. These Vβ2+ Th-cells exhibit markers of effector memory cells (CD45RO+CCR7-). Upon in vitro stimulation, frequencies of IL-4, IFN-γ, IL-17, and IL-21 producing Th cells in response to SEA, SEB, PGN, LTA were similar between SA+ and SA- patients. Notably, a significant increase in the frequency of IL-21- producing Th-cells in response to TSST-1 was observed in SA+ GPA-patients compared to SA- GPA-patients. Importantly, TSST-1 induced the production of both IgG and PR3-ANCA in vitro. Meanwhile, the levels of anti-TSST-1 antibodies were significantly decreased in the plasma of SA+ GPA-patients, compared to those in HCs.

Conclusions: GPA-patients have an inadequate humoral immune response to TSST-1, which hampers the ability to eliminate this superantigen. The persistence of TSST-1 may subsequently contribute to the production of ANCAs by inducing IL-21 secretion in Th cells, thereby promoting disease progression and severity in patients with GPA.

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Disclosures: None.

BREAKOUT SESSION: PEDIATRIC VASCULITIS

O-070

ANCA-Associated Vasculitis at Children's Hospital Colorado: Pediatric Patient Characteristics, Clinical Course, and Outcomes

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Background/Objectives: Anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV) is an understudied, chronic inflammatory disease in children with significant morbidity and mortality. There are few large pediatric cohorts described and no large observational studies or randomized controlled trials to guide management. Our hospital serves the vasculitis community across a seven state catchment area in the United States.

Methods: Retrospective chart review was completed using electronic medical records of patients managed from 2002-2023 at a single institution. Patients diagnosed with AAV at less than 18 years old were identified using ICD-9 and -10 diagnosis codes and confirmed based on provider documentation. Data was manually entered into a HIPPA-compliant REDcap database. Descriptive statistics were then completed to determine means and proportions.

Results: There were 91 children with AAV identified, 62 (68.1%) with granulomatosis with polyangiitis (GPA) and 29 (31.9%) with microscopic polyangiitis (MPA) (**Table 1**). 8 patients had eosinophilic GPA and were not included for analysis. 74 of the children identified were diagnosed after 2010. The cohort is demographically diverse with a mean age of 13.6 years at diagnosis. The majority were female. Many patients were severely ill with diffuse alveolar hemorrhage (43.8%), glomerulonephritis (59.6%), and airway stenosis (11.8%) and required mechanical ventilation (17.6%) and dialysis (27.5%). Lab abnormalities were common. Many patients underwent chest CTs (62.9%) and tissue biopsies, including lung (9%), sinus (6.7%), and renal (45.5%) biopsies. Almost all patients received rituximab (93.3%) while cyclophosphamide (43.3%), azathioprine (37.8%), and mycophenolate (21.3%) were also received. Proportions were also determined for those with GPA only and MPA only.

Conclusions: This is one of the largest described single center cohorts of children diagnosed with AAV in the world. Many children presented with severe manifestations including diffuse alveolar hemorrhage, glomerulonephritis, and airway stenosis requiring intubation and dialysis. Future studies will compare these results to the international pediatric and adult literature, assess the fit of classification criteria, and assess management trends over time. More research efforts must be dedicated to the pediatric vasculitis community moving forward.

References: None.

Table 1. Characteristics, Clinical Course, and Outcomes for Patients Diagnosed with ANCA-Associated Vasculitis in Childhood at Children's Hospital Colorado

	ANCA-Associated Vasculitis Disease Type		
Characteristic	**All N = 91**	**Granulomatosis with Polyangiitis N = 62**	**Microscopic Polyangiitis N = 29**
	Mean (standard deviation) or n (percentage)		
Age at diagnosis	13.6 (2.8)	14.2 (2.1)	12.5 (3.7)
Sex (Female)	56 (61.5%)	30 (48.4%)	26 (89.7%)
Ethnicity			
Hispanic or Latino	17 (18.7%)	5 (8.1%)	12 (41.4%)
Not Hispanic or Latino	73 (80.2%)	57 (91.9%)	16 (55.2%)
Not Reported	1 (1.1%)	0 (0.0%)	1 (3.4%)
Race			
Caucasian/White	71 (78.0%)	51 (82.3%)	20 (69.0%)
Black/African American	2 (2.2%)	2 (3.2%)	0 (0.0%)
Native American/Alaskan	4 (4.4%)	2 (3.2%)	2 (6.9%)
Asian/Pacific Islander	3 (3.3%)	2 (3.2%)	1 (3.4%)
Other	9 (9.9%)	4 (6.5%)	5 (17.2%)
More than one race	2 (2.2%)	1 (1.6%)	1 (3.4%)
ANCA-associated vasculitis subtype			

Characteristic	ANCA-Associated Vasculitis Disease Type		
	All N = 91	Granulomatosis with Polyangiitis N = 62	Microscopic Polyangiitis N = 29
	Mean (standard deviation) or n (percentage)		
Granulomatosis with Polyangiitis	62 (68.1%)	-	-
Microscopic Polyangiitis	29 (31.9%)	-	-
ANCA status			
Positive	90 (98.9%)	61 (98.4%)	29 (100.0%)
Negative	1 (1.1%)	1 (1.6%)	0 (0.0%)
ANCA antibody subtype			
Cytoplasmic-ANCA	59 (66.3%)	57 (93.4%)	2 (7.1%)
Missing (N)	2	1	1
Perinuclear-ANCA	32 (35.6%)	4 (6.6%)	28 (96.6%)
Missing (N)	1	1	0
Anti-serine protease 3	55 (64.0%)	55 (93.2%)	0 (0.0%)
Missing (N)	5	3	2
Anti-myeloperoxidase	34 (39.5%)	7 (12.1%)	27 (96.4%)
Missing (N)	5	4	1
Presenting Symptoms			
Fever	43 (49.4%)	36 (58.1%)	7 (28.0%)
Missing (N)	4	0	4
Arthritis	47 (54.7%)	41 (66.1%)	6 (25.0%)
Missing (N)	5	0	5
Rash	32 (37.6%)	28 (45.9%)	4 (16.7%)
Missing (N)	6	1	5
Nasal or Oral Ulcers	13 (15.3%)	13 (21.3%)	0 (0.0%)
Missing (N)	6	1	5
Cough	52 (60.5%)	41 (67.2%)	11 (44.0%)
Missing (N)	5	1	4
Dyspnea	43 (51.2%)	32 (55.2%)	11 (42.3%)
Missing (N)	7	4	3
Sinusitis	31 (37.3%)	27 (45.7%)	4 (16.7%)
Missing (N)	8	3	5
Scleritis/Episcleritis	15 (17.9%)	12 (20.0%)	3 (12.5%)
Missing (N)	7	2	5
Weight Loss	39 (52.7%)	32 (57.1%)	7 (38.9%)
Missing (N)	17	6	11
Diffuse Alveolar Hemorrhage	39 (43.8%)	32 (52.5%)	7 (25%)
Missing (N)	2	1	1
Hemoptysis	24 (66.7%)	20 (69.0%)	4 (57.1%)
Missing (N)	55	33	22
Glomerulonephritis	53 (59.6%)	29 (48.3%)	24 (82.8%)
Missing (N)	2	2	0
Sinusitis	43 (48.3%)	38 (62.3%)	5 (17.9%)
Missing (N)	2	1	1
Airway Stenosis	10 (11.8%)	10 (17.5%)	0 (0.0%)
Missing (N)	6	5	1
Laboratory Evaluation at Presentation			

Characteristic	ANCA-Associated Vasculitis Disease Type		
	All N = 91	Granulomatosis with Polyangiitis N = 62	Microscopic Polyangiitis N = 29
	Mean (standard deviation) or n (percentage)		
Anti-GBM antibody	2 (6.1%)	0 (0.0%)	2 (18%
Missing (N)	58	40	18
Leukocytosis	53 (60.2%)	41 (68.3%)	12 (42.9%)
Missing (N)	3	2	1
Anemia	61 (68.5%)	40 (65.6%)	21 (75.0%)
Missing (N)	2	1	1
Thrombocytosis	21 (23.9%)	17 (28.3%)	4 (14.3%)
Missing (N)	3	2	1
Elevated erythrocyte sedimentation rate	80 (92.0%)	55 (90.2%)	25 (96.2%)
Missing (N)	4	1	3
Elevated c-reactive protein	68 (87.2%)	54 (91.5%)	14 (73.7%)
Missing (N)	13	3	10
Elevated creatinine	53 (59.6%)	30 (49.2%)	23 (82.1%)
Missing (N)	2	1	1
Hematuria	72 (80.0%)	47 (75.8%)	25 (89.3%)
Missing (N)	1	0	1
Proteinuria	67 (76.1%)	42 (70.0%)	25 (89.3%)
Missing (N)	3	2	1
Imaging and Diagnostic Procedures			
Chest X-ray	86 (95.6%)	60 (98.4%)	26 (89.7%)
Missing (N)	1	1	0
Chest CT	56 (62.9%)	45 (73.8%)	11 (39.3%)
Missing (N)	2	1	1
Sinus CT	25 (28.4%)	24 (39.3%)	1 (3.7%)
Missing (N)	3	1	2
Renal Ultrasound	48 (55.2%)	26 (43.3%)	22 (81.5%)
Missing (N)	4	2	2
Echocardiogram	46 (52.3%)	25 (41.7%)	21 (75.0%)
Missing (N)	3	2	1
Bronchoscopy/Alveolar Lavage	22 (24.7%)	18 (29.5%)	4 (14.3%)
Missing (N)	2	1	1
Lung Biopsy	8 (9.0%)	5 (8.2%)	3 (10.7%)
Missing (N)	2	1	1
Sinus Biopsy	6 (6.7%)	6 (9.8%)	0 (0.0%)
Missing (N)	2	1	1
Renal Biopsy	40 (45.5%)	19 (31.7%)	21 (75.0%)
Missing (N)	3	2	1
Management			
Rituximab	83 (93.3%)	57 (93.4%)	26 (92.9%)
Missing (N)	2	1	1
Cyclophosphamide	39 (43.3%)	25 (41.0%)	14 (48.3%)
Missing (N)	1	1	0
Azathioprine	34 (37.8%)	18 (29.5%)	16 (55.2%)
Missing (N)	1	1	0

Characteristic	ANCA-Associated Vasculitis Disease Type		
	All N = 91	**Granulomatosis with Polyangiitis N = 62**	**Microscopic Polyangiitis N = 29**
	Mean (standard deviation) or n (percentage)		
Mycophenolate Mofetil/Mycophenolic Acid	19 (21.3%)	6 (9.8%)	13 (46.4%)
Missing (N)	2	1	1
Plasmapheresis	25 (28.0%)	19 (31.1%)	6 (21.4%)
Missing (N)	2	1	1
Dialysis	25 (27.5%)	11 (17.7%)	14 (48.3%)
Missing (N)	0	0	0
Mechanical Ventilation	16 (17.6%)	13 (16.7%)	3 (9.7%)
Missing (N)	0	0	0
*Alive**			
Yes	65 (71.4%)	44 (71.0%)	21 (72.4%)
No	2 (2.2%)	1 (1.6%)	1 (3.4%)
Lost to follow-up	25 (26.4%)	17 (27.4%)	7 (24.1%)
*Remission Status**			
Yes	55 (60.4%)	38 (61.3%)	17 (58.6%)
No	21 (23.1%)	17 (27.4%)	4 (13.8%)
Lost to follow-up	15 (16.5%)	7 (11.3%)	8 (27.6%)

Abbreviations: anti-neutrophil cytoplasmic antibody, ANCA; glomerular basement membrane (GBM).

*At time of data collection.

O-071

Clinical course of pediatric-onset Behçet's Disease in young adulthood

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Background/ Objectives: Although Behçet's disease (BD) onset is in the second or third decade, the first symptoms may occur at an earlier age. It may take a longer time for a full disease phenotype development after the first symptom starts in pediatric Behçet's patients. In this study we aimed to assess the clinical course of pediatric onset BD in adulthood period.

Methods: 112 patients diagnosed with BD before the age of 18 from five tertiary clinics were retrospectively assessed. Demographic and clinical characteristics, follow-up and treatment data of the patients were acquired from files. Patients with a follow-up of less than six months were excluded.

Results: Ninety-three patients with pediatric-onset BD were included; 64.5% (n = 60) of the patients were male. The median age of diagnosis was 15 years (4–17), and the median age of the first symptom was 14 years (1–17). Recurrent oral aphtosis is the most common clinical manifestation (96.7%). Major organ involvement was present in 52.5% (n = 49) of the patients. The most commonly affected organ is the eye (n=27). Vascular involvement was observed to be more common in males (28.3%, n = 17) than females (9.1%, n = 3)(p = 0.031).

Sixty-eight (73.1%) patients had follow-up data for a median of 47 months (1–200) in adulthood. At pediatric period, 40 (58.8%) of these patients had only mucocutaneous findings, while 28 (41.2%) patients experienced organ involvement (Table 1).

Major organ involvement developed in 15 (53.3% were male) of 40 patients mean 10.1 (±2.06) years after diagnosis, who had only mucocutaneous findings during pediatric follow-up.

Twenty-eight patients (41.1%) experienced major organ involvement during the pediatric period. During adulthood follow-up, 12 (42.8%) patients developed new major organ involvement and/or relapse of the same organ.

Conclusions: Our results show that more than one-third (39.7%) of pediatric-onset Behcet's patients still have signs of active disease (either relapse or new major organ development) in adulthood.

Disclosures: None.

Table 1: Disease course of pediatric-onset Behçet's patients followed in adulthood.

Patients followed in adulthood	**n=68 (%)**
Major organ involvement in childhood	28 (41.2%)
Relapse or/and new major organ involvement *No relapse or major organ involvement*	*12 (17.7%)* *16 (23.5%)*
Mucocutaneous disease in childhood	40 (58.8%)
New major organ involvement *No major organ involvement*	*15 (22.1%)* *25 (36.7%)*

O-072

HLA class I and II gene polymorphisms in childhood IgA vasculitis

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Background/ Objectives: IgA vasculitis (IgAV) is a small vessel vasculitis occurring predominantly in childhood. Studies concerning the genetic background of IgAV have confirmed that susceptibility to the disease may be influenced by Human Leukocyte Antigens (HLA), with HLA-DRB1 gene showing a strong association with the disease. The objective of this study was to investigate HLA-A, -B and -DRB1 polymorphisms in Croatian patients with IgAV.

Methods: 130 children with IgAV and 202 unrelated healthy individuals were enrolled in study. Genomic DNA was extracted from whole peripheral blood in patients and controls. The HLA-DRB1 genes were analysed using the Next Generation Sequencing (NGS) method, while HLA-A, B and DQB1 polymorphisms were determined by polymerase chain reaction methods in combination with oligonucleotides specific for HLA allelic groups (PCR-SSO).

Results: There were 71 girls and 59 boys with IgAV with median age 6.3 (4.4-8.1) years at the time of diagnosis. All patients had purpuric rash, 108 (83.1%) patients had affected musculoskeletal system, 50 (38.5%) patients had gastrointestinal (GI) system involvement, while 39 (30.0%) patients developed IgA vasculitis nephritis (IgAVN). HLA-A*03 (21.4% vs. 12.38%, p=0.009), HLA-B*37 (2.9% vs. 0.2%, p=0.005) and HLA-DRB1*12 (3.1% vs. 0.7%, p=0.022) alleles were significantly more frequent in IgAV than in controls. High-resolution typing revealed significantly higher frequency of HLA-DRB1*10:01 among IgAV patients with GI involvement in comparison to controls (6.5% vs. 1% p=0.002, CI 1.3%-14.5%) and patients without GI manifestations of the disease (6.5% vs. 0%, p=0.005, CI 1.5%-15.5%). HLA-DRB1*11:03 was also significantly frequent in patients with IgAV who developed GI manifestations compared to control group (3.2% vs. 0.5%, p=0.031, CI 0.1%-10.5%). HLA-DRB1*14:01P occurred significantly more often in the group of patients with IgAVN in comparison with controls (17.5% vs. 4.5%, p<0.001, CI 3.9%-27.6%) and IgAV patients without nephritis (17.5% vs. 5.8%, p=0.024, CI 1.2%-26.4%).

Conclusions: There is an association of HLA-A*03, HLA-B*37 and HLA-DRB1*12 alleles with susceptibility to IgAV in the investigated Croatian pediatric population. Different genes of HLA-DRB1 loci showed an association with the clinical manifestations of the disease itself. Studies aimed at determining the HLA profile may contribute to elucidation of genetic background of IgAV.

SUPPORT: Croatian Science Foundation Project IP-2019-04-8822.

References: Sapina M, Frkovic M, Sestan M et al. Geospatial clustering of childhood IgA vasculitis and IgA vasculitis-associated nephritis. Ann Rheum Dis. 2021; 80(5): 610-6.

Disclosures: None.

O-073

Kidney transplantation in chilldhood-onset ANCA-associated vasculitis: outcomes of a multicentre cohort

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Background: ANCA-associated vasculitis (AAV) is rare among children but may lead to kidney failure in ~30% of cases.[1] Kidney transplantation (KT) is widely performed among adults with AAV while data on children are scarce.[2,3] We report the outcome of KT in a multicentre cohort of recipients with childhood-onset AAV.

Method: Patients with AAV diagnosed at the age ≤18 years who received a KT were identified from databases of one Canadian, one Chinese and 22 European centres. We determined patient and graft survival and the frequency of chronic graft dysfunction (eGFR <60 mL/min), post-transplant AAV relapse, rejection, and infections and analysed predictors of outcome. Eighteen patients had already been reported in previous articles;[1,2] their follow-up was extended and further relevant data retrieved.

Results: We included 72 patients, of whom 53 (74%) had microscopic polyangiitis (MPA) and 19 (26%) granulomatosis with polyangiitis (GPA). The median age at diagnosis and transplantation was 12 (interquartile range, IQR 9-14) and 14 (IQR 11-16) years respectively (**Table**). At the time of transplantation, all patients were in remission and 15/72 (21%) had positive ANCA.

The median follow-up after transplantation was 53 months (IQR 25-95). Seventy patients (97%) were alive at last visit and death-censored graft survival was 86%, while 28/72 (39%) developed chronic graft dysfunction. AAV relapse occurred in 8/72 (11%) a median of 71 months (IQR 30-100) after transplantation and 5/8 (62%) had positive ANCA at transplantation. Graft involvement was observed in 6/8 (75%), which lead to graft loss in 2/6. Acute rejection occurred in 26/72 patients (36%) and was consistent with T cell-mediated rejection in 23/26 (88%). Neither the diagnosis of MPA vs GPA nor the type of ANCA, ie MPO vs PR3, were

Table Main features of patients included

	All N=72	MPA N=53	GPA N=19	P value GPA vs MPA
Demographics				
Female, n (%)	52 (72)	40 (75)	12 (63)	0.37
Caucasian, n (%)	50 (69)	34 (64)	16 (84)	0.14
Age at diagnosis, median (IQR) - years	12 (9-14)	12 (9-14)	12 (10-14)	0.77
ANCA, n (%)				
P-ANCA/MPO ANCA, n (%)	47 (65)	44 (83)	3 (16)	**<0.001**
C-ANCA/PR3 ANCA, n (%)	19 (27)	5 (5)	14 (74)	**<0.001**
Negative, n (%)	3 (4)	2 (4)	1 (5)	1
Pre-transplant immunosuppressive therapy				
Cyclophosphamide, n (%)	59 (82)	43 (81)	16 (84)	1
Rituximab, n (%)	17 (24)	10 (19)	7 (39)	0.12
Other IS agent, n (%)	4 (6)	3 (6)	1 (5)	1
None/glucocorticoids only, n (%)	3 (4)	3 (6)	0	0.56
Time of transplantation				
Age, median (IQR) – years	14 (11-16)	14 (11-16)	14 (13-16)	0.56
Pre-emptive transplant, n (%)	2 (3)	1 (2)	1 (5)	0.46
Date of transplantation				
<2000, n (%)	8 (11)	6 (11)	2 (11)	1
2000-2010, n (%)	24 (33)	19 (36)	5 (26)	0.57
>2010, n (%)	40 (56)	28 (53)	12 (63)	0.59
ANCA at transplantation	N=69	N=50	N=19	
Negative, n (%)	54 (78)	37 (74)	17 (89)	0.20
Positive, n (%)	15 (22)	13 (26)	2 (11)	0.20
Type of donor				
Living, n (%)	25 (35)	17 (32)	8 (42)	0.57
Deceased, n (%)	47 (65)	36 (68)	11 (58)	0.57
Post-transplant immunosuppressive therapy				
GC-TAC-MMF, n (%)	43 (60)	33 (62)	10 (53)	0.58
GC-TAC-AZA, n (%)	13 (18)	7 (13)	6 (32)	0.09
GC-CyA-AZA, n (%)	3 (4)	2 (4)	1 (5)	1
Other, n (%)	8 (11)	7 (13)	1 (5)	0.67
Outcomes at last FU				
Alive, n (%)	70 (97)	52 (98)	18 (95)	0.46
Functioning graft, n (%)	62 (86)	45 (15)	17 (89)	1
Chronic graft dysfunction, n (%)	28 (39)	22 (41)	6 (32)	0.58
AAV relapse (cumulative), n (%)	8 (11)	4 (7)	4 (21)	0.19
Acute rejection (cumulative), n (%)	28 (39)	19 (36)	9 (47)	0.41
Infections (cumulative), n (%)	42 (59)	28 (53)	14 (21)	0.17

significantly associated with graft failure, rate of rejection and post-transplant AAV relapse, but ANCA positivity at transplantation showed a statistically significant association with post-transplant AAV relapse (p=0.004) and chronic graft dysfunction (p=0.002). Forty-two patients (59%) experienced infections, mainly bacterial urinary tract infections (17/42) and cytomegalovirus infections (11/42) of milder severity. Two patients died of infectious complications. Neither cardiovascular events nor cases of malignancy were reported.

Conclusion: We found a high patient and graft survival and a low rate of post-transplant AAV relapse in this large, multicentre cohort of KT recipients with childhood-onset AAV. Positive ANCA at transplantation seems associated with a higher risk of AAV relapse and chronic graft dysfunction.

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Disclosure: None.

BREAKOUT SESSION: ADVANCES IN TREATMENT (II)

O-074

Remission, Glucocorticoid Toxicity, Health-Related Quality of Life, and Safety Outcomes in Patients with ANCA-Associated Vasculitis with Kidney Involvement Treated with Avacopan

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Background/ Objectives: In the phase 3 ADVOCATE trial comparing avacopan to a prednisone taper, 81% of patients with anti-neutrophil cytoplasmic autoantibody (ANCA)–associated vasculitis (AAV) had kidney involvement based on the Birmingham Vasculitis Activity Score.[1] At baseline, this kidney subgroup had a mean estimated glomerular filtration rate (eGFR) of 45.1 mL/min/1.73 m^2.[1] The objective of this analysis was to evaluate efficacy and safety outcomes beyond eGFR and urinary albumin to creatinine ratio for patients with AAV with kidney involvement at baseline.

Methods: This post hoc analysis evaluated remission, glucocorticoid (GC) use, GC toxicity index (GTI), health-related quality of life (HRQoL by SF-36), and safety in patients with kidney involvement at baseline for those treated with avacopan (N=134) vs a prednisone taper (N=134).

Results: Compared with the overall study population, the mean age for the kidney subgroup was similar (62 vs 61 years), but there was a slightly higher proportion of patients with newly diagnosed AAV (74% vs 69%), myeloperoxidase+ ANCA (63% vs 57%), microscopic polyangiitis (52% vs 45%), and use of cyclophosphamide (39% vs 35%). The avacopan group achieved a higher sustained remission rate at week 52 (67.9% vs 56.7%) while receiving a 2.4-/5.3-fold less total GC dose (mean/median) than the prednisone taper group (**Table 1**). The GTI cumulative worsening and aggregate improvement scores were lower at weeks 13 and 26 in the avacopan group compared to the prednisone taper group. At weeks 26 and 52, the avacopan group reported a greater improvement in SF-36 physical and mental component summary scores compared with the prednisone taper group. Serious adverse events occurred in 46% (2 deaths) and 49% (3 deaths) of patients in the avacopan and prednisone taper groups, respectively.

	Avacopan (N=134)	Prednisone taper (N=134)
Baseline characteristics		
Age (years), mean ± SD	60.9 ± 14.6	62.2 ± 13.9
Male / Female, n (%)	84 (63%) / 50 (37%)	76 (57%) / 58 (43%)
Newly diagnosed / Relapsed, n (%)	98 (73%) / 36 (27%)	100 (75%) / 34 (25%)
Proteinase 3+ / Myeloperoxidase+, n (%)	53 (40%) / 81 (60%)	47 (35%) / 87 (65%)
GPA / MPA, n (%)	65 (49%) / 69 (51%)	63 (47%) / 71 (53%)
Rituximab / Cyclophosphamide, n (%)	81 (60%) / 53 (40%)	82 (61%) / 52 (39%)
eGFR (mL/min/1.73 m^2), mean ± SD	44.6 ± 27.7	45.6 ± 27.3
Key Results		
Disease remission at week 26, n (%)	99 (73.9%)	95 (70.9%)
Sustained disease remission at week 52, n (%)	91 (67.9%)	76 (56.7%)
Total all-source glucocorticoid dose during the 52-week period, mg (mean / median)	1,589 / 575	3,801 / 3,028
GTI-CWS at weeks 13 / 26, LSM ± SEM	24.1 ± 3.9 / 38.9 ± 3.9	37.7 ± 4.0 / 58.5 ± 4.0
GTI-AIS at weeks 13 / 26, LSM ± SEM	8.5 ± 3.9 / 11.2 ± 4.0	24.3 ± 4.0 / 24.3 ± 4.0
SF-36 PCS Score, Change from baseline at weeks 26 / 52, LSM ± SEM	4.8 ± 0.8 / 4.9 ± 0.8	1.9 ± 0.8 / 3.1 ± 0.8
SF-36 MCS Score, Change from baseline at weeks 26 / 52, LSM ± SEM	5.2 ± 0.9 / 6.6 ± 1.0	3.5 ± 1.0 / 5.1 ± 1.0
Serious Adverse Events, n patients (%), n events	61 (45.5%) 104 events	65 (48.5%) 148 events
Deaths, n (%)	2 (1.5%)	3 (2.2%)

AIS, aggregate improvement score; CWS, cumulative worsening score; eGFR, estimated glomerular filtration rate; GPA, granulomatosis with polyangiitis; GTI, glucocorticoid toxicity index; LSM, least squares mean; MCS, mental component summary; MPA, microscopic polyangiitis; PCS, physical component summary; SD, standard deviation; SEM, standard error of the mean; SF-36, Short Form-36.

Table 1: Baseline Characteristics, Remission Rates, Glucocorticoid Toxicity, Health- Related Quality of Life, and Safety for Patients with ANCA-Associated Vasculitis with Kidney Involvement in the ADVOCATE Trial.

Conclusions: In the ADVOCATE trial, patients with AAV with kidney involvement at baseline and treated with avacopan achieved higher sustained remission rates while receiving less GCs, experiencing less GC-related toxicity, and reporting greater improvements in HRQoL vs those treated with a prednisone taper.

Reference: 1. Jayne DRW, et al. *N Engl J Med* 2021;384:599-609

Disclosures: AbbVie/Abbott, Amgen, Argenx, AstraZeneca, Aurinia, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Cabaletta, Calliditas, Chinook, CSL Behring, CSL Vifor, Fresenius, Eicos, Electra, Genentech, GlaxoSmithKline, HiBio, InflaRx, Janssen, Jubilant, Kyverna, Merck/Merck Sharp & Dohme (MSD), MiroBio, Neutrolis, Novartis, NS Pharma, Pfizer, Q32, Regeneron, Roche, Sanofi, Sparrow, Takeda, Travere, UpToDate, Valenza Bio, Visterra.

O-075

Real-life Use of the PEXIVAS Reduced-dose Glucocorticoid Regimen in Granulomatosis with Polyangiitis and Microscopic Polyangiitis

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Background/ Objectives: Glucocorticoids (GCs) in combination with rituximab (RTX) or cyclophosphamide are the cornerstone of treatment for patients with severe granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA). GCs are associated with adverse effects, including serious infections. The PEXIVAS trial demonstrated non-inferiority of reduced-dose GC regimen compared to standard dose for the incidence of death or end-stage kidney disease (ESKD), with a significant reduction in serious infections at one year.

However, the primary endpoint did not include disease progression or relapse, the majority of patients received cyclophosphamide as induction therapy, and subgroup analysis showed a trend towards an increased risk of death or ESKD in RTX-treated patients. We aimed to evaluate the efficacy and safety of the reduced-dose GC regimen in a real-world setting.

Methods: We conducted a retrospective, multicentre study comparing the PEXIVAS reduced-dose GC regimen with a standard regimen in patients with severe GPA or PAM flare between January 2018 and April 2022. The primary composite endpoint included the occurrence of death, ESKD, progression before remission requiring treatment modification or relapse, whichever occurred first. Factors associated with the occurrence of the primary endpoint and of, death or ESKD, were estimated using univariate and multivariate Cox models. In a sensitivity analysis, patients were compared after matching on a propensity score.

Results: Of the 234 patients enrolled (93 MPA and 148 GPA), 126 (53.8%) received a reduced GC regimen and 108 (46.2%) received a standard regimen. The primary endpoint occurred in 62/234 (26.5%) of patients during the first year of follow-up: 33.3% of patients on the reduced dose versus 18.5% on the standard dose (p=0.016).

In multivariate analysis, a reduced GC regimen was significantly associated with the occurrence of the endpoint compared to a standard regimen (HR 1.72; 95%CI 1.08-2.74) (Figure 1), but was not associated with an increased risk of death or ESKD (HR 1.62; 95%CI 0.82-3.19). There was no significant difference in serious infections at 1 year (20.6% vs 15.7%, p=0.427).

After propensity score matching, the reduced-dose GC regimen tended to be more likely to meet the primary endpoint than the standard regimen (HR 1.57; 95%CI 0.93-2.64). In the subgroup of patients treated with the reduced-dose GC regimen, patients with creatinine levels above 300 µmol/L were more likely to meet the primary endpoint (RR 2.14; 95% CI 1.14-4.03). Similarly, in the subgroup of patients treated with RTX, the reduced-dose GC regimen tended to be more likely to achieve the primary endpoint (HR 1.61; 95% CI 0.94-2.77) and was more likely to meet death or ESKD (HR 2.42; 95%CI 1.04-5.66).

Conclusions: In patients with severe GPA or MPA, the reduced-dose GC regimen was associated with an increased risk of death, ESKD, progression before remission, or relapse. This risk was even greater in patients with creatinine levels above 300 µmol/L and in those treated with RTX as induction therapy.

Disclosures: No disclosure.

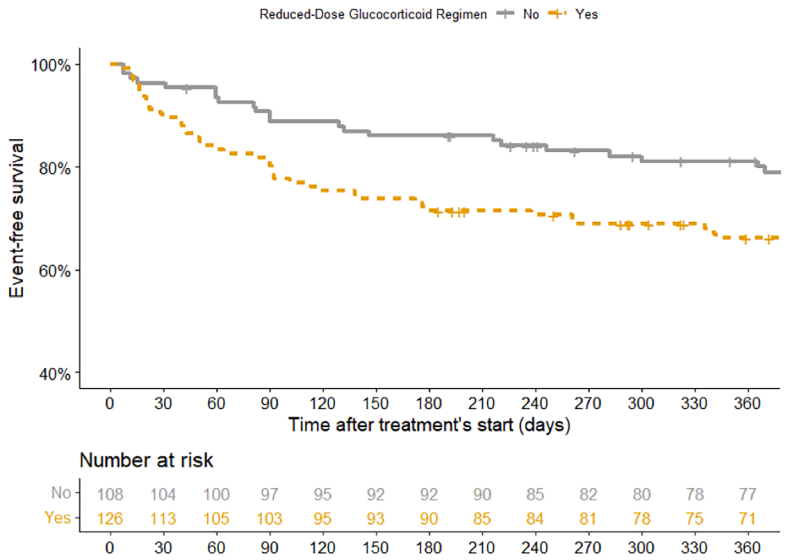

Figure 1: Kaplan-Meier survival curve comparing occurence of primary endpoint at 12 months.

O-076

Kinetics of auto-antibodies removal with immunoadsorption or plasma exchange: results of the CINEVAS study

Marion Sallée[1], Noémie Resseguier[2], Thomas Crepin[3], Daniel Bertin[1], Dominique Bertrand[4], Mickaël Bobot[5], Thierry Krummel[6], Nicolas Maillard[7], Julie Moussi-Frances[8], Marion Pelletier[1], Pascale Poullin[1], Cedric Rafat[9], Thomas Robert[5], Benjamin Terrier[10], Lionel Rostaing[11], Stanislas Faguer[12], Noémie Jourde-Chiche[5].

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Background and objective: The fast removal of auto-antibodies (anti-glomerular basement membrane (GBM) and anti-cytoplasmic neutrophilic (ANCA) antibodies) with apheresis is required in anti-GBM disease, and can be targeted in ANCA-associated vasculitis (1,2). The CINEVAS study tested whether immunoadsorption (IA) allowed a faster removal of ANCA and/or anti-GBM than plasma exchanges (PEx).

Methods: CINEVAS was a prospective multicenter non-randomized study comparing IA to PEx in 40 consecutive patients with ANCA and/or anti-GBM vasculitides. The primary objective was the reduction rate in auto-antibody titers between the beginning of the first and the end of the seventh apheresis session. Secondary objectives were: number of sessions needed to obtain desired reduction rates; removal kinetics of total immunoglobulin (Ig) G, IgA and IgM; tolerance and technical parameters of sessions; and patients' outcome.

Results: The results of 38 patients (16 treated with IA and 22 with PEx), and 43 auto-antibodies, were analyzed. There was no difference in the reduction rates in auto-antibody titers over 7 sessions between IA and PEx (respectively 98% [90-100] vs 96% [78-100], p=0.39, **Figure 1**). The numbers of sessions needed to obtain undetectable auto-antibodies, or 50%, 75% or 90% reductions, did not differ between techniques. Results were similar for anti-proteinase-3, anti-myeloperoxydase and anti-GBM antibodies. Whatever the apheresis technique, greater reduction rates of auto-antibodies were observed when plasma was separated by filtration compared to centrifugation. Total IgG reduction level was higher with IA, while total IgA and IgM reduction levels were lower with IA. PEx sessions required higher volumes of plasma, IA sessions higher volumes of citrate; IA sessions were longer.

Conclusions: Immunoadsorption and plasma exchange were comparable in ANCA or anti-GBM removal kinetics. Faster removal of total IgG, and better preservation of total IgA and IgM, was observed with immunoadsorption.

References:

1. Hellmich B, Sanchez-Alamo B, Schirmer JH et al. EULAR recommendations for the management of ANCA-associated vasculitis: 2022 update. Annals of the Rheumatic Diseases 2023; : ard-2022-223764.
2. Rovin BH, Adler SG, Barratt J et al. Executive summary of the KDIGO 2021 Guideline for the Management of Glomerular Diseases. Kidney International 2021; 100: 753–779.

Disclosures: The CINEVAS study was funded by a research grant from Fresenius Medical Care

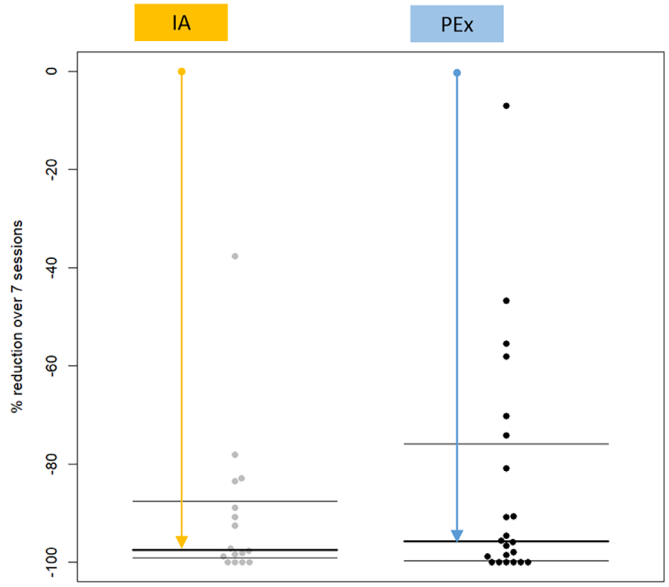

Figure 1. Percent reduction of auto-antibody titers per patient (N = 38) over 7 sessions of apheresis.
IA: immunoadsorption (N = 16); PEx: plasma exchange (N = 22).

BREAKOUT SESSION: OUTCOME PREDICTORS

O-077

Albuminuria after Induction Treatment and Kidney Prognosis in ANCA-associated Glomerulonephritis

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Background/Objectives: Persisting proteinuria has been associated with worse kidney outcomes in ANCA-associated vasculitis (AAV). However, it remains unclear whether this reflects damage from the initial injury or ongoing inflammation.

Methods: A retrospective, single centre study of biopsy-proven ANCA-associated glomerulonephritis (AAGN), excluding those with non-AAV glomerular pathologies. We assessed the presence of albuminuria beyond 6 months, defined as urine albumin-to-creatinine ratio (ACR). The group of "albuminuria" was defined as ACR more than 300mg/g and the group of "no albuminuria", defined as ACR less or equal than 300mg/g at 6months. We sought the clinical and histopathological characteristics from both the initial and subsequent biopsies, and long-term kidney outcomes stratified by albuminuria levels.

Results: 218 patients were included; Within the first six months, 28 (13%) had either died or progressed to end-stage kidney disease (ESKD), categorized as "early progressers". Among the remaining 190 patients, referred to as "late progressers", 37% had an ACR>300mg/g at 6 months. The albuminuria group more frequently presented with a Berden mixed or crescentic class and had higher glomerular activity in the initial biopsy. They were also more often male [odds ratio (OR) 2.69; 95% CI 1.13-6.41], of younger age (OR 0.96; 95% CI, 0.93 to 0.99) and had fewer normal glomeruli in the biopsy (OR 0.96; 95% CI, 0.93 to 0.99) compared to the group without albuminuria. After five years, the recovery in GFR was lower in the albuminuria group (adjusted mean delta GFR -12.5 ml/min per 1.73m^2; 95% CI 9.1 to 15.8). Additionally, the albuminuria group had worse kidney survival (log-rank, p<0.001, fig.1). In multivariable analysis, ACR greater than 300mg/g at 6 months was associated with a higher risk of End-Stage Kidney Disease (ESKD), even after adjusting for age, Berden classification and GFR at diagnosis (Hazard ratio 7.25; 95% CI, 1.62 to 32.47).

Conclusions: In a well-defined cohort of AAGN, one third of the patients, primarily younger males with a lower percentage of normal glomeruli, had persisting albuminuria after induction treatment which was associated with worse kidney outcomes independent of Berden class and GFR.

Disclosures: RJ received fees from GSK, Roche, Vifor. DJ from Amgen, Astra-Zeneca, CSL Vifor, GSK, Novartis, Roche, Takeda. The other authors declared no conflicts of interest.

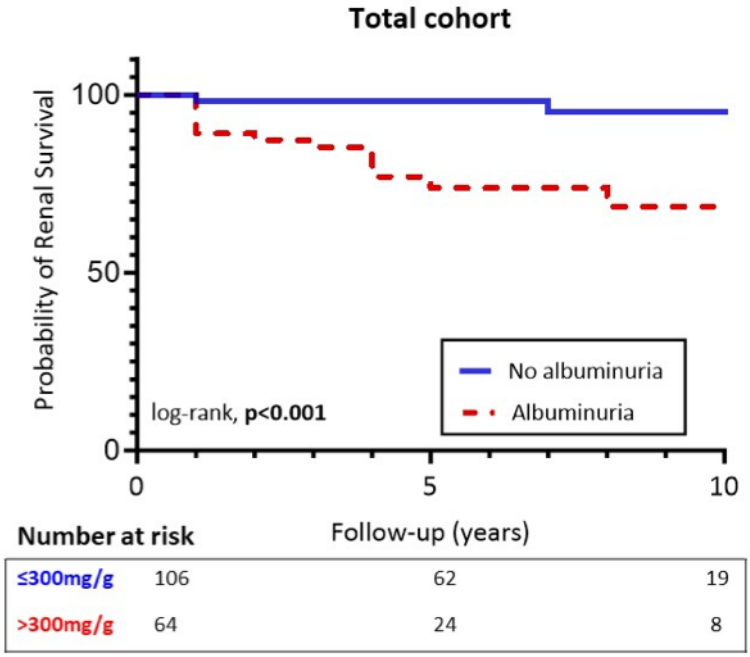

Figure 1. A Kaplan Meier analysis in late progressers cohort of the outcome of end-stage kidney disease according to albuminuria at 6 months

O-078

Frequency and the Effects of Spondyloarthritis-Spectrum Disorders on the Clinical Course and Management of Takayasu Arteritis

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Background: Extravascular findings of Takayasu arteritis (TAK), a chronic large-vessel vasculitis, usually belong to the spondyloarthritis (SpA)-spectrum of diseases. However, the characteristics of these findings and their effect on the vascular manifestations of TAK are not fully known. Therefore, we aimed to investigate the frequency of axial-SpA, inflammatory bowel disease (IBD), and psoriasis in TAK patients and the effect of these associations on the clinical features and management of TAK.

Material and Methods: Patients with TAK followed in 12 tertiary rheumatology clinics across Turkey were included in the study and were evaluated for the presence of axial-SpA, IBD or psoriasis. Demographic characteristics, clinical features, angiographic involvement patterns, disease activity, damage scores and treatments of TAK patients with or without SpA-spectrum disorders were analyzed and compared.

Results: Patients (n=350) classified according to ACR 1990 criteria were included in the study. Mean age (SD) was 45.5 (13.6) years and mean (SD) follow-up 76.1 (65.9) months. Thirty-one (8.8%) patients also had diseases in the SpA-spectrum. Among them, 8 (2.2%) patients had IBD, 8 (2.2%) had psoriasis and 20 (5.7%) had axial SpA. (Figure 1) The symptoms of TAK presented at a significantly earlier age in the TAK with SpA group than without SpA (TAK with SpA: mean (years) (SD): 26.03 (7.49) vs TAK without SpA: 31.59 (12.6), p=0.041). Furthermore, a significantly higher rate of biological therapy use was detected in the TAK with SpA group (TAK with SpA: 22 (70.9%) vs TAK without SpA: 85 (27.9%), p<0.001). Vascular involvement was similar in both groups.

Conclusion: Our study confirmed that diseases in the SpA-spectrum are not rare in TAK patients. TAK symptoms also appeared earlier in the group accompanied by SpA. However, most patients in the TAK with SpA group had an earlier onset of SpA-related symptoms than symptoms attributable to TAK. More aggressive therapy with biological agents was required in the TAK with SpA group and mostly for the severity and activation of TAK. Our results suggest that presence of SpA-spectrum disorders may cause more severe disease course and earlier disease onset in TAK patients.

Disclosure: None.

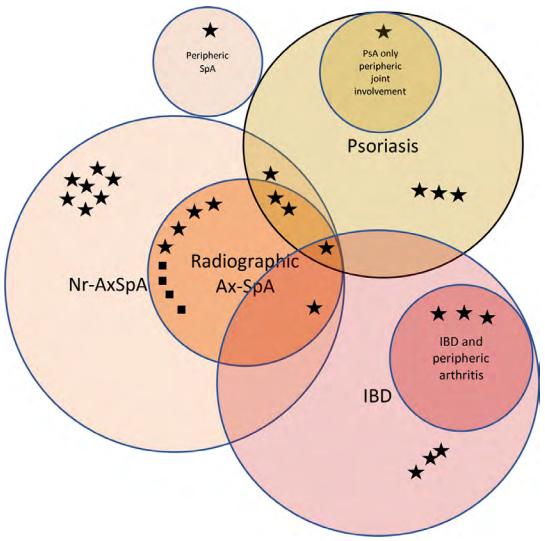

Figure-1. Distribution clusters of TAK and SpA patients within the SpA disease spectrum
(SpA: Spondyloarthritis, Ax-SpA: Axial Spondyloarthritis, Nr-AxSpA: Non-Radiographic Axial Spondyloarthritis, PsA: Psoriatic Arthritis, IBD: Inflammatory Bowel Disease): female,: male patiens.

O-079

ABO Blood Groups and Increased Risk for Vascular Involvement in the Patients with Behçet Disease

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Background/Objectives: Behçet's disease (BD) is classified as a variable vessel vasculitis, and a tendency for thrombosis in association with inflammatory endothelial activation is an important characteristic of vascular involvement in BD. Recent studies suggest an association between ABO blood groups and thrombotic vascular disease in particular in those carrying non-O (A, B, and AB) blood groups [1]. We herein aimed to investigate the potential contribution of ABO blood groups to the risk of vascular involvement in patients with BD.

Methods: We retrospectively analyzed the records of BD patients followed between 1978 and 2022. Patients fulfilling the ISG Criteria for diagnosis of BD were screened, and those with information about ABO blood groups were included in the study. The presence or absence of vascular involvement and its features were recorded using a standard form. The chi-square test, t-test, Mann-Whitney U test, and logistic regression tests were used for statistical analyses.

Results: The study group consisted of 411 patients with available blood group data, and 143 (34.8%) were carrying O [58% men, mean age at diagnosis 31.4±10.1 years, median follow-up period 153 (98-219) months], and 268 (65.2%) were carrying non-O blood groups [60.1% men, mean age at diagnosis 30.7±8.4 years, median follow-up period 148 (92-204) months]. There was no statistical significance between O and non-O groups regarding the potential confounding factors affecting the risk for vascular disease, including sex, age at diagnosis, family history, HLA-B51 positivity, smoking, comorbidities, and prothrombotic mutations. Vascular involvement was observed in 39 (27.3%) patients with blood group O [venous in 35 (24.5%), and arterial in 11 (7.7%)], whereas 109 patients (40.7%) with non-O blood groups had vascular involvement [venous in 95 (35.4%), and arterial in 38 (14.2%)]. The frequencies of total vascular and venous involvement between the two groups were significantly different (p=0.007, p=0.023, respectively). Unadjusted and adjusted ORs with different models in the multivariate logistic regression analyses are shown in **Table 1**. After adjustments for age, sex, and comorbidities, the risk for arterial disease was also found to be increased in association with non-O blood groups.

Conclusions: The results of this preliminary study support the previous reports revealing the potential contribution of ABO blood groups in the development of thrombotic vascular disease in general, and suggest an approximately two-fold increased risk for vascular involvement for BD patients for non-O blood groups.

References: 1. Vasan SK, et al. *Circulation*. 2016;133(15):1449-1457.

Disclosures: None.

	Total involvement		Venous involvement		Arterial involvement	
	p-value	**OR (CI %95)**	**p-value**	**OR (CI %95)**	**p-value**	**OR (CI %95)**
Model 1	0.007	1.8 (1.2-2.8)	0.023	1.7 (1.1-2.7)	0.057	2.0 (0.9-4.0)
Model 2	0.007	1.9 (1.2-3.1)	0.024	1.7 (1.1-2.8)	0.062	2.0 (0.9-4.0)
Model 3	0.005	2.0 (1.2-3.2)	0.022	1.8 (1.1-2.9)	0.038	2.2 (1.0-4.7)
Model 4	0.006	2.0 (1.2-3.2)	0.023	1.8 (1.1-2.9)	0.046	2.2 (1.0-4.6)
Model 5	0.029	1.9 (1.1-3.2)	0.038	1.8 (1.0-3.2)	0.102	2.0 (0.9-4.5)

Table 1. Logistic regression analysis to estimate unadjusted and adjusted risk for vascular events comparing O with non-O blood groups. Model 1: ABO blood group, Model 2: Model 1 plus age at diagnosis and sex, Model 3: Model 2 plus comorbidities, Model 4: Model 3 plus malignancy, Model 5: Model 4 plus smoking (missing value for 84 patients).

O-080

Renal Prognosis of Dialysis dependent Patients at Baseline in ANCA associated Vasculitis

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Background/ Objectives: Renal involvement in ANCA-associated vasculitides (AAV) is an organ- and life-threatening manifestation and therefore an important prognostic factor. However, the identification of predictive factors for renal failure remains a major challenge. Indeed, it may influence the intensity of induction treatment strategies. Furthermore, the benefit of plasma exchange (PLEX) has been questioned in recent years. The aim of this study is to describe the clinical outcome of patients requiring renal replacement therapy (RRT) at baseline and to identify clinical, biological and histological factors at baseline associated with their prognosis at one year.

Methods: This retrospective observational multicentre study included patients with anti-myeloperoxidase or proteinase 3 AAV with biopsy-proven renal involvement. Characteristics were evaluated stratified by dialysis requirement at baseline to identify determinants of renal prognosis. The primary composite outcome was the occurrence of death or end-stage renal disease at one year. Prognostic outcomes were modelized by generalized linear models to quantify the impact of predictors.

Results: Of the 395 patients enrolled, 106 (26.8%) were on dialysis at baseline. The mean age was 63.1±13.6 years and age was not associated with RRT at baseline (p=0.521). PR3-ANCA was associated to a greater prevalence of renal failure.

Among patients with dialysis at baseline, 61 (57.5%) achieved the one-year composite outcome of death or end-stage kidney disease (ESKD), whereas only 29 (10.0%) patients RRT-free at baseline reached the outcome at one year (p<0,001). Thirty (28.3%) patients with RRT at baseline had an eGFR at one year superior to 30 mL/min/1,73m², with a null median of eGFR recuperation at one year (0,00 [IQR 0.00-31.5 mL/min/1,73m²]).

Among patients requiring dialysis at baseline, in multivariate analysis, age at diagnosis was not associated with the composite outcome at one year in multivariate analysis (p=0.744). MPO-ANCA were associated with a higher prevalence of RRT and/or death at one year (OR 3,08; 95%CI 1.21–8.14; p = 0.02). In addition, Brix score at baseline was associated with worse renal prognosis at one year (OR 1.40; 95%CI 1.16–1.73; p=0.001).

Of the patients requiring dialysis at baseline, 80 (75.5%) underwent PLEX. Plasma exchanges were independently associated with a higher estimated glomerular filtration rate (eGFR) at one year of 9.15 mL/min/1.73m² [95%CI 0.26-18.04] (p=0.044). In addition, 41 (91.1%) of the surviving patients who were weaned from RRT at one year had received PLEX, whereas only 39 (63.9%) of the patients with the composite outcome (death or RRT at one year) had received PLEX (p=0.003). Thus, PLEX was associated with a reduced risk of one-year RRT or death in patients receiving dialysis at baseline (OR 0.24, 95%CI 0.06-0.82).

Conclusions: This study describes the clinical evolution of patients with AAV requiring RRT at baseline. It shows a strong association between plasma exchange and improvement in renal function with a higher rate of dialysis weaning. It opens perspectives for further studies in patients who benefit more from PLEX therapy.

References: None.

Disclosures: None.

O-081

The prognostic value of presenting features on the short- and long-term prognosis of giant cell arteritis patients: data from the Italian Society of Rheumatology Group

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Background/objectives: Identifying baseline factors that can predict the prognosis of patients with giant cell arteritis (GCA) could help to define a tailored approach. Here we investigated the impact of presenting features included in the "2022 ACR/EULAR GCA Classification Criteria"[1] on short- and long-term outcome.

Methods: Data of GCA patients from centres belonging to the Italian Society of Rheumatology group were retrospectively reviewed. All the items included in the "2022 GCA classification criteria" were retrieved. Disease-related outcomes at baseline (only for visual loss[VL]) and at 12 and 60 months were evaluated. Univariate and multivariate logistic analyses were performed.

Results: Complete data on baseline clinical and laboratory features were available for 1027 patients. In this cohort, follow-up data were available for 950 (93%) and 494 (48%) patients at 12 and 60 months, respectively. At GCA onset, 197 (19%) patients had VL. At 12 and 60 months, 46 (5%) and 30 (6%) patients developed ascending aorta aneurysm (AAA), 243 (26%) and 245 (50%) patients had a first relapse, respectively. At multivariate analysis, jaw/tongue claudication (OR 1.727[1.225-2.434], p=0.0018) and temporal artery abnormality (OR 1.650[1.163-2.342], p=0.0050) were directly associated with whereas polymyalgia rheumatica (OR 0.618[0.445-0.857], p=0.004) was inversely associated with VL. Jaw/tongue claudication was associated with a lower risk of AAA at 12 months (OR 0.313[0.127-0.772], p=0.0117) and new-onset headache with a lower risk of AAA at 60 months (OR 0.456[0.210-0.991], p=0.0474). Polymyalgia rheumatica (PMR) was associated with a higher risk of 1st relapse over both 12 (OR 1.431[1.066-1.919], p=0.0169) and 60 months (OR 1.859[1.300-2.657], p=0.004).

Complete data on baseline clinical, laboratory, imaging/histological features were available for 290 patients. In this cohort, follow-up data were available for 262 (90%) patients at 12 months and for 113 (39%) patients at 60 months. At GCA onset, 44 (15%) patients had VL. At 12 and 60 months, 18 (7%) and 30 (11%) patients developed AAA, and 66 (25%) and 60 (53%) patients had a relapse, respectively. At multivariate analysis, jaw/tongue claudication was directly associated (OR 2.473[1.186-5.158], p=0.0158) whereas axillary involvement was inversely associated (OR 0.109[0.024-0.493], p=0.0040) with VL. Jaw/tongue claudication (OR 0.107[0.014-0.829], p=0.0324) and ESR>50 mm/h (OR 0.313[0.112-0.872], p=0.0264) were both associated with a lower risk of AAA at 12 months. PMR was associated with a higher risk of 1st relapse over 12 months (OR 2.191 [1.242-3.866], p=0.0067).

Conclusions: In this large cohort of Italian GCA patients, cranial symptoms were confirmed to increase the risk of VL but appeared to reduce the risk of AAA. PMR reduces the risk of VL but is associated with a higher risk of flare. Imaging data provide little additional prognostic information.

Reference:

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BREAKOUT SESSION: OTHER FORMS OF VASCULITIS

O-082

Methotrexate as a steroid-sparing agent in chronic periaortitis (idiopathic retroperitoneal fibrosis): a multicentre randomised clinical trial

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Background/Objectives: The standard therapy for chronic periaortitis (CP), also known as idiopathic retroperitoneal fibrosis, is based on high-dose glucocorticoids, which are progressively withdrawn within a 9-month period. The present study aims at evaluating whether methotrexate (MTX) is an effective steroid-sparing agent in CP.

Methods: This is a multicentre, randomized trial (NCT 01240850) comparing the efficacy of a 9-month course of standard-dose prednisone (PDN) and that of a 9-month course of low-dose PDN and MTX. Patients aged 18-80 and with a new diagnosis of CP were enrolled between April 2007 and January 2014. Patients assigned to the PDN group received 1 mg/kg/day of PDN for the first month, 0.5 mg/kg/day for the second month, 0.25 mg/kg/day for the third and fourth months, gradually tapered to zero over the subsequent 5 months. Those assigned to the PDN+MTX group were given 1 mg/kg/day of PDN for the first month, then MTX (0.3 mg/kg/week) was added, and PDN dose was reduced as follows: 0.25 mg/kg/day for the second month, 0.125 mg/kg/day for the third and fourth months, tapered to zero over the 5 subsequent months; both PDN and MTX were withdrawn at the end of the ninth month. The primary endpoint was remission (absence of symptoms, normal acute-phase reactants and no hydronephrosis, stent-free or nephrostomy-free) at the end of the 9-month treatment course. Secondary endpoints included relapses, the reduction in size of the retroperitoneal mass, and treatment-related side-effects.

Results: Of the 60 patients enrolled, 31 were assigned to the PDN group and 29 to PDN+MTX group. Twenty-five (80.6%) patients of the PDN group and twenty-six (89.7%) patients of the PDN+MTX group achieved remission at month 9 (p=0.549). Mean CP thickness reduction did not differ between treatments. No significant difference was observed between groups in terms of therapy-related adverse events. During the 16-month follow-up period after the achievement of remission, no significant difference was observed in terms of relapses (p=0.813). A statistically significant difference in terms of cumulative PDN doses between the two groups was observed: the mean dose in the PDN group was 4805±723 mg, whereas in the PDN+MTX group reached 3554±525 mg (p<0.001).

Conclusions: A 9-month treatment regimen based on the use of MTX in combination with low-dose PDN has comparable efficacy and safety in inducing CP remission to that of a 9-month regimen based on standard-dose PDN, which represents to date the reference treatment. The difference between cumulative PDN doses between the groups is remarkable.

References: None.

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O-083

Histopathological evaluation of IgG4-RD using the 2019 ACR/EULAR scoring system

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Background/ Objectives: IgG4-RD (Immunoglobulin G4-Related Disease) is a chronic immune-mediated disease in which nearly every organ can be affected. The diagnostic process can be challenging and often requires a multidisciplinary approach.[1] In 2019, American College of Rheumatology/European League against Rheumatism (ACR/EULAR) classification criteria for IgG4-related disease[2] came out including a step-wise scoring system in which histopathology scores are given in step 3 for those cases meeting entry criteria (step 1) and not meeting exclusion criteria (step 2). We here present the first data of a patient cohort from a large university hospital focussing on the evaluation of the histology findings.

Methods: We performed a search for biopsy reports from a 10-year period (11 May 2013 – 10 May 2023) containing the phrase 'IgG4'. A total of 922 reports were found from 777 patients. We excluded 195 from our analysis, mainly because of insufficient/missing material or data - or because the term IgG4 was used in the text but had no relation to a consideration of IgG4-RD. We categorized the remaining results of 727 pathology reports into: 1. definite IgG4-RD; 2. indicative of IgG4-RD and 3. no histopathological evidence of IgG4-RD. We then re-evaluated the findings of the first 2 categories according to the proposed ACR/EULAR scoring system. All scores were given by 2 pathologists and consensus meetings solved cases with interobserver variability.

Results: There were 645 reports with no histopathological evidence of IgG4-RD. Original biopsy slides of 82 cases, 31 with definite IgG4-RD and 51 indicative of IgG4-RD, came from a variety of organs with pancreas, head and neck specimens and hematology specimens being the most frequent and accounting for 39 of 82 cases. All biopsies except one showed a dense inflammatory infiltrate. 10/82 cases had obliterative phlebitis; 22/82 cases had storiform fibrosis; 68/82 cases had more than 50 IgG4+ cells/HPF and in 13/82 the IgG4:IgG ratio was > 70. Comparing those cases with findings 'definite' or 'indicative' of IgG4-RD we found that in the former category, the total histology score was significantly higher than in the latter ($\chi^2 = 8.2$; $p < 0.05$) – which was largely due to the presence of storiform fibrosis (score: 13).

Conclusions: In this large, single center cohort of patients with IgG4-RD we found consistency between the original histopathological conclusion and the newly introduced ACR/EULAR scoring system, distinguishing between a histopathological diagnosis that is either indicative or definite for IgG4-RD. We are currently assembling the clinical data and outcome of this cohort to gain insight into the predictive value of the histopathological findings.

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Disclosures: None.

O-084

Rituximab in adult-onset IgA Vasculitis and crescentic IgA Nephropathy. A multicentre study

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Background: Adult-onset IgA Vasculitis (IgAV) is poorly responsive to glucocorticoids (GC) and conventional immunosuppressive therapies, such as cyclophosphamide. Rituximab has been successfully used in a few cases and may represent a safer and potentially more effective option.[1] Crescentic IgA Nephropathy (cIgAN), a rare entity that shares features of renal vasculitis with IgAV, is also frequently refractory to cyclophosphamide, while response to rituximab is unknown. We investigated outcomes after rituximab in a multicentre European cohort of adult-onset IgAV and cIgAN.

Methods: We screened clinical records of patients followed at 18 European consorted centres who were ≥18 years old at the onset of IgAV and received ≥1 rituximab dose. Furthermore, we identified patients with cIgAN (≥25% crescentic glomeruli and rapidly progressive glomerulonephritis), who were treated with rituximab. Remission was defined as Birmingham Vasculitis Activity Score (BVAS) <3 at month 6 after rituximab and renal response as stable or improved eGFR and ≥50% proteinuria reduction. Relapse was defined as an increase in BVAS requiring a change in immunosuppressive therapy. Outcomes of IgAV with severe nephritis (eGFR <60 mL/min) were compared with those of cIgAN.

Results: We included 61 patients with IgAV and 15 with cIgAN (**Table**). Rituximab was administered as initial therapy in 23/61 (38%) patients with IgAV and 13/15 with cIgAN (87%), while the remainder had refractory or relapsing disease. Active skin involvement was present in 49 patients (80%) and nephritis in 55 patients (90%) with IgAV at the time of starting rituximab. This

Table Main features of patients with IgAV and cIgAN

	All IgAV N=61	Non-severe IgAV nephritis N=31	Severe IgAV nephritis N=24	cIgAN N=15	P values*
Age at diagnosis, median (IQR)	43 (27-55)	38 (22-49)	52 (40-62)	33 (24-52)	**0.025**
Male, n (%)	39 (64)	18 (58)	19 (79)	11 (73)	0.71
IS therapy before rituximab					
Glucocorticoids, n (%)	41 (67)	23 (74)	13 (54)	2 (13)	**0.017**
Cyclophosphamide, n (%)	16 (26)	8 (26)	5 (21)	2 (13)	0.68
Other	17 (28)	12 (39)	4 (17)	0	0.458
Indications to rituximab					
1st line, n (%)	23 (38)	9 (29)	11 (46)	13 (87)	**0.017**
Relapsing disease, n (%)	15 (24)	6 (19)	6 (25)	0	0.06
Refractory disease, n (%)	23 (38)	16 (52)	6 (25)	2 (13)	0.44
Active extra-renal organ involvement					
Skin, n (%)	49 (80)	23 (74)	19 (79)	/	/
GI tract, n (%)	35 (57)	19 (61)	10 (42)	/	/
Joints, n (%)	38 (62)	18 (58)	13 (54)	/	/
BVAS, median (IQR)	14 (10-21)	12 (6-16)	16 (10-21)	/	/
Renal involvement	55/61 (90)				
eGFR, median (IQR), mL/min	73 (28-100)	89 (80-105)	26 (15-35)	28 (16-38)	0.45
Renal replacement therapy, n (%)	3 (5)	/	3 (12)	2 (13)	1
Proteinuria, g/day	2.1 (1.2-4.3)	1.8 (0.8-2.6)	2.8 (1.6-6.2)	4.2 (2.4-6.3)	0.58
Concomitant IS therapy					
None, n (%)	13 (21)	8 (26)	5 (21)	0	0.13
Glucocorticoids, n (%)	48 (79)	23 (74)	19 (79)	15 (100)	0.13
Cyclophosphamide, n (%)	9 (15)	2 (6)	7 (29)	6 (40)	0.50
Other, n (%)	9 (15)	5 (16)	1 (4)	5 (33)	**0.023**
Remission, n (%)	52 (85)	27 (87)	22 (92)	7 (47)	**0.003**
Relapse, n (%)	15/52 (29)	6/27 (22)	7/22 (32)	4/7 (57)	0.37
eGFR >60 mL/min at last FU, n (%)	45 (74)	28 (90)	11 (46)	2 (13)	**0.044**
Kidney failure at last FU, n (%)	5 (8)	2 (6)	3 (12)	10 (66)	**0.001**

*Comparison between patients with severe IgAV nephritis and cIgAN (Mann-Whitney or Fisher test). P<0.05 was considered a statistically significant result

was given alone in 13/61 (21%) or combined with GC in 48 (79%) patients with IgAV and in all those with cIgAN. Furthermore, cyclophosphamide was used in 15% of patients with IgAV and 40% of those with cIgAN. Remission at 6 months was achieved by 52 (85%) patients with IgAV and 12/13 (92%) of those treated with rituximab alone. A renal response was observed among 49/55 (89%) of those with nephritis. Patients with IgAV and severe nephritis had similar eGFR to those with cIgAN at the time of starting rituximab, but the latter had lower rate of remission and a higher frequency of kidney failure. A relapse occurred in 15/52 patients (29%) who achieved remission a median of 13 months (10-15) after rituximab. Eight patients resumed rituximab and achieved again remission.

Conclusions: Rituximab alone or in combination with GC and immunosuppressants appeared to achieve a high rate of remission in this cohort of adult-onset IgAV. Renal response among those with severe nephritis was also good, while this was worse among patients with cIgAN, suggesting substantial differences among these conditions despite similar histological appearances.

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Disclosures: None.

CASE REPORT AND PANEL DISCUSSION (II)

O-085

Giant cell arteritis in patients with systemic sclerosis: a case series

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Background/Objectives: Giant cell arteritis (GCA) in patients with systemic sclerosis (SSc) is a rare entity for which only case reports are available. High-dose glucocorticoid use has been relatively contraindicated in SSc patients due to the concern of scleroderma renal crisis (SRC). Optimal treatment strategies for this group of patients have not been reviewed.

Methods: A single-institution retrospective study was performed reviewing all patients that had diagnosis codes for both SSc and GCA between January 1, 1996, and December 31, 2020. Medical records were reviewed individually, and data was abstracted regarding demographic characteristics, clinical presentation, diagnostic modalities, treatments, and outcomes. Diagnosis of both SSc and GCA by a rheumatologist was required for inclusion. Number of ACR/EULAR classification criteria met for 2013 SSc criteria and 2022 GCA criteria were documented.

Results: Eight patients were retrospectively identified, all of which were female. Seven patients fully met both respective ACR/EULAR classification criteria sets. One patient fulfilled GCA criteria and had 8/9 points for SSc criteria plus an esophagogram which was consistent with clinical diagnosis of SSc. Mean±SD age at diagnosis was 60.5±17.1 years for SSc and 74.8±6.9 years for GCA. Six patients (75%) developed SSc before GCA. Mean±SD time from SSc diagnosis to GCA diagnosis was 19.6±15.7 years. Two patients (25%) developed GCA before SSc. Mean±SD time from GCA diagnosis to SSc diagnosis was 1.8±1.1 years. Mean±SD follow-up time after GCA diagnosis was 5.2±4.2 years. Main clinical symptoms, diagnostic modalities, treatments used, complications and outcomes are presented in **Table 1**. Three patients had a previous history of SRC prior to GC initiation for GCA. No episodes of SRC occurred after high-dose GC. Two patients with history of SRC were on ACE inhibitors at the time of GC initiation. One of these patients developed a hypertensive episode without end-organ damage or SRC while on 40mg of prednisone after GCA diagnosis. This occurred due to cessation of a thiazide diuretic and resolved with reinitiation. Most patients in this study were diagnosed with SSc and GCA prior to the FDA approval of tocilizumab for either GCA or SSc, limiting the number of patients that received this treatment. In total, three patients were treated with tocilizumab (TCZ). One patient developed a diverticular perforation secondary to TCZ requiring colonic resection and colostomy, one patient discontinued TCZ after a medication-unrelated complication and one patient has remained in remission off GC on TCZ for 19 months as of last follow-up.

Conclusions: Herein we present the largest single-institution series of patients that present both GCA and SSc, an uncommon combination. High-dose glucocorticoid treatment for GCA did not appear to precipitate development of SRC in this series of patients. Further investigation regarding the benefit of tocilizumab in patients with SSc and GCA is required.

References: None.

Disclosures: K.J.W.: Kiniksa, Amgen, Sanofi, BMS, Eli Lilly; M.J.K.: Amgen; Others: none.

	Systemic Sclerosis				Giant Cell Arteritis					Outcomes	
Case	Age SSc DX	SSc subtype, Sx & Serology	Tx for SSc prior to GCA Dx	Hx SRC	Age GCA Dx	Method GCA Dx	GCA Sx & IMs at Dx	Initial GC dose	GCA GC-sparing agents used	Complications	Status
#1	57	lcSSc CC, DU, GERD, RP, SD, TE. ANA, Anti Scl-70	CCB, E1RA, HCQ, PDE$_5$-I	Yes, 1 episode	66	Clinical	HA, PMR, ST CRP: 22 mg/L ESR: 55 mm/h	40mg	None	GCA: None SSc: pHTN, ILD	Deceased: Complications of Scleroderma
#2	45	dcSSc DU, GERD, IA, RP, SD, TE. Anti-RNA Pol III	Penicillamine (D/C AE), HCTZ, ACEI	Yes, 1 episode	73	Clinical	HA, JP, PMR, ST, VS CRP: 66 mg/L ESR: 46 mm/h	40mg	None	GCA: GC-related: IHG, OP & VCFs SSc: ILD, severe HTN episode without SRC	Deceased: Cause of death N/A
#3	43	dcSSc CC, DU, ED, GERD, RP, SD, TE. Anti Scl-70	CCB	No	86	Biopsy	HA, JC, JP, PMR, VS CRP: N/A ESR: 73 mm/h	40mg	None	GCA: None SSc: ILD, hand contractures, finger autoamputations.	Deceased: Ruptured sigmoid volvulus
#4	81	dcSSc ED, GERD RP, SD, TE. Anti-RNA Pol III	None (SSc Dg after GCA)	No	78	Clinical	HA, PMR, ST, FE, NS CRP: N/A ESR: 60 mm/h	60mg	None	GCA: N/A SSc: ILD, severe dysphagia.	Deceased: Failure to thrive due to severe dysphagia.
#5	76	lcSSc GERD, RP, SD, TE. ANA, ACA	CCB	No	79	Biopsy	JC, PMR, VS CRP: 86.8 mg/L ESR: 72 mm/h	60mg	TCZ	GCA: PVFD SSc: None	GCA: Remission, on TCZ 4mg/kg IV q4wks. SSc: Stable, on CCB, PPI
#6	34	lcSSc DU, GERD, RP, SD. ANA	PDE$_5$-I, AZA, CYC, HCQ, LEF, MTX, MMF	Yes, 1 episode	63	Biopsy + LV Imaging	HA, PMR, VS CRP: 22 mg/L ESR: 43 mm/h	60mg	1st line: TCZ (D/C AE) 2nd line: LEF (D/C AE) 3rd line: MTX	GCA: Diverticular perforation 2ry to TCZ, PVFD, adrenal insufficiency 2ry to GCs. SSc: Hand contractures	GCA: clinically stable on prednisone 15mg + MTX SSc: stable, PDE$_5$-I
#7	69	lcSSc DU, ED, GERD, IA, RP, SD, TE. ACA.	HCQ, CCB, ACEI	No	75	Biopsy	HA. CRP: N/A ESR: 40 mm/h	60mg	None	GCA: None. SSc: None.	GCA: Remission, off Tx SSc: Stable, lost to F/U 2013 (but using HCQ, CCB, PPI)
#8	79	lcSSc GERD, RP, TE. ANA, ACA	None (SSc Dg after GCA)	No	78	Clinical, LV imaging for relapse (aortitis)	HA, PMR, JC CRP: N/A ESR: 103 mm/h	40mg	TCZ	GCA: Aortitis (relapse), GC-related OP. SSc: None	GCA: Remission, off Tx SSc: Stable, on CCB

ACA = Anti-centromere antibody, ACEI = Angiotensin Converting Enzyme inhibitor, ANA = Antinuclear antibody, AZA = Azathioprine, CC = Calcinosis cutis, CCB = Calcium channel blocker, CRP = C Reactive Protein, CYC = Cyclophosphamide, D/C AE = Discontinued due to Adverse Event(s), dcSSc = diffuse cutaneous Systemic Sclerosis, DU = Digital Ulcerations, E1RA = Endothelin 1 Receptor Antagonist, ED = Esophageal Dysmotility, F = Female, FE = Fever, GC = Glucocorticoid(s), GC-IHG = Glucocorticoid-induced hyperglycemia, GCA = Giant Cell Arteritis, GERD = Gastroesophageal Reflux Disease, HA = Headache, HCQ = Hydroxychloroquine, HCTZ = Hydrochlorothiazide, IA = Inflammatory Arthritis, ILD = Interstitial Lung Disease, IMs = Inflammatory Markers, JC = Jaw claudication, JP = Jaw Pain, LEF = Leflunomide, lcSSc = limited cutaneous Systemic Sclerosis LV = Large vessel, MTX = Methotrexate, MMF = Mycophenolate Mofetil, N/A = Not Available, NS = Night sweats, OP = Osteoporosis, PDE5-I = Phosphodiesterase 5 inhibitor, pHTN = Pulmonary Hypertension, PMR = Polymyalgia Rheumatica, PPI = Proton pump inhibitor, PVFD = Permanent Visual Field Defect, RP = Raynaud's Phenomenon, SD = Sclerodactyly, SRC = Scleroderma Renal Crisis, SSc = Systemic Sclerosis, ST = Scalp Tenderness, TCZ = Tocilizumab, TE = Telangiectasia(s), Tx = Treatment, VCFs = Vertebral compression fractures, VS = Visual symptoms.

Table 1. Characteristics and outcomes of patients with giant cell arteritis and systemic sclerosis.

O-086

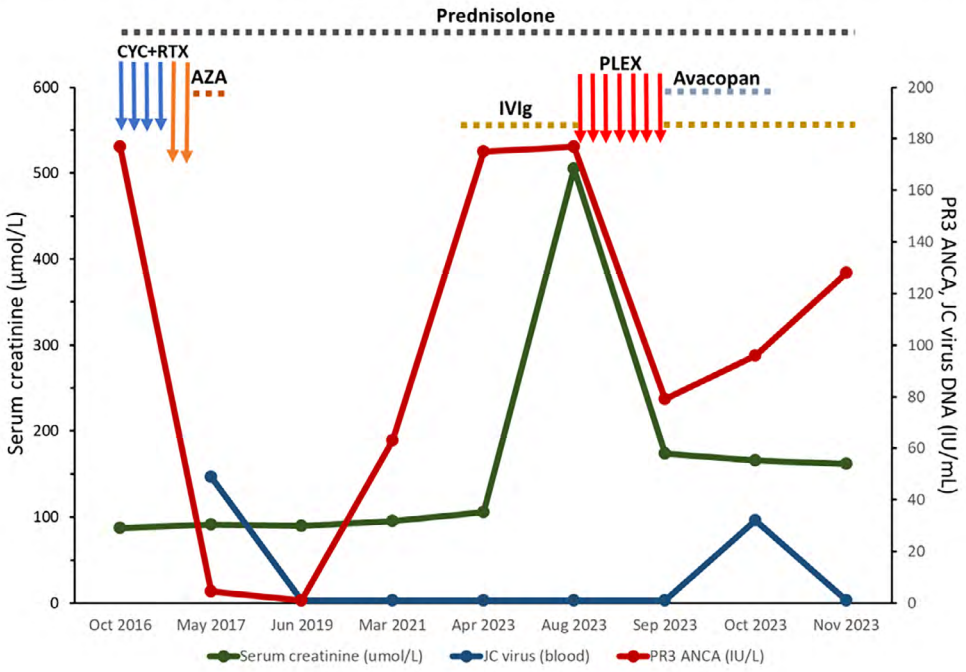
Managing relapse and progressive multifocal leukoencephalopathy in PR3 ANCA-positive vasculitis: the balance between immunosuppression and immunocompetence

Giorgio Trivioli[1], Toby Humphrey[1], Kevin Loudon[1], Eoin Mckinney[2], Lisa Willcocks[1], Andrew Carmicheal[1], Amanda Cox[1], Alasdair Coles[2], Rachel Jones[1], David Jayne[2], Rona Smith[2].

[1]Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom; [2]University of Cambridge, Cambridge, United Kingdom.

Presentation of Case: A 74-year-old man was diagnosed with PR3 ANCA vasculitis manifesting as *mononeuritis multiplex* in 2016 and treated with glucocorticoids (GC) and intravenous cyclophosphamide (cumulative dose 3.5g). Rituximab (2g) was added in December 2016 due to progressive mononeuritis. Six months later, his vasculitis was in remission (PR3 negative) on low dose prednisolone and azathioprine, but he developed dysarthria and incoordination. MRI head showed cerebellar lesions and polymerase chain reaction (PCR) of cerebrospinal fluid (CSF) was positive for JC virus, consistent with progressive multifocal leukoencephalopathy (PML).[1] Of note, he was lymphopaenic at the time of diagnosis. He continued low-dose prednisolone while azathioprine was withdrawn and he commenced 3 monthly IV immunoglobulins (IVIg). His neurological condition stabilised and JC virus in blood became undetectable. However, his PR3 ANCA returned positive in 2021 and in August 2023, he developed pulmonary infiltrates and acute kidney injury (creatinine 505µmol/L, **Figure**).

Figure Trends of serum creatinine, PR3 ANCA and blood PCR of JC virus and immunosuppressive therapy



Diagnostic Testing and management: A kidney biopsy revealed a pauci immune crescentic glomerulonephritis, consistent with vasculitis relapse. He received IV GC and plasma exchange (7 sessions) but no immunosuppressive agents, in light of the history of PML. He commenced avacopan 30mg twice daily, in view of perceived low risk of viral reactivation but the requirement to control active vasculitis.

Outcome and follow-up: Clinically, he improved and renal function recovered substantially (creatinine 170µmol/L), and his PR3 level reduced. On discharge, blood PCR for JC virus was negative. However, he noted deterioration in his mobility over the following weeks and blood PCR in October 2023 returned positive for JC virus. Avacopan was stopped and treatment with the antiviral cidofovir planned. Surprisingly, PCR of CSF taken 1 week after avacopan was stopped returned negative for JC virus. PCR of blood was then negative on three consecutive assessments in the following month, hence cidofovir was not administered in view of risk of nephrotoxicity. He continues under close follow up on 15mg prednisolone, 3 monthly IVIg, with vasculitis in remission and undetectable JC virus in blood and CSF, although his PR3 level is again rising.

Discussion: Achieving sufficient immunosuppression to control vasculitis activity, while minimising infection risk is a common issue in vasculitis practice. However, the management of vasculitis relapse in this patient with PML was particularly challenging because of the very fine balance between immunosuppression and immunocompetence. Our patient relapsed with a severe pulmonary-renal syndrome, which was heralded by reappearance of PR3 ANCA, and was successfully treated with PLEX, GC, avacopan and IVIg. Notably, timing of avacopan therapy was associated with reappearance and disappearance of JC virus, suggesting it exerts a non-negligible immunosuppressive effect on viral surveillance.

References:

1. Cheema K *et al.* Deciphering neurological symptoms in ANCAassociated vasculitis, uncontrolled disease or a complication of therapy. *Rheumatology* 2021;60:iii67–iii69.

Disclosures: None.

O-087

VEXAS masquerading as Granulomatosis with Polyangiitis (GPA)

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Presentation of Case: A 70-year-old man presented with a two-year history of episodic constitutional symptoms, myalgia, arthralgia and a widespread rash primarily on his legs and forearms. His medical history included chronic unexplained neutropenia, with an inconclusive bone marrow biopsy, and open angle glaucoma. Over the preceding six months, he'd had two hospital admissions for similar symptoms, each with significantly elevated inflammatory markers. During these admissions, the rash was treated as cellulitis. Bilateral peri-orbital swelling was attributed to open-angle glaucoma and managed conservatively. Examination revealed multiple discrete circular erythematous lesions surrounding small tender palpable subcutaneous nodules, mainly around his wrists and legs.

In addition to high inflammatory markers (CRP 191 mg/L) his bloods were notable for normocytic anaemia (Hb 120 g/L) and hypoalbuminemia (21 mg/L). Serology was negative for ANA and ANCA, with normal complement levels. Viral screening for hepatitis A, B, C, HIV, CMV, and EBV were unremarkable. Urine dipstick analysis showed 1+ protein and normal protein creatinine ratio. CT scan of neck, chest, abdomen and pelvis showed no malignancy.

He re-presented with left sided peri-orbital swelling, erythema, proptosis with limitation of eye movements, injected conjunctiva and reduced visual acuity (9/13). Inflammatory markers were again elevated. MRI of the orbit revealed left rectal muscle swelling and inflammatory changes within the left orbital roof, involving the superior rectus and levator palpebrae muscle complex, with mild left proptosis. This was consistent with an orbital inflammatory syndrome (figure 1).

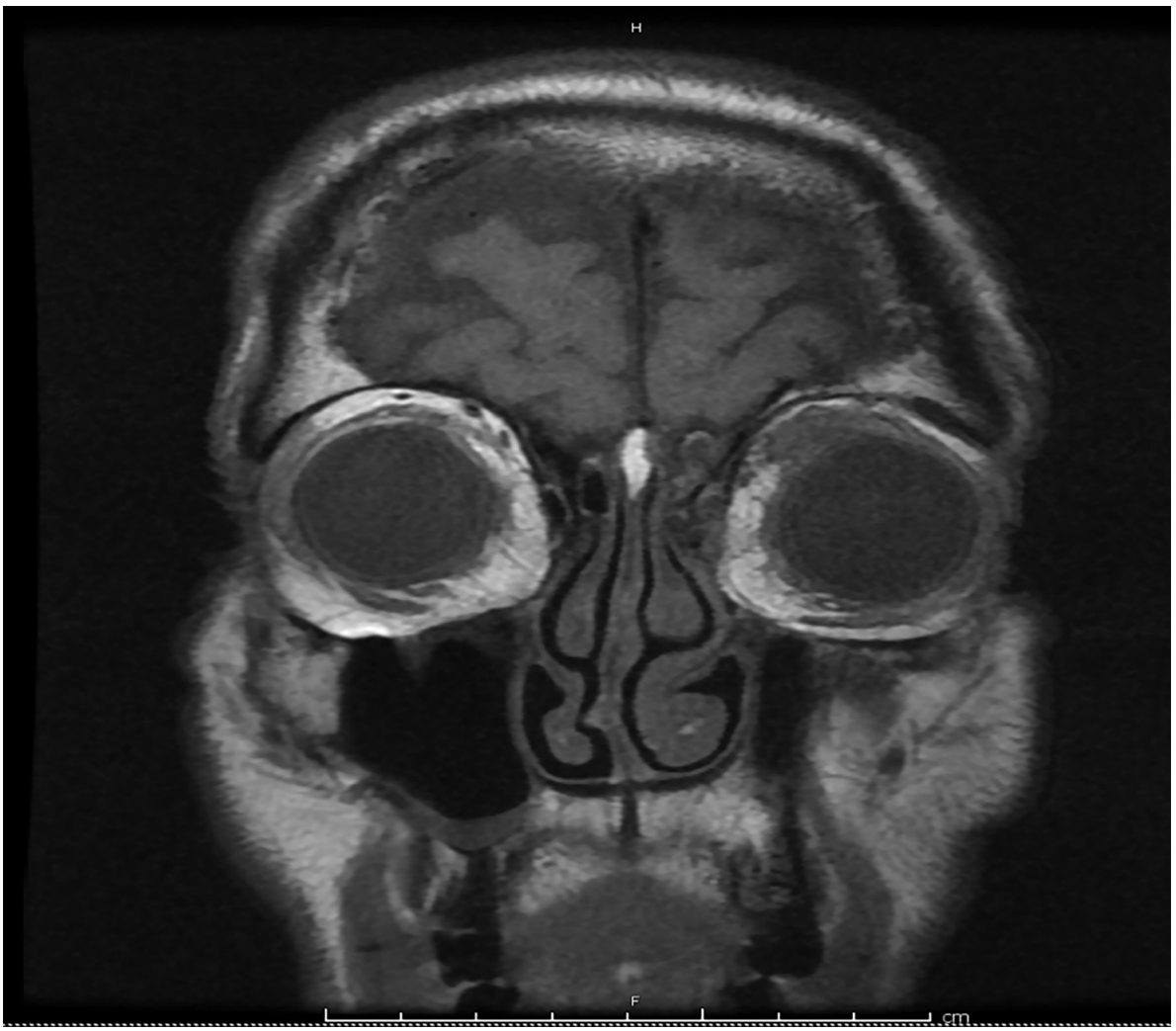

Figure 1. MRI Orbit: Left superior rectus muscles swelling and inflammatory changes on a Coronal T1 fat-sat image.

Skin biopsy revealed a granulomatous vasculitis of medium sized vessels with fibrinoid necrosis. A diagnosis of Granulomatosis with Polyangiitis was made. Due to his previous history of mild intermittent neutropenia, he was initiated on Rituximab along with a high dose Prednisolone. He had a poor response to Rituximab and this primary inefficacy raised the suspicion of an alternate diagnosis. Genetic testing for the UBA1 gene mutation was positive, confirming the diagnosis of VEXAS.

Discussion of Management: The presence of medium-sized granulomatous vasculitis in a man with ocular, cutaneous and constitutional involvement led to a diagnosis of GPA, despite negative ANCA serology. Approximately 10-20% of patients with GPA are ANCA negative. The sub-optimal response to Rituximab prompted exploration for an alternative diagnosis. Genetic testing for UBA1 gene mutation confirmed the diagnosis of VEXAS syndrome.

VEXAS syndrome, caused by an X-linked somatic mutation, is a multisystem auto-inflammatory condition primarily affecting males. Common clinical features include fever, cutaneous involvement, pulmonary infiltrates, chondritis of ears and nose, venous thromboembolism and macrocytic anaemia.

Conclusion: ANCA negative vasculitis, refractory disease and pre-existing cytopenia in males over the age of 50 should raise suspicion of VEXAS.

Disclosures: None.

O-088

Paraneoplastic MPO+ ANCA vasculitis in Chronic Lymphocytic Leukemia

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Presentation of Case: A 77 year old female with a history of neuroendocrine tumor, breast cancer, and untreated chronic lymphocytic leukemia (CLL) presented with rising creatinine up to 2.69 mg/dl (baseline 1.4 mg/dl), gross hematuria, proteinuria, and intermittent arthritis. Review of systems was otherwise negative except for intermittent cramping in her feet, and she had no recent medication changes. Physical exam was unremarkable. A renal biopsy was performed prior to referral.

Diagnostic Testing:

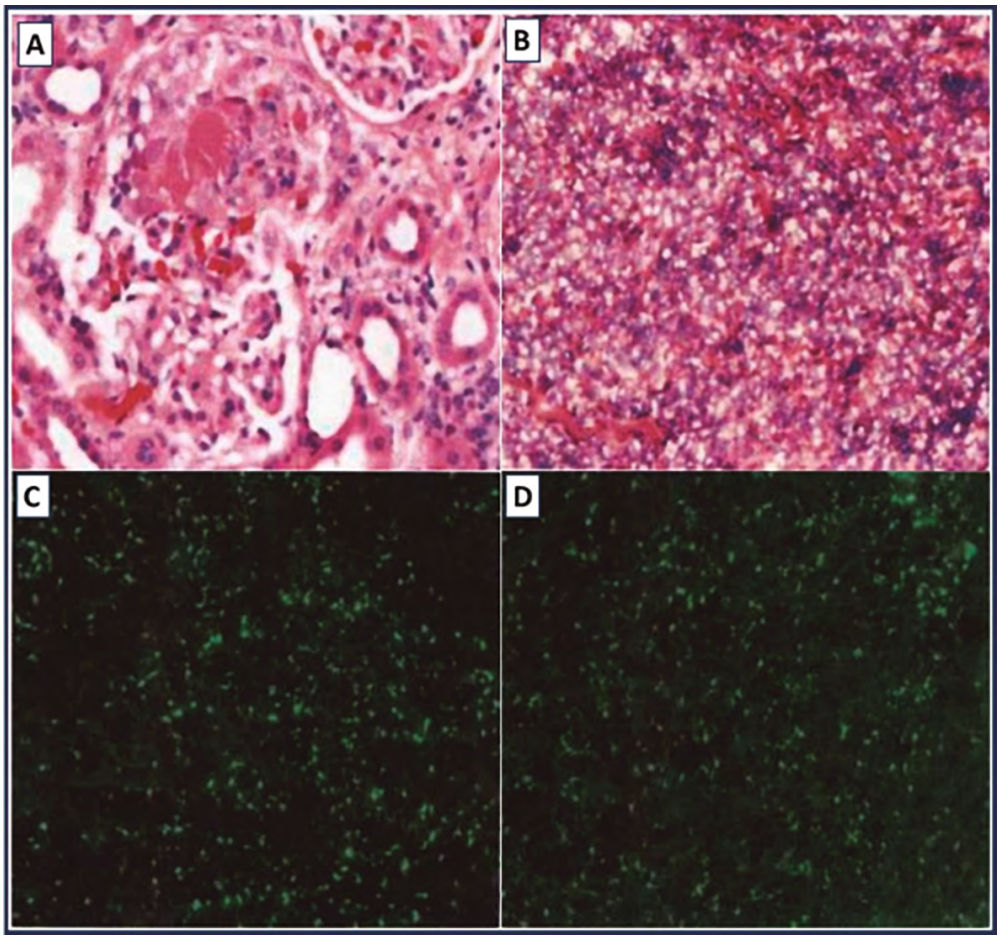

Figure 1. Renal biopsy A. Glomerular cellular crescent and fibrinoid necrosis. B. Dense lymphocytic interstitial infiltrate. C. IgG immunofluorescence (IF) of infiltrate. D. Kappa IF of infiltrate.

- Renal biopsy: pauci-immune focal necrotizing glomerulonephritis (GN) with 13% crescents, segmental fibrinoid necrosis, diffuse mononuclear interstitial inflammation and dense infiltrate at the end of the biopsy core. IF of that infiltrate demonstrated diffuse granular mostly cytoplasmic and perinuclear staining with antiserum for IgG and kappa light chains. (Figure 1)
- Leukopenia with 70% lymphocytes, anemia, thrombocytopenia.
- Urine sediment with 50 RBC/hpf (>20% with dysmorphic features), rare mixed cellular casts, 7-10 WBC/hpf.
- Urine protein/creatinine ratio 1507 mg/g.
- Positive perinuclear-ANCA pattern, MPO-ANCA (102.5 U/ml).
- SPEP with irregularity in the gamma region; faint monoclonal component typed as IgG Kappa on immunofixation; Kappa/Lambda free light chain ratio 2.3.
- Peripheral blood flow cytometry demonstrated CD5 positive kappa restricted B-cell population consistent with CD5+/CD23+ mature B-cell leukemia/lymphoma, representing 50% of the peripheral white blood cells.

Differential & Final Diagnosis: Differential: Idiopathic ANCA vasculitis (AV), sarcoidosis, paraneoplastic disease, infection-related GN.

Final Diagnosis: MPO+ ANCA vasculitis secondary to CLL.

Discussion of Management: Though treatment for AV with crescentic disease typically involves cyclophosphamide and steroids, the abnormal infiltrate consistent with CLL prompted discussion with oncology. Rarely, renal involvement and AV have been reported with CLL.[1-2] Given the suspicion of paraneoplastic AV, treatment of the underlying CLL was felt to be indicated. She was started on obinutuzumab monotherapy with later addition of venetoclax and achieved remission of CLL and demonstrated significant renal recovery (creatinine 1.2 mg/dl). Both CLL and AV have remained in remission off therapy.

Conclusions: AV may rarely be associated with hematologic malignancies. We present a unique case of an MPO-positive AV thought to be a manifestation of CLL. The patient was treated for underlying CLL with remission of AV. In the context of underlying indolent B cell malignancy, treatment of AV directed toward the underlying malignancy should be considered.

References:

1. Wanchoo et al. Renal involvement in chronic lymphocytic leukemia. Clin Kidney J. 2018 Oct;11(5):670-680.
2. Henriksen et al. Rare association of chronic lymphocytic leukemia/small lymphocytic lymphoma, ANCAs, and pauci-immune crescentic glomerulonephritis. Am J Kidney Dis. 2011 Jan;57(1):170-4.

Disclosures: None.

O-089

A case of a puerperal granulomatosis with polyangiitis relapse

Cliona Cowhig[1], Liam Plant[1], Nóirín E. Russell[2], Michael Clarkson[1], Sarah Moran[1].

[1]Cork University Hospital, Cork, Republic of Ireland; [2]Cork University Maternity Hospital, Cork, Republic of Ireland.

Presentation of Case: A 35-year-old female with a 15-year history of PR3-ANCA associated vasculitis (AAV) presented at 23 weeks' gestation with mono-arthritis, proteinuria, acute kidney injury and foetal intrauterine growth restriction. Her background history was significant for AAV with renal, skin, nasal, nerve, and joint involvement. A frequently relapsing disease course was experienced with ultimate progression to end stage renal failure and transplantation eight years post diagnosis. PR-3 titres were persistently elevated post-transplant, however, only one clinical relapse occurred which was managed with an oral steroid pulse. Her AAV had been quiescent for 2 years at the time and there had been an uncomplicated obstetric course prior to the 23rd week of pregnancy.

Diagnostic Testing: Laboratory data was significant for a creatinine of 102umol/L (baseline 74 umol/L), urinary protein creatinine ratio was 724.4mg/mmol. Liver function tests, haemoglobin and platelets were unremarkable. She was persistently c-ANCA positive with a PR-3 of 181 IU/ml one month prior to this presentation (prior PR3 range 50-150 IU/ml in the post transplant period).

Differential & Final Diagnosis: Pre-eclampsia (PET) was the initial clinical diagnosis and emergent C-section was arranged for obstetric indications at week 23+5. Prednisolone was increased peri-operatively. Placental histopathology was significant for maternal vascular malperfusion with foci of infarction, and perivillious fibrinoid deposition.

6 weeks post-partum the patient presented with bilateral pulmonary emboli, cardiomyopathy and a further rise in ANCA titre. On reinterrogation of the case the patient had experienced migratory arthralgias, and features concerning for episcleritis peripartum. A clinical diagnosis of a ANCA vasculitis relapse in the setting of pregnancy was reached. This case outlines the complexity of diagnosing an AAV relapse, potentially concurrent PET, and subsequent cardiomyopathy in pregnancy and the post-partum period.

Discussion of Management: Rituximab and induction steroids were commenced 6 weeks post-partum with co-trimoxazole anti-microbial prophylaxis. The evidence base regarding the use of rituximab and co-trimoxazole during breastfeeding in premature neonates is limited. At six-month follow-up the patient had returned to baseline immunosuppression, recovered cardiac function, and had no evidence of active AAV.

Conclusions: Pregnancy in the setting of vasculitis poses diagnostic and therapeutic challenges, and an increased frequency of maternal and foetal complications. This case emphasises the difficulty in differentiating AAV relapse from pre-eclampsia in the late second trimester and underscores the need for employing existing biomarkers such as soluble fms-like tyrosine kinase 1 (sFlt-1), and urinary CD163 to clarify diagnosis and thus optimise management. Furthermore, it highlights the urgent need to explore new biomarkers of vasculitis disease activity.

Disclosures: None

PLENARY SESSION: END-ORGAN DAMAGE AND REPAIR

O-090

Classical monocyte-derived and *SPP1* lipid-associated macrophages orchestrate inflammatory and fibrotic processes in ANCA-associated glomerulonephritis

Yosta Vegting[1], Aldo Jongejan[1], Annette Neele[1], Nike Claessen[1], Gal Sela[1], Koen Prange[1], Jesper Kers[1], Joris Roelofs[1], Joost Van Der Heijden[2], Onno De Boer[1], Ester Remmerswaal[1], Liffert Vogt[1], Frederike Bemelman[1], Menno De Winther[1], Perry Moerland[1], Marc Hilhorst[1].

[1]AmsterdamUMC, Amsterdam, Netherlands; [2]Spaarne Gasthuis Hospital, Hoofddorp, Netherlands.

Background/ Objectives: Kidney macrophage infiltration is a histological hallmark of vasculitic lesions and is strongly linked to disease activity in anti-neutrophil cytoplasmic antibodies (ANCA)-associated glomerulonephritis (AGN). A recent single-cell peripheral blood monocyte study showed increased proportions of activated CD14⁺ monocytes[1]. The precise mechanisms by which kidney macrophages influence local inflammation and long-term damage remain largely unknown.

Methods: Kidney macrophage diversity was studied using single cell transcriptome analysis of CD45⁺ immune cells from freshly retrieved kidney biopsies of five AGN patients, a lupus nephritis and nephrectomy control (NC). Myeloid cells were selected and reclustered to identify disease-specific macrophage subtypes and functionality was assessed by a gene set enrichment analysis. Findings were validated using multicolor immunofluorescence stainings and flowcytometry, and correlations between monocyte and macrophage subsets and clinical and histological markers were assessed. Last, differences between serological subsets were examined.

Results: Data from 25 485 high-quality kidney immune cells were retrieved. Detailed subclustering identified a novel SPP1⁺ lipid-associated macrophage (SPP1 LAMs) subtype exhibiting distinctive upregulation of fibrotic genesets (**Fig 1b, 1d**). Evaluating kidney macrophage subsets revealed a markedly increased proportion of CD163⁺ macrophages in AGN compared to NC tissue, predominantly composed of highly inflammatory classical monocyte-derived macrophages (MDMs) (ANCA vs. NC, 52% vs. 38%), accompanied by resident-like C1Q macrophages, and SPP1 LAMs (**Fig 1a-c**). Our findings indicate a critical role for classical MDMs in the inflammatory response by neutrophil and monocyte recruitment (CXCL2, CXCL3, CXCL8, CCL3) and pro-inflammatory cytokine production (IL1β, TNF), while SPP1 LAMs coordinate fibrotic processes. An analogous trend in the expansion of peripheral blood classical monocytes during active disease was found (**Fig 1e**).

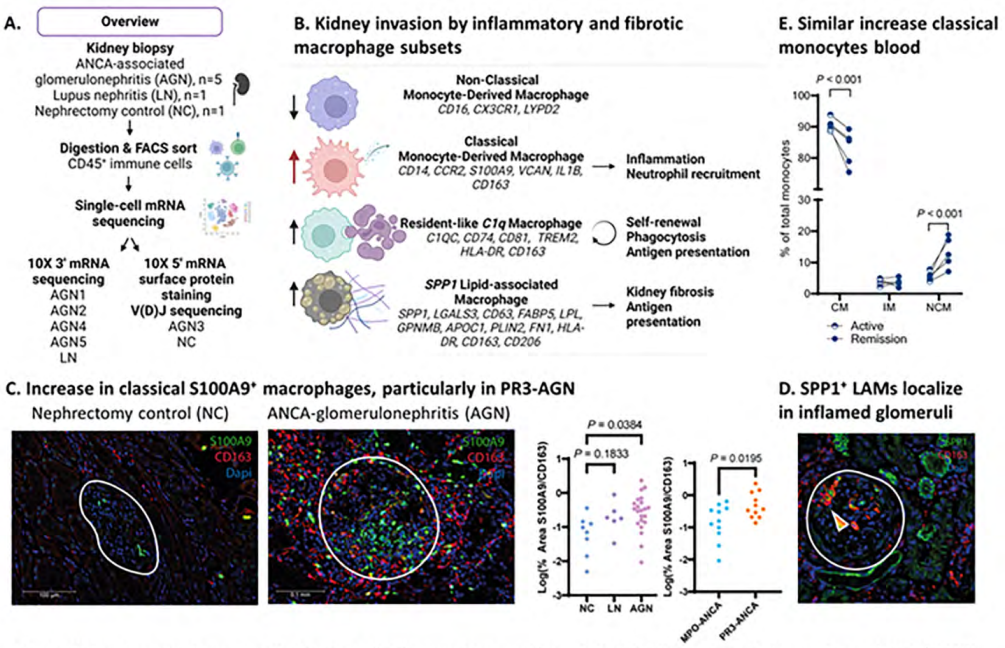

Fig. 1: Kidney macrophages are instigators of inflammation and fibrosis in ANCA-associated glomerulonephritis (AGN) **A,** Overview methods single-cell RNA sequencing kidney biopsies. **B,** Summary findings kidney macrophage subsets, markers and functionality. **C-D,** Multi-color immunofluorescence stainings of kidney biopsies of AGN, LN and NC. **C,** Semi-quantification shows significantly increased CD163/S100A9 macrophages (representing classical MDMs) in AGN, particularly in PR3-ANCA subtype. **D,** SPP1/CD163 macrophages are located in areas of inflammation. **E,** Flowcytometric analysis of peripheral blood monocyte subsets. CM, classical monocyte; IM, intermediate monocytes; NCM, Non-classical monocytes

Conclusions: Kidney macrophages are not just bystanders, but instigators of inflammation and fibrosis in AGN. Classical monocyte dysregulation and kidney infiltration seems to be a key event in the pathogenesis, challenging the prevailing focus on neutrophils. Targeting classical monocyte infiltration and *SPP1* LAM formation may potentially control the inflammatory cascade and attenuate resulting fibrosis in AGN and kidney disease in general.

References:

1 Nishide et al. Single-cell multi-omics analysis identifies two distinct phenotypes of newly-onset microscopic polyangiitis. Nat Commun 14, 5789 (2023).

Disclosures: None related to this research.

O-091

Activated B-cells induce fibroblast activation and cytokine production in giant cell arteritis

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University Medical Center Groningen, Groningen, Netherlands.

Background/Objectives: Giant cell arteritis (GCA) is a large vessel vasculitis characterized by arterial wall inflammation and remodelling. We previously showed that highly organized B-cell clusters are present in GCA-affected arteries, particularly in the adventitia[1]. Fibroblasts, the predominant cell type in the adventitia, may interact with B-cells owing to their location and phenotypic plasticity. As stromal cells, fibroblasts play a crucial role in orchestrating immune responses. In GCA arterial lesions, both B-cells and fibroblasts produce cytokines. This study aims to explore the heterogeneity/subtypes of fibroblast in B-cell clusters of GCA-affected aorta tissues, and to investigate the impact of B-cells on fibroblast activation and cytokine production through in vitro analyses.

Methods: Immunohistochemistry, detecting several fibroblast markers (CD90, fibroblast activation protein alpha (FAP), podoplanin (PDPN), CD248, alpha-smooth muscle actin (αSMA)) and B-cells (CD20), was performed on GCA-affected (n=9) and atherosclerotic (AS, n=11) aorta tissues. B-cells isolated from peripheral blood mononuclear cells (PBMCs) of GCA patients (n=6) and healthy donors (n=10), were incubated with/without CpG oligodeoxynucleotides (ODN) 2006, phorbol 12-myristate 13-acetate (PMA) and calcium ionophore (CaI) for 72 hours. Human aortic adventitial fibroblasts were then cultured with B-cells or with B-cells-conditioned medium for 24 hours in either a co-culture or transwell system. IL-6 levels in medium were measured by ELISA. RNA expression of IL-6, FAP, PDPN, granulocyte macrophage colony-stimulating factor (GM-CSF) and αSMA in fibroblasts was examined by qPCR.

Results: Abundant protein expression of CD90, PDPN, and CD248 was observed in B-cell clusters in the aorta, with no significant differences in fibroblast phenotypes between GCA-affected aorta and AS aorta. Fibroblasts showed enhanced RNA expression of IL-6 (Figure 1A), GM-CSF, PDPN, FAP, but not αSMA, when cocultured with activated B-cells or activated B-cells-conditioned medium. Coculture with activated B-cells also promoted IL-6 secretion by fibroblasts (Figure 1B). Mechanistically, soluble factors rather than cell-cell contact seemed to mediate effects of activated B-cells on fibroblasts.

Conclusions: Activated B-cells may steer fibroblasts towards a proinflammatory phenotype, possibly contributing to disease progression in GCA. If proven, B-cell-targeted therapy may alleviate both B-cell and fibroblast-related inflammation in GCA.

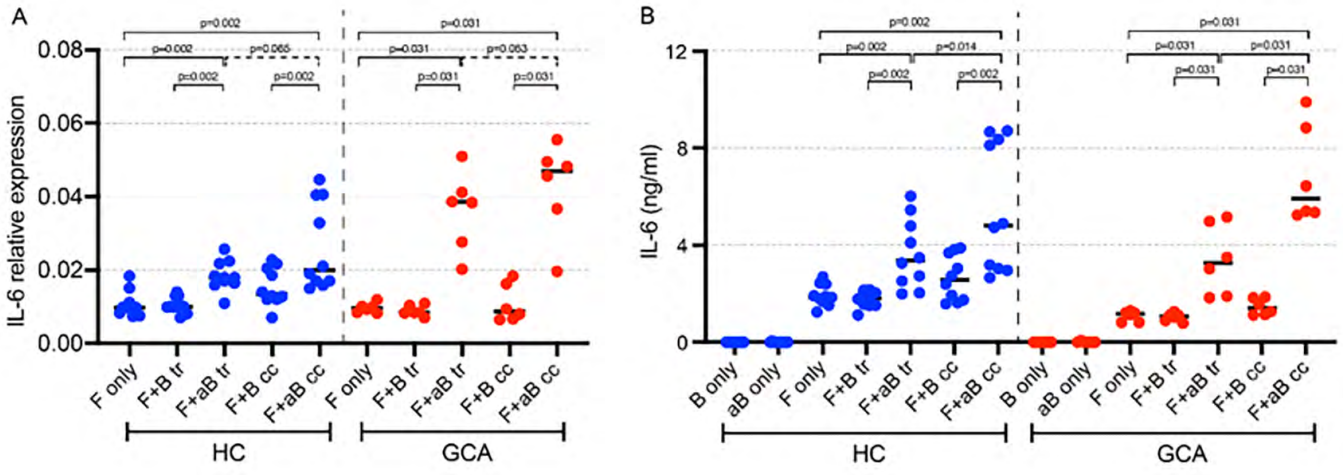

Figure 1. Activated B-cells promote interleukin-6 (IL-6) expression and secretion in human aortic adventitial fibroblasts. (A) IL-6 mRNA levels (relative to GAPDH) in fibroblasts, cultured with/without B-cells from healthy donors (HC) or GCA patients. (B) IL-6 levels in coculture medium. Abbreviations: GCA=giant cell arteritis, F=fibroblasts, B=B-cells, aB=activated B-cells, tr=transwell, cc=cell cell contact.

References:

1. Graver JC, et al. Front Immunol. 2019; 10: 83.

Disclosures: None.

O-092

Long-term Observational Study of Interstitial Lung Disease in ANCA-Associated Vasculitis: European Multicentre Study

Aglaia Chalkia[1], Rachel Jones[1], Ajay Kamath[2], Aladdin J. Mohammad[3], Sara Monti[4], Chetan B. Mukhtyar[2], Viral Nanda[2], Ioannis Petrakis[5], Dimitrios Petras[6], Ashnish Sinha[7], Pasupathy Sivasothy[8], Rona Smith[1], Konstantinos Stylianou[5], Dimitrios Vassilopoulos[6], David Jayne[9].

[1]University of Cambridge, Department of Medicine, Cambridge, United Kingdom; [2]Norfolk and Norwich University Hospital, Norwich, United Kingdom; [3]Lund University, Lund, Sweden; [4]Fondazione IRCCS Policlinico San Matteo, Pavia, Italy; [5]University Hospital of Heraklion, Heraklion, Greece; [6]General Hospital of Athens Hippokration, Athens, Greece; [7]Norfolk and Norwich University Hospital, Norwich, Greece; [8]Vasculitis & lupus Clinic, Addenbrooke's Hospital, Cambridge, United Kingdom; [9]University of Cambridge, Department of Medicine, Cambridge, Greece.

Background/Objectives: Given the limited data on the epidemiology and outcomes of patients with Interstitial Lung Disease (ILD) associated with ANCA-associated Vasculitis (AAV) or positive ANCA and the conflicting results regarding the effectiveness of immunosuppressive treatments, our objective is to describe the long-term outcomes and evaluate the impact of immunosuppressive therapy on lung function.

Methods: A European multicentre retrospective study encompassed patients with ILD-associated with AAV or ANCA. The diagnosis of ILD was confirmed by a CT chest pattern of usual interstitial pneumonia (UIP), non-specific interstitial pneumonia (NSIP), organising pneumonia or chronic hypersensitivity pneumonia. Time-to-event analyses were employed to evaluate both survival and respiratory survival, defined as independency from long-term oxygen treatment. The impact of immunosuppressive therapy was assessed by the relative change in percentage of predicted Forced Vital Capacity (FVC) and Diffusing Capacity for Carbon Monoxide (TLCOc) between treatment initiation and 12 months.

Results: 173 patients with ILD were included. 135 had ILD with ANCA positivity with vasculitis (AAV-ILD) and 38 had ILD with ANCA positivity without vasculitis (ANCA-ILD). The mean age at ILD diagnosis was 70±11 years, and 82% was positive for MPO-ANCA. The most prevalent radiological pattern observed was UIP (66%).

Median survival was 9.8 years, with a trend favouring earlier mortality in ANCA-ILD compared to AAV-ILD (log-rank, p=0.053, fig.1). Median respiratory survival for the entire cohort was 13 years. Over a median follow-up of 4.9 years (interquartile range 2-8), the adjusted mean annual rates of absolute decline were -3.1% for FVC % and -3.8% for TLCOc %. In multivariate Cox regression analysis age (Hazard ratio (HR) 1.1; 95% CI, 1.06 to 1.16), baseline FVC % (HR 0.9; 95% CI, 0.96 to 0.99), baseline TLCOc % (HR 0.9; 95% CI, 0.96 to 0.99), and long-term oxygen requirement (HR 2; 95% CI, 1.08 to 3.88) were identified as significant predictive factors for mortality.

90% of the cohort, received immunosuppressive treatment, which included cyclophosphamide (CYC) in 52%, rituximab (RTX) in 17%, combination in 12%, mycophenolate mofetil (MMF) or methotrexate in 9% as part of the induction regimen. Evaluating the impact of immunosuppression on lung progression over 12 months revealed slowing of the decline of FVC % and TLCO %, most evident in CYC and RTX-treated patients.

Conclusions: Our study provides insights into the long-term outcomes of AAV and ANCA associated ILD, where lung severity emerged as a predominant risk factor for mortality. Immunosuppressive treatment appeared to retard progression of lung disease in the short term.

Disclosures: RJ received fees from GSK, Roche, Vifor. DJ from Amgen, Astra-Zeneca, CSL Vifor, GSK, Novartis, Roche, Takeda. The other authors declared no conflicts of interest.

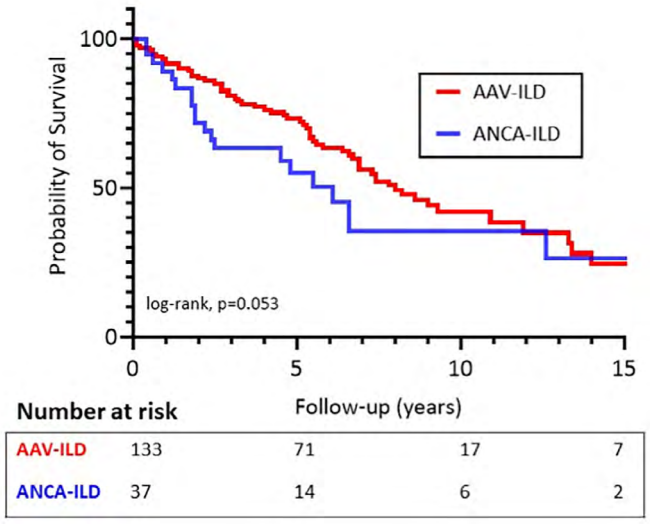

Figure 1. Kaplan Meir survival curve according to AAV-ILD and ANCA-ILD.

BREAKOUT SESSION: IMAGING IN DISEASE ASSESSMENT

O-093

Association of extent of vascular inflammation on cranial MRI with visual complications in giant cell arteritis

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[1]University of Pennsylvania, Philadelphia, United States; [2]St. Joseph's Hospital, Hamilton, Canada; [3]University of Southern California, Los Angeles, United States.

Background/Objectives: Vessel wall MRI can detect inflammation of multiple cranial arteries beyond the temporal arteries and may be useful to assess disease severity. This study evaluated disease extent on MRI and its association with visual complications from GCA ("ocular GCA").

Methods: Patients with newly-diagnosed or relapsing cranial GCA who underwent cranial vessel wall MRI were included. Active cranial GCA and ocular involvement were determined by a rheumatologist and/or neuro-ophthalmologist. MRI enhancement of 7 arteries and 2 muscles (either right or left side) as well as a global imaging diagnosis (GCA or non-GCA) were determined by a single radiologist blinded to all clinical data. In a subset of patients, repeat MRIs were performed at month 1, 6 and 12. Using a mixed effects model that combines information from all structures on MRI, a new continuous global patient-level score, named the Propensity for Enhancement for GCA (PEG) score, was derived. The PEG score ranges from 0-1 and corresponds to the degree and extent of vascular inflammation. Groups were compared using Wilcoxon rank-sum and chi-square tests. Linear test for trend assessed longitudinal changes in the PEG score.

Results: A total of 64 patients were included: 12 ocular GCA, 13 non-ocular GCA, and 39 non-GCA. A greater proportion of arteries and muscles had abnormal MRI enhancement in GCA vs non-GCA and ocular vs non-ocular GCA (**Figure 1A**). Similarly, PEG score was higher in ocular vs non-ocular GCA (median PEG score [IQR] 0.46 [0.26-0.69] vs 0.08 [0.03-0.46], P = 0.07, **Figure 1B**). We compared the PEG score in GCA patients with vs without orbital MRI enhancement (regardless of visual symptoms) and found they were significantly different (median PEG score [IQR] 0.46 [0.46-0.72] vs 0.07 [0,03-0.15], P < 0.01, **Figure 1B**). Among 11 patients with GCA who underwent repeat MRIs, the PEG score significantly improved over time and reached normal levels by month 12 (**Figure 1C**).

Conclusions: MRI reveals a greater extent of cranial vascular inflammation in patients with ocular vs non-ocular GCA. The PEG score, a novel continuous global MRI score, was higher in ocular vs non-ocular GCA and in patients with vs without abnormal orbital MRI enhancement. The PEG score significantly improved over time with treatment. These results provide proof of principle that comprehensive assessment of multiple cranial arteries using vessel wall MRI may be useful as an imaging biomarker of disease severity in GCA and future studies could determine if MRI-guided clinical decision-making improves outcomes in patients with GCA.

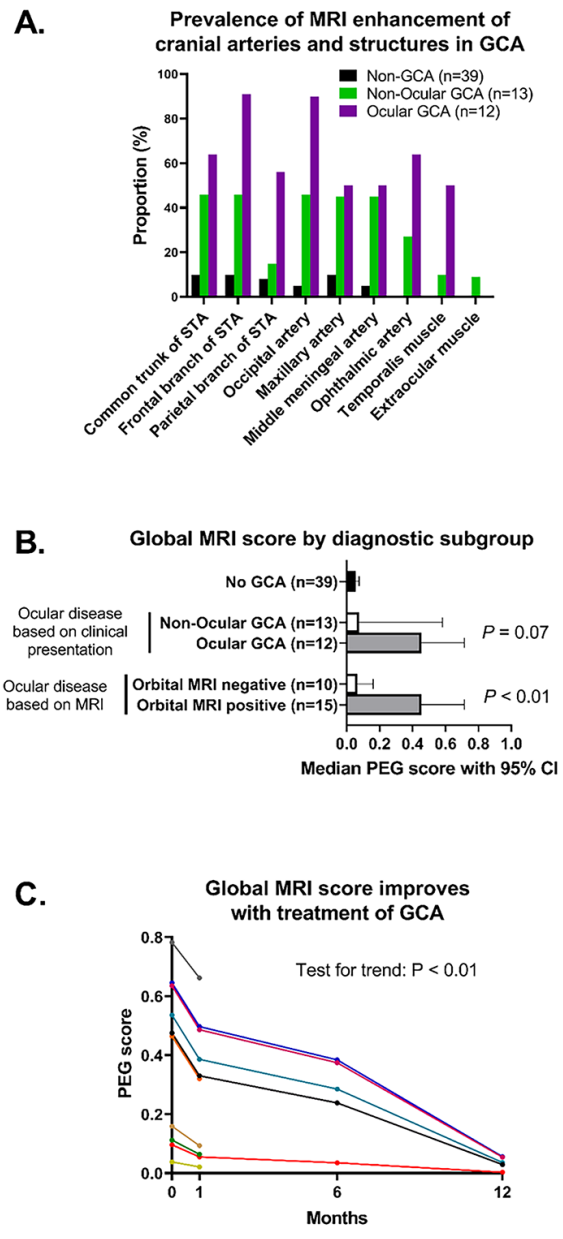

Figure 1. Ocular involvement in giant cell arteritis is associated with greater disease extent on cranial vessel wall MRI. Compared to GCA patients without ocular disease, patients with ocular involvement have more enhancing structures on MRI (A) and a higher Propensity for Enhancement for GCA (PEG) score, which is a novel continuous global MRI score (B). Line plots of individual patients with GCA (n=11) demonstrates that PEG score significantly decreases over time with treatment (C). Abbreviations: GCA, giant cell arteritis; STA, superficial temporal artery.

O-094

Imaging and clinical predictors of outcome in chronic periaortitis

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Background: Treatment with glucocorticoids (GC), often combined with immunosuppressants, effectively induces remission in the majority of cases (75-95%) of chronic periaortitis (CP). However, a significant proportion of patients (up to 75%) experience relapses. Limited literature exists on predictors of these outcomes.

Objective: The aim of this study was to identify predictors of remission and relapse in patients with CP.

Methods: We retrospectively reviewed consecutive adult CP patients referred to dedicated outpatient clinics at three Italian hospitals between January 2006 and February 2021. To be included, patients were required to have baseline and post-treatment CT, 18F-FDG PET, or MRI scans.

Statistical Analysis: Logistic univariate and multivariate regression models were employed to assess remission probability based on baseline demographic and clinical parameters. Risk of relapse, at baseline, month 4, and end of treatment (EOT), was evaluated with Cox univariate and multivariate regression models. Measurement of vascular uptake at 18F-FDG PET was graded using a 4-point semiquantitative scale. Metabolic responses were classified as complete, partial, stable or progressive disease according to PERCIST criteria. Remission was defined as the disappearance of disease-related symptoms, normalization of ESR and CRP and a decrease/stabilization of the mass on imaging. Relapse was defined as recurrence of disease-related symptoms or enlargement of the mass on imaging.

Results: One hundred and fifteen patients, with a mean follow-up of 33 (17-57) months, were included in this study. Baseline characteristics and treatments are reported in Table 1. Of the 115 patients, 101 (87%) achieved remission, with a median time to remission of 4 (3-5) months. Among those who achieved remission, 42 out of 101 (42%) experienced a relapse, with a median time to relapse of 14 (8-26) months. Smoking habit (OR 0.34, 95% CI 0.11-0.99, p=0.049) and an atypical CP localization (ie, pelvic, pre-sacral, peri-ureteral involvement, OR 0.11, 95% CI 0.02-0.52, p=0.005) were identified as negative independent predictors of remission. Conversely, PET-CT uptake at baseline (grade 0 vs grade 1-3) emerged as a positive predictor of remission (OR 11.51, 95% CI 1.35-98.20, p=0.025). In terms of predictors of relapse, thoracic vessel involvement and a positive 18FDG-PET at EOT were identified as positive independent predictors of relapse (HR 2.61, 95% CI 1.19-5.68, p=0.016 and HR 3.47, 95% CI 1.54-7.82, p=0.003 respectively).

Conclusions: To our knowledge this is the largest study aiming at evaluating factors influencing remission and relapse in CP patients. These findings provide valuable insight into discerning patients who may require intensified immunosuppressive therapy to attain remission and to prevent relapse. This underscores the potential necessity for tailoring treatment approaches to specific subtypes of the disease.

Baseline characteristics	
Men	40/115 (34.8%)
Age	55 [50-63]
Clinical features	
Idiopathic retroperitoneal fibrosis	105/115 (91.3%)
Perianeurysmal retroperitoneal fibrosis	10/115 (8.7%)
Symptoms	107/115 (93%)
Hydronephrosis	78/114 (68.4%)
Deep vein thrombosis	19/114 (11.8%)
Established atherosclerotic disease	13/111 (11.7%)
Associated autoimmune disease	38/114 (33.3%)
Fibro-inflammatory disease	19/114 (16.7%)
Laboratory findings	
Erythrocyte sedimentation rate (mm/h)	50 [34-73]
C-reactive protein concentration (mg/L)	13.1 [5.4-33]
Serum creatinine (mg/dL)	1.2 [0.9-2-2]
IgG4 above normal range	18/92 (19.6%)
Characteristics of CP at CT/MR	
Typical CP localization	97/115 (84.3%)
Atypical CP localization	18/115 (15.6%)
Thoracic involvement	21/114 (18.4%)
Lesion thickness (max, mm)	15 [10.3-22]
Uptake at ^{18}F-FDG PET	96/115 (83.5%)
Grade 0	6/96 (6.2%)
Grade 1	5/96 (5.2%)
Grade 2	30/96 (31.3%)
Grade 3	55/96 (57.3%)
Treatment regimens	
Glucocorticoids only	71/115 (62%)
Glucocorticoids + MTX	22/115 (19%)
Glucocorticoids + MMF	16/115 (14%)
Glucocorticoids + RTX	6/115 (5%)

Table 1.

O-095

Predicting Disease Relapse in ANCA Associated Vasculitis with Radiomics of Lung Nodules/Masses

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Background/Objective: Pulmonary nodules are common manifestations of granulomatosis with polyangiitis (GPA) as compared to the other syndromes of ANCA-associated vasculitis (AAV)[1]. It has been postulated that granulomatous manifestations including lung nodules predispose patients to relapsing disease[1,2]. Despite advances in our understanding of the pathogenesis and treatment for AAV, relapses are common. For this reason, we sought to develop a radiomic model utilizing quantitative imaging data from CT chest to predict risk of relapsing AAV.

Methods: We retrospectively reviewed patients at Mayo Clinic sites between 1/1/2006 and 9/1/2022 with pulmonary nodules at time of diagnosis. Inclusion criteria were age over 18 years, meeting Chapel Hill and ACR/EULAR consensus definitions of GPA or Microscopic Polyangiitis (MPA), and imaging with high-resolution CT chest at initial diagnosis of AAV. Quantitative CT analytics with CANARY (Computer Aided Nodule Analysis and Risk Yield) was applied to pulmonary nodules. A texture-based radiomic analysis of the lung with Computer-Aided Lung Informatics for Pathology Evaluation and Rating (CALIPER) was then performed. Following radiomic feature extraction, least absolute shrinkage and selection operator (LASSO) reduction was used to identify the candidate features best fit to build a radiomic model predictive of relapsing disease.

Results: In total N=49 patients were included, N=27 with non-relapsing disease and N=22 patients with relapsing disease. Median age at diagnosis was 56 years (IQR 45-66) with N=23 (46%) females. Patients were predominantly c-ANCA/PR3 positive (N=34/N=34) and classified as GPA in 93% (N=46) of patients Median Birmingham Vasculitis Activity Score for Wegener´s Granulomatosis (BVAS/WG) at diagnosis was 3 (1-7). An ensemble model integrating radiomic features from two existing models yielded a sensitivity of 91%, specificity of 89%, and ensemble AUC of 0.94 predictive of relapsing diseases relapse as illustrated in Figure 1.

Conclusion: We demonstrated the feasibility of novel radiomic model to predict risk of relapse based on CT scan at initiation presentation with AAV.

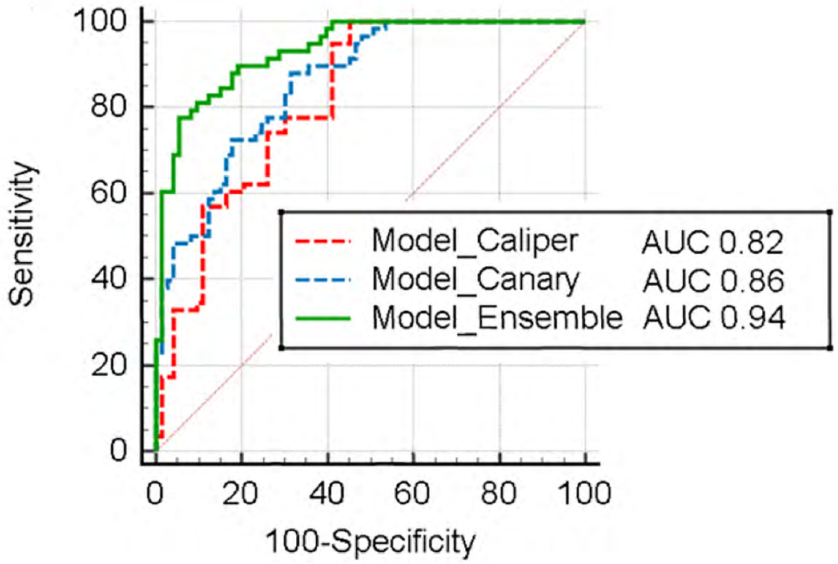

Figure 1: Area under the curve (AUC) illustrating model performance for prediction of relapse risk with CANARY based anaylysis (red dashed), CALIPER (blue dashed) , and an ensemble model (green) with radiomic features dervied from both models yielding the highest absolute AUC.

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Disclosures: Specks – Consulting/Advisory Boards: Amgen, Argenix, AstraZeneca, Boehringer Ingelheim, CSL Vifor. Research Grant/Support: Amgen, AstraZeneca, Bristol Myers Squibb, Genentech, GSK, Northstar Medical Radioisotopes, Takeda.

O-096

Use of FDG-PET to Monitor Disease Activity in Patients with Giant Cell Arteritis on Tocilizumab

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Background: The use of tocilizumab for treatment of giant cell arteritis (GCA) is supported by recent society guidelines[1,2]. Because tocilizumab has a direct effect on acute phase reactants, the optimal way to monitor disease activity in this subset of patients remains uncertain.

The objective of this study was to assess the value of FDG-PET scans in monitoring disease activity in patients with GCA on treatment with tocilizumab.

Methods: Patients with GCA treated with tocilizumab were selected from an ongoing prospective, observational cohort. All patients fulfilled the 2022 ACR/EULAR classification criteria for GCA. At each study visit, patients underwent clinical, laboratory, and imaging assessments, including both FDG-PET and non-invasive angiography.

A single reader reviewed all PET scans, blinded to clinical data. Qualitative assessment of FDG uptake relative to liver uptake by visual assessment (scale 0-3) was assessed in 9 arterial territories. A summary score, PET vascular activity score (PETVAS), was calculated (scale 0-27).

Fisher's exact or Wilcoxon rank sum test were used to compare characteristics of patients with and without PET activity.

Results: Thirty-five patients with GCA underwent FDG-PET imaging while on tocilizumab treatment for ≥ 6 months. Four patients had persistent clinical disease activity on tocilizumab treatment and FDG-PET scans were active in all 4 patients (PETVAS: 19, 20, 22, 19). Of the remaining 31 patients who achieved clinical remission on tocilizumab treatment, FDG-PET was performed after median tocilizumab treatment duration of 254 days (IQR 189-558), on a median prednisone dose of 0 mg/day (IQR 0-6), and with a median disease duration of 1070 days (IQR 401-1415). FDG-PET was active in 17 patients (55%) and inactive in 14 patients (45%). There were no differences observed between patients with and without PET activity with respect to age, sex, disease duration, tocilizumab treatment duration, acute phase reactants, glucocorticoid dose, or use of other immunosuppressants **(Table).**

Of the 31 patients who achieved clinical remission on tocilizumab, no patient with or without PET activity had angiographic progression over the follow-up period. A total of 17 patients discontinued tocilizumab (15 patients due to sustained clinical remission, 2 patients due to side effects attributed to tocilizumab) after a median treatment duration of 1.8 years (IQR 0.8-2.3). Five of the 17 patients (29%) who discontinued tocilizumab subsequently had a clinical relapse a median of 1.3 years (IQR 0.6-2.8) after stopping tocilizumab and no patient who remained on tocilizumab had a clinical relapse. Among the 5 patients who had a clinical relapse, there were no differences in whether PET scan was active (n=3, 18%) or inactive (n=2, 14%) during established clinical remission on tocilizumab (p=0.80) **(Table).**

Conclusions: FDG-PET, when performed in patients with GCA while in clinical remission on treatment with tocilizumab, has limited value to guide management decisions or inform prognostic risk for relapse.

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Disclosures: None.

Table: Characteristics of patients with GCA on Tocilizumab who had an FDG-PET scan during established clinical remission.

	PET active n=17	**PET inactive** n=14	**p value**
Age	70 (58-83.2)	72 (66.75-78.25)	0.36
Female Sex	13 (76%)	8 (57%)	0.44
Disease Duration (days)	1103 (468-1528)	713 (343-1362.5)	0.35
Duration on TCZ (days)	203 (167-776.5)	370.5 (200-562.25)	0.44
ESR	2 (2-5)	2 (2-2)	0.98
CRP	0.4 (0.25-1.3)	0.4 (0.25-1.3)	0.13
Prednisone	0 (0-5.5)	3.75 (0-8.5)	0.49
Methotrexate	1 (6%)	2 (14%)	0.58
PETVAS	22.5 (19-25.25)	16 (14-18.5)	<0.01
Clinical relapse	3 (18%)	2 (14%)	0.80

*Continuous variables are expressed as medians (interquartile range) and categorical variables are expressed as number (%).

O-097

Comparing Clinical and Imaging assessment in Three Takayasu's Arteritis Cohorts by using the Takayasu's Arteritis Disease Activity Index

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Background/ Objectives: The Takayasu' s Arteritis Disease Activity Index (TAIDAI) is a recent tool which integrates clinical and imaging evaluations[1]. We evaluated clinical and imaging assessment in 3 TAK cohorts and compared performance of TAIDAI.

Methods: Clinical data was collected retrospectively in 2 cohorts (Rheumatology Clinics of the Universities of Istanbul and Reggio Emilia). In the other cohort (National Insitutes of Health, NIH) data was obtained prospectively in an ongoing observational study. All patients underwent clinical assessment and fluorodeoxyglucose positron emission tomography (FDG-PET) scans. In the NIH cohort adult patients received a fixed dose of FDG and images were acquired after a 2-hours uptake. In Italy and Turkey, the dose was based on the weight and images were collected after 1 hour.

Physician global assessment (PhGA) was scored to define clinical disease activity, as well as the certainty or uncertainty of the clinical assessment blinded to imaging.

The PET Vascular Activity Score (PETVAS) was calculated for each scan, and TAIDAI was derived. The sensitivity and specificity of TAIDAI was evaluated relative to physician assessment, restricted to cases where clinical assessment was certain.

Results: 211 patients were enrolled. Baseline data are reported in **Table 1**. The mean prednisone dose was significantly lower in the Turkish cohort (2.3, $p<0.001$).

PhGA was lowest in the NIH cohort ($p<0.001$). There were no differences in clinical symptoms except headache was more common in the NIH cohort ($p<0.001$).

PETVAS was significantly higher in the NIH cohort ($p<0.001$).

TAIDAI also differed significantly and had a sensitivity of 100% in the NIH cohort, whereas in the Italian and Turkish cohort was 44% and 38%, respectively. On the contrary, the specificity was 100% in the Italian cohort, but 80% in the NIH and 67% in the Turkish one.

Conclusions: In different cohorts of TAK, the relationships between clinical and imaging- based assessment of disease activity are substantively different. Performance of TAIDAI to discriminate active disease varied due to the heterogeneity of these approaches. Standardization of clinical and imaging assessment is pre-requisite to the conduct of successful multi-center clinical trials in TAK.

References:

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Disclosures: None.

Baseline data	NIH n=96	ITALY n=47	TURKEY n=67
Females	80 (82.5%)	41 (87.2%)	55 (82.1%)
Disease duration	65.37 months (87.7)	34.4 months (49.2)	55 months (74.5)
Age at diagnosis	28.3 (13.9)	30.7 (10.7)	37.6 (14.4)
Physician global assessment	1.44 (2.1)	2.51 (1.7)	4.65 (2.2)
PETVAS	14.6 (7.1)	3.94 (5.2)	5.21 (7.1)
CRP	11.9 mg/dl (22)	2.3 mg/dl (3.3)	18.1 mg/dl (24.2)
ESR	16.5 mm/1st hour (18.4)	33.2 mm/1st hour (28.5)	38.6 mm/1st hour (25.0)
TAIDAI	1.2 (1.8)	0.4 (1.0)	0.6 (1.0)
Active visits	35 (36.1%)	21 (44.7%)	50 (74.6%)
Confident assessment	13 (37.1%)	18 (85.7%)	26 (52%)
Prednisone dose	7.2 mg daily (13.3)	9.9 mg daily (14.4)	2.3 mg daily (9.9)

Table 1. Baseline features of the cohorts.

O-098

Protocolised ultrasonography led pathway has a high sensitivity for diagnosis of primary large vessel vasculitis

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Background/ Objectives: Ultrasonography (US) for diagnosis of large vessel vasculitis (LVV) is a recommended first line diagnostic procedure.[1] Our county has an annual incidence of 57.5/million for primary LVV.[2] Our protocolised fast-track US pathway has reduced visual loss from 18.7% to 11.5%.[3] We present the results of our first 1000 unique referrals. Our objectives were to assess the sensitivity and negative predictive value of our pathway, and to determine the need for scanning beyond the superficial temporal artery.

Methods: Unique requests for US from January 2017 were analysed. Protocolised US examination includes the superficial temporal artery (STA), the axillary artery, followed by other arteries as necessary. Halo sign in at least two different arteries was needed for diagnosis. A temporal artery biopsy (TAB) or positron emission tomography (PET) were requested if the US was negative AND CRP was ³20mg/L (or missing) AND an alternate explanation for the raised CRP was not immediately apparent. Where a second test was not needed OR if it was negative, prednisolone was tapered rapidly. A patient-initiated follow-up allowed rapid re-assessment. If a second test was not done when indicated, GCA was diagnosed on clinical grounds and the pathway was considered to have failed.

Results: The median (IQR) age was 73 (13); 11/1000 referrals were for people <50 years of age. The median (IQR) delay for the US was 4 (4) days. Median (IQR) duration of prednisolone was 4 (5) days.

279/1000 (28%) US scans demonstrated vasculitis. Of the 721 cases with negative US, pre-steroid CRP was unavailable in 7 and was ³20mg/L in 283 cases. An alternate explanation for the CRP was found in 102 cases; 181 were referred for a second test; 7 received a clinical diagnosis of GCA without a second test. The second test was diagnostic in 31/181 (17%) - 24/139 (17%) TAB, 7/42 (17%) PET.

The pathway missed 8 cases - 3 with a negative second test and 5 with CRP <20mg/L were diagnosed with GCA on follow-up. The delayed diagnosis did not result in visual loss.

202/279 (72%) US positive cases had bilateral STA involvement. Additional axillary artery imaging picked up 53 (19%) cases; 24 (9%) cases needed imaging of other arteries.

The sensitivity and negative predictive value of the pathway are 95% (310/325) and 98% (675/690) respectively.

Conclusions: Protocolised US led pathway for diagnosis of LVV is highly sensitive allowing disease exclusion with high certainty. Routine US of the superficial temporal artery and the entire axillary artery capture 91% of cases but ability to scan more arteries improves yield in 9% of cases. Composite testing with US plus second test, stratified by CRP levels can be recommended as a gold standard diagnostic tool for LVV.

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Disclosures: None.

BREAKOUT SESSION: CO-MORBIDITIES

O-099

Comprehensive evaluation of long-term cardiovascular comorbidities among patients with AAV

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Background: ANCA associated vasculitis (AAV) is closely correlated to elevated cardiovascular disease (CVD) rates, positioning it a one of the leading causes of death among these patients. The impact of AAV on the risk of CVD has not been described in large prospective cohorts with a long-term follow up. The aim of our study was to evaluate the occurrence of cardiovascular events, encompassing major adverse cardiovascular events (MACE), to delineate associated risk factors, and to draw comparisons with other cohorts of patients diagnosed with CKD.

Methods: We included 848 patients with a diagnosis of AAV who participated in 7 EUVAS RCTs, recruited from 74 centers in 17 European countries. The three-point MACE outcome was defined as acute myocardial infarction (AMI), stroke, or death from cardiovascular event. We used multivariate logistic regression analysis to assess the risk factors of MACE. Patients from our cohort were compared to the patients from the Chronic Renal Insufficiency Cohort (CRIC), which is a multicenter, prospective observational cohort study of participants with CKD.

Results: During the median FU of 8 years (range 0-24.5, IQR: 2.9-13.6), 100 (11.8%) patients developed diabetes, 98 (13.4%) coronary heart disease (CHD), 90 (12.1%) hypertension, 70 (9.6%) deep vein thrombosis (DVT), 43 patients (5.9%) had a stroke and 28 (3.8%) an AMI. The number of MACE during FU was 144 (17%). MACE was more frequent among patients older than 65 years (n=62 (43.1%); p-value: 0.013). CVD was the primary cause of death in 43 patients (14%). During the first 5 years after randomization, there was a significant increase in the number of cardiovascular events compared to the period 6 years- end of follow up (CHD: n=55 vs n=23, p=<0.001; DVT: n=55 vs n=29; p <0.001; stroke: n=35 vs n=24, p-value < 0.001).

The prognostic factors for MACE in our cohort were hemodialysis dependency during RCT, age, male sex, previous history of CHD and stroke, and occurrence of diabetes during follow up.

Within the subset of patients who underwent kidney biopsy, those in the crescentic class (n=16) followed by the mixed class (n=15) exhibited a significant higher incidence of MACE (p=0.02).

When compared to the cohort of patients with CKD from the CRIC study, the risk for CHD was higher (13.4% (95%CI: 11.16-16.11) vs 5.4% (95% CI 4.5-6.5); respectively; RR: 2.49 (95% CI 1.91-3.24); p-value<0.01). Additionally, there was a higher risk for stroke (5.6% (95% CI 4.2-7.4) vs 2.8% (95% CI 2.2- 3.7); RR 1.97 (95% CI: 1.33- 2.91) p-value: 0.0006).

Conclusions: Patients with AAV had an increased risk of stroke and CHD compared to patients with CKD from other etiologies. During the first years after diagnosis, there is an increased risk for CVD occurrence.

The prognostic factors for MACE in our cohort were hemodialysis dependency, age, male sex, previous story of CHD and stroke, and diabetes during follow up.

Patients with AAV should be considered at high cardiovascular risk; therefore, the therapeutic approach should include the management of traditional cardiovascular risk factors and lifestyle modification. Efforts should be made to meet strict therapeutic targets and to implement early CVD detection programs.

Disclosures: None.

O-100

Prevalence, predictors, and prognosis of serious infections in Takayasu arteritis – a cohort study

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Background/ Objectives: Takayasu arteritis (TAK) is more common in tropical countries, where infections are more common. This study aims to analyze serious infections and their prognostic relevance in an ambispective, monocentric large cohort of TAK from India.

Methods: Serious infections (infections resulting in hospitalization or death or unusual infections such as tuberculosis) were identified from a cohort of TAK. Corticosteroids and disease-modifying anti-rheumatic drug (DMARD) use at the time of serious infection was noted. Baseline demographic characteristics, clinical presentation, angiography), and disease activity scores were compared between TAK with or without serious infections [categorical variables using univariable logistic regression (odds ratios (OR) with 95%CI) and continuous variables with unpaired Student's t test]. Mortality in TAK who developed serious infections vs those without was compared using hazard ratios (HR, with 95%CI).

Results: 38/238 TAK (15.97%) had developed serious infections (50 episodes: one episode, n=30; two episodes, n=7; six episodes, n=1). 11/38 initial episodes occurred in TAK not on corticosteroids and 14/38 in TAK not on DMARDs. Among 39/50 episodes of serious infections, the mean(SD) dose of daily prednisolone was 13.03 (10.41) mg. Pneumonia (n=19) was the commonest infection, followed by tuberculosis (n=12), gastrointestinal infections (n=6), urinary tract infection (n=5), sepsis (n=4), and others (n=4). Three serious infections resulted in death. TAK who developed serious infections (vs those without) had more disease activity at baseline (active disease 97.37% vs 69.50%, ITAS2010 12.66(7.29) vs 10.16(7.02), DEI.TAK 11.21(6.14) vs 8.76(6.07), p<0.05 for all), were more likely to have been initiated on corticosteroids (86.84% vs 70%, p=0.033) or DMARDs (84.21% vs 67%, p=0.034) and had been treated with more number of DMARDs [mean(SD) 1.32(0.96) vs 0.98(0.92), p=0.042]. TAK with serious infections were more likely to have abdominal aorta involvement (OR 2.20, 1.01-4.77), renal artery (left 2.25, 1.11-4.58; right 2.42, 1.18-4.95), or iliac artery involvement (left 5.66, 2.03-15.81; right 3.98, 1.32-11.94). Since the proportional hazards assumption was not met, hazard ratios calculated using exponential parametric regression survival-time model revealed increased risk of death in TAK who developed serious infections (HR 5.52, 95%CI 1.75-17.39, Fig 1), even after adjustment for baseline ITAS2010 (4.65, 95%CI 1.48-14.65), DEI.TAK (4.50, 95%CI 1.43-14.18), disease activity by physician global assessment (4.65, 95%CI 1.48-14.65), use of corticosteroids (5.47, 95%CI 1.73-17.23), DMARDs (5.31, 95%CI 1.69-16.74), number of DMARDs (5.23, 95%CI 1.64-16.64), or differences in angiography (5.91, 95%CI 1.77-19.71).

Conclusions: Serious infections occurred even in the absence of treatment with corticosteroids or DMARDs in about one-third of TAK and were associated with increased risk of death even after adjustment for baseline disease activity.

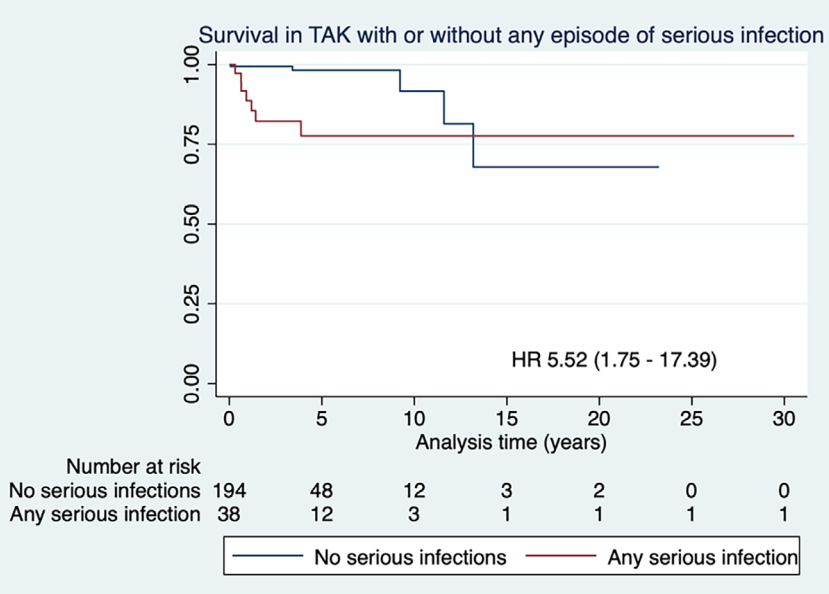

Figure 1: Risk of mortality in TAK with or without serious infections.

References: None.

Disclosures: None.

O-101

Hypogammaglobulinemia in patients with ANCA-associated vasculitis, treated with Rituximab

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Objective: The anti CD20 monoclonal antibody Rituximab (RTX) is a standard treatment for induction and maintenance treatment of ANCA-associated vasculitis. Treatment with RTX, a B-cell depleting agent, entails the risk for hypogammaglobulinemia (HG) thereby increasing the risk of infections. Earlier studies have demonstrated that HG is a common side effect of RTX. This study aims to characterize the occurrence of HG in patients treated with RTX in a population-based cohort of AAV from Sweden.

Methods: Cases with AAV from the AAV cohort (cases with incident AAV between 97-2019, population-based, defined geographic area in southern Sweden) that were treated with RTX either as induction or maintenance treatment were identified. Case records were analysed for the occurrence of HG (defined as IgG<6.7g/L) and demographics, serology, and other treatment received were studied. The incidence rate and predictors of HG were studied. Using a Cox regression model, sex, kidney involvement, glucocorticoid dose at first RTX, age and levels of IgG at RTX start were studied as predictors. Follow- up was from time of first RTX administration to date of HG, death, or end of study (March 2023).

Results: Eighty-four patients (51% female, GPA n=25, MPA n=57, EGPA=2) received RTX. Thirty-eight patients (45%) developed HG anytime during 236 years of follow up resulting in an incidence rate of 16.1 (95%CI 11—21.2) per 100 person-years of follow-up. Two patients (5%) developed severe HG (IgG <3 g/L), 10 (26%) moderate HG (IgG >3 to <4.9g/L) and 26 (68%) mild HG (IgG=4.9—6.69g/L). There was no association with age and no differences in clinical features or other laboratory findings were observed between those with vs with no HG, except for low IgG at start of first RTX (Table 1). Severe infection was observed in 29 of the 84 patients treated with RTX (35%), but only 5 of those cases exhibited HG. Median time from first RTX to HG was 3.5 (IQR 0.7—6) months. Low levels of IgM were observed in 26 (31%) and low IgA in 14 (17%) of cases. Low levels of IgG at RTX start were the only independent factor predicting HG with a HR of 0.85 (95%CI 0.76—0.95) for each 1g increase in IgG at RTX start.

Conclusion: HG is common in patients with AAV, treated with RTX, occurring in almost half of patients. However, an association of HG with the occurrence of severe infections was not observed in our study. Low IgG prior to RTX treatment was the only independent predictor of HG. IgG level at start should warrant close monitoring by the treating physician.

Table 1. Demographics, serology and clinical parameters at diagnosis and time of 1st RTX -treatment.

	All n=84	HG n=38	No HG n=46	
Age at diagnosis in years, mean ±SD	59.32 ± 16	59.42 ±14	59.24 ±17	0.9
Sex, Female, n (%)	43 (51.2)	19 (50)	24 (52.2)	1.0
Age at first RTX treatment, mean ±SD	61.8 ± 15	62.2 ± 13	61.5 ± 17	0.8
Diagnosis, GPA/MPA/EGPA	25/57/2	9/28/1	16/29/1	
PR3–ANCA +, n (%)	58 (69.0)	27 (71.1)	31 (67.4)	0.7
MPO–ANCA +, n (%)	24 (28.6)	10 (26.3)	14 (30.4)	0.7
RTX induction, n (%)	28 (33.3)	12 (31.6)	16 (34.8)	0.4
Plasma–exchange, n (%)	14 (16.7)	5 (13.2)	9 (19.6)	0.5
CYC, n (%)	65 (77.4)	30 (78.9)	35 (76.1)	0.7
BVAS at diagnosis, median (IQR)	16.5 (12—19)	16 (12—22.5)	17 (12—19)	0.36
S–creatinine, µmol/l, (IQR)	97 (74—153)	100 (82.5—144)	88.5 (72.7—176.2)	0.21
eGFR ml/min x1,73m^2, median (IQR)	62 (38—76)	58 (34—74)	70 (43.5—77)	0.27
At time of first RTX treatment				
Prednisolon, mg/day	30.3±21.3	35.5±21.9	28.4±20.8	0.3
IgG g/L ±SD	9.4±3.5	8.5±3.4	10.2±3.4	0.03
IgA g/L ±SD	2.3±1.2	1.9±0.8	2.5±1.3	0.02
IgM g/L ±SD	0.92±0.7	0.8±0,7	1.0±.07	0.06

GPA: granulomatosis with polyangiitis, MPA: microscopic polyangiitis, EGPA: eosinophilic GPA, eGFR estimated glomerular filtration rate (MDRD), BVAS: Birmingham vasculitis activity score, PR3: proteinase 3, MPA: myeloperoxidase. RTX: rituximab, Ig G/A/M: immunoglobuline G/A/M. Data on immunoglobulins prior to RTX available was in 80 cases, 20 (25%) cases show hypogammaglobulinemia before RTX (15 mild, 4 moderate, 1 severe).

O-102

Hospitalization rates and features of a large multicentric cohort of patients with ANCA-associated vasculitis

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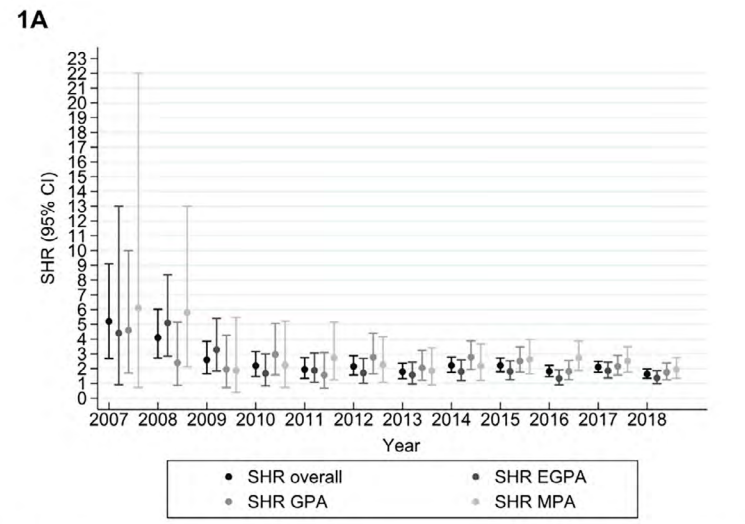
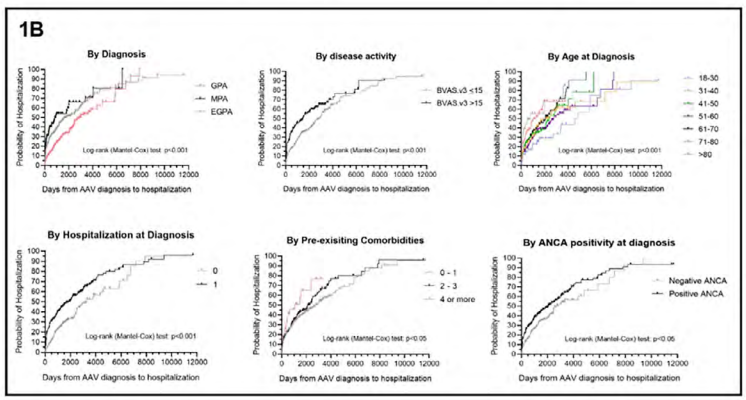
Background/ Objectives: To determine hospitalization rates and features in a large cohort of patients with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV).

Methods: Hospitalization dates, features, length of stay, primary discharge diagnoses and patient data were abstracted from charts of AAV patients from 13 Italian hospitals, between 2007 and 2018. Age- and sex-standardized hospitalization rates (SHR) were calculated by an indirect method, per year and for the study period, using the 2007–2018 hospitalization data provided by the Italian Ministry of Health. Multivariable and survival models were used to explore associations between these outcomes, clinical parameters at diagnosis, and pre-existing comorbidities.

Results: A total of 610 hospitalizations occurred during follow up 47.1% of the 635 patients with AAV (19.4% microscopic polyangiitis, MPA; 34.6% granulomatosis with polyangiitis, GPA; 46.0% eosinophilic GPA, EGPA) during a 12-year observation; in 19.8% for life-threatening conditions and leading to death in 2.3%. The median hospitalization length was 8 days (25-75%IQR, 8-14).





These rates of hospitalization were stably higher in AAV and GPA, MPA and EGPA subsets as compared to general population (2018 SHR (95%CI) for AAV: 1.64 (1.35, 1.97); **Figure 1A:** Age- and sex-SHR by year during 2007-2018).

The main causes of hospitalization in patients with AAV were infectious diseases (18.7%), followed by major relapse and diagnostic re-evaluation (17.2% each), and cardiovascular diseases (10.8%). Among AAV patients hospitalized during follow-up, 55.5% had only 1 hospitalization, 18.7% had 2, and 25.6% had 3 or more hospitalizations. Patients with a diagnosis of GPA or MPA (versus EGPA), higher vasculitis activity (assessed by BVAS), ANCA positivity at diagnosis, and hospitalization at diagnosis ($p<0.001$), more pre-existing comorbidities and older age ($p<0.05$), were more likely to be hospitalized during follow-up (**Figure 1B:** Kaplan-Meier plots of the probability of hospitalization after AAV diagnosis). In a multivariate model, only GPA diagnosis (b coefficient (2.5%-97.5% CI): 0.564 (0.258-0.871)) and higher BVAS at diagnosis (0.038 (0.017-0.058)) were independent predictors of hospitalization during follow-up (both $p<0.0001$).

Conclusions: Patients with AAV experience higher rates of hospitalization than the general population. Approximately half of the patients is hospitalized during follow-up, with identified risk profiles of patients more likely to be hospitalized, requiring more active vigilance.

References: Wallace, Z. et al. Arthritis Care Res. 2016.

Disclosures: SS worked at the IRCCS San Raffaele Scientific Institute at the time of the study and is now an employee of Bristol Myers Squibb.

POSTER

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Poster Tour 1A: Advances in treatment

PT-1A-01

Randomized, Controlled, Double-Blind Trial on the Impact of Rosuvastatin on Sublinical Markers of Atherosclerosis in Patients With ANCA-Associated Vasculitis

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Background: Despite more effective therapeutic strategies in ANCA-associated vasculitis (AAV), there is still a significant risk of morbidity and mortality, mainly due to infection, and cardiovascular disease. Carotid intima-media thickness (cIMT) is a marker of subclinical atherosclerosis associated with cardiovascular risk factors and is predictive of major cardiovascular events (MACE). We hypothesized that patients with AAV might benefit from statin treatment in primary prevention to reduce subclinical markers of atherosclerosis and the incidence of major cardiovascular events.

Methods: This phase 3, multicentre, randomized, controlled, double-blind, superiority study compared rosuvastatin with placebo in reducing the progression of subclinical markers of atherosclerosis. Patients with AAV in remission after a first flare or relapse were randomized 1:1 to receive the experimental strategy based on the use of rosuvastatin 20 mg/day or placebo for 24 months. The primary endpoint was the mean change in mean cIMT (distal wall of primary carotid arteries) at 24 months.

Results: A total of 111 participants underwent randomization (55% male, mean age 54.8 (13.3) years, 63.1% GPA, 28.8% EGPA, 8.1% MPA), with 54 participants assigned to receive rosuvastatin and 57 to placebo.

The primary endpoint was not met. The mean change in cIMT at month 24 was not different between the two study groups (difference -0.002 [-0.034 ; 0.030], p=0.89) (**Figure 1**). The annualized rate of change in mean cIMT was 0.0110 (0.0617) mm/year in the rosuvastatin group and 0.0189 (0.0556) mm/year in the placebo group (difference -0.0062 [-0.0318 ; 0.0193], p=0.61). Similar results were found for the mean change in the number of plaques in the carotid and femoral arteries and abdominal aorta (difference 0.01 [-0.39 ; 0.42], p=0.94).

Mean LDL-cholesterol levels were significantly different between the two study groups at all time points evaluated (P<0.001, P<0.001, and P<0.001 for reductions between the rosuvastatin and the placebo groups at months 6, 12 and 24, respectively). Also, high-sensitivity CRP levels were significantly different between the two study groups at month 24 (difference -3.16 [-5.58 ; 0.74], p=0.011 for reductions between the rosuvastatin and the placebo groups).

There was only one MACE in the rosuvastatin group. Vasculitis relapse-free survival did not differ between the two groups (HR 1.59, 95%IC = [0.81 ; 3.09], p=0.18).

Eleven and seventeen patients discontinued intervention in the rosuvastatin and the placebo groups, respectively. The incidence of serious adverse events was similar in the two groups: 27.8% in the rosuvastatin group and 22.8% in the placebo group.

Conclusion. Among patients with ANCA-associated vasculitis, 24 months of rosuvastatin reduced LDL-cholesterol but did not reduce the progression of subclinical markers of atherosclerosis or the incidence of major cardiovascular events (Funded by the French Ministry of Health; STATVAS ClinicalTrials.gov number, NCT02117453).

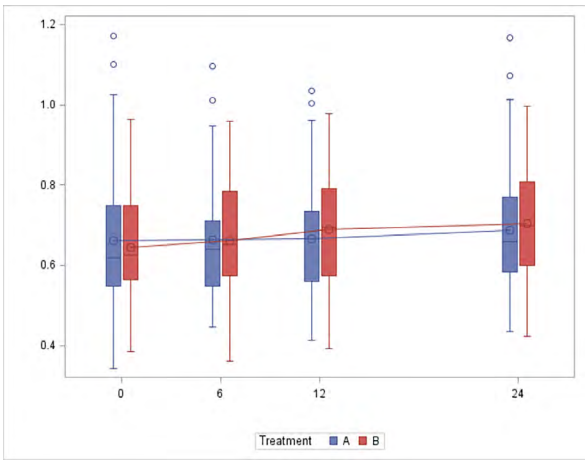

Figure 1. Evolution of mean carotid intima-media thickness during the study period in the two groups. Rosuvastatin arm is group A and placebo arm is group B.

PT-1A-02

Characterizing Treatment Response, Tolerability, and Rationale for Choosing Avacopan Therapy in Patients with ANCA-Associated Vasculitis: A Multicenter Observational Study in a Real-World Setting

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Background/ Objectives: In ANCA-associated vasculitis (AAV) treatment with Avacopan (C5a-receptor blocker) demonstrated steroid-sparing effects, reduction of side effects, increased remission maintenance, and improved kidney function, leading to its approval in January 2022. Limited global experience, particularly outside clinical intervention studies, emphasizes the need of further evaluation. This multicenter observational study aims to assess treatment response, tolerability, safety, and decision-making factors in a real-world setting.

Methods: Patients with active AAV (>18 years) treated with Avacopan from 03/2022 to 06/2023, with treatment durations of at least 3 months, were included. The combined primary endpoint was remission (Birmingham Vasculitis Activity Score (BVAS) of 0 and ≤7.5mg prednisolone at 6 months), and sustained remission at 6 and 12 months. Secondary endpoints included renal response (hematuria, proteinuria, and S-creatinine after 3 months), relapses, adverse events (AEs), and the rationale for choosing Avacopan therapy.

Results: This study included 39 patients with an average BVAS of 16. Remission was achieved in 91% (29/32), sustained remission in 91% (21/23). Renal response was observed in 76% (25/33) and 4 patients experienced a relapse (10%). The cumulative prednisolone dose over 52 weeks was 3229mg. The primary reasons for selecting Avacopan therapy included improved renal outcome, steroid-sparing, and relapsing disease or need for therapy intensification. Avacopan was discontinued in 21% (8/39) of cases due to AEs, including fever and leukopenia (2), gastrointestinal issues (2), severe cough and respiratory mucus production (2), and increased transaminases (2). Serious AEs were reported in 31% of patients, potentially glucocorticoid-associated AEs in 64.1%.

Conclusion: In this study, patients treated with Avacopan showed high rates of both remission and sustained remission. Renal Response was reached in 76% of cases but was ultimately reached by most participants – further emphasizing Avacopan´s benefit for kidney-related outcomes. The cumulative Prednisolone dose was higher than in ADVOCATE, yet significantly lower compared to the Prednisolone group in ADVOCATE or low-dose group in PEXIVAS. In clinical practice, a more rapid tapering of Prednisolone when using Avacopan is advised to further reduce side effects. Overall, Avacopan appears to be an effective and relatively safe therapy, but vigilant monitoring for potential side effects is essential as they can lead to treatment discontinuation.

Disclosures: Financial support was received from CSL Vifor.

PT-1A-03

Infections during the avacopan early access program (EAP) for anca-associated vasculitis (AAV)

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Background: Infections remain a concern with many immune targeted therapies. Infections are one of the common causes of early mortality in AAV.[1] Avacopan, a selective C5aR inhibitor is approved for the treatment of adults with severe and active AAV in combination with rituximab or cyclophosphamide.[2] Avacopan does not block C5b-9 production, leaving the membrane attack complex (MAC) intact.[3] Integrated safety data from two Phase 2 and one Phase 3 studies in 439 AAV patients have shown fewer infections in patients on avacopan versus comparator groups. [4] Our objective was to assess infections in patients under real world conditions by analysing avacopan EAP data.

Methods: Pharmacovigilance data for EAP participants was obtained for the period February 2019 and September 2023. Criteria for EAP participation included newly diagnosed or relapsing AAV and high unmet need.

Results: Data from 216 patients were analyzed with a median treatment duration of 6 months (range 1- 45 months). 14 episodes of infections were reported in 10 patients (5%). Eight were classified as serious, with four resulting in hospitalization and one with fatal outcome. The patient who died had a relapsing MPA with pulmonary involvement and died due to complicated pneumothorax and multiple infections in an intensive care unit setting. COVID 19 was the most frequent type of infection, occurring in 4 patients with full resolution in 3 and in one outcome unknown. One patient required hospitalization. Eight events in four patients were assessed as related to avacopan by the reporter, leading to permanent avacopan withdrawal, temporary avacopan withdrawal, no change and unknown action in 1 patient each.

Conclusions: Infection in these patients appears similar to what would be expected in this immunosuppressed population. Limitations of this program include potential underreporting and incomplete data.

Table 1: infections reported in 216 AAV Patients Enrolled in the Early Access Program.

PT Name	Non Serious (n)	Serious (n)	Assessed as related according to the reporter	Onset of action	Grand Total (n)
COVID-19	3	1		240 days; Unknown; Unknown; Unknown	4
Dacryocystitis		1	1	163 days	1
Gastroenteritis	1		1	133 days	1
Infection	1	1	1	Unknown; On the day of Avacopan initiation	2
Joint abscess		1	1	20 days	1
Klebsiella infection		1	1	30 days	1
Muscle abscess		1	1	20 days	1
Rhinitis	1			Unknown	1
Staphylococcal bacteraemia		1	1	50 days	1
Urosepsis		1	1	30 days	1
Grand Total	6	8			14

n: number of patients.

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3. Jayne D, et al. N Engl J Med 2021;384(7):599–609.
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Disclosures: JV has received consulting fees from CSL Vifor. TP and AO are employees of CSL Vifor.

PT-1A-04

Avacopan in the treatment of ANCA-associated Vasculitis with Hypoxic Pulmonary Haemorrhage

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Background/Objectives: Pulmonary haemorrhage with hypoxia caused by ANCA-associated vasculitis (AAV) has a high early mortality. Avacopan, an oral C5a receptor antagonist, is an approved treatment for AAV, but patients with pulmonary haemorrhage requiring invasive pulmonary ventilation support were excluded from the ADVOCATE trial.

Methods: A retrospective, observational, multicentre case series of AAV patients with hypoxic pulmonary haemorrhage, requiring oxygen support or mechanical ventilation, who received avacopan.

Results: Eight patients (62.5% female), median age 64 years (range 17-80), seven with kidney involvement, median glomerular filtration rate (GFR) 11 (range 5-99) ml/min per 1.73m^2, were followed for a median of 6 months from presentation. Seven were newly diagnosed (87.5%), five were MPO-ANCA and three PR3-ANCA positive. All had hypoxia, four requiring mechanical ventilation (three invasive and one non-invasive). Intensive care unit (ICU) stay for the four patients lasted a median of 9 days (range 6-60). Four received rituximab and cyclophosphamide combination, three rituximab and one cyclophosphamide. Four underwent plasma exchange and one received two months of daily extracorporeal membrane oxygenation (ECMO) therapy. Following the initiation of avacopan after a median of 10 days (range 2-40), pulmonary haemorrhage resolved in all patients, even two who had one month of refractory pulmonary haemorrhage prior to avacopan. Additionally, after one month, the median prednisolone dose was 5 mg/day (range 0-50), with three patients successfully discontinuing steroid use. Two patients suffered serious infections, two discontinued avacopan, one permanently due to a rash and one temporarily after three months due to neutropenia. All patients survived and no re-hospitalization occurred.

Conclusions: We report the use of avacopan as a component of the treatment for pulmonary haemorrhage with hypoxia in AAV. Despite the life-threatening presentations all patients recovered, but attribution of the positive outcomes to avacopan is limited by the concomitant therapies and retrospective observational design.

Disclosures: OF fees from Vifor. RJ fees from Roche, GSK, Vifor. TS fees from Vifor. LW fees from Otsuka. DJ fees from Astra-Zeneca, CSL Vifor, GSK, Novartis, Roche, Takeda, Amgen. The other authors declared no conflicts of interest related to this work.

PT-1A-05

Avacopan for the treatment of ANCA Vasculitis. First experiences in Spain

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Introduction: ANCA-associated vasculitis (AAV) are chronic diseases with relapses that associate organic damage because of the disease and its treatment. Avacopan, a selective C5a receptor antagonist, is indicated for the treatment of adult patients with severe and active granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) in combination with a regimen of rituximab (RTX) or cyclophosphamide (CF). We present the first experiences with avacopan in Spain as part of an Early Access program.

Material and methods: Patients with GPA/PAM who started treatment with avacopan between June 2022 and September 2023 were included. Below, we describe the baseline characteristics, reasons for indicating avacopan, and evolution.

Results:24 patients were analyzed, mean age 55.2±20 years, 58.3% women, 77% new diagnoses and 83% MPO+. 79%(19/24) had kidney involvement(with a mean serum Creatinine of 274umol/ L±151); followed by ENT (45.5%), Pulmonary (33.3%), skin (25%) and neurological (16.6%).

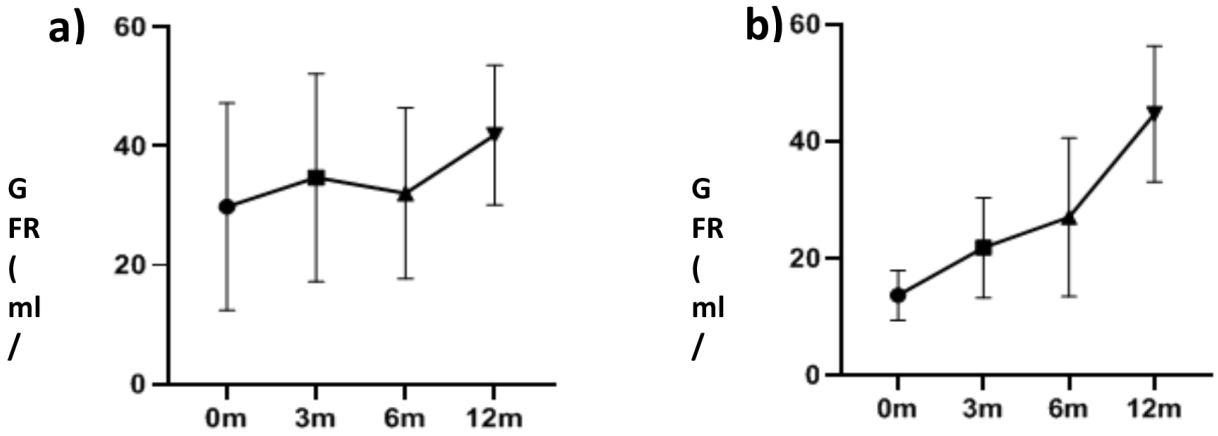
In 55% of the cases avacopan was indicated due to risk of event (AE) related to glucocorticoids (GC), the main causes being diabetes, hypertension, osteoporosis, infections, frailty, cardiovascular risk and cumulative dose of GC. 25% of patients presented AE prior to GC and 7% were steroid dependent. In 25% of cases, avacopan was requested due to refractory disease and in 13% of patients due to the potential for recovery of renal function.

RTX alone was used for induction in 50% of patients, associated with CF in 34.61% of cases. Additionally, 67% received bolus methylprednisolone, 100% received oral prednisone, and 19.2% received plasma exchange. Median follow-up was 8.6±4.7 months. Remission of the disease was described in 96% of the patients with 1(4%) relapse reported during follow-up.

The mean change in eGFR at 6 and 12 months were 5.7±13.9 and 13.2±19.3 ml/min/1.73m2.For patients with baseline GF<20 ml/min/1.73m2, mean change in eGFR at 6 and 12 months were 13.3±12 and 28±14.1ml/min/1.73m2 (Figure 1).

Prednisone was discontinued in 70% of patients (13.25±5.9 weeks). 3 AEs have been reported (diarrhea, urinary infection and neutropenia) and treatment was discontinued in one patient.

Discussion: The combination of avacopan and standard AAV induction treatment in clinical practice presents a good safety profile and provides added value by contributing to the control of AAV activity, increase GFR, AND the reduction/removal of GC.



PT-1A-06

Real-world experience comparing Avacopan use to high dose steroids as part of remission induction therapy in ANCA-associated vasculitis

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Background: Avacopan, an oral complement C5a receptor antagonist, has been demonstrated to be as effective as tapering glucocorticoids, alongside Rituximab (RTX) or Cyclophosphamide (CYC), at inducing remission in ANCA-associated vasculitis (AAV). We describe our early experience of using Avacopan compared to high-dose glucocorticoids, alongside standard immunosuppression, in a tertiary vasculitis referral centre in the UK over the last 18 months.

Methods: This retrospective analysis includes 60 patients with a new diagnosis or relapse of AAV over the last 18 months managed through our centre. Patients with eGFR < 15 ml/min at diagnosis were excluded as we do not currently use avacopan in those patients. Patients were treated with either, avacopan with or without low dose glucocorticoids, or standard high dose glucocorticoids, alongside RTX or CYC. We collected clinical and safety outcomes over a 26 week follow up period.

Results: 30 patients were treated with avacopan alongside RTX or CYC. 80% of these patients received a 2 week low-dose prednisolone course alongside avacopan. Our standard steroid protocol in avacopan treated patients is to administer 30mg prednisolone for 1 week, 20mg prednisolone for 1 week and then stop. 30 patients received standard high dose prednisolone alongside RTX or CYC and no avacopan. These patients were either diagnosed prior to NICE approval of avacopan or had a contraindication to commencing avacopan, including abnormal liver function tests (LFTs) or a diagnosis of eosinophilic granulomatosis with polyangiitis (n=2). The demographics of both groups were similar at presentation in respect to age, gender, ethnicity, organ involvement and MPO or PR3 positivity. No patients required dialysis treatment. eGFR at presentation was lower in avacopan treated patients at 47 mL/min (IQR 19-82), compared to 64 (25-90) in the no avacopan group, but this difference was not statistically significant. By the end of 26 weeks of follow up, 5 patients in the avacopan group had discontinued avacopan. Two patients discontinued avacopan due to side effects (abnormal liver function and GI upset). Three patients required transfer to high dose steroids due to persistent ENT disease. In the remaining patients, there was no difference between patients treated with avacopan versus patients treated with high dose steroids in terms of attainment of remission, eGFR (Figure 1), proteinuria or CRP by 26 weeks of follow up. There was also no difference in the change in eGFR from baseline between the two groups.

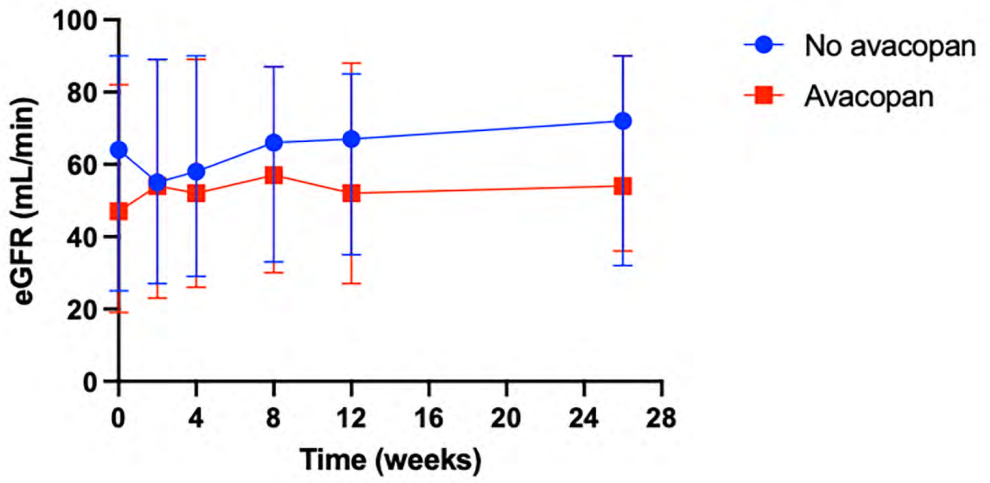

Figure 1: Median eGFR over 26 weeks follow up in those treated with avacopan or not:

Conclusions: We report our real world experience of avacopan for the treatment of AAV with an eGFR > 15 ml/min in the context of minimal steroid use in the avacopan treated patients. Avacopan was discontinued in 5 out of 30 patients. Three out of those 5 patients required transfer to high dose steroids for persistent ENT disease. In the remainder of patients, avacopan with minimal steroid use was as efficacious as high dose steroids for the management of AAV.

Disclosures: C.King is funded by an MRC CRTF fellowship.

PT-1A-07

Efficacy and Safety Experience with Avacopan beyond 52 weeks in Early Access Program (EAP)

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Background: Avacopan, a selective C5aR1 inhibitor, has demonstrated efficacy and safety over 52 weeks in patients with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis.[1] However, efficacy and safety data on avacopan beyond 52 weeks are limited. Here, we describe the experience with avacopan beyond 52 weeks from the Early Access Program (EAP).

Methods: Safety data in patients with severe, active granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) within the EAP were recorded in a global safety database from Feb 2019 – Apr 2023. Adverse events (AE) included a lack of effect and other events (i.e., relapse or worsening of disease).

Results: A total of 19 patients were treated with avacopan beyond 52 weeks within the EAP. Average age was 47 years, with 13 patients (68%) diagnosed with GPA and 6 (32%) with MPA. The median duration of therapy was 17 months (range 12–45). A total of 9 AEs were recorded in 2 patients (10.6%) (Table 1). One vasculitis flare was recorded 6 months after avacopan initiation and coincided with an unintended dose reduction to 20 mg BID, due to a product supply issue during COVID. The event was well-managed with rituximab, with no additional use of glucocorticoids, and avacopan 30 mg BID was reinstated. No further cases of a lack of effect, worsening of disease, or disease relapse were reported. Data regarding concomitant medications did not indicate a decline in the patients' status during treatment. No treatment discontinuations due to AEs were recorded.

Conclusion: These results suggest that continuation of avacopan beyond 52 weeks is generally well-tolerated in patients with GPA and MPA and may be effective in terms of disease control. Limitations of this program include low patient number, potential underreporting, and incomplete data.

References: 1. Jayne DRW, et al. Avacopan for the Treatment of ANCA-Associated Vasculitis. *N Engl J Med*. 2021;384(7):599–609.

	No. of events
Patient 1	
General disorders and administration site conditions *Malaise*	1
Infections and infestations *COVID-19*	1
Injury, poisoning, and procedural complications *Product dose omission issue*	1
Product issues *Product supply issue*	1
Patient 2	
General disorders and administration site conditions *Pain*	1
Musculoskeletal and connective tissue disorders *Psoriatic arthropathy* *Arthritis*	2
Surgical and medical procedures *Therapy interrupted*	1
Vascular disorders *Vasculitis*	1
Total	**9**

Table 1. **Overview of Safety Events Reported in 2 of 19 Patients Receiving Avacopan Beyond 52 Weeks in the Early Access Program.**

PT-1A-08

Efficacy and safety of combination therapy with rituximab and low-dose cyclophosphamide in ANCA-associated renal vasculitis

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Introduction: Current guidelines recommend the use of cyclophosphamide or rituximab as induction therapy for ANCA-associated vasculitis (AAV) with renal involvement. Some authors have described the combination of cyclophosphamide and rituximab in the treatment of severe AAV, and recently a 6-cycle regimen of low-dose cyclophosphamide combined with rituximab has been described with good results. This study aimed to compare the efficacy and safety of treatment with lower doses of cyclophosphamide (2-3 cycles) combined with rituximab versus standard treatment.

Material and methods: We performed a retrospective study of 14 patients with histologically confirmed AAV diagnosis, treated with an induction treatment scheme with corticosteroids, rituximab and 2-3 cycles of intravenous cyclophosphamide. We performed a case-control analysis with 16 patients who received only corticosteroids and rituximab in the same period, matched by propensity score for age, creatinine at presentation and histological parameters (percentages of sclerosed glomeruli, epithelial crescents and normal glomeruli). Renal and overall survival and complications due to immunosuppression were compared in both groups.

Results: At presentation, patients treated with the combination regimen had a mean age of 67±12.1 years, mean glomerular filtration rate estimated by CKD-EPI of 19.8 ± 11.1 ml/min/1.73m2, proteinuria of 1.6 (0.81-1.84) g/24 hours and baseline BVAS score of 18.5±6.9. Of the patients, 78.6% were anti-MPO positive and 21.4% were anti-PR3 positive. According to Berden's classification, 85.7% had a mixed variant on renal biopsy, 7.1% crescentic and another 7.1% sclerotic. The mean dose of cyclophosphamide was 1445±384 mg, and of rituximab was 2g. Twenty-eight-point six percent of patients required dialysis at debut, of which 75% recovered renal function. The duration of steroid treatment was 8 (4.6-16.9) months. The remission rate at 6 months was 71.4%, and after a median follow-up of 20 (15-35) months, 92.9% had remitted. During follow-up, 50% of the patients had severe infections; and at the end of follow-up, 7.1% progressed to end-stage renal disease (ESRD), with 21.4% of the total dying.

In the comparison with the control group, the patients who received the combined treatment had a higher remission rate (92.9% vs 75%), a lower relapse rate (15.4% vs 35.7%), less progression to ESRD (7.1% vs 20%) and lower mortality (21.4% vs 37.5%), with no differences in the rate of serious infections.

Conclusions: The association of low doses of cyclophosphamide to rituximab treatment in ANCA-associated renal vasculitis could improve the prognosis of these patients.

PT-1A-09

Timing B cell Return for Maintenance Rituximab

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Introduction: Continuous B cell depletion with rituximab (RTX) is highly effective in maintaining remission in ANCA associated vasculitis (AAV). However, even after over 2 years of continuous B cell depletion with RTX, relapse rates remain high when treatment is discontinued, and side effects develop if treatment is continued. The MAINTenance of ANCA VASculitis study (MAINTANCAVAS Dublin 2022, in press), showed that the time to B cell return is variable between patients, but that prolonged treatment with RTX redosing at B cell return (based on monitoring B cells every 3 months), is highly effective in maintaining remission. This study examines a simple and efficient strategy for timing subsequent RTX doses to B cell return based on the individual's track record without the need for extensive B cell monitoring.

Methods: We analyzed data from 56 patients with AAV after individual RTX doses and were monitored for B cell return every 3 months. B cell return was defined as ³10 B cells/uL.

Results: Out of 56 patients, 47 had B cell return at least twice: 8 at 6 months, 21 at 9 months, 15 at 12 months, and 3 at 15 months. There was no statistically significant difference in absolute B cell counts at the same time point (6, 9, or 12months) after the 1st, 2nd, or 3rd RTX infusions (Figure 1A-C, P>0.05 for all comparisons). We then evaluated the correlation between B cell counts at 9 months after the 1st infusion with B cell counts at 9 months after the 2nd infusion and found they were highly correlated (r = 0.75, 95% confidence interval 0.47-0.89, P<0.001, Figure 1D). We also evaluated the association between the time to B cell return after the 1st RTX infusion (t1) with time to B cell return after the 2nd RTX infusion (t2) and found that they were highly correlated (r = 0.87, 95% confidence interval 0.77-0.92, P<0.001, Fig 1E). T2 could be estimated based on t1 using the following equation: t2 = 0.999*T1 + 1.579, where the coefficient for t1 is 0.999 (95% CI: 0.825-1.172) with a R^2 = 0.75 and P<0.001 for the model.

Conclusion: The pattern of B cell return after RTX dosing is variable between patients. However, for individual patients, the pattern of B cell return is remarkably consistent. Indeed, after each dose, the next B cell count can be estimated based on the B cell count at the same time point after a precedent dose. Conversely, time to B cell count >10 B cells/uL remains similar over multiple doses.

When using extended interval dosing, this information can be used to time the next dose to help achieve an optimal peripheral B cell count: low enough to limit the risk of relapse but high enough to preserve a degree of immune function.

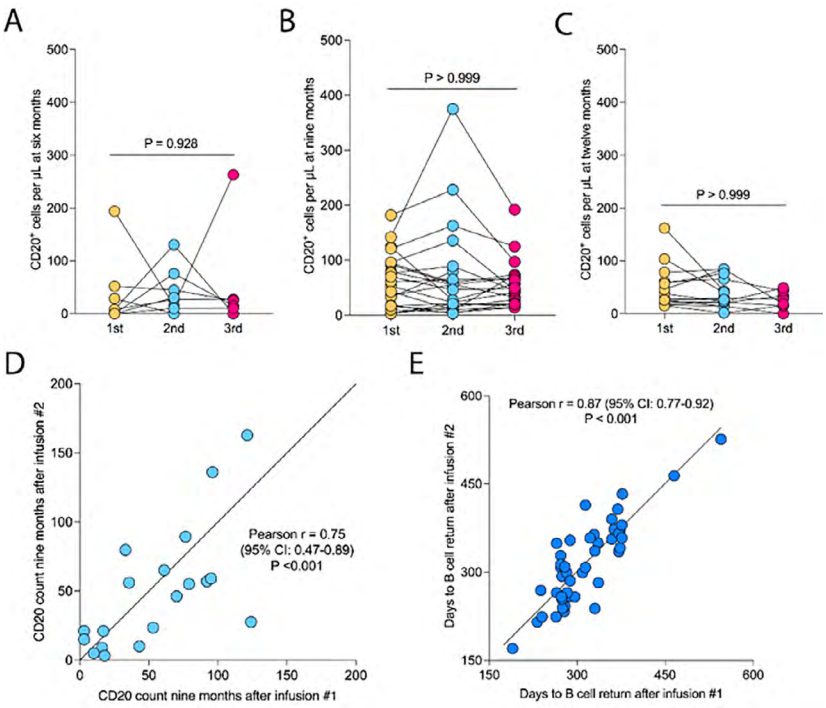

Figure 1. B cell counts after RTX in individuals with AAV. (A) B cell counts 6, (B) 9, and (C) 12 months after the 1st, 2nd, and 3rd RTX infusions in individuals who have had B cell counts measured 3 times after RTX infusions. (D) Association between B cell counts at 9 months after the 1st RTX infusion with B cell counts at 9 months after the 2nd RTX infusion. (E) Association between time to B cell return after the 1st and 2nd RTX infusions. Statistics by (A-C) Friedman test and (D-E) Pearson correlation.

PT-1A-10

Rituximab vs. Combination of Rituximab and Cyclophosphamide Induction Therapy for ANCA-associated vasculitis: A retrospective study

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Background/ Objectives: In ANCA-associated vasculitis (AAV), the use of rituximab (RTX) alone or RTX in combination with cyclophosphamide (RTX/CYC) was non-inferior to oral CYC [1] or intravenous pulse CYC alone followed by azathioprine (CYC-AZA) for the induction of remission, respectively [2]. However, there is a lack of comparative real-world data between both RTX-based therapy regimens. Moreover, the RAVE trial was not powered to determine the efficacy of RTX alone for remission induction in patients with severe renal involvement [1]. Our study aimed to compare the efficacy of RTX alone with combined RTX/CYC or intravenous CYC-AZA [3] for remission induction in AAV including patients with severe renal involvement in a monocentric cohort.

Methods: In this comparative effectiveness retrospective monocentric study, 166 patients with new-onset or relapsing AAV including patients with severe renal involvement (granulomatosis with polyangiitis [GPA] n=97; microscopic polyangiitis [MPA], n=69) were treated first-line either with RTX-, RTX/CYC-, or CYC-AZA -based regimen similar to RAVE-, RITUXVAS, and CYCLOPS trial regimens for the induction of remission between January 2010 and November 2021. The primary outcome was the relapse rate at 24 months. Clinical and laboratory data were assessed at baseline and every 6 months up to 24 months. RTX- and RTX/CYC-based regimen were followed by RTX-maintenance.

Results: Of the 166 patients, 81 received first-line RTX alone (RAVE), 23 RTX/CYC (RITUXVAS) and 62 CYC-AZA. At baseline, there was no difference between RTX and RTX/CYC treatment groups with respect to disease activity. In AAV, RTX and RTX/CYC was not inferior to treatment according to CYC-AZA for the induction of remission (*figure 1*). Moreover, RTX was not inferior to RTX/CYC (HR 0.61, *P*=0.1356, *figure 1*). Interestingly, a subgroup analysis showed that RAVE was slightly superior to RITUXVAS in GPA (HR: 0.48, *P*=0.0408, *figure 1*). RTX and RTX/CYC were superior to CYC-AZA in prednisolone dose reduction at 12 months (AAV: *P*=0.0074; GPA: *P*=0.0048). In RTX-based treatment regimens lower prevalence of adverse events was seen in contrast to RTX/CYC and CYC-AZA (P=0.0499).

Conclusions: In AAV, RTX and the combination of RTX/CYC were non-inferior to CYC-AZA for remission induction. The combination of RTX and CYC was not superior to RTX alone. Prednisolone dose tapering was faster with RTX-based regimens than with CYC-AZA.

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Disclosures: No conflict of interests.

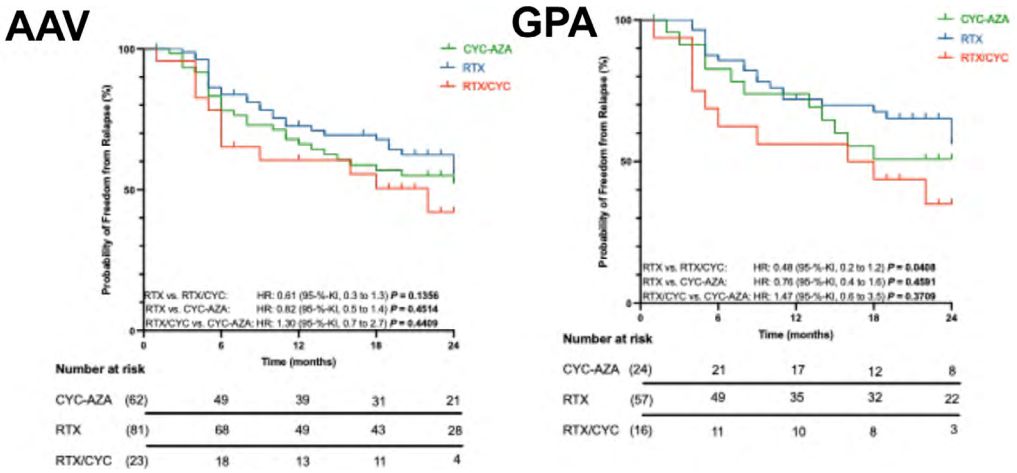

Figure 1 Kaplan-Meier survival analysis. RTX- and RTX/CYC-based regimen were *non-inferior* to CYC-AZA -based regimen. Specifically, RTX-based regimen was *superior* to RTX/CYC-based regimen in GPA (HR:0.48; *P* = 0.0408), but not in MPA (HR:0.69; *P* = 0.2397; *data not shown*).

Poster Tour 2A: Advances in treatment

PT-2A-11

Differences between glucocorticoids, conventional DMARDs and tocilizumab in achieving disease remission and in preventing the progression of damage in giant cell arteritis patients

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Background/Objectives: Various treatment regimens are available for patients diagnosed with large vessel vasculitis (LVV), each characterized by distinct efficacy and safety profiles. The aim of the present study was to assess the effectiveness of different regimens in achieving clinical or metabolic remission and in preventing the progression of damage, as well as the safety profiles. Treatment included glucocorticoids (GC), conventional disease modifying anti-rheumatic drugs (cDMARDs) and tocilizumab (TCZ).

Methods: Consecutive LVV inpatients and outpatients, classified as giant cell arteritis (GCA), were prospectively enrolled in three referral centers. We included all patients with new diagnosis or relapsing disease who underwent to at least 2 consecutive 18F-FDG PET-CT or MR scan between March 2011 and November 2023.

Before every PET scan demographic, clinical data and disease activity were assessed. Remission was defined as absence of signs and symptoms attributable to GCA and normalization of acute phase reactants (ESR <30 mm/H) and C-reactive protein (CRP <1 mg/dL). For each PET scan the vessel's metabolic activity was evaluated using the PETVAS score. The damage was evaluated using the LV-Vasculitis Index of Damage (LVVID). Patients were compared according to treatment regimens.

Results: The study included 80 LV-GCA patients (age at diagnosis: GC 66 [60-72], 62.3% female, cDMARDs [58-73], 62.9% female, TCZ 64 [59-71], 29.1% female) exposed to a total of 112 treatment regimens (n = 53 GC monotherapy, n = 35 cDMARDs, n = 24 TCZ). Overall clinical remission rate during the follow-up was 71.7 % in GC-treated patients, 51.4 % in cDMARDs-treated and 91.7 % in TCZ-treated (p = 0.004). Improvement in PETVAS was observed in all patients: GC treated 10 [4-21] vs 6 [2-12], cDMARDs treated 15 [6-21] vs 5 [1-18], and TCZ - treated 13 [9-20] vs 3 [1-8], with a difference at baseline and at last follow-up between the three groups (p = 0.530 and p = 0.210, respectively). Significant improvement in PETVAS was observed in TCZ-treated patients (ΔPETVAS= -75% [-97% to -61%], p=0.05). Daily prednisone dose at last examination was 5 [0-6.25] mg/d in the cDMARDs group vs 0 [0-2.5] mg/d in the TCZ group (p = 0.005).

At last evaluation LVVID was similar in the three groups (2 [1-3] vs 2 [1-4] vs 2 [1-4], p = 0.256), but TCZ was associated with significantly lower increase in damage accrual (p = 0.044). No statistically significant differences were observed between the three groups in terms of infections (p = 0.197), but a higher frequency of adverse events was observed in TCZ-treated patients (p = 0.045).

Conclusion: ^{18}F-FDG PET may be useful in assessing disease activity and monitoring response to therapy. Tocilizumab therapy significantly reduce vessel's metabolic activity over time, when compared to conventional treatment. A persistent low grade uptake during remission is common features in LVV patients, irrespectively of treatment regimens. None of the three different treatment regimens reduce the progression of the damage. No safety differences were observed.

Characteristics of patients (n=112)	GC (n = 53)	TCZ (n= 24)	cDMARDs (n = 35)	p
Female, n %	33 (62.3)	7 (29.1)	22 (62.9)	0.014
Age at diagnosis, y, median (IQR)	66 (60-72)	64 (59-61)	65 (58-73)	0.752
Clinical remission, n %	38 (71.7)	22 (91.7)	18 (51.4)	**0.004**
Reason for treatment discontinuation:				
Primary failure, n %	4 (7.5)	0 (0)	2 (5.7)	0.841
Secondary failure, n %	15 (28.3)	0 (0)	10 (28.6)	**0.044**
Adverse events, n %	0 (0)	4 (16.7)	2 (5.7)	**0.045**
Remission, n %	8 (15)	4 (16.7)	4 (11.4)	0.829
PETVAS baseline, y, median (IQR)	10 (4-21)	13 (9-20)	15 (6-21)	0.530
PETVAS LFU, y, median (IQR)	6 (2-12)	3 (1-8)	5 (1-18)	0.210
Δ PETVAS, %, median (IQR)	- 33 (-83; 0)	- 75 (-97;-61)	- 33 (-92;0)	0.053
GC baseline, y, median (IQR)	50 (25-50)	8.75 (5-32.5)	25 (12.5-50)	**0.001**
GC LFU, y, median (IQR)	5 (2.5-10)	0 (0-2.5)	5 (0-6.25)	**0.005**
LVVID baseline, y, median (IQR)	0 (0-1)	3 (0-3)	0 (0-1)	**0.001**
LVVID LFU, y, median (IQR)	2 (1-3)	3 (1-4)	2 (1-4)	0.256
Δ LVVID, y, median (IQR)	+1 (0-2)	0 (0-1)	+ 1(0-2)	0.044
Infection rate, n %	19 (35.8)	9 (37.5)	7 (20)	0.221
Total infection, y, median (IQR)	0 (0-3)	0 (0-3)	0 (0-2)	0.197

PT-2A-12

Effectiveness of conventional and biologic DMARDs in treatment of non-infectious aortitis

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Background/Objectives: Aortitis is a rare form of large vessel vasculitis with infectious and non-infectious aetiologies. There is limited data on the management of non-infectious aortitis and no studies reporting efficacy of disease-modifying drugs (DMARDs). The primary objective is to investigate the efficacy and side effects of DMARDs in non-infectious aortitis.

Methods: We retrospectively reviewed patients with a diagnosis of non-infectious aortitis at the Oxford University Hospitals NHS Foundation Trust, United Kingdom between 2010-2020. Medical notes were reviewed using local electronic patient records. DMARDs included Methotrexate, Cyclophosphamide, Leflunomide, Azathioprine and Mycophenolate as well as biological drugs such as Tocilizumab and Rituximab. Efficacy rates for a drug were determined by calculating the percentage of patients on the drug who achieved drug-free remission. Analysis was performed using R version 4.2.2.

Results: Between 2010-2023, 110 adults were diagnosed with non-infectious Aortitis. 59% were female, and the median age was 77 (±9.71). The majority identified as White British or another white background (94.5%), while smaller percentages were South-Asian (3.6%), mixed-background (0.9%), and Black African (0.9%). 7 patients were excluded due to death during therapy (4.5%) or incomplete data (1.8%). Among the remaining 103 patients, 54.4% achieved drug-free remission (n=56) after a median treatment duration of 46.4 months (IQR=26-6-65.6, range 12-122.4 months), requiring a median of 2 DMARDs (IQR=1-3, range 1-6). 16 patients achieved remission with methotrexate monotherapy (28.6%).

Methotrexate was used by 95% of patients (n=53) and Methotrexate with Leflunomide (14.3%, n=8) was the commonest DMARD combination regimen. Cyclophosphamide showed the highest efficacy rates, achieving remission in 87% (20/23 patients). It was discontinued in 3 patients due inefficacy (8.7%, n=2) or recurrent urinary tract infections (4.3%, n=1). Figure 1 shows all efficacy and tolerance rates of DMARDs. Azathioprine exhibited the lowest efficacy rates with 22% (4/18 patients) attaining remission. The primary reasons for discontinuing Azathioprine included inefficacy (27.7%, n=5), gastrointestinal intolerance (44.4%, n=8) and abnormal liver function test results (5.6%, n=1). Finally, Mycophenolate exhibited efficacy rates of 50% (n=7/14) with the primary reason for discontinuation being inefficacy and gastrointestinal intolerance (each comprising 14.3%, n=2/14). Tocilizumab was the most common biological drug given (16%, n=9), achieving remission in 77.8% of the patients (n=7), but was discontinued in 22% due to neutropenia.

Conclusions: Patients with non-infectious Aortitis were on treatment with DMARDs for around 3.8 years and required several DMARDs to achieve remission, with Cyclophosphamide and Tocilizumab being most effective.

Disease-modifying drug	Efficacy rates	Tolerance rates
Cyclophosphamide	87% (n=20/23)	95.7% (n=22/23)
Tocilizumab	77.8% (n=7/9)	77.8% (n=7/9)
Mycophenolate	50% (n=7/14)	64.2% (n=9/14)
Leflunomide	50% (n=10/20)	60% (n=12/20)
Methotrexate	41.5% (n=22/53)	71.7% (n=38/53)
Azathioprine	22% (n=4/18)	50% (n=9/18)

Figure 1.

PT-2A-13

Clinical description and associated treatment in 78 patients with Takayasu's arteritis: results from the Spanish Registry of Systemic Vasculitis (REVAS)

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Background/ Objectives: Takayasu arteritis (TAK) is a rare disease with a high variable clinical course. We aimed to describe the clinical characteristics of patients included in the REVAS Registry and to analyse the treatment used in this cohort.

Methods: Retrospective study that evaluated all patients with TAK included at the REVAS Registry. Variables are described as mean (standard deviation), median (quartile 1 – quartile 3) or proportions, as appropriate. Statistical analysis was performed using StataIC/16.1.

Results: We included 78 patients, 66 (84.6%) women, with a mean age at diagnosis of 39.2 (14.8) years. Diagnostic delay was 32 (8-144) weeks. Symptoms at diagnosis were fever in 23 (29.5%) patients, constitutional syndrome in 22 (28.5%), arthralgia/ arthritis in 27 (34.6%), Raynaud in 10 (20.4%), erythema nodosum in 5 (10.2%), carotidina in 6 (13.0%) and limb claudication in 44 (57.1%). Twelve (15.4%) suffered from a stroke, 4 (5.1%) a transient ischemic attack, 8 (10.3%) amaurosis fugax and 2 (2.6%) diplopia. Other symptoms were heart failure in 13 (16.7%), coronary artery disease in 12 (15.4%) and gut angina in 5 (6.4%).

Blood tests at diagnosis showed an erythrocyte sedimentation rate of 37 (16-76) mm/h and a C reactive protein of 2 (0.5-9) mg/ dL. Anemia was present in 29 (40.8%) patients. Vascular involvement at diagnosis showed stenosis of the subclavian artery in 68 (95.8%) patients and stenosis of renal artery in 34 (47.9%). Thoracic and abdominal aortic involvement was present in 30 (42.9%) patients. Mesenteric and coronary arteries were less prevalently involved (20 (27.8%) and 11 (15.3%) patients).

Regarding therapy, 64 (82.1%) patients received steroids with a median initial dosage of 60 (30-60) mg/day. Immunosupressive drugs were frequently given, and its use was associated with the administration of biological therapy (Table 1).

	Overall	No BT	BT	Significance
Methylprednisolone bolus	11 (14.1%)	6 (10.9%)	5 (21.7%)	0.29
Methotrexate	40 (51.3%)	23 (41.8%)	17 (73.9%)	0.01
Azathioprine	16 (20.5%)	7 (12.7%)	9 (39.1%)	0.01
Cyclophosphamide bolus	9 (11.5%)	1 (1.8%)	8 (34.8%)	<0.001
Mycophenolate	5 (6.4%)	3 (5.5%)	2 (8.7%)	0.63

Table 1. Association of biological therapy and immunosuppressive drugs. BT = biological therapy.

Forty-one (68.3%) patients presented at least one relapse, being the mean number of relapses 1.6 (1.0).

Biological therapy was used in 23 cases, including tocilizumab in 17 patients, adalimumab in 9 patients and infliximab in 3. Tocilizumab was given in 2 patients at disease onset while the remaining ones received this drug during follow-up. In 3 patients adalimumab was previously administered and two of them had also previously received infliximab. Tocilizumab was well tolerated, just 1 patient had to withdraw the drug due to leucopenia. In 3 patients tocilizumab was not associated to immunosuppressive drugs. Infliximab and adalimumab were always given with immunosuppressive drugs.

Conclusions: TAK is a highly recurrent disease that needs multiple drugs to reach remission. Immunosupressive drugs are frequently used due to complications of the disease and its use is associated with the start of biological drugs.

References: None.

Disclosures: None.

PT-2A-14

Safety and efficacy of long-term treatment with Tocilizumab in a cohort of patients affected by Giant Cell Arteritis: an Italian monocentric retrospective study

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Background/ Objectives: Tocilizumab (TCZ) is the only biologic disease modifying synthetic rheumatic drug approved for the treatment of giant cell arteritis (GCA), having both clinical trials and real-life studies outlined its effective and safe use in that disease. However, optimal duration of the treatment has yet to be determined, since its early interruption has been associated with an increased risk of relapse, while, on the other hand, prolonged schemes of therapy may rise safety concerns. We designed a retrospective study to evaluate the incidence of adverse events (AEs) and remission/relapse rate in a cohort of GCA patients treated with TCZ and an accelerated steroid tapering scheme, over a follow-up period of 24 months.

Methods: We included the patients referring to our "Vasculitis clinic" from January 2019 to November 2021 who were diagnosed with GCA and started subcutaneous TCZ treatment (162 mg/week) following adequate infective screening and immunoprophylaxis. They also received up to 62,5 mg prednisone, tapered according to an accelerated six-month withdrawal scheme. Follow-up visits were performed at 3 (T1), 6 (T2), 12 (T4), 18 (T5) and 24 (T6) months, then annually if sustained remission was achieved. Safety was evaluated based on the incidence of AEs during the follow-up, while effectiveness outcomes included the assessment of relapses, diagnostic imaging analysis and GCs dose at the last observation point and/or GCs discontinuation over time.

Results: A total of 38 patients was collected, with a mean age of 76,4 years and an average duration of TCZ treatment of 22,3 months. AEs occurred in 11 (28,9%) subjects, and only one episode of serious adverse event was reported; 7 (18%) patients permanently discontinued TCZ. At the end of follow-up, all the patients continuing treatment showed clinical remission, 23 (85%) discontinued GCs and among those who continued steroid treatment, mean dosage was <5 mg PDN equivalent. We registered 3 (7,8%) minor relapses under TCZ, after an average interval of 15 months; relapse rate following TCZ discontinuation was 30%.

Conclusions: This is one of the few studies assessing subcutaneous TCZ treatment in GCA patients over a period of 2 years. Considering the limited sample size, we nevertheless recorded an excellent GCs-free remission rate, with no increase in the burden of AEs and/or serious infections in the long-term. Prolonged TCZ therapy then emerges as feasible and crucial to achieve adequate control of disease activity; not least, the administration of moderate GCs doses for the shortest possible duration can certainly play a pivotal role in its overall tolerability.

Disclosures: None.

PT-2A-15

Treatment of Giant Cell Arteritis with Ultra-short Glucocorticoids and Tocilizumab: results from the extension to 76 weeks

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Background/ Objectives: The efficacy and safety of one year of Tocilzumab (TCZ) monotherapy after 3 boluses of intravenous methylprednisone in inducing remission in patients with GCA and large vessel involvement (TOPAZIO Study) was previously reported[1].

We present the results of the six-month observation period after the withdrawal of TCZ.

Methods: Patients who completed the 52-week part and were in clinical remission stopped TCZ and were eligible to enter the second part, a 24-week observational follow-up. Clinical assessment was performed every 12 weeks, and fluorodeoxyglucose positron emission tomography (FDG-PET) was repeated at week 76. The PET Vascular Activity Score (PETVAS) and the diameters of the aorta at 3 different levels were calculated by a single nuclear medicine physician and a radiologist.

Clinical remission was defined by the absence of any clinical signs and symptoms due to GCA, including normalization of the acute phase reactants, independently by imaging evaluation.

Aortic dilation was defined by a diameter >40 mm in the ascending aorta, ≥40 mm in the descending aorta, and ≥30 mm in the abdominal aorta.

The primary endpoint was the variation of PETVAS at week 76 compared with baseline and week 52 and the proportion of patients with clinical remission at week 76. The secondary endpoint was the proportion of patients with new aortic dilation at week 76.

Results: 13 patients were in clinical remission at week 52 stopped TCZ and entered in the 6 months follow-up period without any treatment. 2 patients relapsed 8 and 22 weeks after TCZ suspension, respectively. 11 PET were performed at week 76.

Compared to baseline, a significant reduction of PETVAS was observed at week 76. However, after suspension of TCZ, a significant increase of PETVAS was observed at week 76 compared to week 52 (**Table 1**). 4 of the 11 PET/CT (36%) were considered active by nuclear medicine physician's interpretation.

The proportion of patients with clinical remission at week 76 was 85% (95% CI 55-98).

At week 76, one patient showed a new aortic dilation. 2 patients who presented an aortic dilation at week 52 were in clinical remission at weeks 52 and 76. Still, both showed further aortic dilation at CT performed at week 76.

Conclusions: One year of TCZ monotherapy was able to maintain sustained clinical remission in a sizeable proportion of patients with GCA. However, after the withdrawal of TCZ, there was a significant increase in the FDG uptake and a new aortic dilation. Whether this persistence of activity despite clinical remission may indicate future relapses is still unknown.

References:

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Disclosures: None.

Outcome	Week 76
Primary endpoints	
PETVAS compared with baseline, mean differences (95% CI) p value	-6.6 (-9.5 to -3.7) 0.004
PETVAS compared with week 52, mean differences (95% CI) p value	4.6 (0.7 to 8.5) p=0.016
Proportion of patients with clinical remission, n (%, 95% CI)	85% (95% CI 55-98),
Secondary endpoints	
Proportion of patients with new aortic dilation, n (%, 95% CI)	1/11 (9, 0-41)

Table 1. Clinical Outcomes.

PT-2A-16

Risk of major adverse cardiac events among patients with giant cell arteritis who received tocilizumab

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Background: Exposure to glucocorticoids among patients with giant cell arteritis (GCA) may increase the rate of major adverse cardiac events (MACE), including congestive heart failure (CHF), cerebrovascular accidents (CVA), and myocardial infarctions (MI. The steroid-sparing agent tocilizumab may decrease glucocorticoid use among patients with GCA, thereby decreasing subsequent MACE. The objective of the study was to define the risk of MACE among patients with GCA who did or did not receive tocilizumab.

Methods: We performed a retrospective cohort study of incident cases of GCA using the US-based TriNetX electronic health records database from 1/1/2010 to 4/23/2023. Patients were included if they had 2 ICD-9CM/ICD10-CM codes for GCA separated by 30 days but within 1 year and received any dose of prednisone within 30 days of the first GCA code. The index date was defined by the first prescription for prednisone within 30 days of the index date; exposure to tocilizumab was defined by receiving one or more prescriptions for tocilizumab within the first 6 months after the index date. The primary outcome of interest was a composite of MACE, which included MI, CVA, CHF, or death. Events were identified using a single ICD-9-CM/ICD-10-CM code and the incidence of MACE was reported as unadjusted incidence rate ratios. The clone-censor-weight approach was then used to account for confounding and immortal time bias. After cloning, censoring, and weighting using inverse probability of censoring, time-updated multivariable Cox proportional hazards models were used to calculate the hazard ratio (HR) and 95% confidence intervals for the risk of MACE.

Results: During the study period, 5,743 patients met the inclusion criteria (932 tocilizumab exposed and 4,811 tocilizumab unexposed) who were followed for an average of 3.1 years (SD 2.7 years). The majority were female (4,065, 70.8%) and white (4,139, 72.1%). In unadjusted analysis, tocilizumab exposure was associated with a lower rate of MACE (incidence 77.0/1,000 person-years vs 102.8/1,000 person-years, incidence rate ratio 0.75, 95% confidence interval (CI) 0.60-0.94) (Figure 1). After implementing the clone-censor-weight approach to mitigate confounding and time-related biases, tocilizumab exposure was not associated with a decreased risk of MACE overall (HR 0.98, 95% CI 0.87-1.09). With respect to the components of the composite MACE outcome measure, patients who received tocilizumab had a lower risk of CVA (HR 0.86, 95% CI 0.79-0.93) and a similar risk of CHF (HR 0.96, 95% CI 0.87-1.03) and MI (HR 0.99, 95% CI 0.76-1.19) as compared to those who did not receive tocilizumab.

Conclusion: In this retrospective cohort study of patients with incident GCA, tocilizumab initiation was not associated with a lower rate of MACE, though there was a small reduction in the risk of CVA. Future studies with longer follow-up and more granular glucocorticoid prescribing information should be performed to corroborate these results.

Disclosures:

Author 1 has nothing to disclose.

Additional contributors:

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Author 4: reports research support from Astra Zeneca, Abbvie and receives consulting fees from Novartis.

PT-2A-17

Outcomes of Vascular Intervention in Takayasu Arteritis Patients: A Tertiary Centre Experience From Turkey

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Background and Objectives: Takayasu arteritis (TAK) is a chronic, granulomatous large vessel vasculitis involving the aorta and its main branches.[1] Segmental stenosis, occlusion, dilatation and/or aneurysm may develop due to inflammation in the vessel wall.[2] Vascular intervention may be required in the presence of symptomatic signs of arterial stenosis (limb claudication, stroke, syncope, uncontrolled renovascular hypertension, etc.) and severe aneurysm.[3] The aim of this study was to evaluate the frequency, outcomes and complications of vascular intervention in patients with TAK.

Methods: Patients with a diagnosis of TAK who underwent vascular intervention at Marmara University Rheumatology Clinic were evaluated retrospectively. The indication for vascular intervention, the stage of the disease, the type of vascular intervention, complications, early and late results were recorded. Control imaging data were not available. Restenosis was evaluated when they were symptomatic or according to the results of imaging studies performed for any reason.

Results: 55 patients and 107 lesions (102 stenosis and occlusions, 5 aneurysms or dissections) were included. 16 (14%) balloon angioplasty, 69 (64%) stents, 20 (18%) bypass grafts, 2 (1%) endarterectomy were performed. 52.3% (n=56) of the procedures were performed after the diagnosis of TAK. The most common indication was limb claudication in 56.7%. Only 6% (n=7) interventions were performed for emergency indications. Of the procedures, 87.8% (n=42) were performed while taking steroids (11.1% (n=6) high dose), 23.2% while taking biologic agents (n=13), and 64.3% (n=36) while taking DMARDs.

6 (5.6%) vascular interventions resulted in early failure. Graft infection, hematoma and embolism developed in one patient each. Restenosis occurred in 47 (43.9%) lesions during follow-up. The median time to restenosis was 24 (6-80) months. The risk of restenosis was highest in the subclavian artery compared to other vessels (10.6%). Repeat procedures were frequently needed in patients with involvement of lower extremity vessels. There was no significant difference between comorbidities and restenosis/complications.

Conclusion: Endovascular and surgical procedures can be safely performed in patients with TAK in the presence of appropriate indications. Considering that 47.7% of vascular procedures are performed before diagnosis, it is important for the relevant departments to raise awareness and refer patients for rheumatologic evaluation when necessary. Suppression of inflammation with immunosuppressive therapy before the intervention may reduce restenosis and complication rates.

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Poster Tour 3A: Advances in treatment

PT-3A-18

Effectiveness of dupilumab on refractory chronic rhinosinusitis with nasal polyps in eosinophilic granulomatosis with polyangiitis: a clinical and cytological study

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Background/ Objectives: Eosinophilic granulomatosis with polyangiitis (EGPA) is frequently associated with refractory chronic rhinosinusitis with nasal polyps (CRSwNP), despite current treatments. Dupilumab demonstrated efficacy in the treatment of severe and uncontrolled CRSwNP.

We aimed to assess safety and efficacy of dupilumab in refractory CRSwNP in EGPA and analyze changes in nasal smears and tissue infiltrates.

Methods: Consecutive EGPA patients suffering from refractory CRSwNP were enrolled prospectively between December 2021 and October 2023. Demographic, clinical, biological data and nasal cytology were collected at each evaluation.

Assessment included patient-reported outcomes such as Asthma Control Test (ACT), Nasal Congestion Score (NCS), Sino-Nasal Outcome Test (SNOT-22), Visual Analogue Scales (VAS)), as well as objective measures including Peak Nasal Inspiratory Flow (PNIF), Nasal Polyp Score (NPS) and Sniffin' Sticks Identification Test (SSIT).

Complete response was defined by Birmingham Vasculitis Activity Score (BVAS)=0 and prednisone dose ≤4 mg/day, and partial response by BVAS=0 and prednisone dose >4 mg/day.

Results: The study included 9 EGPA patients (age at diagnosis 51 [46-59] years, male 66.6%), with BVAS at diagnosis of 16 [11.5-19.5]. Median eosinophils at diagnosis were 4810/mmc [2100-9180], reduced to 330/mmc [175-640] at dupilumab initiation. Dupilumab was mainly used as third-line therapy, after a median disease duration of 66 [65-128] months. Two (22.2%) patients were previously treated with anti-IL5/IL-5R therapy. Median duration of treatment with dupilumab was 8 [3.5-6] months.

	T0 (n=9)	T3 (n = 9)	P value (T0-T3)	T6 (n=6)	P value (T3-T6)	T12 (n=4)	P value (T6-T12)	T LFU (n=9)	P value (T0-TLFU)
Eosinophils count (/mm3), median (IQR)	330 (175-640)	540 (165-1700)	-	465 (255-880)	-	615 (260-1000)	-	790 (245-2170)	0.036
Eosinophils > 1500, n (%)	0 (0)	2 (22.2)	-	0 (0)	-	0 (0)	-	3 (33.3)	-
BVASv3, median (IQR)	0 (0-0)	0 (0-0)	-	0 (0-0)	-	0 (0-0)	-	0 (0-0)	-
VDI, median (IQR)	5 (4-6)	5 (3-6)	-	5 (3.25-6.75)	-	4.5 (3.25-6.5)	-	5 (4-6)	-
CRP (mg/L), median (IQR)	2 (1-3)	2.9 (1.25-31.66)	-	4.69 (4.38-4.69)	-	2.7 (0.64-5.10)	-	2.79 (0.64-31.75)	-
Complete response, n, (%)	0 (0)	3 (33.3)	-	5 (83.3)	-	3 (75)	-	5 (55.5)	-
Partial response, n (%)	0 (0)	1 (11.1)	-	0 (0)	-	0 (0)	-	0 (0)	-
Concomitant therapy									
PDE, mg, median (IQR)	0 (0-5)	1.6 (0-20)	0.285	0 (0-2.5)	1.00	0 (0-1.87)	1.00	1.25 (0-20)	0.465
Adverse events, n (%)	1 (11.1)	3 (33.3)	-	0 (0)	-	0 (0)	-	1 (25)	-
Patient reported outcomes									
ACT, median (IQR)	23 (20-24.5)	24 (22-24.5)	0.672	24 (22.5-25)	0.083	25 (20.5-25)	0.655	25 (24-25)	0.5
SNOT-22, median (IQR)	55 (38-74)	30 (21-50)	0.050	21 (3.75-47.5)	0.686	25 (3.5-47.25)	0.461	28 (14-43)	0.05
VAS nasal obstruction, median (IQR)	8 (6-10)	2 (0-6)	0.017	1.5 (0-3.75)	0.854	1 (0-5.75)	0.654	2 (0-6)	0.011
VAS anterior rhinorrhea, median (IQR)	6 (5-8)	2 (1-6)	0.049	0 (0-0)	0.713	0 (0-5.25)	0.317	0 (0-6)	0.043
VAS posterior rhinorrhea, median (IQR)	7 (4-8)	2 (1-5)	0.078	2 (0-5.75)	1.00	1 (0-6.5)	0.655	1 (0.5-4.5)	0.273
VAS facial pain, median (IQR)	3 (2-7)	1 (0-3)	0.136	0 (0-0)	0.414	0.5 (0-6.25)	0.180	0 (0-2)	0.107
VAS sleep disorders, median (IQR)	5 (3-8)	0 (0-2)	0.042	0 (0-0)	0.317	0 (0-0)	1.00	0 (0-0)	0.042
VAS smell, median (IQR)	10 (9.5-10)	6.5 (1.75-9.75)	0.043	3 (0-6.25)	0.705	3 (0-3)	0.180	5 (2-9.5)	0.028
NCS, median (IQR)	2 (2-3)	1 (0-2)	0.016	0.5 (0-1.25)	0.317	1 (0.25-1.75)	0.157	0.5 (0-1.75)	0.016
Objective measure									
NPS, median (IQR)	6 (4-7)	4 (1-6)	0.051	3 (0-6.25)	0.317	2 (2-4.25)	0.564	2 (0-6)	0.011
PNIF, median (IQR)	120 (60-185)	150 (78-180)	0.236	142.5 (110-255)	0.916	135 (75-300)	0.715	150 (82.5-200)	0.309
SSIT, median (IQR)	3/12 (3-4)	6/12 (4-10)	0.075	7/12 (6-9)	0.655	8/12 (7-8)	1.00	6/12 (3-8)	0.216
Nasal smears tissutal infiltrates	n=6	n = 5		n = 4		n = 3		n = 4	
Eosinophils cells HPF, median (IQR)	8 (2-13)	1 (1-4)	0.225	0.3 (0-1.8)	1.00	0,2 (0-0.2)	0.180	16.2 (6-16.2)	
Neutrophils cells HPF, median (IQR)	6 (2-9)	2 (2-7)	0.500	1.1 (0-3.7)	0.715	0 (0-0)	0.317	5 (1.4-5)	
Hair cells HPF, median (IQR)	0 (0-1)	0 (0-0)	0.285	0.8 (0-3.55)	0.180	1.6 (0.6-1.6)	0.655	0.3 (0-0.3)	

A total of 26 nasal cytology tests were performed (min 2 – max 4 for each patient). At baseline, 66.7% patients showed a nasal cytology with eosinophilic patterns, 16.7% a neutrophilic pattern and 16.7% a mixed (eosinophils-neutrophils) pattern. The median eosinophils count was 8 (2-13) cells per field at the start of dupilumab, reduced to 0.2 (0-0.2) at 12 months, whereas median neutrophils count was (2-9) cells per field at the start of dupilumab, reduced to 0 (0-0) at 12 months.

No differences were observed in median eosinophils count, prednisone dose and VDI during follow-up.

Significant improvement was observed in VAS-nasal obstruction (p=0.011), VAS-smell (p=0.028), VAS anterior rhinorrhea (p=0.043), VAS sleep disorders (p=0.042), NCS (p=0.016), SNOT-22 (p=0.05) and NPS (p=0.011).

At last follow-up complete response was achieved by 6 (66.6%) patients. Adverse events were reported in 4 (44.4%) patients. Hypereosinophilia occured in 2 (22.2%) patients within the first 3 months, leading to dupilumab discontinuation.

Conclusions: Dupilumab showed improvement in patient reported outcomes and objective measures when used in refractory CRSwNP in EGPA. Treatment was associated with a good safety profile.

References: None.

Disclosures: None.

PT-3A-19

Prognosis of essential mixed cryoglobulinemia and connective tissue disease-related cryoglobulinemia after rituximab-induced remission

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Background/Objectives: The treatment and prognosis of cryoglobulinemia vasculitis (CryoVas) depend on etiology. Rituximab (RTX) and corticosteroids (CS) are the first line treatment for mixed essential (ME) CryoVas and connective tissue disease (CTD)-related CryoVas (1,2,3). The prognosis and long term outcomes of these forms of CryoVas are as yet unknown. The aim of this study was therefore to describe the risk of relapse and treatment-related morbidities in patients with ME and CTD-related CryoVas.

Methods: A retrospective study was conducted of 63 patients in remission of ME or CDT-related CryoVas after RTX-CS therapy, with a median follow-up time of 58 months (interquartile range, 33–88 months).

Results: Thirty-nine out of 63 patients (62%) had a relapse a median of 42 (23–65) months after the initial flare. The relapse incidence was 38% at 2 years and 46% at 3 years. The factors associated with relapse were purpura at the time of the qualifying flare (HR, 2.2; 95% confidence interval (CI), 1.1–4.4; $p = 0.002$) and prior history of CryoVas flares (HR, 1.9; 95% CI, 1.0–3.7; $p = 0.04$). Maintenance therapy was associated with a lower risk of relapse 6–24 months after the initial flare (HR, 0.27; 95% CI, 0.09–0.78; $p = 0.02$), but not thereafter (HR, 2.0; 95% CI, 0.7–5.7; $p = 0.21$). The most common form of maintenance therapy was 500 mg RTX every 6 months. The most frequent complication was infection, and maintenance RTX therapy was associated with a higher risk of severe infection (HR, 2,2; 95% CI, 0.9–5,6; $p = 0.08$).

Conclusion: In this group of patients in RTX-CS remission of ME and CTD-related CryoVas, relapses were common and the risk of relapse was significantly associated with purpura during the qualifying flare and a prior history of relapse. Maintenance RTX was associated with a lower risk of relapse but was also associated with an increased risk of severe infection.

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Disclosures: None.

PT-3A-20

Tocilizumab for Polyarteritis Nodosa with cutaneous involvement

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Backgrounds: Immune checkpoint inhibitors (ICIs) have dramatically improved the prognosis for many cancers. The therapeutic effect of ICIs is based on their ability to release the brakes on lymphocyte activation. However, this brake release can trigger immune-related adverse events (IrAEs) in up to 60-80% of cases. Few observations of ICI-induced large vessel vasculitis (LVV) have been reported. We aimed to describe the characteristics and outcomes of LVV occurring after or during ICI therapy, compared with non-induced LVV.

Methods: We conducted a European, multicenter, retrospective study of patients who received at least one infusion of ICI and subsequently presented with LVV between March 2018 and January 2023. Each case was compared with four patients with non-induced LVV matched for sex and age (+/5 years). LVV patients either satisfied the 2022 ACR/EULAR classification criteria for giant-cell arteritis (GCA) or had an imaging or histological proof of LVV.

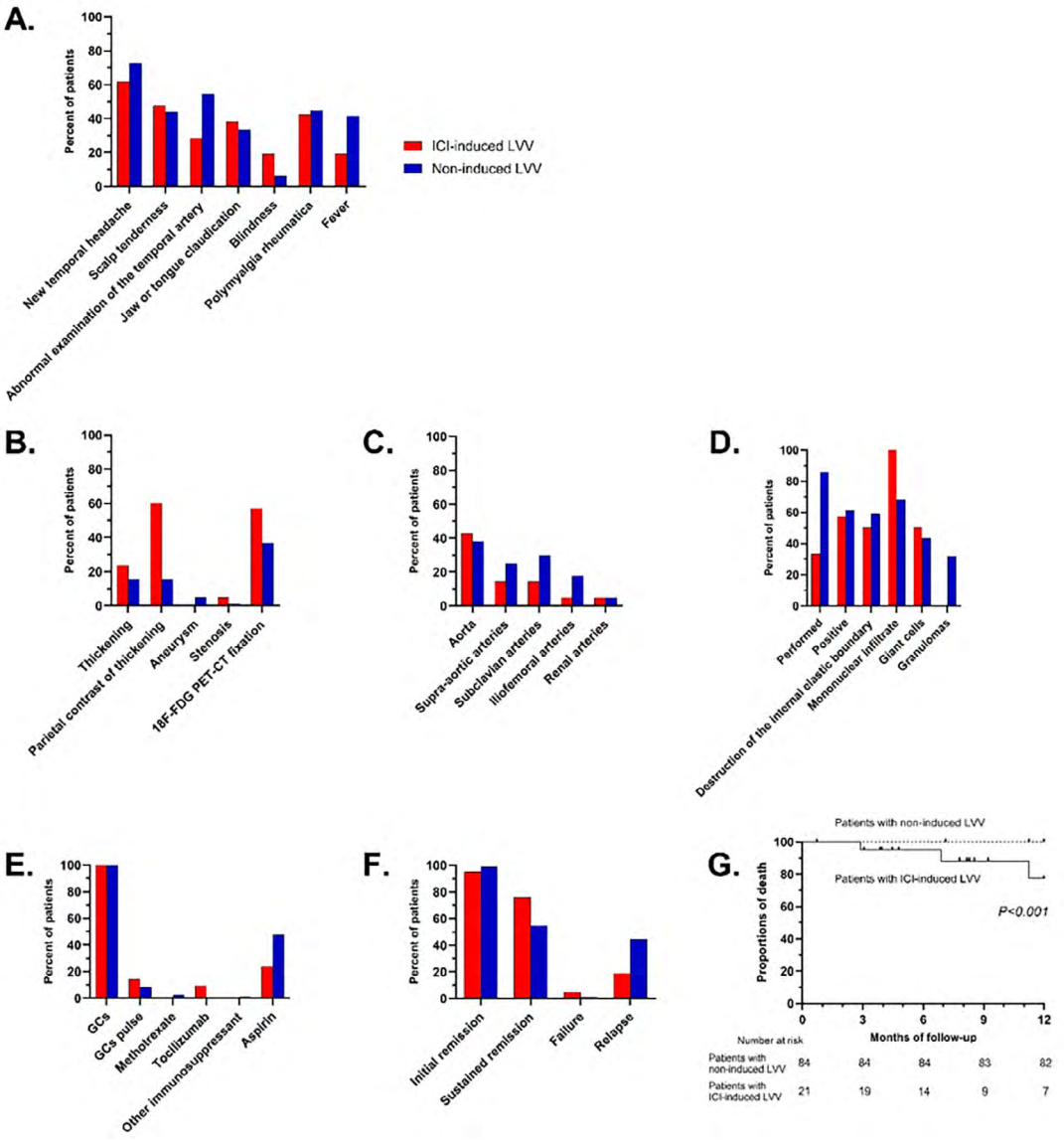

Figure 1.

Results: Twenty-one patients were included (median age 70 (IQR 61-74) years). Previous history of PMR or GCA was noted in 4 (19%) patients. The two most common cancers treated with ICIs were melanoma (38%) and renal cell carcinoma (24%). Five (29%) patients received a combination of nivolumab and ipilimumab, while the rest received a monotherapy of anti-PD-1/PD-L1. First LVV manifestations occurred after a median of 5 (IQR 3-22) ICI infusions and a median time of 3 (IQR 2-18) months since the first ICI infusion. Thirteen (62%) patients were diagnosed of LVV within the first six months after ICI initiation.

Clinical manifestations were overall similar compared to controls (**Figure 1A**). Blindness occurred in 4 (19%) patients compared to 5 (6%) controls. Aorta was the main artery involved (**Figure 1B & 1C**). Temporal artery biopsy was positive in 4/7 cases (**Figure 1D**). Five (26%) patients had other IrAEs, mainly hepatitis.

All patients received oral glucocorticoids. The median initial prednisone dose was 0.7 g/kg/d (IQR 0.7-1). Two (11%) patients received tocilizumab as first-line therapy (**Figure 1E**).

ICI was rechallenged or continued for 6 (29%) patients and stopped for 15 (71%) patients.

Median follow-up after LVV diagnosis was 8 months (IQR 4-16). Sustained remission was achieved in 16 (76%) patients. Four (19%) patients relapsed after first line therapy while 37 (44%) had relapsed in the control group (**Figure 1F**). Relapse or failure after first line therapy occurred in 3/6 (50.0%) patients who continued ICI compared with 3/15 (20.0%) patients who discontinued it. At the end of follow-up, 5/21 (24%) patients had died, 4 of cancer and 1 of acute coronary syndrome, while only two (2%) had died in the control group (**Figure 1G**).

Conclusion. LVV is a rare IrAE that usually occurs early after the initiation of ICI. Unexplained elevations in acute phase reactants in ICI-treated patients should prompt clinicians to look for signs of LVV, as severe ischaemic manifestations such as visual loss may occur. While patients who were maintained on ICI or rechallenged had a more refractory or relapsing course, physicians should prioritize cancer management as it is the leading factor affecting early prognosis.

PT-3A-21

Combination rituximab & low-dose IV cyclophosphamide induction therapy for severe multi-system eosinophilic granulomatosis with polyangiitis

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Background/Objectives: Current guidelines advise rituximab (RTX) or cyclophosphamide treatment for organ-threatening disease in eosinophilic granulomatosis with polyangiitis (EGPA). However, conventional treatment is often limited by partial efficacy, toxicity, high relapse rate and steroid dependency. We investigate the use of a combined RTX, low-dose cyclophosphamide, and steroid regimen for treatment of severe EGPA.

Methods: Single-centre retrospective cohort study of patients treated with a combination induction regimen for severe EGPA between 2012-23. Data reported as median (±IQR).

Results: Eighteen patients (10 male; age 56 years [52-62]) are included. At treatment, BVAS was 16.3 [14-20], peak eosinophil count 9.3x10^9/L [5-13], C-reactive protein (CRP) 122mg/L [80-193]. Eleven cases were ANCA positive (10 MPO-, 1 PR3-ANCA.) The proportions of patients affected by active/new respiratory, ENT, neurological, and gastrointestinal disease were 18/18 (100%), 14/18 (78%), 11/18 (61%), and 1/18 (6%), respectively. 11/18 (61%) had cardiac involvement (troponin 10345ng/L [1240-7621]) and 6/18 (33%) had necrotising glomerulonephritis confirmed by renal biopsy (creatinine 123µmol/L [83-167]).

Cumulative cyclophosphamide dose was 3.5g [3.0-3.5] and total RTX dose was 2g. Initial prednisolone dose was 0.5-1.0mg/kg/day, and this was rapidly weaned to 5mg daily at a median time of 6.1 months [3.9-7.2], and 9/18 (50%) had steroids withdrawn completely by 11.7 months [4.6-20.6]. First-line maintenance treatment was azathioprine or MMF.

By 6 months, all achieved disease remission as assessed by BVAS (all 0) and improved laboratory parameters: CRP 1mg/L, eosinophil count 0.1x10^9/L, and ANCA testing negative. In those with renal disease, kidney function improved or stabilised in all (creatinine 95µmol/L).

In those with cardiac disease (11/18), magnetic resonance imaging was performed at baseline and at follow up (median time of 3.7 months) in all patients. Of these, 9/11 (82%) had oedema on initial scan and this improved in all cases; 10/11 (91%) had late gadolinium enhancement at baseline, which persisted in every case, though with significantly lower burden.

The median follow-up period was 38 months [14-55]. At 1, 3 and 5 years, 100%, 92% and 76% of patients were in sustained remission (Figure 1A). Three patients experienced relapse; one patient had major relapse with skin involvement requiring reinduction treatment; two patients had minor ENT relapse requiring retreatment with glucocorticoids. Infection-free survival at 1, 3 and 5 years was 94%, 78%, 62%, respectively (Figure 1B). There were no deaths.

Conclusions: This regimen provided rapid disease control in patients with severe multi-system EGPA, including those with life-threatening cardiac manifestations, and enabled rapid glucocorticoid tapering and withdrawal. Disease-free remission was sustained during long-term follow up. Combination induction regimens may have a role in the treatment of organ-threatening disease in EGPA.

References: None.

Disclosures: None.

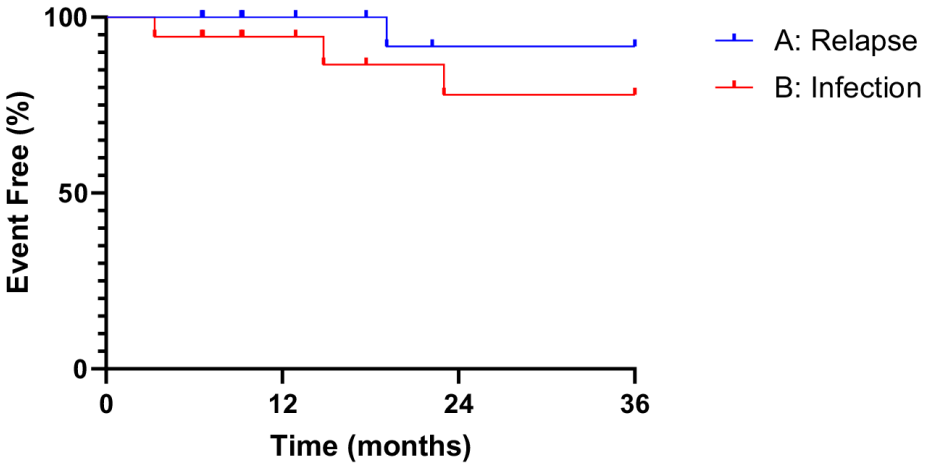

Figure 1: Time to event analysis for relapse (A) and first infection (B) during median follow-up period of 36 months.

PT-3A-22

Efficacy and drug survival of biologic agents in Behçet's disease: a real-life observational monocentric study

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Background/ Objectives: Biologic disease-modifying anti-rheumatic drugs (bDMARDs) are effective in treating Behçet's disease (BD), with most of the evidence concerning anti-TNF, while limited data are available on long-term effectiveness and retention rate. The aim of the study is to assess their effectiveness and 10-year retention rate.

Methods: We included patients treated with Infliximab (IFX), Adalimumab (ADA), Apremilast (APR), and Tocilizumab (TCZ) between 2009-2023. Treatment approaches were compared. Survival rates were analysed with Kaplan-Meier and compared with Log-rank test. Japan's Behçet activity criteria were used to assess disease activity.

Results: We included 32 BD patients (34[29-39] years, 53.1% female) exposed to 53 treatment regimens (23=IFX,10=APR,16=ADA,4=TCZ), of which 68.75% received at least one conventional DMARD. The first bDMARD was prescribed 32.5[13-131] months after diagnosis, with anti-TNF administered earlier (p=0.044) and in individuals with ocular involvement (p=0.033). Previous administration of colchicine was more frequent in patients treated with APR (p=0.035). Anti-TNF treatment duration was longer compared to others bDMARDs (p=0.011). Male patients exhibited a better retention rate for every bDMARD (p=0.001), while there were no differences according to type of bDMARD (p=0.554) or previous use of cDMARDs (p=0.471). Treatment with bDMARDs resulted in a significant reduction in disease activity (92.7%vs44.4%,p<0.001). Daily prednisone dose was significantly reduced in patients treated with IFX (10[5-21.25]vs5[0-10],p=0.015), while no differences were noted in acute phase reactants. Primary failure was observed in 11.3% of cases, while secondary in 24.5%. Discontinuation of bDMARDs was due to intolerance (3.7%), remission (3.7%) and adverse events (15.1%).

Conclusions: Treatment of BD with bDMARDs treatment is effective and its retention rate is affected by female sex, but not by concomitant cDMARDs. Anti-TNF had the longer survival, when compared to others bDMARDs.

PT-3A-23

Rituximab in addition to plasma exchange, cyclophosphamide and steroids for treatment of anti-GBM disease

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Background/ Objectives: Anti-GBM disease is a rare antibody-mediated vasculitis, usually treated with plasma exchange (PEX), cyclophosphamide (CYC) and steroids. There are limited data regarding the use of B-cell depleting therapies such as rituximab (RTX).

Methods: Ten-year (2012-2023) single-centre retrospective cohort study of patients with anti-GBM disease treated with or without rituximab, in addition to standard care, as first-line therapy. A Cox-proportional hazards regression model incorporating age, sex, ANCA status, dialysis at presentation, lung haemorrhage, CYC (oral or IV) and RTX treatment was used to identify disease/treatment factors associated with outcome (death, end-stage kidney disease [ESKD], infection).

Results: Forty-five patients were included; baseline demographics, disease characteristics, treatments and outcomes are summarised in Table 1.

Table 1: Demographics, disease features, and outcomes (data reported as median [IQR])

	All	RTX	No RTX
Demographics			
Number	45	30	15
Age, years	62 [45-75]	61.5 [45-74]	62 [46-76]
Sex, M:F	19:26	12:18	7:8
Disease at Baseline			
Dialysis (%)	26/45 (58)	19/30 (63)	7/15 (47)
Creatinine, µmol/L	647 [314-957]	763 [296-1344]	531 [348-795]
Lung Haemorrhage (%)	14/45 (31)	8/30 (27)	6/15 (40)
ANCA (neg/MPO/PR3)	26 / 14 / 5	16 / 10 / 4	10 / 4 / 1
Anti-GBM, iu/L	144 [53-497]	101 [40-623]	165 [106-349]
Treatment			
PEX, number	14 [7-17]	10 [7-14]	19 [15-21]
CYC dose, g	4.0 [3.0-6.1]	3.6 [3.0-4.8]	6.4 [4.2-7.1]
Outcomes			
Time to anti-GBM negative, months	1.6 [0.47-4.17]	1.75 [0.24-3.86]	1.6 [0.97-4.7]
1 year survival (%)	38/45 (84)	27/30 (90)	11/15 (73)
1 year ESKD-free survival (%)	18/45 (40)	11/30 (37)	8/15 (53)
Hypogammaglobulinemia (%)	5/45 (11)	5/25 (20)	0/15
Post-treatment diabetes (%)	3/45 (7)	3/30 (10)	0/15
Malignancy (%)	1/45 (2)	1/30 (3)	0/15

All patients were treated with PEX, CYC (oral or IV), and steroids. Patients treated with or without RTX had similar baseline demographic and disease features. The addition of RTX treatment was associated with reduced number of PEX (10 *versus* 19 with no RTX, $p<0.01$) and lower total CYC dose (3.6g *versus* 6.4g, $p<0.05$), with equivalent time to circulating anti-GBM negativity.

In the Cox regression model, only increasing age was associated with risk of death (HR 1.08 [95% CI 1.02-1.17]). Age (HR 1.04 [1.01-1.08]), female sex (HR 4.93 [1.80-14.87]), and dialysis need at presentation (HR 5.28 [1.54-17.53]) were associated with ESKD-risk. Increasing age (HR 1.04 [1.00-1.09] and ANCA positivity (HR 3.08 [1.14-8.71]) were associated with risk of infection. The addition of rituximab was not significantly associated with risk of death (HR 0.82 (0.24-2.87), ESKD (HR 1.54 [0.64-3.96]) or infection 2.06 [0.67-5.71].

Conclusions: Addition of rituximab to standard treatment for anti-GBM disease was not associated with improved renal outcome or survival benefit. However, rituximab use permitted lower cumulative doses of CYC and reduction in the number of PEX, without an increased risk of infection. Rituximab may have a limited role as a CYC- and PEX-sparing treatment in patients with anti-GBM disease.

References: None.

Disclosures: None

PT-3A-24

De Novo Manifestations During Adalimumab Treatment in Behçet Syndrome

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Background/ Objectives: Monoclonal antibody tumor necrosis factor alpha inhibitors, particularly infliximab (IFX) and adalimumab (ADA), are the most commonly used biological agents in the treatment of Behçet's syndrome (BS). Treatment response may show variability across organ manifestations of BS. We aimed to determine the frequency of de novo manifestations during ADA treatment.

Methods: We conducted a chart review of 338 BS patients who received ADA in our center. Demographic data, reasons for initiating ADA, concurrent medications, previous treatments, and treatment outcomes were recorded. We defined de novo manifestations as new BS manifestations that had not emerged prior to ADA treatment in addition, for patients with vascular involvement, a new vascular event at another vessel site.

Results: The main reasons for ADA use among our 338 patients were uveitis in 128 patients (38%), vascular involvement in 80 (24%), arthritis in 62 (18%), mucocutaneous involvement in 50 (15%), gastrointestinal (GI) involvement in 10 (3%), and parenchymal central nervous system (CNS) involvement in 8 (2%). Among these patients, 14 (4%) developed a de novo manifestation. De novo manifestations that occurred in 14 patients were vascular involvement in 5 patients, arthritis in 3, anterior uveitis in 2, parenchymal CNS involvement in 2, GI system involvement in 1, and epididymitis in 1 patient. The primary reasons for ADA treatment were vascular involvement in 5 patients, uveitis in 4, arthritis in 3, and mucocutaneous involvement in 2. Among these 14 patients, 9 (64%) were using concomitant conventional immunosuppressive treatment when de novo manifestations occurred (Table).

Table. Characteristics of the BS patients who developed a de novo manifestation

Age at ADA initiation, gender	BS manifestations	Manifestation requiring ADA	Previous drugs	Time to new manifestation (months)	New manifestation	Tx for new manifestation
24, M	O, G, E, U	Epididymitis	AZA	2	Arthritis	GC and IFX
51, M	O, G, J, EN, STM	Arthritis	AZA, SZP, MTX, ETA, IFN	32	DST	ADA intervals ↓
26, M	O, G, J, EN, Budd-Chiari, CT	MK	AZA, CYC, MMF, IFX	35	Uveitis	Topical steroid and tropicamide
26, M	O, G, P, DVT, PAT, VCI, CT	DVT	AZA, CYC, IFN, IFX	3	DST	Pulse MP and AZA
39, W	O, G, EN	Lower extremity DVT	AZA, CYC, IFN, IFX	12	Upper extremity DVT	GC
44, M	O, G, U, DVT, PAT, PAA, STM	PAI	AZA, CYC, IFX	30	MVT and PVT	Pulse MP and ADA intervals ↓
34, M	O, G, P, EN, U, PAT, DVT	Uveitis	AZA, CY-A, CYC, MMF, IFN	9	NBS	Pulse MP, IFX and MMF
51, M	O, P, EN, DVT, STM	DVT	AZA	18	Arthritis	GC
15, W	O, G, P, GIS, J	Arthritis	AZA	12	Uveitis	Topical treatment
62, W	O, G, P, EN, J, U, PA	Arthritis	AZA, CY-A, IFN	26	NBS	Pulse MP, CZP
57, W	O, G, EN, U	Uveitis	AZA, CY-A	26	Arthritis	COL
25, M	O, G, P, EN, U,	Uveitis	AZA, GC	14	PAT	ADA intervals ↓
30, W	O, G, U	Uveitis	AZA, CY-A, IFN, IFX, GC	46	GIS	Pulse steroid, IFX
19, M	O, G, U, DVT, Budd-Chiari, PAT	Vascular	AZA, CYC, IFN, IFX	48	Epididymitis	GC

ADA treatment was intensified in 3 patients by shortening the intervals to 1 week, along with the addition of high dose glucocorticoids (GC) in one patient. In the 4 patients, ADA was switched to another agent (IFX in 3 patients, certolizumab in 1 patient). Only GC were added in 3 patients, azathioprine along with high dose GC in one patient, and colchicine in one patient. Two patients who had developed anterior uveitis were initiated topical treatment (Table).

Conclusions: De novo manifestations occurred in 14 (4%) of 338 BS patients treated with adalimumab. Majority of these (71%) were major organ involvement, mainly vascular involvement. None of the patients developed posterior uveitis, however, de-novo anterior uveitis of two patients were controlled with topical agents.

References: None.

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Poster Tour 4A: Outcomes and Predictors

PT-4A-25

A prospective study of complications and sequelae of glucocorticoid therapy in ANCA-associated vasculitis

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Background/ Objectives: Glucocorticoids (GC) are a cornerstone of induction treatment in ANCA-associated vasculitides (AAV). However, the often severe disease course and frequent relapses lead to high cumulative GC doses which adds to morbidity and mortality in AAV patients. The aim of this study was to assess the frequency of GC-associated complications and sequelae in patients with AAV, as these have been rarely systematically investigated to date due to a lack of proper instruments.

Methods: Patients with a confirmed diagnosis of AAV were included in this monocentric prospective study. Age- and gender-matched subjects who had never received GC were included as controls. The incidence of GC toxicity was assessed by structured patient interviews, clinical examination, and electronic medical record analysis. The Glucocorticoid Toxicity Index (GTI)[1] consisting of the aggregate improvement score (GIT-AIS) and the cumulative worsening score (GTI-CWS) was used to calculate GC toxicity between 2 time points (t1 and t2), the GTI-AIS showing change in GC toxicity over a 6-month period and the GTI-CWS showing cumulative GC toxicity over the entire disease duration. The minimal clinical important difference (MCID) of the GTI is ≥ 10[2]. We used regression analyses to assess the relationship between GTI and GC exposure, toxicity, and disease activity. A ROC analysis was used to calculate a critical GC threshold dose beyond which toxicity becomes likely.

Results: We included 138 patients with AAV and 68 controls. The median cumulative GC was 9014.0 mg. The most frequent GC-associated adverse events in patients with AAV were skin atrophy, osteopenia, osteoporosis, and myopathy. GC exposure and GC toxicity in the observation period were significantly correlated ($p<0.001$). Current GC exposure and GTI-AIS were significantly higher in active disease compared to patients in remission ($p<0.001$). Cumulative GC dose was significantly higher in patients in remission ($p=0.004$). Weight gain, diabetes, hypertension, and sleep disturbance occurred more frequently in patients with active disease (Table 1). Patients with a cumulative GC dose of 935 mg or more showed an 80% likelihood for a clinically meaningful change in GTI scoring.

Conclusions: Patients with AAV and active disease are at significantly increased risk for acute metabolic GC side effects due to high daily GC exposure. Patients in stable remission have a greater impact on the risk of chronic complications due to lower daily but higher cumulative GC dose. The GTI is capable of capturing GC toxicity in AAV and identifies patients at increased risk for GC side effects. Our data support efforts to limit GC-exposure in patients with AAV[3].

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Table 1: GC toxicity according to disease activity.

	Active disease	Stable remission	p
N	29	109	
Diagnosis type			
GPA	15 (51.7)	56 (51.4)	
MPA	7 (24.1)	18 (16.5)	0.545
EGPA	7 (24.1)	35 (32.1)	
Age (years)	59.03 ± 15.377	56.21 ± 15.234	0.378
Female	17 (58.6)	59 (54.1)	0.666
Cumulative GC dose (mg)	5700.0 (3205.0-11036.0)	10282.0 (5390.0-18104.0)	0.004
Average daily GC dose (mg/d)	11.9 (8.5-24.5)	7.3 (5.9-10.0)	0.001
Duration of illness (months)	10.0 (7.0-98.5)	61.0 (30.5-110.0)	0.001
Vasculitis damage index (VDI)	1.0 (0.5-3.0)	1.0 (1.0-2.0)	0.764
Cumulative GC dose in the GTI-AIS calculation period (mg)	1745.0 (1206.5-2542.0)	240.0 (0.0-733.0)	0.001
GTI-AIS calculation period (days)	184.0 (159.5-217.0)	182.0 (161.0-198.0)	0.672

	Active disease	Stable remission	p
GTI AIS (at t2)	23.0 (0.0-74.0)	0.0 (0.0-0.0)	0.001
Subjects (N) with GTI-AIS < 0	2 (6.9)	25 (22.9)	
Subjects (N) with GTI-AIS = 0	8 (27.6)	62 (56.9)	0.001
Subjects (N) with GTI-AIS > 0	19 (65.5)	22 (20.2)	
GTI CWS (at t2)	57.0 (30.5-92.5)	59.0 (29.0-105.5)	0.664
Subjects (N) with GTI-CWS = 0	3 (10.3)	8 (7.3)	
Subjects (N) with GTI-CWS > 0	26 (89.7)	101 (92.7)	0.595
GC-associated complications and sequelae (at t2)			
Metabolism			
Weight gain	8 (27.6)	3 (2.8)	0.001
Lipodystrophy	2 (6.9)	3 (2.8)	0.288
Diabetes/glucose intolerance	11 (37.9)	12 (11.0)	0.001
Adrenal insufficiency	0	2 (1.8)	1.000
Dyslipidemia	6 (20.7)	8 (7.3)	0.034
Musculoskeletal and skin			
Skin atrophy	3 (10.3)	42 (38.5)	0.004
Easy bruising	4 (13.8)	26 (23.9)	0.243
Osteopenia	2 (6.9)	14 (12.8)	0.374
Osteoporosis	5 (17.2)	17 (15.6)	0.830
Myopathy/muscle weakness	4 (13.8)	13 (11.9)	0.786
Acne	0	7 (6.4)	0.543
Striae rubrae	1 (3.4)	3 (2.8)	1.000
Infections	6 (20.7)	9 (8.3)	0.056
Neuropsychiatric symptoms			
Sleep disturbances	9 (31.0)	16 (14.7)	0.042
Mood swings	3 (10.3)	13 (11.9)	0.813
Depression	2 (6.9)	12 (11.0)	0.514
Dizziness	3 (10.3)	6 (5.5)	0.348
Tinnitus	0	8 (7.3)	0.133
Headaches	3 (10.3)	6 (5.5)	0.348
Irritability	2 (6.9)	7 (6.4)	0.927
Nervousness	0	2 (1.8)	1.000
Cardiovascular			
Renal dysfunction	0	1 (0.9)	1.000
Edema	5 (17.2)	9 (8.3)	0.154
Disturbance of electrolyte balance	1 (3.4)	1 (0.9)	0.377
Arterial hypertension	8 (27.6)	11 (10.1)	0.015
Atherosclerosis	0	1 (0.9)	1.000
Angina pectoris	1 (3.4)	0	0.210
Gastrointestinal			
Gastritis	0	1 (0.9)	1.000
Ophthalmological			
Cataract	2 (6.9)	16 (14.7)	0.269
Glaucoma	0	2 (1.8)	1.000

Legend: Data as n (%), mean ± SD or median (IQR). GPA, Granulomatosis with polyangiitis; MPA, Microscopic polyangiitis; EGPA, Eosinophilic granulomatosis with polyangiitis.

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PS has no conflicts of interest.

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PT-4A-26

Manifestations and predictors of neurologic involvement in Behçet's disease: results from a monocentric study

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Background/ Objectives: Behçet's disease (BD) is a multisystem inflammatory disorder primarily affecting mucocutaneous tissues. Central nervous system (CNS) involvement, Neuro-BD (NBD), is a potentially severe manifestation of BD with a variable prevalence depending on the diagnostic criteria and ethnicity of the patients [1-5]. We aim to characterize BD patients with CNS involvement and to identify predictors of this clinical subtype.

Methods: Single-centre observational retrospective study using data from patients with a diagnosis of BD registered at Reuma.pt. NBD was defined according to International Consensus Recommendation Criteria for NBD diagnosis.

Results: We included 160 patients with BD, 42 (26%) males, 129/147 (88%) Caucasian with a median [IQR] age at diagnosis of 31.9 [16.5] years and a median follow-up of 11.0 [12] years. NBD was diagnosed in 24 patients, in 2 at disease onset. The median age at NBD diagnosis was 31.0 [13] years; 3.8 [5.9] years after BD onset. Fifteen (63%) patients had parenchymal involvement, eight (33%) had nonparenchymal involvement, and one (4%) had mixed involvement. Imaging abnormalities were found in 22/22 (100%) patients and cerebral spinal fluid abnormalities in 6/11 (55%) patients. Most of the patients (79%) had a single episode; 17% had a progressive form with relapses and 4% had a relapsing remitting form.

	All patients (N= 160)	NBD patients (N=24)	Patients without CNS manifestation (N=136)	*p*-value*
Demographics				
Age at symptom onset$^{\theta}$, years (median, IQR)	24.6 (19.1)	27.0 (13.6)	24.1 (19.8)	0.220
Age at BD diagnosis$^{\theta}$, years (median, IQR)	31.9 (16.5)	31.0 (12.3)	32.3 (17.7)	0.913
Diagnostic delay$^{\theta}$, years (median, IQR)	3.0 (10.9)	1.8 (9.2)	3.0 (11.9)	0.095
Symptom duration$^{\theta}$, years (median, IQR)	11.0 (12.0)	11.5 (18.0)	11.0 (11.0)	0.979
Male gender (n, %)	42 (26)	6 (25)	36 (26)	0.880
Caucasian ethnicity$^{\theta}$ (n, %)	129 (88)	16 (73)	113 (90)	**0.031**
Comorbidities (n, %)				
Arterial hypertension$^{\theta}$	34 (22)	4 (17)	30 (23)	0,497
Current smokers$^{\theta}$	26 (21)	6 (32)	20 (20)	0.240
Diabetes mellitus$^{\theta}$	11 (7)	2 (8)	9 (7)	0.680
Dyslipidemia$^{\theta}$	26 (17)	4 (17)	22 (17)	1.000
Manifestations at disease onset (n, %)				
Oral ulcers$^{\theta}$	138 (88)	20 (91)	118 (88)	1.000
Genital ulcers$^{\theta}$	59 (38)	15 (68)	44 (33)	**0.002**
Ocular manifestations[1]$^{\theta}$	22 (14)	6 (27)	16 (12)	0.090
Cutaneous manifestations[2]$^{\theta}$	39 (25)	6 (27)	33 (25)	0.699
Articular manifestations[3]$^{\theta}$	18 (12)	1 (5)	17 (13)	0.470
Vascular manifestations[4]$^{\theta}$	6 (4)	2 (10)	4 (3)	0.187
Gastrointestinal manifestations[5]$^{\theta}$	1 (1)	0 (0)	1 (1)	1.000
Constitutional symptoms$^{\theta}$	11 (7)	0 (0)	11 (8)	0.362
Manifestations at disease onset and during disease follow up (n, %)				
Oral ulcer, ever	156 (96)	23 (96)	131 (96)	1.000
Genital ulcer, ever	130 (80)	19 (79)	109 (80)	1.000
Ocular manifestations[1]$^{\theta}$, ever	60 (38)	13 (57)	47 (35)	**0.047**
Cutaneous manifestations[2]$^{\theta}$, ever	115 (73)	15 (65)	100 (74)	0.378
Articular manifestations[3]$^{\theta}$, ever	71 (45)	11 (46)	60 (44)	0.900
Vascular manifestations[4]$^{\theta}$, ever	24 (15)	5 (21)	19 (14)	0.364
Gastrointestinal manifestations[5]$^{\theta}$, ever	17 (11)	2 (8)	15 (11)	1.000
Constitutional symptoms	23 (14)	7 (29)	16 (12)	0.051
Positive pathergy test$^{\nabla}$	32 (35)	8 (62)	24 (30)	0.055
Positive HLA-B51 haplotype$^{\nabla}$	36 (45)	6 (50)	30 (44)	0.706
ISG, 1990 Criteria fulfillment	128 (80)	20 (83)	108 (79)	0.787
Treatment (n, %)				
Glucocorticoids$^{\phi}$	128 (81)	23 (100)	105 (78)	**0.008**
csDMARDs$^{\phi}$	102 (65)	18 (86)	84 (62)	**0.035**
bDMARDs$^{\phi}$	22 (14)	6 (29)	16 (12)	0.085
Cyclophosphamide$^{\phi}$	12 (8)	10 (48)	2 (1)	**<0.001**
Prognosis (n, %)				
Mortality	6 (4)	4 (17)	2 (1)	**0.005**

θ Missing data <10%; ϕ Missing data 10-20%; β Missing data 20-25%; ∇ Missing data 25-50%.
* Independent samples t-test for continuous variables and Chi2 for categorical variables.
NBD – neuro-Behçet's disease; CNS – central nervous system; ISG – International Study Group; csDMARD: conventional synthetic disease modifying antirheumatic drugs; bDMARD: biologic disease modifying antirheumatic drugs.

[1]Ocular manifestations included anterior and/or posterior uveitis, retinal vasculitis, and central retinal vein or artery occlusion; [2]Cutaneous manifestations included erythema nodosum, pseudofoliculitis, and papulopustular or acneiform lesions; [3]Articular manifestations included inflammatory arthralgia or arthritis; [4]Vascular manifestations included superficial phlebitis, deep vein thrombosis, large vein thrombosis, and arterial thrombosis or aneurysm; [5] Gastrointestinal manifestations included abdominal pain, diarrhea, bowel obstruction, and bowel perforation.

Table 1: Comparison of demographic and disease characteristics between Behçet's disease patients with and without CNS involvement.

Table 1 shows the difference between patients with and without NBD. Patients with NBD were more frequently non-Caucasian (27% vs 10%, p=0.031), had more genital ulcers at disease onset (68% vs 33%, p=0.002), more ocular manifestations (57% vs 35%, p=0.047) during the disease course, were more frequently treated with systemic glucocorticoids (p=0.008), csDMARDs (p=0.035) and cyclophosphamide (p<0.001) and had a higher mortality rate (17% vs 1%, p=0.005) than patients without NBD. On multivariate analysis, genital ulcers at presentation (OR 3.36, 95%: 1.20-9.43) and constitutional symptoms during the disease course (OR 3.41, 95%: 1.02-11.32) were independent predictors of CNS involvement, irrespective of sex, ethnicity and age at symptom onset.

Conclusions: In our cohort, CNS involvement occurred in 15% of patients with BD, most commonly with a parenchymal phenotype. Non-Caucasian ethnicity, genital ulcers at presentation and constitutional and ocular manifestations during the disease course were associated with an increased risk of developing NBD. Given the high mortality rate verified in NBD, a potential tailored treatment approach in patients with these disease characteristics may be justified during follow-up.

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Disclosures: None.

PT-4A-27

Evolution and clinical implications of cranial and large vessel FDG-PET/CT activity in giant cell arteritis: a five-year cohort study

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Background/ Objectives: Giant cell arteritis (GCA) is characterised by cranial ischaemia at diagnosis and late aortic complications. The longitudinal pattern of activity by vascular territory has not been studied as a tool to predict and explain these phenomena. We assessed the distribution of FDG-PET/CT detected vascular activity at diagnosis, 6 months, and 5 years in an inception GCA cohort and the relationship with cranial symptoms and aortic dilatation on long-term follow-up.

Methods: Patients were eligible for this 5-year study if they had been enrolled in the Giant Cell Arteritis and PET Scan (GAPS) cohort[1] in 2016 or 2017, had a clinical diagnosis of GCA and a positive temporal artery biopsy (TAB) and/or a positive FDG-PET/CT scan at diagnosis. Patients underwent an FDG-PET/CT scan including assessment of cranial and large vessels, non-contrast MRI of the aorta, blood collection and clinical assessment. PET/CT scans were dual reported by 2 blinded nuclear medicine physicians. Scans were reported overall positive or negative for disease activity and a visual grading of FDG avidity in each vascular territory was made with comparison to blood pool. MRI was reported by a single blinded cardiovascular radiologist and thoracic aortic dilatation was defined as external diameter >= 40 mm in ascending or >= 30 mm in the descending aorta.

Results: 16 of the original 64 “suspected GCA” patients in the GAPS cohort met inclusion criteria and 11 participated in the 5-year study (3/16 deceased, 2/16 declined). The median age was 75, 73% were female and all were in clinical and serological remission with a median CRP of 1 (range 1 - 8). 4/11 (36%) patients had aortic dilatation (range 40 - 43mm) and 5/11 (45%) had globally active FDG-PET/CT scans. The distribution of FDG-PET/CT detected activity changed from a mix of cranial (9/11 patients) and large vessel disease at diagnosis to exclusively large vessel disease at 5-years. Aortitis developed in 4 patients who previously had inactive aortas. All 6 patients with inactive scans were taking an immunosuppressive agent (methotrexate, leflunomide, azathioprine or tocilizumab) at 5 years while all patients with active scans were not on therapy (p=0.02). There was a trend towards a higher median aortic diameter in those with positive scans at 5 years (42 mm vs 35 mm, p=0.08) but aortic avidity at diagnosis did not predict 5-year dilatation.

Conclusions: The distribution of PET/CT vasculitis activity changed from mixed cranial and large vessel to exclusively large vessel by 5-years and this may explain the preponderance of early cranial and late aortic complications in GCA. Aortic avidity at diagnosis did not predict dilatation at 5 years but 4 patients developed new aortitis on follow-up indicating the pitfalls of static PET/CT assessment. Long-term use of steroid sparing agents may protect against smouldering large vessel vasculitis.

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Disclosures: Nil

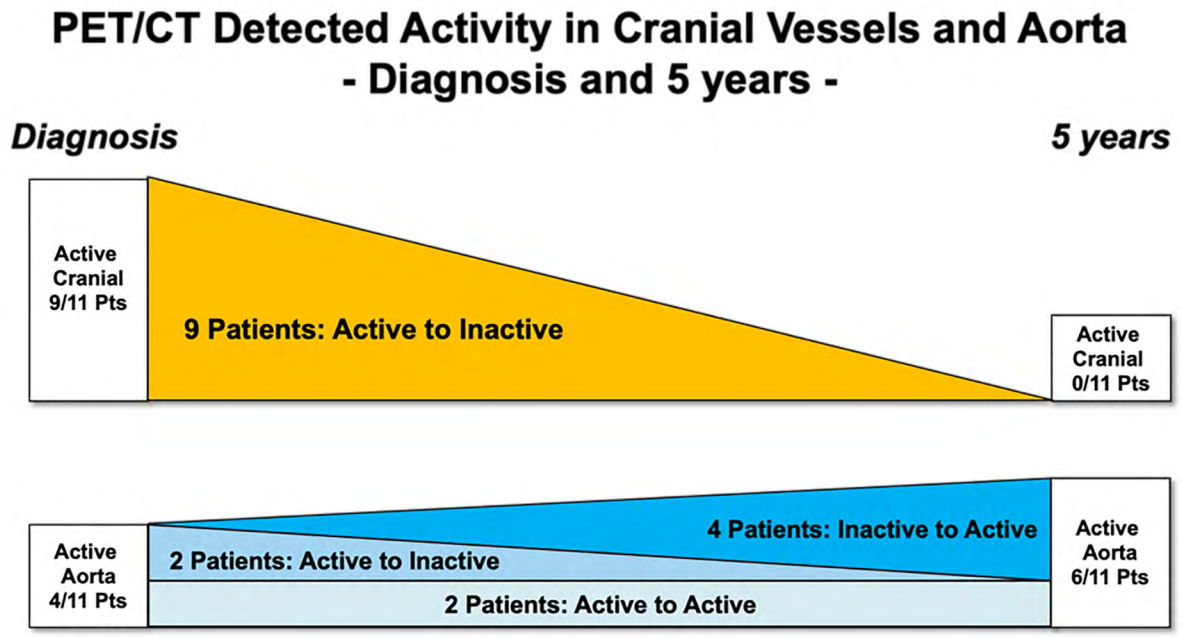

Figure: FDG-PET/CT activity by vascular region at diagnosis and 5 years.

PT-4A-28

Aortic aneurysm/dilatation development in a prospective cohort of patients with biopsy-proven giant-cell arteritis

Javier Marco-Hernández[1], Ana García-Martínez[1], Sergio Prieto-González[1], Andrea Suso[1], Georgina Espígol-Frigolé[1], Pedro Arguis[2], Rosa Gilabert[2], Maria Cinta Cid[1].

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Background/ Objectives: Around 10-33% of patients with giant-cell arteritis (GCA) develop aortic structural damage (ASD), typically involving the ascending aorta[1,2]. The aim of the study was to investigate the prevalence of thoracic ASD in a large prospective cohort of patients with GCA subjected to periodic imaging and to evaluate its association with features at diagnosis.

Methods: Patients were included in the study and prospectively followed if they consented, had biopsy-proven GCA and met the 1990 ACR criteria for GCA classification. Since 1995 patients were subjected to systematic imaging screening aimed to detect thoracic ASD. Until November 2006 it consisted of a chest X-ray repeated every 4 years. Since November 2006, most of patients were prospectively studied with CT angiography at diagnosis, after 1 year and every 4 years. The diagnosis of thoracic ASD was always confirmed by CT, defined as an aortic diameter > 4 cm at the ascending aorta or ≥4 cm at the aortic arch or descending aorta.

Data regarding demographic characteristics, cardiovascular risk factors, GCA symptoms, laboratory tests, chronic medication and GCA treatment were recorded. Kaplan-Meier survival plot was used to present the cumulated incidence of thoracic ASD over time.

We also investigated which variables present at the time of GCA-diagnosis were associated with future development of thoracic ASD after a follow-up period of 8 ± 1 years from the time of GCA diagnosis.

Results: Thoracic ASD was confirmed by CT in 58 patients (21.6% of the patients with systematic image screening diagnosed from 1995 to 2018) after a median follow-up of 4.7 years (0.05-7.5). Ascending aorta was involved in 56 patients (96.5%). Figure 1 shows the number of patients with thoracic ASD detected during follow-up.

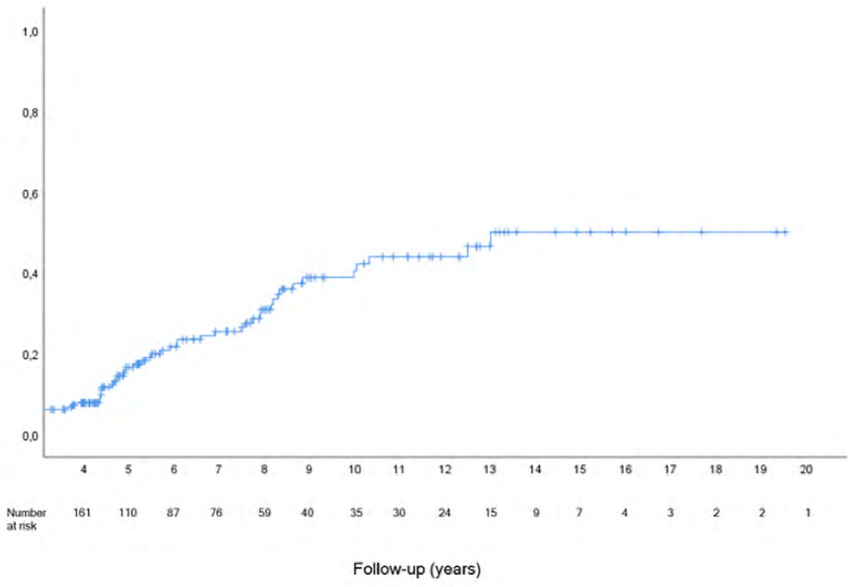

Figure 1: Kaplan-Meier survival curve showing thoracic ASD development over time.

Thoracic ASD was detected within the first 4 years from GCA-diagnosis in 19 out of the 58 patients who developed ASD (32.7%). Most ASD was detected between 5 and 9 years after GCA-diagnosis.

Patients who developed ASD during follow-up experienced less often cranial ischemic symptoms (14.8% vs 41.1%; p=0.003) or polymyalgia (33.3% vs 51.8%; p=0.057), and less frequently had a previous diagnosis of hypertension (66.7% vs 82.1%; p=0.081) at the time of GCA-diagnosis. Age, sex, clinical or laboratory findings or chronic therapies used at the time of GCA-diagnosis were not significantly different between groups. After multivariate analysis, the presence of cranial ischemic symptoms (HR 0.180, 95% CI 0.065-0.495, p=0.001) and polymyalgia rheumatica (HR 0.329, 95% CI 0.136-0.793, p=0.013) remained inversely associated with thoracic ASD development.

Conclusions: ASD is frequent and probably an underdiagnosed complication of GCA. In our prospective cohort, the presence of cranial ischemic symptoms or polymyalgia rheumatica were inversely associated with thoracic ASD development.

Supported by MTV3 2014/20150730.

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Disclosures: None.

PT-4A-29

Sleep Disturbances Among Patients with Vasculitis

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Background/Objectives: Sleep deprivation can impair health-related quality of life and increase the risk of cardiometabolic and neuropsychiatric disease. There is a lack of studies describing sleep disorders in patients with vasculitis. This study aimed to determine the frequency of sleep disorders and to identify factors associated with sleep disorders in patients with vasculitis.

Methods: This study was a cross-sectional online survey of patients registered with the Vasculitis Patient-Powered Research Network (VPPRN). The questionnaire included the following validated measures: the Epworth Sleepiness Scale (ESS), the Functional Outcomes of Sleep Questionnaire-10 (FOSQ-10), and the Multivariable Apnea Prediction Index (MVAP). Patients were also asked about previously diagnosed sleep disorders, characteristics of their vasculitis, medication use, behaviors and demographics. Responses were collected from February 1 to April 1, 2023. Multivariable logistic regression was performed to identify factors associated with any sleep disturbance (defined as ESS ≥ 11, FOSQ-10 < 18, MAPV ≥ 0.6, and/or physician-diagnosed insomnia, obstructive sleep apnea (OSA), restless leg syndrome (RLS) and/or narcolepsy).

Results: There were 1,104 patients with vasculitis that participated in the study: 737 with anti-neutrophilic cytoplasmic antibody-associated vasculitis (AAV), 132 large vessel vasculitis (LVV), and 235 with other types of vasculitis. The study sample was 74% female. The mean (SD) age and disease duration were 59.5 (13.6) and 9.7 (8.4) years, respectively. At least 1 sleep disturbance was reported by 82% of respondents. Excessive daytime sleepiness occurred in 25%, impaired daily function in 76%, and 17% were at high risk for OSA. Previously diagnosed OSA, insomnia, and RLS were reported by 20%, 14%, and 11% of patients, respectively. Prevalence of OSA among this sample was higher than what is reported for the general population (6-17%). The risk of OSA was higher in males (36% vs. 10% in females; p<0.0001). Daily functional impairment and insomnia were more common in females (80 vs. 66%; p<0.0001 and 16 vs. 9%; p=0.003, respectively). In multivariable analyses, perceived financial difficulties, low physical activity, high body mass index, history of psychiatric and/or cardiovascular disease, higher pain scores, sino-nasal symptoms, renal involvement, and worse symptoms of vasculitis were associated with sleep disturbances (Table 1).

Conclusion: Sleep disturbances are common in patients with vasculitis. Males had a higher risk of OSA, but other sleep disturbances were more common in females. Modifiable socioeconomic, behavioral, co-morbid and disease-related factors were associated with sleep disturbances; addressing these factors may improve sleep and quality of life in patients with vasculitis.

Table 1. Factors associated with any sleep disturbance in patients with vasculitis.

Factors included in the Model*	OR (95% CI)		
	All (n=1013)	Females (n=753)	Males (n=260)
Age	1.01 (0.99-1.02)	1.01 (0.99-1.03)	1.01 (0.97-1.05)
Male Sex	1.04 (0.83-1.29)		
Perceived financial difficulties	1.66 (1.13-2.45)	1.64 (1.05-2.57)	1.84 (0.78-4.38)
Smoking	1.33 (1.01-1.75)	1.37 (0.97-1.92)	1.29 (0.77-2.18)
Physical activity (low vs. moderate)	1.91 (1.16-3.15)	1.99 (1.12-3.53)	2.05 (0.67-6.32)
BMI	1.10 (1.05-1.15)	1.07 (1.02-1.12)	1.25 (1.12-1.40)
Type of vasculitis (AAV vs. LVV)	1.24 (0.77-1.98)	1.42 (0.83-2.43)	0.75 (0.22-2.55)
Pain VAS	1.44 (1.25-1.66)	1.40 (1.19-1.66)	1.62 (1.18-2.23)
Vasculitis symptom VAS	1.16 (1.03-1.31)	1.21 (1.05-1.40)	1.06 (0.82-1.36)
Current prednisone use	1.00 (0.80-1.25)	0.93 (0.71-1.23)	1.12 (0.72-1.73)
Co-Morbidities:			
Cardiovascular disease	1.46 (1.02-2.07)	1.35 (0.86-2.12)	1.73 (0.93-3.22)
Hypertension	0.72 (0.57-0.89)	0.74 (0.57-0.97)	0.71 (0.46-1.09)
Psychiatric illness	1.77 (1.31-2.39)	1.77 (1.27-2.48)	1.97 (0.94-4.12)
Disease manifestations at diagnosis			
Sino-nasal	1.26 (0.96-1.67)	1.57 (1.10-2.22)	0.95 (0.56-1.60)
Renal	1.40 (1.10-1.77)	1.11 (0.83-1.49)	2.02 (1.28-3.20)

**included based on knowledge from prior literature and goodness of fit using the Akaike information criterion; OR(95%CI)=odds ratio with 95% confidence intervals; VAS=visual analogue score.*

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PT-4A-30

The predictive performance of the renal risk score in patients over 65 years of age with renal ANCA-associated vasculitis

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Background/objectives: In 2018, Brix *et al.* developed the ANCA Renal Risk score (ARRS) to predict end-stage kidney disease (ESKD)(1). However, the validation cohorts in previous studies(2–4) have not focused on elderly adults presenting a high cardiovascular comorbidity burden, prevalent microscopic polyangiitis and aging kidneys. The objective of the present study was to assess the ARRS's predictive performance for the renal prognosis in older patients (aged 65 or over) with inaugural flare-up of ANCA-associated glomerulonephritis (AAGN).

Methods: We retrospectively studied a multicentre cohort of 192 patients (median [interquartile range] age: 73 [68; 78]) with biopsy-proven inaugural flare-up of AAGN. The primary endpoint was the cumulative incidence of ESKD (i.e. maintenance of dialysis for at least 3 months) at 12 months, with death considered as a competing event.

Results: The median serum creatinine concentration at diagnosis was 300 [202; 502] µmol/L, and 48 (25.0%) patients required dialysis at presentation. The ARRS was high in 43 (22.4%) patients, medium in 106 (55.2%), and low in 43 (22.4%). The cumulative incidence of ESKD at 12 months was 0% in the low ARRS, 13.0% [7.6-20.0] in the medium ARRS, and 44.0% [29.0-58.0] in the high ARRS (p<0.001). None of the low ARRS patients achieved ESKD. The analysis of the 149 patients presenting a medium or high ARRS revealed that dialysis at diagnosis, a high ARRS, and the Five factor score were independently associated with ESKD at 12 months (medium ARRS was considered as reference). HRs [95%CI] were respectively 4.96 [2.04-12.10] (p<0.001), 2.01 [1.01-3.99] (p = 0.047), and 2.29 [1.15-4.56] (p = 0.020). The ARRS had a C-index of 0.66 [0.58-0.74] for the prediction of ESKD at 12 months; this rose to 0.86 [0.80-0.90] when dialysis status at diagnosis was included.

Conclusion: The ARRS was a poor predictor of kidney survival at 12 months among patients aged 65 or over with renal AAV involvement – especially in the high ARRS. Taking into account the dialysis status at diagnosis might improve the ARRS's predictive performance.

Keywords: ANCA-associated vasculitis, older adults, glomerulonephritis, predictive performance, ANCA renal risk score.

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Disclosures: None.

PT-4A-31

Magnetic resonance imaging reflects diseaseactivity in the "giant cell arteritis treatment with ultra-short glucocorticoids and tocilizumab" trial: the gusto trial

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Background/ Objectives: Magnetic resonance imaging (MRI) is well established for diagnosing giant cell arteritis (GCA). Its role in monitoring disease activity has yet to be determined. We investigated vascular and musculoskeletal inflammation using MRI in the patients of the GUSTO trial to assess the utility of MRI in monitoring disease activity.

Methods: Eighteen patients with newly diagnosed GCA received 500 mg methylprednisolone intravenously for 3consecutive days [1]. After that, GC treatment was discontinued, and a single dose of tocilizumab (TCZ) was administered intravenously, followed by weekly subcutaneous TCZ injections from day 10 until week 52. Cranial, thoracic and abdominal MRI exams were performed at baseline (active, new-onset disease), and at weeks 24, 52 (remission on-treatment), and 104 (remission off-treatment). MRI findings typical for polymyalgia rheumatica (PMR) as well as extent and severity of vasculitic disease were rated as previously reported (grade 0-3, grade≥2 considered as vasculitis) [2,3]. Up to 10 cranial, 13 large vessel and 18 musculoskeletal segments were assessed.

Results: In total, 673 vascular segments and 943 musculoskeletal regions in 55 thoracic/abdominal MRI and 490 vascular segments in 49 cranial MRI scans of 18 patients were analyzed. Vasculitic vessels were still detectable in one in four cranial segments at week 24. At weeks 52 and 104, no cranial vascular segment showed a vasculitic manifestation. Large vessels, except for the ascending aorta, and PMR displayed little or no decrease in inflammatory findings over time. The proportion of segments with inflammatory findings (red numbers) summarized over all patients (black numbers=number of segments or regions assessed) is displayed in Figure 1.

Conclusions: Vasculitic manifestations in the cranial vessels normalized after 52 weeks of treatment, whereas large vessel and PMR findings persisted despite lasting full remission. The dynamics of cranial vessel signals suggest that MRI of these arteries might qualify as a potential diagnostic tool for monitoring disease activity and for detecting relapse after 52 weeks of treatment.

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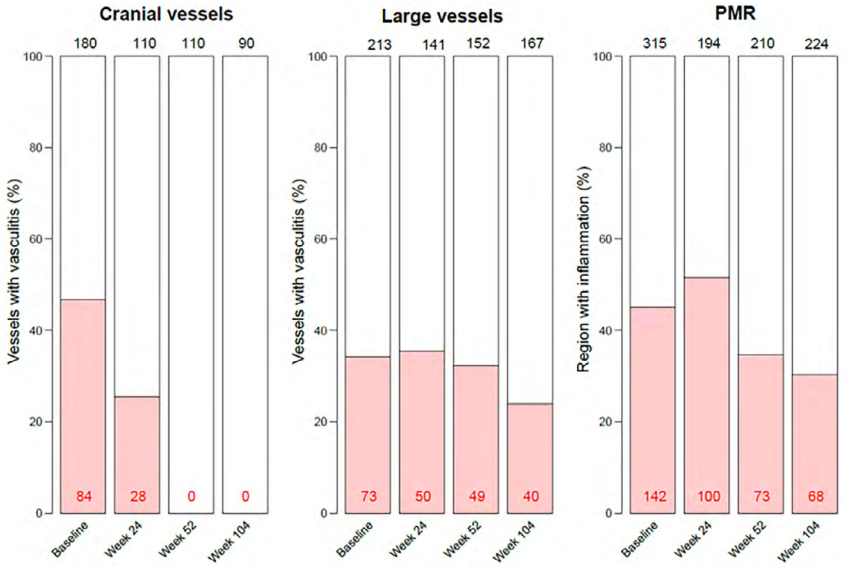

Figure 1.

Poster Tour 1B: Outcomes and predictors

PT-1B-32

The 2022 ACR/EULAR classification criteria for Takayasu arteritis predict mortality better than the 1990 ACR classification criteria: a cohort study

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Background/ Objectives: The prognostic relevance of the 2022 American College of Rheumatology (ACR)/European Alliance of Associations for Rheumatology (EULAR) criteria scores for Takayasu arteritis (TAK) is unknown (1). We compared the performance of 2022 ACR/EULAR classification criteria for the prediction of mortality with 1990 ACR classification criteria from a cohort of TAK.

Methods: Fulfilment of 2022 ACR/EULAR and 1990 ACR classification criteria for TAK and number of items scored were assessed in patients diagnosed with TAK from an ambispective monocentric cohort. The area under the receiver operating characteristics (ROC) curve (AUC, with 95% CI) for prediction of mortality was calculated using the "roctab" option on STATA 16.1 I/C (StataCorp, USA). The performance of a range of scores on the 2022 ACR/EULAR and 1990 ACR classification criteria to predict mortality in TAK was explored and compared using Youden index.

Results: The cohort comprised 238 patients with TAK (172 females, mean follow-up duration 43.8 months). Twelve deaths had been recorded in the cohort (2). Across the range of scores, the 2022 ACR/EULAR criteria (AUC 0.756, 95%CI 0.630-0.882) moderately predicted mortality. However, the 1990 ACR criteria (0.578, 95%CI 0.444-0.712) poorly predicted mortality (Figure 1A). At the prescribed cut-offs, both the 1990 ACR criteria (≥3 points, AUC 0.547, 95%CI 0.527-0.565) and the 2022 ACR/EULAR criteria (≥5 points, AUC 0.522, 95%CI 0.509-0.536) poorly predicted mortality (Figure 1B). At modified 2022 ACR/EULAR cut-offs of ≥6 or ≥7 or with the cut-off of ≥5 after excluding the point scored for female sex proposed from an earlier study (2), the ability of the scores to predict mortality only improved marginally (AUC 0.540-0.575, **Figure 1C**). At a cut-off ≥12, the 2022 ACR/EULAR criteria (sensitivity 83.33%, specificity 56.64%, Youden index 39.97) optimally predicted mortality. The Youden index for 2022 ACR/EULAR criteria scores between 12-15 ranged from 33.93 to 39.97 (AUC ranging from 0.674-0.700, **Figure 1C**). The best prediction of mortality with the 1990 ACR criteria was at a score ≥4 (sensitivity 83.33%, specificity 32.30%, Youden index 15.63, **Figure 1C**).

Conclusions: Higher 2022 ACR/EULAR criteria scores predicted mortality. This possibly reflects their utility as extent scores in TAK and merits exploration of their prediction of other outcomes such as damage accrual and immunosuppressive requirement.

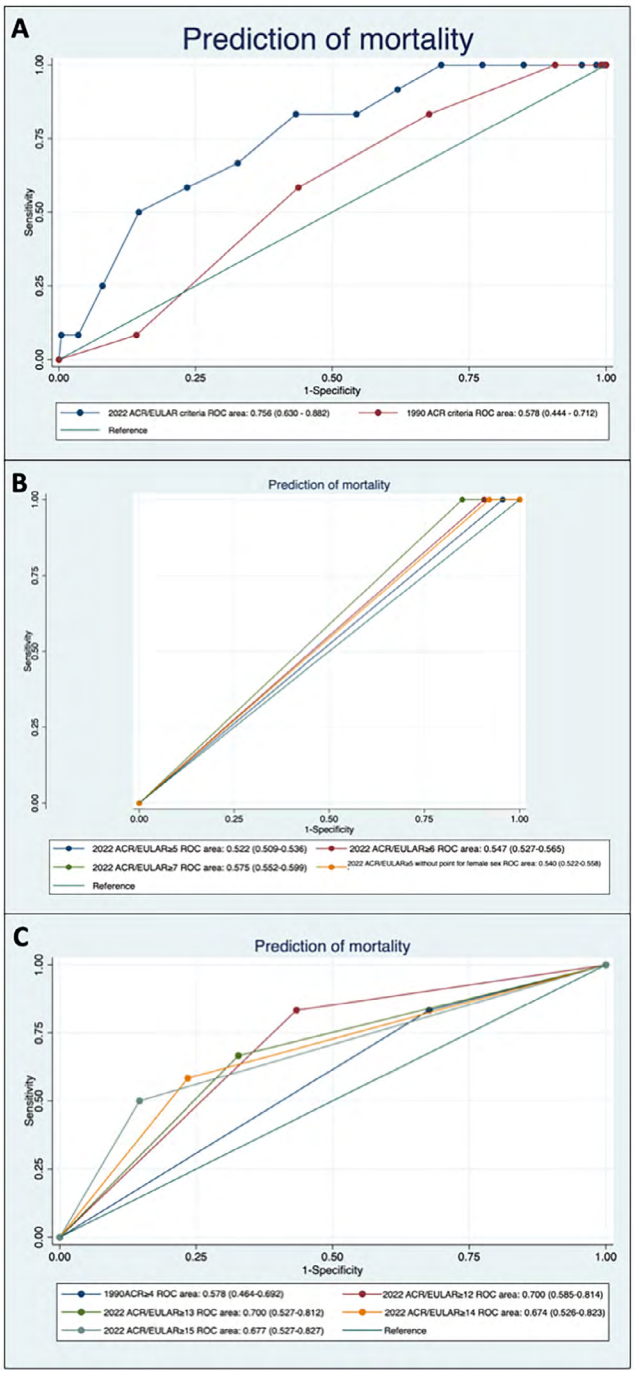

Figure 1: A. Prediction of mortality with 2022 ACR/EULAR and 1990 ACR TAK classification criteria scores. B. Prediction of mortality with 2022 ACR/EULAR classification criteria scores at the original and modified cut-offs. C. Prediction of mortality with 2022 ACR/EULAR classification criteria scores at cut-offs ≥12-15 or with 1990 ACR TAK classification criteria ≥4.

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Disclosures: None.

PT-1B-33

Assessment of the Extent and Accrual of Damage in Takayasu's Arteritis

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Background/Objectives: Damage is the irreversible consequence of disease or its treatment**.** This study aimed to evaluate the accrual of damage in Takayasu's arteritis (TAK) using 2 currently-available indices of damage.

Methods: Patients with TAK enrolled in a multicenter, prospective, observational cohort from North America, and a single-center in Turkey were included. Damage was assessed at baseline and last visits using the Vasculitis Damage Index (VDI) and the Large-Vessel Vasculitis Index of Damage (LVVID).

Results: The study included 350 patients with TAK, mean±SD age 40.3 (13.4) years, 91% female, median (25^{th}, 75^{th} percentile) disease duration 69 (1.6, 274) weeks. 313 (89%) had at least 1 follow-up visit, median (25^{th}, 75^{th}) duration 4.5 (2.1, 8.0) years. Damage was present at first visit in 83% on VDI and 89% on LVVID, with median (range) number of damage items on VDI 3 (0, 10) and on LVVID 3 (0, 13). Most items of damage at baseline visit were captured in the peripheral vascular (83% VDI, 89% LVVID) and cardiac (42% VDI, 44% LVVID) categories.

At last follow-up, damage items were noted in 95% on VDI and 95% on LVVID, mainly in the peripheral vascular (97% VDI, 89% LVVID) and cardiac (60% VDI, 59% LVVID) categories. *New* damage was captured in 52% patients on VDI and 53% on LVVID. In patients with *new items, the* median (range) numbers of *new* items were 1 (range 1, 13) on VDI and 2 (1, 17) on LVVID. The majority of *new* items of damage were disease-related and on VDI were in the peripheral vascular (18%), and cardiac (18%) categories, and on LVVID in the cardiovascular category (37% total, 26% peripheral vascular, 20% cardiac) and "Other" (22%) categories. The most frequent *new* items of damage at last visit are in **Table 1**. Damage captured on VDI but not LVVID included major vessel stenosis (83%), pulse loss (98%), elevated diastolic blood pressure (40%), second pulse loss (12%); items of damage captured on LVVID but not VDI included hypertension (40%), arterial thrombosis (41%), renal artery stenosis (28%), damage requiring vascular intervention (8% angioplasty alone, 20% angioplasty with stent), bypass surgery (22%), aortic aneurysms (14%). 12 of 64 items (19%) on VDI and 20 of 87 items (23%) on LVVID were never applicable to any patient with TAK but 13 of the 20 (65%) items not used on LVVID were in the ocular category with manifestations that can occur in giant cell arteritis.

Conclusions: Damage is present in >80% of patients with TAK at first visit. During follow-up, new damage items, mostly disease related, are observed in 50% of patients, including new cardiovascular damage in nearly 40%. LVVID captures *new* damage items in the cardiovascular category more comprehensively than VDI but many damage items were captured in the "Other" category on both measures. Based on these results, LVVID can be modified and streamlined to more efficiently measure damage in TAK and perhaps focus on disease-related damage. Despite treatment, disease-associated damage accrues in TAK and assessment of damage should be included in therapeutic trials.

Disclosures:

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C.L: GlaxoSmithKlein(GSK) (grant/research support).

C.P: AstraZeneca (advisor, consultant, speaker), GlaxoSmithKlein(GSK), (advisor, speaker), Otsuka (Advisor, consultant, grant/research support, speaker), Pfizer (grant/research support), Roche (consultant).

P.S: Amgen (advisor), Janssen (advisor).

A.S: Bristol Myers Squibb (employee).

K.W: Bristol-Myers Squibb(BMS) (grant/research support), Chemocentryx (Advisor, speaker), Eli Lilly (grant/research support), kiniksa (grant/research support).

H.D: AbbVie/Abbott (advisor, grant/research support, speaker), Amgen, (speaker), celltrione (advisor, speaker), Pfizer (Grant, speaker), UCB (grant/research support, speaker).

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Table 1: Most frequent new items of damage in patients with Takayasu's arteritis at last visit observation

Organ System	VDI	LVVID
Peripheral vascular, N (%)[a]	**55 (17)**	**83 (46)**
Claudication	22 (7)	---
Left arm claudication	---	17 (5)
Right arm claudication	---	10 (3)
Left leg claudication	---	4 (1)
Right leg claudication	---	4 (1)
Arterial thrombosis/occlusion	---	20 (6)
Renal artery stenosis	---	10 (3)
Pulse loss	15 (5)	---
Second episode absent pulse in one limb	11 (3)	---
Major vessel stenosis	16 (5)	---
Aortic aneurysm		11 (3)
Angioplasty alone		6 (2)
Angioplasty with stent		16 (5)
Bypass		10 (3)
Cardiac, N (%)[a]	**58 (18)**	
Angina/Angioplasty	25 (8)	---
Hypertension		28 (9)
Diastolic blood pressure ≥95 mm Hg or requiring treatment	30 (10)	---
Coronary artery disease	---	7 (2)
Valvular disease	28 (9)	---
Aortic valve regurgitation	---	17 (5)
Tricuspid regurgitation	---	17 (5)
Mitral regurgitation	---	14 (4)
Other, N (%)	**34 (11)**	**70 (22)**
Weight gain >10 pounds	---	37 (12)
Damage requiring surgical intervention	---	22 (7)
Other (free texted)	13 (4)	8 (3)
Ocular	**37 (12)**	**37 (12)**
Left low vision	---	9 (3)
Right low vision	---	11 (3)
Left cataract	---	11 (3)
Right cataract	---	11 (3)
Visual Impairment	11 (3)	---
Cataract	14 (4)	---
Retinal change	16 (5)	---
Musculoskeletal, N (%)	**26 (8)**	**27 (9)**
Osteoporosis, vertebral collapse	13 (4)	13 (4)
Avascular necrosis	7 (2)	7 (2)
Neurologic, N (%)	**12 (4)**	**12 (4)**
Cerebrovascular accident	10 (3)	---
Cerebrovascular accident, ischemic	---	9 (3)
Cerebrovascular accident, hemorrhagic	---	2 (1)

N = number, % = percentage, VDI=Vasculitis Damage Index, LVVID=Large-Vessel Vasculitis Index of Damage,
--- =Not applicable (ie item not queried on index)
[a]Cardiovascular category on LVVID

PT-1B-34

Age, Hypertension and Anticoagulant Therapy at Presentation are Associated with Cranial Ischaemic Complications in Giant Cell Arteritis

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Background: Accurate risk assessment of ischaemic manifestations in giant cell arteritis (GCA) is essential to improve treatment outcomes for patients(1). Previous studies have highlighted a link between cardiovascular (CV) risk factors and ischaemic complications in GCA(2, 3). However, work establishing these associations in larger cohorts is limited. Here, cranial ischaemic complications (including vision loss, cranial nerve palsies, stroke, scalp/tongue necrosis) at GCA presentation were tested for association with pre-existing CV risk factors, CV disease (CVD) or genetic risk of CV-related traits.

Methods: This observational study describes 1,946 GCA subjects with detailed clinico-demographic data available from disease presentation. Univariate associations were tested between pre-existing CV traits (including calculated polygenic risk scores [PRS]) and cranial ischaemic complications, and a multivariate model predictive of cranial ischaemic complications was optimized using elastic net regression. Finally, positional gene mapping of associated PRS was performed to inform biological understanding of the outcome.

Results: In 1,946 GCA patients (median age=71.2), 68.7% were female, and 17% had cranial ischaemic complications. Univariate analyses revealed associations between 10 clinical variables and increased risk of complications. Following adjustment for clinical, sociodemographic and genetic factors, two traits remained associated: anticoagulant therapy pre-GCA (adjusted OR[95% CI]=0.21[0.05 to 0.62], P=4.95x10^{-3}) and age at GCA diagnosis (adjusted OR[95% CI]=1.6[0.73 to 3.66], P=2.52x10^{-3}, for the highest versus the lowest decade). Sensitivity analyses omitting anticoagulant therapy from fully adjusted models were performed, revealing an association between pre-existing hypertension and cranial ischaemic complications (adjusted OR[95%CI]=1.35[1.03 to 1.75], P=0.03). Finally, positional gene mapping of an associated transient ischaemic attacks PRS identified the *TEK*, *CD96* and *MROH9* loci.

Conclusions: In this work, age and hypertension were found to be risk factors for developing cranial ischaemic complications in GCA, and a potentially protective role of anticoagulant therapy prior to diagnosis was identified. Furthermore, a role for immune and coagulation-related pathways were highlighted through positional gene mapping.

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Disclosures: None for the analyses performed in this study.

PT-1B-35

Presentation and outcome of silent giant cell arteritis: a retrospective cohort study

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[1]Department of General Internal Medicine, UZ Leuven, Department of Microbiology, Immunology, and Transplantation, KU Leuven, Leuven, Belgium; [2]Department of Nuclear Medicine, UZ Leuven, Leuven, Belgium; [3]Interuniversity Institute for Biostatistics and Statistical Bioinformatics (I-BioStat), KU Leuven and Hasselt University, Leuven, Belgium.

Background/ Objectives: A subgroup of patients with giant cell arteritis (GCA) only have constitutional symptoms and/or raised inflammatory markers, which is sometimes called 'silent GCA'. These patients are commonly excluded from therapeutic trials. Our objective was to evaluate the prevalence, characteristics and outcome of patients with silent GCA.

Methods: Patients with a diagnosis of GCA between 2000 and 2020 who were followed for ≥12 months at the University Hospitals Leuven, were included retrospectively. Silent GCA is defined as a final diagnosis of GCA with only constitutional symptoms and/or raised inflammatory markers without the presence of cranial symptoms, polymyalgia rheumatica (PMR) or limb claudication. PET scans were visually scored (0-3) in 7 vascular areas and a total vascular score (TVS) was calculated, ranging from 0 to 21. FDG uptake ≥ grade 2 was considered indicative for vasculitis. Patients with and without silent GCA were compared.

Results: We included 398 GCA patients, of which 57 (14%) had silent GCA. Patients with silent GCA more frequently reported constitutional symptoms (91% vs 73%, p=0.003) and dry cough (37% vs 14%, p<0.001). Patients with silent GCA had lower hemoglobin (11.1 vs 11.9 g/dL, p<0.001) and albumin (36.2 vs 38.5 g/L, p=0.004) without differences in other laboratory markers. There was no difference in FDG uptake in the large vessels (77% vs 69%, p=0.25) and in the cranial vessels (36% vs 48%, p=0.16) nor in the proportion of patients with a positive temporal artery biopsy (63% vs 67%, p=0.80). However, patients with silent GCA have a higher TVS (12 vs 4, p=0.007). In contrast to other GCA patients, those with silent GCA were never treated with high dose intravenous glucocorticoids (GC) at diagnosis (0% vs 16%, p<0.001), but non-linear mixed effect models showed no differences in the initial oral GC dose (31.5 vs 34.2 mg methylprednisolone, p=0.14) and the GC doses during follow-up **(Figure 1)**. In addition, the median duration of GC treatment was comparable between both groups (24 vs 25 months, p=0.48). Logistic regression analyses showed no difference in the proportion of patients able to stop GC at last follow-up (67% vs 67%, OR 1.00 [95%CI 0.56-1.85], p=0.99) and in the proportion of patients with relapse (58% vs 56%, OR 1.08 [95%CI 0.61-1.92], p=0.79).

Conclusions: Of GCA patients, 14% only had constitutional symptoms and/or raised inflammatory markers. These patients had a similar relapse rate and similar duration and doses of GC treatment as patients with clinical symptoms typical for GCA. Hence, patients with silent GCA are an important subgroup with a similar long term prognosis who should be included in therapeutic trials.

References: None.

Disclosures: LM: Roche; DB: Roche, GSK, Eli Lily; LB, GM, AB, SV: none.

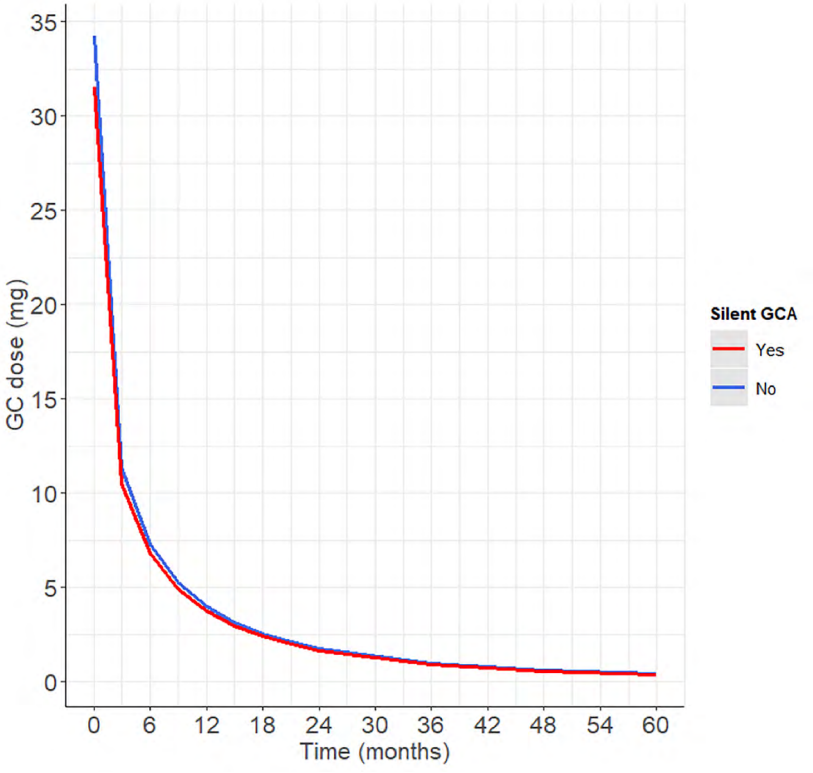

Figure 1: Change in GC dose (expressed in methylprednisolone equivalents) in patients with and without silent GCA.

PT-1B-36

Five-year analysis of patient reported outcomes in a longitudinal cohort of giant cell arteritis and polymyalgia rheumatica patients

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Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) are overlapping inflammatory diseases that occur in people older than 50 years. Both diseases can affect the quality of life, due to the burden of vascular inflammation and ischemia-related symptoms (GCA), joint symptoms (PMR) and systemic symptoms (GCA and PMR) and the side-effects of long-term treatment with glucocorticoids. Commonly used patient reported outcome measures (PROMs) include the Short Form (SF)-36, Groningen Frailty Index (TFI) and Health Assessment Questionnaire-Disability Index (HAQ). The goal of this study was to analyze PROMs in our prospective GCA/PMR cohort and set out to identify which symptoms, laboratory parameters or treatments are associated with impaired quality of life.

We prospectively followed treatment-naïve GCA (n=56) and PMR (n=42) patients since diagnosis for up to five years. Data were compared to HCs (n=70) selected based on frequency matching of 10-year age cohorts stratified for gender, who were also followed for up to five years. PROM data, laboratory measurements, disease symptoms and medication use were recorded at every visit.

At diagnosis, PROMs were substantially worse in GCA and PMR patients compared to HCs. During the 5-year follow-up, we recorded only a partial improvement in PROMs during the first year. We found that weight loss at diagnosis was associated with particularly low PROM scores, whereas inflammatory markers did not (PMR) or only moderately (GCA) associate with PROMs. Both at diagnosis as well as two year after diagnosis, we surprisingly found no association of PROMs with the physician general disease assessment (GDA) score. PROMs at the two-year visit (Figure 1) did correlate with the Fatigue score and patient GDA. Equivalent to the baseline visit, laboratory markers such as CRP correlated with PROMs in GCA, but not PMR patients at the two-year visit. The glucocorticoid dose associated with worse PROMs in GCA patients, whereas methotrexate was associated with better PROMs. In contrast, in PMR patients we found glucocorticoid use associated with better scores on the SF-36.

GCA and PMR patients experience both short-term and long-term impact on their frailty, daily functioning and quality of life. Medication use appears to be important in determining the patient's quality of life, although surprisingly, glucocorticoid and methotrexate use appear to affect GCA and PMR patients differently. Importantly, the physician GDA or inflammatory markers do not associate strongly with PROMs, particularly in PMR patients, indicating a need for better understanding of the disease and treatment impact on patient's quality of life.

GCA	SF-36 domains										Physician GDA	Fatigue score	Patient GDA
	PF	RP	RE	EN	EW	SF	BP	GH	GFI	HAQ			
Physician GDA	-0.06	-0.19	0.06	-0.00	-0.14	-0.13	-0.16	-0.21	0.15	0.19			
Fatigue score	-0.69**	-0.44*	-0.28	-0.68**	-0.66**	-0.66**	-0.54**	-0.61**	0.63**	0.34			
Patient GDA	-0.43*	-0.38	-0.07	-0.19	-0.36	-0.35	-0.48*	-0.32	0.37	0.46*			
CRP	-0.43*	-0.45*	0.03	-0.38	-0.08	-0.43*	-0.16	-0.28	0.19	0.20	0.28	0.23	0.21
ESR	-0.44*	-0.52**	-0.01	-0.26	-0.33	-0.42*	-0.33	-0.24	0.28	0.43	0.27	0.31	0.31
Leukocytes	-0.37	-0.36	-0.22	-0.37	-0.17	-0.36	-0.04	-0.44*	0.34	0.39	0.19	0.34	0.05
Thrombocytes	0.05	-0.25	-0.05	-0.11	-0.24	-0.09	-0.11	-0.03	0.03	0.27	0.15	0.12	0.01
Hb	0.3	0.49*	0.42*	0.36	0.35	0.41*	0.43*	0.14	-0.30	-0.04	-0.07	-0.07	0.03
Daily GC use	-0.18	-0.21	-0.34	-0.43*	-0.36	-0.38*	-0.13	-0.41*	0.42*	0.13	0.33	0.17	0.33
Cumulative GC use	0.13	-0.00	-0.12	-0.26	-0.28	-0.33	-0.01	-0.13	0.19	0.03	0.23	0.10	0.34
Daily MTX use	0.41*	0.28	0.29	0.24	0.13	0.09	0.30	0.48*	-0.41*	-0.23	-0.25	-0.32	-0.01
Cumulative MTX use	0.44*	0.34	0.08	0.14	0.03	0.01	0.24	0.42*	-0.29	-0.32	-0.24	-0.19	0.10

PMR	SF-36 domains										Physician GDA	Fatigue score	Patient GDA
	PF	RP	RE	EN	EW	SF	BP	GH	GFI	HAQ			
Physician GDA	0	0.02	-0.24	-0.15	-0.03	-0.17	-0.23	-0.06	-0.07	0.03			
Fatigue score	-0.68**	-0.69**	-0.59*	-0.68**	-0.48*	-0.41	-0.62**	-0.33	0.49	0.67*			
Patient GDA	-0.66**	-0.82**	-0.45	-0.60**	-0.40	-0.40	-0.70**	-0.38	0.31	0.49			
CRP	-0.01	-0.19	-0.44*	-0.18	-0.14	0.08	-0.14	-0.05	0.40	0.50	-0.06	0.50*	0.04
ESR	-0.38	-0.15	-0.23	-0.01	-0.20	-0.26	-0.26	-0.36	0.31	0.35	0.14	0.32	0.17
Leukocytes	-0.17	-0.04	0.17	-0.08	0.14	0.12	-0.19	0.12	0.12	0.08	0.19	0.35	0.24
Thrombocytes	-0.12	-0.13	-0.30	-0.09	-0.24	-0.19	-0.19	0.11	-0.12	-0.18	-0.03	0.07	-0.01
Hb	0.25	0.19	-0.16	-0.01	-0.13	-0.04	0.35	0.08	-0.26	-0.06	0.01	-0.53*	-0.41
Daily GC use	0.05	0.08	0.46*	0.29	0.44*	0.47*	0.02	-0.01	0.14	-0.11	-0.10	0.00	0.02
Cumulative GC use	0.07	-0.19	0.18	-0.10	0.26	0.43*	0.18	-0.17	0.13	0.18	-0.01	0.14	0.08
Daily MTX use	-0.01	0.16	0.14	-0.25	-0.01	0.13	0.13	0.20	-0.27	-0.21	0.16	-0.05	-0.10
Cumulative MTX use	-0.02	0.10	0.02	-0.34	-0.03	0.14	0.05	0.15	-0.11	-0.21	0.31	0.11	0.00

Figure 1: Factors associating with PROMs at the two-year follow-up visit for GCA and PMR patients. Shown are Spearman R coefficients; cell colors are based on strength of association. Orange colors indicate that worse PROMs associate with unhealthy scores on the other parameters (low Hb and high levels of all the other factors and more medication use).

PT-1B-37

Imaging to predict relapses after treatment discontinuation in patients with large vessel giant cell arteritis – a cohort study

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Background/Objectives: To date, no reliable biomarkers are available for the prediction of relapses after treatment discontinuation in patients with large vessel giant cell arteritis (LV-GCA) (1). The aim of this study was to investigate the value of [^{18}F]fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) and magnetic resonance imaging (MRI) in predicting relapse after treatment stop in patients with LV-GCA.

Methods: This study included patients at the University Hospital Basel with LV-GCA whose treatment was discontinued between 2018-2023. All patients underwent PET/CT and/or MRI at the time of treatment stop in clinical remission. Imaging findings of the aorta and supraaortic vessels were compared between patients who relapsed within 4 months after treatment stop and those who did not.

Results: Forty patients were included (median age 67 years, interquartile range (IQR) 61-74; 78% females). The duration from diagnosis to treatment stop was 20.3 months (IQR 13.1-36.4). Eleven patients (28%) relapsed after treatment stop. Patients with and without subsequent relapses were comparable with respect to signs attributable to active vasculitis on MRI and/or PET/CT (54.5% vs. 58.6%, p=1) (Figure 1). There was no difference between relapsing and non-relapsing patients regarding the number of affected segments on MRI (0, IQR 0.0-1.5, vs. 2, IQR 0.0-3.0, p=0.221) or PET/CT (2.5, IQR 0.5-4.5 vs. 0, IQR 0.0-1.5, p=0.085). The modified PET vascular score (PETVAS) was 4.5 (IQR 0.75-8.25) in patients with vs. 0 (IQR 0.0-3.0, p=0.172) in patients without relapses.

Conclusions: PET/CT or MRI at treatment stop did not predict relapse and may not be suited to guide treatment decisions in patients with LV-GCA in clinical remission.

References:

1. Berger CT et al. The clinical benefit of imaging in the diagnosis and treatment of giant cell arteritis. Swiss Med Wkly. 2018. Aug 13;148:w14661.

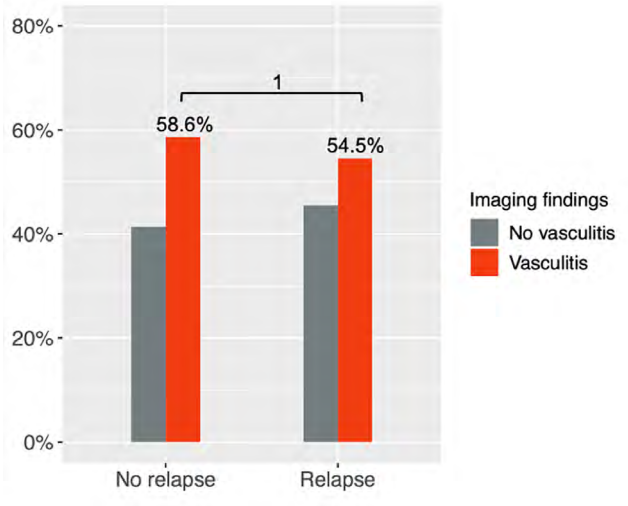

Figure 1: Signs attributable to active vasculitis on MRI and/or PET/CT in patients who remained in remission (N=29) compared to patients who relapsed (N=11).

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PT-1B-38

Patients experiences of Polymyalgia Rheumatica: A Qualitative Literature Synthesis Review

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Background: Qualitative research is needed to better understand the concepts of remission and relapse in Polymyalgia Rheumatica (PMR). Remission, relapse, and disease activity have been defined heterogeneously in clinical studies which exclude the patient view leading to a discrepancy between physician and patient perspectives when evaluating disease activity.

Aims: The present work is part of a project of the PMR Working Group of Outcome Measures in Rheumatology (OMERACT), which is a global, volunteer-driven, non-profit research group aiming to improve outcome measures in rheumatic diseases. We carried out a synthesis of findings from multiple qualitative studies to provide a range and depth of meanings, experiences, and perspectives of participants across health-care contexts to explore the patient perspectives of disease activity in PMR.

Methods: A professional librarian carried out a systematic search of qualitative research studies in PMR across Ovid (Medline), EMBASE and CINAHL databases from inception to 19/10/23. Research synthesis was carried out in accordance with the ENTERQ criteria by three researchers with qualitative research experience.

Results: Twelve studies of interest were identified following the initial database search, abstract review and and hand-searching reference lists of included manuscripts. There were three main over-arching ideas identified within the published work: 1. Pathway to diagnosis, 2. Managing uncertainty and 3. Challenges to everyday life. Within these three over-arching ideas there were sub-themes identified within the conceptual scaffold, which were underpinned with the expression of self and control. The domain of “pathway to diagnosis” included making sense of the condition, normalisation of symptoms and struggles navigating care systems. Within the domain of “managing uncertainty”, concepts of self and illness and the positive and negative effects of treatment with steroids predominated. The ”challenges to everyday life” domain concentrated on day to day living, adaptation and psycho-social burden of disease.

Conclusion: This research synthesis of qualitative studies in PMR has identified three over-arching domains and provides a rich narrative of the patients’ lived experience which may assist in the development of future collaborative definitions of remission and relapse.

Disclosure: Nonspecific to this study.

PT-1B-39

Relapses in large vessel vasculitis occur in a different arterial territory as compared to diagnosis

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Background/ Objectives: Ultrasonography (US) for diagnosis of large vessel vasculitis (LVV) is a recommended first line diagnostic procedure.[1] We have been running an US led diagnostic pathway in our centre since January 2017.[2] This pathway is also used to diagnose relapsing disease. We present the anatomical distribution of relapses consecutive patients diagnosed with relapsing disease.

Methods: Patients in whom new and relapsing disease was diagnosed using US were included. Protocolised US examination of the common carotid system of arteries and those of the subclavian system of arteries were carried out at diagnosis and relapse. Halo sign in at least two different arteries was needed for establishing new or relapsing disease. Disease characterisation was classified as being in the carotid system, subclavian system, or both. The nature of the disease at relapse was compared to that at diagnosis.

Results: 279 patients were diagnosed with LVV using US since Jan 2017. 57 (20%) were diagnosed as having a relapse using US. 43/57 (75%) and 28/57 (49%) had involvement of the carotid system at baseline and relapse respectively. 22/57 (39%) and 44/57 (77%) had involvement of the subclavian system at baseline and relapse respectively. A Sankey Graph comparing the nature of involvement at diagnosis and relapse is as in Figure 1.

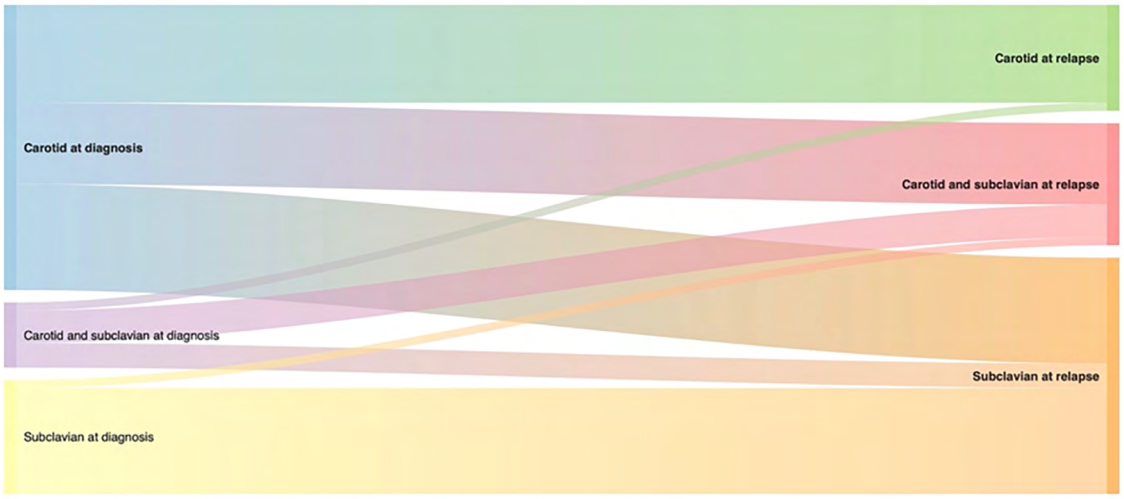

Figure 1. Sankey graph demonstrating nature of vasculitic involvement at diagnosis and relapse.

Conclusions: The branches of the common carotid artery (external carotid artery) are commonly involved at diagnosis, but relapse tends to occur more frequently in the subclavian artery branches. This is especially true where baseline disease was established in the carotid system. The presentation of patients with subclavian system disease is often with only constitutional symptoms and with shoulder girdle pain and stiffness. This may be mistaken for being a polymyalgia rheumatica relapse. It is essential to examine the subclavian system of arteries before diagnosing polymyalgia rheumatica relapse in individuals with LVV.

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1. Hellmich B, et al. 2018 Update of the EULAR recommendations for the management of large vessel vasculitis. Ann Rheum Dis. 2020 Jan;79(1):19-30.
2. Mukhtyar C, et al. Improving the quality of care for people with giant cell arteritis. Clin Med (Lond). 2021 Jul;21(4):e371-e374.

Disclosures: None.

PT-1B-40

Polymyalgia rheumatica is a risk factor for more recalcitrant disease in giant cell arteritis: a retrospective cohort study

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Background/ Objectives: To evaluate differences in presentation and outcome of patients with giant cell arteritis (GCA) with and without polymyalgia rheumatica (PMR) symptoms.

Methods: Patients with a diagnosis of GCA between 2000 and 2020 who were followed for ≥12 months at the University Hospitals Leuven, were included retrospectively. FDG PET scans were visually scored in 12 articular (score 0-2) and 7 vascular regions (score 0-3). The 12 articular regions were summed to a total skeletal score (TSS). FDG uptake ≥ grade 2 was considered indicative for vasculitis. Patients with and without PMR symptoms were compared.

Results: We included 398 GCA patients, of which 181 (45%) with PMR symptoms. Patients with PMR symptoms had a significantly longer time to diagnosis (10 vs 5 weeks, p<0.001). They less frequently had fever (19% vs 28%, p=0.04), fatigue (51% vs 63%, p=0.01), dry cough (10% vs 24%, p<0.001) and permanent vision loss (16% vs 28%, p=0.02). Those with PMR symptoms had a lower c-reactive protein (68 vs 79 mg/L, p=0.02) and ferritin (290 vs 366 µg/L, p=0.04) and higher albumin (39 vs 37 g/L, p=0.005). Temporal artery biopsy was less frequently positive in patients with PMR symptoms (60% vs 72%, p=0.02). They also less often had FDG uptake in the cranial arteries (40% vs 52%, p=0.04), while there was no difference in FDG uptake in the large vessels (69% vs 71%, p=0.83). TSS was significantly higher in those with PMR symptoms (12 vs 4, p<0.001). Patients with PMR symptoms were treated with a lower initial glucocorticoids (GC) dose (30.4 vs 36.7 mg methylprednisolone, p<0.001) **(Figure 1A)**, but there was no difference in the cumulative oral GC dose in the first 2 years (4.4 vs 4.3 g methylprednisolone, p=0.67). However, those with PMR symptoms were treated with higher GC doses during the longer follow-up (p<0.05 from 35 months after diagnosis) **(Figure 1A)** and had a lower probability of stopping GC at last follow-up (HR 0.74 [95% CI 0.58-0.94], p=0.02) **(Figure 1B)** with a longer median duration of GC treatment (29 vs 23 months, p=0.02). In addition, presence of PMR symptoms was associated with an increased risk of relapse (HR 1.36 [95%CI 1.05-1.77], p=0.02) **(Figure 1C)** with a higher number of relapses (1.15 vs 1.45 relapses, p=0.008).

Conclusions: GCA patients with PMR symptoms less frequently had permanent vision loss at diagnosis, but had more recalcitrant disease with a higher risk of relapse and longer duration of GC treatment with need for higher GC doses.

References: None.

Disclosures: LM: Roche; DB: Roche, GSK, Eli Lily; LB, GM, AB, SV: none.

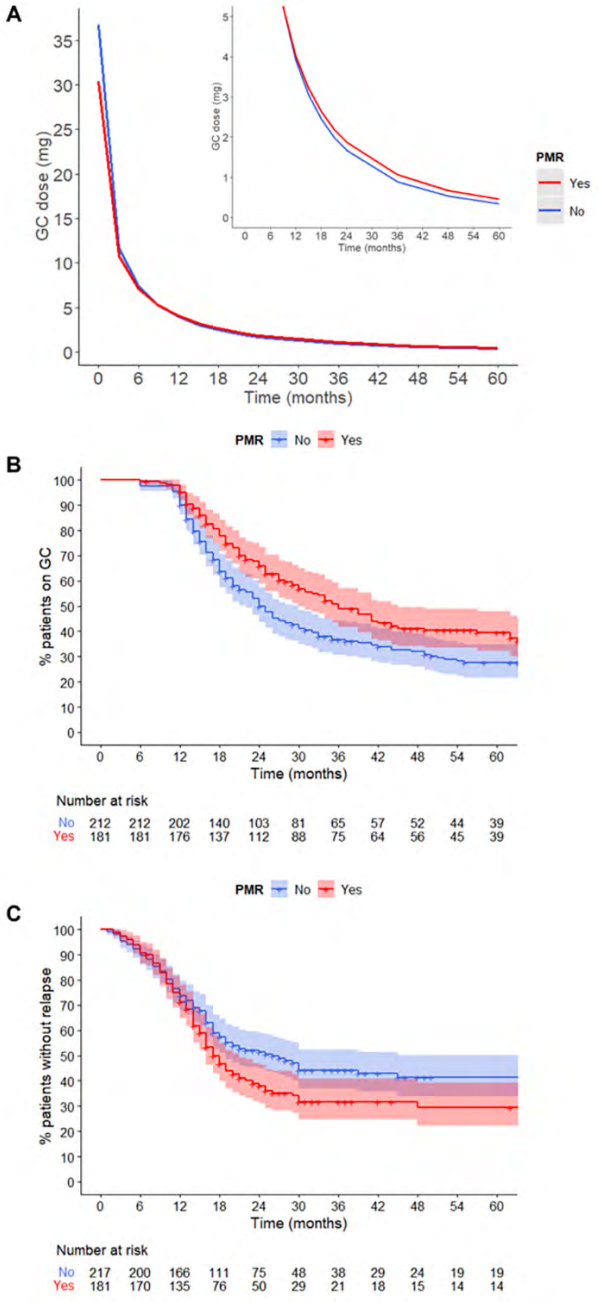

Figure 1: (A) Non-linear mixed-effects model estimates for the change in GC dose (expressed in methylprednisolone equivalents) **(B)** Kaplan-Meier estimates for the proportion of patients on GC treatment and **(C)** for the proportion of patients without relapse comparing GCA patients with and without PMR symptoms.

PT-1B-41

Severe ischemic events in Takayasu's Arteritis –A multi-national retrospective study

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Background/ Objectives: Our current knowledge and understanding of the cumulative incidence of ischemic events in Takayasu's arteritis (TAK), their presentations, recurrence rate of ischemic events, and outcomes are limited. We conducted a multinational retrospective study to estimate incidence rate of severe ischemic events (SIE), describe patient and disease characteristics associated with SIE, and identify predictive risk factors of SIEs.

Table 1. Demographic features and clinical characteristics of Takayasu's arteritis patients with/without SIE

	No SIE (n=144)	SIE (n=48)	P value
Female	125 (86.8)	38 (79.2)	0.1
Age at diagnosis, years (median, IQR)	31 (22-40)	32 (23-41)	0.7
Symptom duration before initiation of immunosuppressive treatment, months (median, IQR)	6 (2-24)	12 (2-24)	0.5
Ethnic ancestry			0.7
White	84 (58.3)	31 (64.6)	
Asian/Middle East	45 (31.2)	14 (29.2)	
Hispanic	8 (5.6)	2 (4.2)	
Black	7 (4.9)	1 (2.1)	
Arterial cluster*			**0.04**
Abdominal predominant	36 (25.2)	6 (12.5)	
Aortic arch predominant	88 (61.5)	39 (81.2)	
Focal disease	19 (13.3)	3 (6.2)	
Cardiovascular disease (CVD) risk factors*			
Diabetes Mellitus	18 (12.6)	8 (16.7)	0.3
Hypertension	62 (43.4)	22 (45.8)	0.4
Dyslipidemia	36 (25.2)	19 (39.6)	**0.04**
Smoking, ever	21 (14.7)	14 (29.8)	**0.02**
Atrial Fibrillation	3 (2.1)	2 (4.2)	0.3
Osteoporosis	7 (4.9)	4 (8.3)	0.2
Obesity	10 (7.0)	5 (10.4)	0.3
Family history of cardiovascular disease	3 (2.1)	3 (6.5)	0.1
Other autoimmune disease	31 (22.0)	6 (12.5)	0.1
Treatments for TAK*			
No treatment	10 (7.0)	1 (2.1)	0.1
Glucocorticoids only	13 (9.1)	0 (0)	**0.02**
Glucocorticoids + immunosuppressants	120 (83.9)	46 (97.9)	**0.01**
Methotrexate	100 (69.9)	34 (72.3)	0.7
Azathioprine	54 (37.8)	16 (34.0)	0.6
Leflunomide	28 (19.6)	3 (6.4)	**0.03**
Mycophenolate mofetil	11 (7.7)	3 (6.4)	0.5
Cyclophosphamide	21 (14.7)	14 (29.8)	**0.02**
Glucocorticoids + biologics	59 (41.3)	20 (42.6)	0.5
TNF-inhibitors	44 (30.8)	12 (25.5)	0.4
Tocilizumab	25 (17.5)	10 (21.3)	0.5
Rituximab	4 (2.8)	1 (2.1)	0.6
Antiplatelet agents	86 (60.6)	44 (95.7)	**<0.0001**
Anticoagulant	11 (7.7)	11 (23.9)	**0.003**
Statins	32 (22.7)	19 (41.3)	**0.01**

Data are presented as numbers (%) of patients unless otherwise indicated.
*TAK: Takayasu arteritis, SIE: Severe ischemic events, IQR: Interquartile range,
*CVD risk factors and Arterial cluster were available in 191 patients, treatment data for TAK was available for 190 patients, treatment data for antiplatelet agents, anticoagulants and statins were available for 188 patients.

Methods: A review of available records of patients with a diagnosis of TAK at each of the 5 participating centers (in Canada, Turkey, Sweden, Saudi and UK) was performed. SIEs were defined as stroke, transient ischemic attack (TIA), acute coronary syndrome (ACS), ischemic cardiomyopathy, or ischemia induced blindness. The incidence rate (IR) of SIEs was estimated using the number of first SIE as the numerator and the sum of person-year (py, defined as time from date of TAK diagnosis to first SIE, death, or end of study) of follow-up as the denominator. We compared clinical characteristics of patients with or without SIEs, and analysed the factors associated with SIEs using Cox regression analysis.

Results: A total of 192 patients with TAK were included (Canada,n=107; Turkey,n=57; Sweden, n=12; Saudi,n=11; UK,n=5). Forty-eight patients had experienced at least one SIE (Table 1). Of these, forty occurred three months before the diagnosis of TAK or any time thereafter were included in the IR during 1876 py of follow-up, resulting in an IR of 21.3 per 1000 py (95% CI 14.7-27.9); 30.6 (95% CI 6.1-55.1) among males compared to 20.2 (95% CI 13.4-27.0) among females. The IR of stroke was 11.7 (95% CI 6.8-16.6) per 1000 py. Time from TAK onset to the initiation of immunosuppressive treatment was longer in patients with SIEs. Dyslipidemia and smoking were more prevalent among those with SIEs (Table). Aortic arch predominant disease was more frequently observed in patients with SIEs (p = 0.043), while no differences were observed for relapse of TAK rates.

Two thirds of the SIEs occurred before or at the time of diagnosis of TAK (n=30, 62.6%), mostly being the presentation symptoms of the patients (n=21, 43.8%). Fifteen patients with SIE 15/48 had multiple SIE during the study period. In multivariate analysis, carotid artery involvement (HR 2.2, 95% CI 1.1-4.0, p=0.01), and ever smoking (HR 2.1, 95% CI 1.0-4.3, p=0.04), were independently associated with occurrence of SIEs.

Majority of the patients with SIEs were treated with a combination of glucocorticoids and immunosuppressants rather than glucocorticoids alone (p=0.022). During the disease course, patients with SIEs received antiplatelet agents, anticoagulants and antihyperlipidemic agents more frequently.

Conclusions: This multi-national large study identified that SIEs are not rare in TAK, and occur mostly around the time of diagnosis. An early diagnosis and primary prevention is important, particularly in patients with carotid artery involvement and traditional risk factors for SIE.

Disclosures: None.

Poster Tour 2B: Outcomes and predictors

PT-2B-42

Identification of ANCA associated vasculitis relapse risk factors for building model for personalized maintenance therapy scheme

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Background/ Objectives: ANCA associated vasculitides (AAV) are a heterogeneous group of rare diseases with unknown etiology and the clinical spectrum ranging from life-threatening systemic disease, through single organ involvement to minor isolated skin changes. Individual disease course prediction, prognosis, and maintenance treatment regimen selection create difficulties due to the heterogeneity of the AAV. The ability to predict the risk of relapse in AAV course is crucial for decision about maintenance therapy duration. It also forms an important unmet need in actual guidelines [1].

Methods: We conducted a national multicenter study of all adult patients diagnosed with AAV (648–GPA, 170–MPA) [2]. Their clinical and laboratory data were collected in the registry by 12 referral centers. Cox proportional hazards analyses were applied to calculate hazard ratios for the first relapse as the main endpoint. First, one-dimensional models were used to identify potentially relevant variables. Then, using stepwise regression with different order of inclusion and exclusion of variables, a multidimensional model was obtained

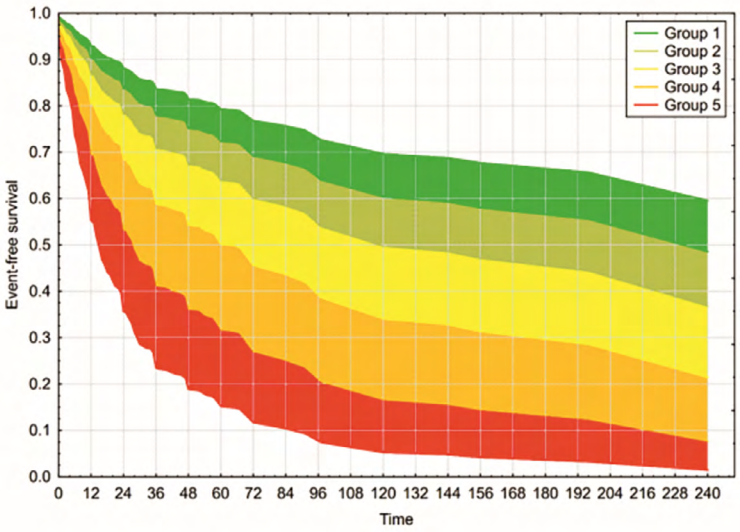

Figure 1. Relapse free survival rates for 5 AAV subgroups.

Results: Data analysis from 818 patients identified seven significant risk factors of AAV relapse: gender, skin, ENT or eye involvement, maximal ever creatinine < 475 umol and CRP > 10 ng/ml at baseline. In the next step AAV patients were divided into 5 groups with different risk of relapse (HP) over time (Figure 1) using following algorithm:

$$HP = \prod_{i=1}^{7} [1 + x_i * (h_i - 1)],$$

$h_i, i \in \{1,\ldots 7\}$ are hazard ratios obtained in analysis.*HP* value determines to which group the patient belongs: Group 1: HP≤1.5, Group 2: 1.5<HP≤2, Group 3: 2<HP≤3, Group 4: 3<HP≤5, Group 5: HP>5.

As shown in fig. 1 the relapse free survival curves differ between identified subgroups. For the group 1 the first 24 months are crucial with ca 50% of cases having no relapse during next 240 months. Whereas within group 5 patients almost all will experience the AAV relapse in long term perspective.

Conclusions: POLVAS registry data analysis identified AAV relapse risk factors for and allowed to build a model able to define AAV patients' subsets characterized by different probability of disease relapse which may help to guide personalized decisions about the duration of maintenance therapy.

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Disclosures: None.

PT-2B-43

Long-term Safety of Rituximab (Mabthera) in Granulomatosis with Polyangiitis (GPA) or Microscopic Polyangiitis (MPA): Rituximab Surveillance Study in VAsculitis (RIVAS)

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Background: Rituximab is a leading treatment for remission induction and prevention of relapse in ANCA-associated vasculitis (AAV). There is a paucity of real-world data on the long-term safety of rituximab in patients with AAV. This study evaluated the incidence of safety events in a rituximab cohort and a cohort treated with other therapies up to 15 years from first exposure.

Methods: RIVAS was a single-centre retrospective observational study including patients with GPA/MPA who received rituximab (MabThera) or other treatments between 2003 and 2017 followed up until September 2018. Time 0 was defined as initiation of MabThera treatment for the rituximab cohort or time of first disease flare/diagnosis for the control cohort. The primary endpoint was time to first SAE. Secondary endpoints were time to first pre-categorized SAE including serious infection.

Results: 392 patients were enrolled: 247 in the rituximab and 145 in the control cohort with a total of 2,217 person-years (mean study duration 5.7 years). Mean age was 61 years, 77% had GPA and 23% MPA. The median disease duration at baseline was 25.0 months in the rituximab and 1.6 months in the control arm. Observed differences in the baseline characteristics between groups reflected the predominant use of rituximab for relapsing or refractory disease. Three hundred and eighty-six SAEs occurred in 134 patients (54%) in the rituximab and 114 in 58 patients (40%) in the control groups (Table 1). Sixty-five patients (26%) in the rituximab and 18 (12%) in the control group experienced serious infections. Twenty-one patients (9%) in the rituximab group developed severe hypogammaglobulinemia (IgG <3 g/L) requiring change of treatment and 19 (8%) received immunoglobulin replacement for hypogammaglobulinemia compared to 3 (2%) and 1 (0.7%) of patients in the control group. We found no evidence of differences in incidence rates for malignancy, cardiovascular events or renal insufficiency. Time to first SAE was shorter in the rituximab group (HR 1.55, 95%CI 1.07-2.26, p=0.022). Time to first serious infection was shorter in the rituximab group (HR 2.34, 95%CI 1.079-5.07, p=0.031), while no between-group differences were found for other SAE categories. Predictors of first SAE were higher vasculitis damage scores and chronic pulmonary or kidney disease. The risk of serious infection and additional safety events was higher in the rituximab group (unadjusted relative risk (RR) 2.12, 95%CI 1.31-3.43; RR 1.86, 95%CI 1.30-2.65).

Conclusions: Over 40% of patients with GPA/MPA experienced at least one SAE. Although the risk of first SAE and infection were higher in the rituximab group, baseline imbalances, particularly in disease duration and prior immunosuppressive use, due to the study design were a cause of bias and require cautious interpretation.

Disclosures: RJ: GlaxoSmithKline, Roche, CSL Vifor. RS: GlaxoSmithKline, Union Therapeutics. RL: BMS Celgene, CSL Vifor, GlaxoSmithKline, Roche. DJ: GlaxoSmithKline, CSL Vifor, AstraZeneca, Novartis, Roche, Takeda, Chinook, Hansa, Aurinia. Other authors: none.

Event type	Events(n)/ Patients (n(%)) Rituximab	Events(n)/ Patients (n(%)) Control
All SAEs	386/ 134 (**54%**)	114/ 58 (**40%**)
Serious infection	121/ 65 (**26%**)	28/ 18 (**12%**)
Cardiovascular disorder	28/ 23 (9%)	17/ 15 (10%)
Hematological events	9/ 8 (3%)	2/ 2 (1%)
Malignant events	11/ 11 (4%)	8/ 8 (6%)
Renal Insufficiency	19/ 14 (6%)	19/ 15 (10%)
PML	1/ 1 (0.4%)	0/ 0 (0%)
Additional safety events*	197/ 95 (**38%**)	40/ 30 (**21%**)

*This category includes 'Any other SAEs of unclear categorization (most common)', 'Hypogammaglobulinemia (IgG<3g/L) requiring change of treatment', 'Hypogammaglobulinemia requiring immunoglobulin replacement', 'Serious disease flares', 'Serious infusion-related reaction' and 'Vaccination failure'.

Table 1. Serious adverse events (SAEs) by event category.

PT-2B-44

Is there any advantages of the use of the Glucocorticoid Toxicity Index among the patients with vasculitis?

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Background/ Objectives: The Glucocorticoid Toxicity Index (GTI) is a novel, outcome-based tool for monitoring glucocorticoid-induced adverse effects. Even the purpose of the tool is to measure the change glucocorticoid (GC) toxicity in time, there is no prospective study conducted among patients with vasculitis in the literature yet. This study aimed to evaluate the GC toxicity by using the GTI in a prospective cohort of vasculitis patients treated with GC.

Methods: Patients at the Vasculitis Clinic with newly prescribed/currently using GC were evaluated for the study between January 2021 and June 2022. Patients treated with GC for more than two years were excluded from the study due to the difficulty in cumulative dose calculation. Suitable patients were divided into two groups: GC-naive and GC-experienced (treated with GC for £2 years). Cumulative GC dose and data for eight GTI domains (body mass index [BMI], blood pressure, glucose tolerance, lipid metabolism, myopathy, skin toxicity, neuropsychiatric effects, and infections) excluding bone mineral density were recorded at baseline (t0), 3rd month (t3) and 6th (t6) month and then the GTI scores were calculated accordingly.

Results: In total, 97 patients (53.6% female) with a median (IQR) age of 54 (28) years were included; 49 patients in the GC-naive and 48 patients in the GC-experienced group. Among the patients, 24.7% had ANCA-associated vasculitis, 17.5% had Ig-G4 related disease, 16.5% had Takayasu arteritis, and 13.4% had giant cell arteritis. 54 (55.7%) patients (38 in GC-naive and 16 in GC-experienced group) experienced at least one GC-related toxicity during study period and the most common toxicity observed was an increase in blood pressure in the GC-naive patients and lipid disturbances in GC-experienced patients. While no improvement in GC toxicity was seen in the GC-naive patients over 6 months since the baseline, 48.9% (n=23) of GC-experienced patients showed improvement. Although the median (IQR) baseline GTI scores were higher in GC-experienced patients, these scores were higher in GC-naive patients at both 3rd and 6th month ($p<0.001$). Our results showed a strong correlation in the cumulative GC doses received by patients throughout the study period and GTI scores (3rd month $r=0.774$, $p<0.001$; 6th month $r=0.736$, $p<0.001$). However, no significant association was observed between the GTI scores and the cumulative GC dose in GC-experienced patients, if the 'previously received total dose' is also included in the analysis ($r=0.176$, $p=0.236$).

Conclusions: Changes in glucocorticoid toxicity during the treatment period were detected by the GTI. Glucocorticoid-related toxicities were observed to be higher in patients newly started on glucocorticoid therapy, in correlation to cumulative doses in vasculitis treatment. In patients using glucocorticoid for relatively longer periods, an observed change in toxicity is limited. Therefore, GTI should be considered to be integrated into clinical practice for monitoring glucocorticoid toxicity in patients who are new to glucocorticoid therapy.

Disclosures: None.

Table. Cumulative GC doses and GTI scores of GC-naive and GC-experienced patients.

	Cumulative prednisolone dose, mg median (IQR)			Baseline GTI median (min-max)	Changes in GTI median (min-max)			
					GTI-AIS		GTI-CWS	
	t_0	between t_0 and t_3	between t_0 and t_6	t_0	t_3	t_6	t_3	t_6
GC-naive (n=49)	0	2820 (2401.3)	4065 (3804.4)	50.0 (0-139)	42.0 (0-101)	42.5 (0-190)	42.5 (0-101)	50.5 (0-190)
GC-experienced (n=48)	*	490.6 (545.3)	1000 (805.0)	105.0 (0-184)	0 (-32 to 82)	0 (-63 to 29)	0 (0-82)	0 (0-82)

GC: Glucocorticoid, GTI-AIS: Glucocorticoid Toxicity Index Aggregate Improvement Score, GTI-CWS: Glucocorticoid Toxicity Index Cumulative Worsening Score, t_0: baseline visit, t_3: 3rd month, t_6: 6th month.

*previously received total dose until the baseline visit, median (IQR): 7483.1 (6272) mg

PT-2B-45

Clinical presentations and outcomes in seronegative versus seropositive ANCA associated glomerulonephritis - An international cohort study

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Background: Seronegative ANCA associated glomerulonephritis (AAGN) has previously been reported to occur in up to 30% of pauci-immune glomerulonephritides[1,2]. The absence of detectable circulating ANCA is thought to indicate a distinct spectrum of the disease, with more renal limited involvement and poorer outcomes despite being a younger age[2,3]. Due to the rarity of the disease and frequent exclusion from clinical trials, there remains unanswered questions regarding the pathophysiology, diagnosis and management of patients with seronegative AAGN.

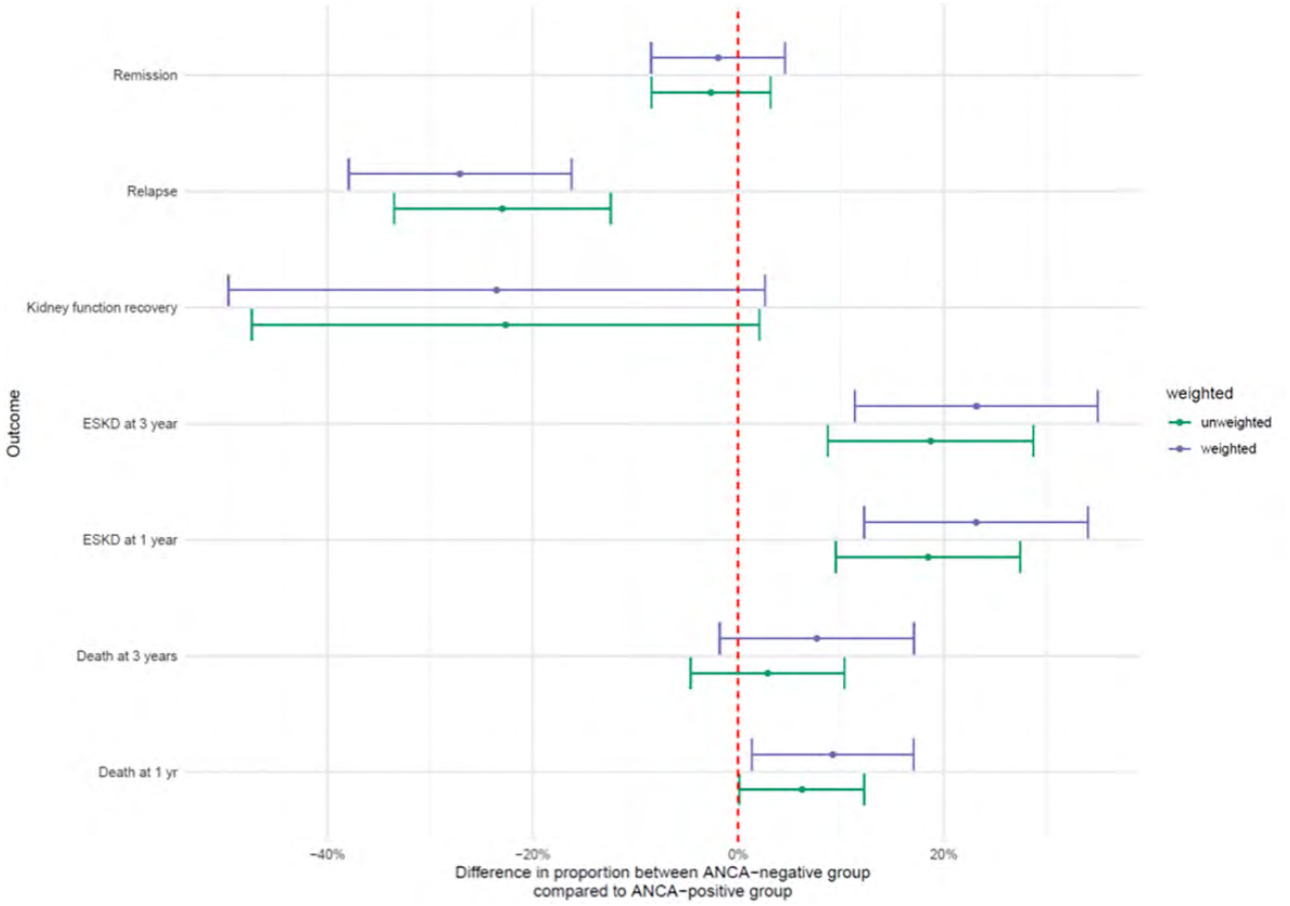

Fig 1 Clinical outcomes of seronegative vs seropositive AAGN when adjusting for pre diagnostic variables.

Methods: A retrospective, multicentre cohort study from 2002-2022 was carried out to include ANCA negative patients. Inclusion criteria included small vessel systemic vasculitis according to EMEA criteria with biopsy proven pauci-immune glomerulonephritis in those aged >18 years. Patients were required to be ANCA negative on IIF and ELISA at presentation and throughout the study period. A control cohort of anti-MPO or anti-PR3 ANCA positive patients were recruited to achieve a 1:1 ratio. Data including demographics, clinical presentation, histopathology, treatment and clinical outcomes were collected.

Results: A total of 132 ANCA negative and 127 ANCA positive patients (PR3 n=62, MPO n=65) with AAGN were included from 14 international centres. The mean age of ANCA negative patients was lower than that of ANCA positive patients (56.6 $\pm$17.0 vs 63.6 $\pm$14.5 yrs). ANCA-negative patients tended to present with more renal-limited disease (n=69, 52.3% vs n=39, 30.7%). When comparing clinical outcomes, using inverse probability weighting to control for age, gender, ethnicity and recruiting centre, ANCA-positive patients had higher relapse rates (35.7% vs 12.3%, P<0.001), whilst ANCA-negative patients had higher rates of ESKD at 1 year and 3 years (P<0.001). They also had marginally increased risk of death at 1 year (P=0.02), Fig.1. Standard induction therapy was used in 93.9% of ANCA negative compared to 97.6% ANCA positive patients. Fewer ANCA negative patients received ongoing maintenance therapy (n=107, 82.3% vs n=119, 92.4%).

Conclusion: Seronegative AAGN is seen more commonly in younger patients with a tendency for renal limited disease. The precise pathophysiology of seronegative AAGN and the factors contributing to its clinical phenotype, such as the propensity to affect predominantly the kidney and lower relapse rates remain unclear, but suggests a distinct disease entity separate from seropositive AAGN. While seropositive and seronegative AAGN exhibit similar histopathological features, ANCA negative disease is associated with higher rates of ESKD and mortality. The poorer outcomes may be attributed to uncertainties among physicians and a reluctance to treat in the absence of positive serology. A lack of robust biomarkers and reliance on histology can create delays in diagnosis, potentially resulting in more severe disease at presentation.

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Disclosures: None.

PT-2B-46

Influence of histological tempol artery biopsy findings on outcomes of biopsy-proven giant cell arteritis in Italian patients : a long single center follow-up study

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Background/ Objectives: Few studies have evaluated the influence of histological features of temporal artery biopsy (TAB) on disease outcome in giant cell arteritis (GCA) patients. Our aim was to investigate potential associations between TAB histological characteristics and outcomes of GCA in a long term single centre retrospective follow-up study.

Methods: Two hundred and four Italian patients with biopsy-proven GCA resident in Reggio Emilia area (Italy) followed up for at least 12 months entered the study (median duration of FU 130 months (range 13-435 months). The following histological findings of TAB were recorded : localisation of inflammatory infiltrate (small vessel vascultis (SVV), inflammation limited to adventitia (ILA), trans mural inflammation TMI), presence of giant cells (GC), presence of infiltrating neutrophils, plasma cells, histiocytes, eosinophils, presence of laminar necrosis (LN), vessel wall calcifications, luminal trombosis (LT) and intimal hyperplasia (IH). The severity of inflammation (SI) was graded on a semiquantitative scale (mild, moderate and severe), the severity of IH (was graded as mild <25% reduction in lumen diameter, moderate from 25% to 75%, and severe >75%).

The following data were recorded during follow up : presence of relapses, long term remission (LTR), cumulative steroid dose at 6, 12 months and at end of FU, duration of steroid treatment and of LTR, and mortality. Survival curve were compared with K-M method using log rank test. A Cox proportional hazards model was used to assess the relationship between pathologic parameters at diagnosis and disease outcomes (flares, steroid withdrawal and survival).

Results: Forty-two % of the patients relapsed during a median FU period of 130 months (limits 13-435). First relapse time was significantly influenced by presence of GC (140 vs 207 months, p=0.025), presence of LT (91 vs 171 months, p=0.036) and histological subtype (80 vs 156 vs 249 months for SVV, ILA and TMI respectively, p=0.017). Fifty-seven % of patients were able to withdraw steroids for at least 12 month. Histological subtypes influenced the duration of treatment (SVV 2.7 months, ILA 17.9 months, TMI 32.0 months, p=0.019). Seventy % of patients died during the follow up period. TAB histological factors with impact on survival time were : SI severe vs mild infiltrate (107 months vs 155 months, p=0.006), presence of GC (112 vs 154 months, p=0.049), presence of LN (96 months vs 132 months, p=0.029), histological subtypes (TMI 115 months vs ILA 161 months vs SVV 195 months, p= 0.017). In a Cox multivariate model only TMI was associated with a significantly increased mortality (HR 3.864; 95% CI 1.061- 14.072) and no other pathological findings maintained statistical significance.

Conclusion: Histological findings of TAB influenced survival time, first relapse time and duration of steroid treatment in GCA pts.

Disclosure: None.

PT-2B-47

Immune Checkpoint Inhibitors-Induced Large Vessel Vasculitis: Data from a Multicenter Study

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Backgrounds: Immune checkpoint inhibitors (ICIs) have dramatically improved the prognosis for many cancers. The therapeutic effect of ICIs is based on their ability to release the brakes on lymphocyte activation. However, this brake release can trigger immune-related adverse events (IrAEs) in up to 60-80% of cases. Few observations of ICI-induced large vessel vasculitis (LVV) have been reported. We aimed to describe the characteristics and outcomes of LVV occurring after or during ICI therapy, compared with non-induced LVV.

Methods: We conducted a European, multicenter, retrospective study of patients who received at least one infusion of ICI and subsequently presented with LVV between March 2018 and January 2023. Each case was compared with four patients with non-induced LVV matched for sex and age (+/5 years). LVV patients either satisfied the 2022 ACR/EULAR classification criteria for giant-cell arteritis (GCA) or had an imaging or histological proof of LVV.

Results: Twenty-one patients were included (median age 70 (IQR 61-74) years). Previous history of PMR or GCA was noted in 4 (19%) patients. The two most common cancers treated with ICIs were melanoma (38%) and renal cell carcinoma (24%). Five (29%) patients received a combination of nivolumab and ipilimumab, while the rest received a monotherapy of anti-PD-1/PD-L1. First LVV manifestations occurred after a median of 5 (IQR 3-22) ICI infusions and a median time of 3 (IQR 2-18) months since the first ICI infusion. Thirteen (62%) patients were diagnosed of LVV within the first six months after ICI initiation.

Clinical manifestations were overall similar compared to controls (**Figure 1A**). Blindness occurred in 4 (19%) patients compared to 5 (6%) controls. Aorta was the main artery involved (**Figure 1B & 1C**). Temporal artery biopsy was positive in 4/7 cases (**Figure 1D**). Five (26%) patients had other IrAEs, mainly hepatitis.

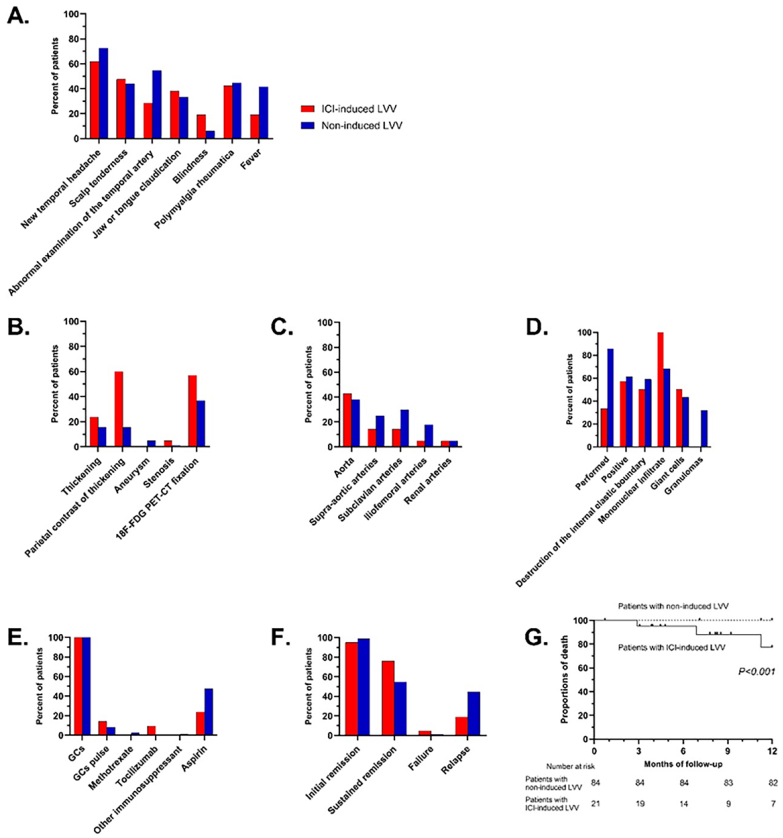

Figure 1.

All patients received oral glucocorticoids. The median initial prednisone dose was 0.7 g/kg/d (IQR 0.7-1). Two (11%) patients received tocilizumab as first-line therapy (**Figure 1E**).

ICI was rechallenged or continued for 6 (29%) patients and stopped for 15 (71%) patients.

Median follow-up after LVV diagnosis was 8 months (IQR 4-16). Sustained remission was achieved in 16 (76%) patients. Four (19%) patients relapsed after first line therapy while 37 (44%) had relapsed in the control group (**Figure 1F**). Relapse or failure after first line therapy occurred in 3/6 (50.0%) patients who continued ICI compared with 3/15 (20.0%) patients who discontinued it. At the end of follow-up, 5/21 (24%) patients had died, 4 of cancer and 1 of acute coronary syndrome, while only two (2%) had died in the control group (**Figure 1G**).

Conclusion: LVV is a rare IrAE that usually occurs early after the initiation of ICI. Unexplained elevations in acute phase reactants in ICI-treated patients should prompt clinicians to look for signs of LVV, as severe ischaemic manifestations such as visual loss may occur. While patients who were maintained on ICI or rechallenged had a more refractory or relapsing course, physicians should prioritize cancer management as it is the leading factor affecting early prognosis.

PT-2B-48

ANCA vasculitis with renal involvement. Is age an issue?

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Background: Older patients with antineutrophil cytoplasmic autoantibody-associated vasculitis (AAV) commonly experience renal impairment and poor prognosis (1). The European Vasculitis Study Group trials showed that approximately 16.7% and 22.5% of older patients with AAV suffered from end-stage renal disease (ESRD) in 5- and 10-year durations (2). The aim of this study was therefore to analyze differences in course and outcome of patients with AAV with respect to age.

Material and methods: This retrospective observational study included patients with diagnosis of AAV and biopsy proven renal involvement between 2000-2021. Patients were divided into two groups according to age: ≥65 or <65 years old. We recorded baseline characteristics and clinical data during follow-up. Response was defined as a BVAS reduction of at least 50% or BVAS of 0, while receiving prednisone dose higher than 4 mg; and remission as BVAS of 0 while receiving prednisone dose of 4mg or less.

Results: We included 42 patients with AAV diagnosis, 47.6% of which were 65 years-old or older. Mean age of the older age group was 77±8 years. No differences were found between older and younger patients at baseline (BVAS, FFS extra-renal symptoms, serum creatinine at diagnosis, hematuria), Patients > 65 years were significantly more likely to present p-ANCA positive MPA, as shown in Table 1.

	Age <65 years (n=20)	Age >65 years (n=22),	p value
BVAS at diagnosis, mean ± SD	18.18 ± 1,92	19.57 ± 4.66	0.36
FFS at diagnosis, mean ± SD	1,23 ± 0.69	1.37 ± 0.59	0.49
ANCA-associated vasculitis type:			
- MPA, n (%)	8 (36.4)	15 (75)	**0.01**
- GPA, n (%)	13 (59.1)	3 (15)	**0.003**
- EGPA, n (%)	1 (4.5)	2 (10)	0.59
Clinical features at diagnosis:			
- General symptoms, n (%)	1 (5)	6 (27.3)	0.053
- Pulmonary, n (%)	9 (45)	8 (36.4)	0.57
- Other extra-renal symptoms, n (%)	16 (80)	19 (86.4)	0.58
Analytical features at diagnosis:			
- c-ANCA, n (%)	14 (63.6)	3 (15)	**0.001**
- p-ANCA, n (%)	8 (36.4)	16 (80)	**0.004**
- Anti-MPO, n (%)	10 (47.6)	19 (95)	**0.001**
- Anti-PR3, n (%)	12 (54.5)	1 (5)	**0.001**
- Serum creatinine (mg/dl), mean ± SD	3.44 ± 2.34	3.61 ± 2.17	0.8
- Hematuria, n (%)	19 (95)	20 (95.2)	1
- Proteinuria, n (%)	17 (85)	22 (100)	0.09
Induction treatment:			
- Methylprednisolone pulses, n (%)	21 (95.5)	18 (90)	0.59
- Cyclophosphamide, n (%)	17 (77.3)	14 (70)	0.59
- Rituximab, n (%)	5 (22.7)	5 (25)	1
Maintenance treatment:			
- Prednisone, n (%)	6 (40)	9 (60)	0.23
- Rituximab, n (%)	10 (45.5)	9 (45)	0.97
- Mycophenolic acid, n (%)	15 (68.2)	15 (75)	0.63
- Azathioprine, n (%)	5 (22.7)	2 (20)	0.41
Response:			
- 6 months, n (%)	18 (81.8)	17 (85)	1
- 1 year, n (%)	19 (90.5)	17 (94.4)	1
- Last visit, n (%)	20 (90.9)	17 (85)	0.66
Remission:			
- 6 months, n (%)	6 (28.6)	5 (25)	1
- 1 year, n (%)	14 (66.7)	11 (57.9)	0.57
- Last visit, n (%)	15 (69.2)	15 (75)	0.63
Relapse, n (%)	17 (40.5)	6 (30)	0.22
Renal outcome:			
- End-stage kidney disease, n (%)	8 (36.4)	12 (60)	0.13
- Hemodialysis, n (%)	4 (18.2)	6 (30)	0.48
Death, n (%)	2 (9.1)	9 (45)	**4.9 (0.01)**

Table 1: Clinical and analytical features at diagnosis, treatment choice and outcome, compared by age. SD: standard deviation; ANCA: antineutrophil cytoplasmic autoantibody; MPA: microscopic polyangiitis; GPA: granulomatosis with polyangiitis; EGPA: eosinophilic granulomatosis with polyangiitis; Anti-MPO: Anti-Mieloperoxidase; Anti-PR3: Anti-Proteinase 3.

There was no difference in initial or maintenance immunosuppressive therapy between the two groups. No differences were found between older and younger patients with regard to treatment response. Although we found no statistical differences, older patients had worse renal outcomes. The older adult group had a higher mortality rate, p 0.01. The average time to death was 27 months for patients over 65 years and 34.5 in those who were younger (p 0.71).

Conclusions: No differences were found between older and younger patients with regard to treatment response. However, mortality was higher during follow-up in the group of older patients. Our results suggest that more attention should be paid to older patients with severe renal impairment.

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Disclosures: None.

Poster Tour 3B: Outcomes and predictors

PT-3B-49

All-Cause and Cause-Specific Mortality In ANCA-Associated Vasculitis: a Population-based Study

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Background/ Objectives: Mortality is elevated in ANCA-associated Vasculitis (AAV). Early deaths in patients with AAV are often attributed to vasculitis and infections secondary to treatment. The objective of this study is to examine the rate and cause of death in AAV compared to the general population.

Methods: Two large population-based cohorts of AAV in Sweden were utilized. Diagnoses of AAV were confirmed by case record review. Patients were classified into granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic GPA (EGPA) using the European Medicine Agency algorithm. For each patient with AAV, 20 controls were selected, matched for age, sex, and residency. Data on all-cause mortality were extracted from The Swedish Cause of Death Register. Person-year (py) of follow-up was calculated from date of diagnosis of AAV (or index-date for controls) to death or December 31, 2020. Rate of death for patients and controls was calculated and rate ratios (death rate in AAV: controls) were estimated. Survival was studied using the Kaplan Meier curves and Log Rank tests. Primary cause of death was grouped into the following categories: vasculitis, infection, cardiovascular, cancer and other.

Results: A total of 561 patients and 11131 controls were included. Patients were classified as: GPA 290, MPA 248 and EGPA 23. The rate of death was 56.1/1000 py in AAV patients vs. 33.5/1000 py in controls resulting in a rate ratio of 1.7 (95% CI 1.5-1.9), Table 1. During the first year the rate of death was 110.7/1000 py in patients vs 27.2/1000 py in controls. During the first year from diagnosis, the main cause of death was vasculitis, cardiovascular diseases in patients vs. cardiovascular, other and cancer in controls. Infection contributed to death in 28% of deaths in patients and 18% in controls during the first year. The 1, 5 and 10-years cumulative survival was 90%, 73% and 57% in patients and 97%, 86% and 73% in controls (p <0.0001),

Conclusions: Mortality rate was higher in patients with AAV compared to matched controls. Death rate is higher in the first year after diagnosis and remains elevated in long-term follow-up. Specific causes of death differ from the matched controls with vasculitis dominating as the primary cause of death in the first year.

	AAV patients			*Controls*			*AAV:Controls*	
Time since diagnosis	**Person yrs**	**Deaths**	**Rate**	**Person yrs**	**Deaths**	**Rate**	**Rate Ratio**	**p**
0-1 year	524	58	110.7	10979	299	27.2	4.1 (3-5.4)	<0.0001
1-5 years	1664	83	49.9	37270	1118	30.0	1.7 (1.3-2.1)	<0.0001
5-10 years	1255	58	54.5	29373	989	43.1	1.4(1.0-1.8)	0.04
>10 years	998	50	50.1	25476	1047	41.1	1.2 (0.9-1.6)	0.21
All	4440	249	56.1	103098	3453	33.5	1.7 (1.5-1.9)	<0.0001

Table 1. Rate of death (per 1000 years of followup) among 561 patients compared with 11131 matched controls.

References: None.

Disclosures: None.

PT-3B-50

Patient-reported sinonasal symptoms and risk of relapse in ANCA-associated vasculitis

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Background/Objectives: Relapses are frequent and difficult to predict in ANCA-associated vasculitis (AAV), resulting in long-term use of immunosuppression. Although sinonasal disease is associated with relapse of AAV, detailed characterization of sinonasal symptoms is lacking. The 22-item Sinonasal Outcome Test (SNOT-22) is a validated patient-reported outcome measure to assess symptoms and quality of life in chronic rhinosinusitis but has not been well-studied in AAV. We investigated longitudinal changes in SNOT-22 scores associated with disease activity and the relationship between SNOT-22 and risk of relapse in patients with AAV.

Methods: This was a prospective, longitudinal study of AAV and healthy individuals. Relapse was defined as BVAS greater than zero. SNOT-22 questionnaires were collected at every visit with higher scores indicating greater disease burden. For the SNOT-22, both total scores and individual domain scores (e.g., rhinologic domain) were analyzed. Generalized estimating equation and Cox proportional hazard models evaluated the association between SNOT-22 and relapse and adjusted for disease duration, concomitant seasonal allergies, and use of antibiotics, immunosuppressive medications, and sinus rinses. Cut-points were generated using Youden method (maximum sum of sensitivity and specificity).

Results: There were 773 visits (106 active disease visits) from 168 patients with AAV and 51 controls. Median SNOT-22 at remission was higher in AAV vs. controls (20 vs. 5, p<0.001) and higher during active disease vs. remission (p<0.001). Higher SNOT-22 rhinologic scores were observed months to years before relapse (**Figure 1A**) and were associated with increased risk of relapse in AAV (HR 2.9 [95% CI 1.4-6.4], P<0.01)(**Figure 1B**). Similar relationships were observed when evaluating other domain scores and the total score. Subgroup analyses of patients with vs. without sinonasal disease and after removal of relapses limited to the ear, nose, and throat alone yielded similar results.

Conclusions: In AAV, a patient-reported outcome measure, the SNOT-22, not only tracks with disease activity but also is associated with a higher risk of future relapse, months-to-years prior to systemic relapse. These findings support the possibility that, in AAV: 1) the SNOT-22 score may be able to enhance our ability to predict relapse and, 2) persistent sinonasal disease activity may play an important role in disease re-activation. Future studies are needed to determine if incorporation of the SNOT-22 score into a clinical prediction model can inform therapeutic decision-making and improve patient outcomes.

Disclosures: PAM - AbbVie, Amgen, AstraZeneca, Boeringher-Ingelheim, Bristol-Myers Squibb, GlaxoSmithKline, InflaRx, Takeda, ArGenx, Cabaletta, CSL Behring, Dynacure, HiBio, Janssen, Novartis, NS Pharma, Regeneron, Vistera, Eicos, Electra, Forbius, Genentech/Roche, Genzyme/Sanofi, Neutrolis, Kyverna, Q32, Sparrow, UpToDate.

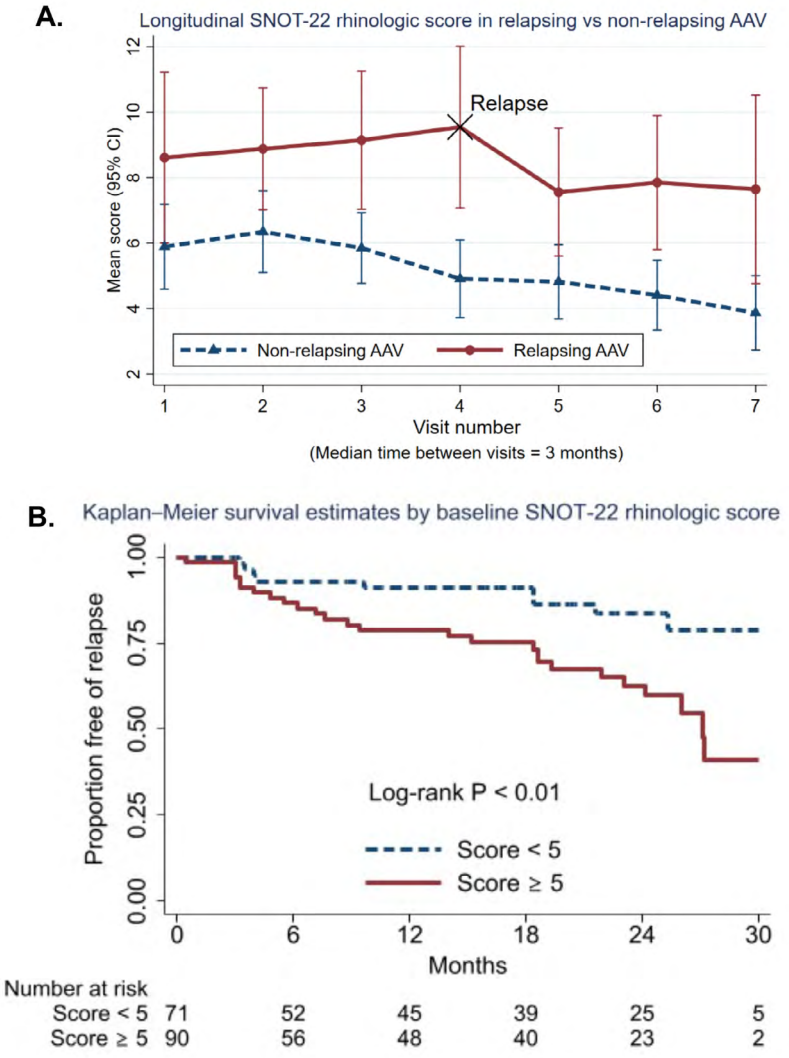

Figure 1. Higher SNOT-22 scores are associated with increased risk of relapse in AAV. (A) Line plot of mean rhinologic SNOT-22 score (95% CI) across consecutive visits (median 3 months between visits) in relapsing AAV (red solid line, n=35) vs non-relapsing AAV (blue dashed line, n=73). In relapsing AAV, relapse visits are aligned at visit 4. Relapsing AAV without an accompanying remission visit not included. (B) Kaplan-Meier curve for relapse-free survival (in months) by baseline rhinologic SNOT-22 score in 161 AAV patients.

PT-3B-51

The Impact of Chronologic vs Biologic Age on Outcomes in Older Adults with ANCA-Associated Vasculitis

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Background/ Objectives: Older adults with ANCA-associated vasculitis (AAV) have distinct clinical presentations and outcomes when compared to younger adults. Studies have focused on age as a risk factor for poor outcomes. Frailty, a syndrome associated with increased morbidity and mortality, provides a more holistic assessment in older adults.

Our objective was to compare the impact of age and frailty on early (≤2 years of diagnosis) end-stage renal disease (ESRD), death, and severe infection in adults with incident AAV who are ≥75 years (y) vs 65-74y.

Methods: Patients ≥65y were included from the 2002-2019 Mass General Brigham AAV cohort. EGPA patients were excluded. Covariates including demographics, comorbidities, disease characteristics, and disease activity were assessed at baseline. Baseline frailty was measured using the claims-based frailty index; pre-established cut-offs defined degrees of frailty (robust, pre-frail, mildly frail, and moderately/severely frail).

The cumulative incidence of the ESRD/death (composite outcome) and severe infections at 2-years were estimated. Multivariable analysis was performed to compare the association of age and frailty with ESRD/death and severe infections within 2 years of treatment initiation.

Results: There were 298 patients included. Most were female (61%), white (86%), MPO-ANCA+ (80%), and had renal involvement (72%). Patients ≥75y old (n=156) had a median age of 81y, while median age was 69yin the 65-74y group.

The cumulative incidence at 2 years of ESRD/death (23.1% [95% CI 16.5, 29.7]) vs 5.6% [95% CI 1.8, 9.4]) and severe infection (34.0% [95% CI 26.5, 41.4] vs 12% [95% CI 6.6, 17.3]) were higher in AAV patients ≥75 vs 65-74y. In the multivariable analysis, age ≥ 75y was associated with an increased risk of composite outcome (hazard ratio (HR) 3.71, 95% CI 1.81, 7.58); frailty was not (HR 1.93, 95% CI 0.44, 8.46) (Table 1). In contrast, both frailty (HR 8.62, 95% CI 2.08, 35.66) and age ≥75 years (HR 2.98, 95 CI% 1.82, 4.88) appeared to be independent risk factors for severe infections at 2-year follow-up; the association with frailty appeared greater. In the interaction term analysis, the association with frailty appeared stronger and higher in the 65-74 vs ≥75y groups (HR 13.40 vs 3.41, p=0.02).

Conclusions: AAV patients aged ≥75 vs 65-74y had a higher incidence of ESRD/death and severe infections. Older age was associated with ESRD/death and severe infection risk. Frailty was a strong risk factor for severe infection, and this effect was more pronounced in the 65-74y group.

Disclosures: Sattui: Bristol Myers Squibb Foundation (research funding); AstraZeneca and GlaxoSmithKline (clinical trials); Sanofi and Amgen (consulting/advisory board, funds toward research support).

Wallace: NIH/NIAMS [K23AR073334, R03AR078938, R01AR080659], Rheumatology Research Foundation [K Supplement] (research funding); Amgen, Bristol-Myers Squibb, and Principia/Sanofi (research support); Amgen, Viela Bio, Horizon, Zenas Biopharma, PPD, and MedPace (consulting); Amgen, Horizon, Sanofi, Shinogi, and Visterra/Otsuka (advisory boards).

Factors	Composite outcome (ESRD/Death)		Severe infection	
	Univariable analysis HR (95% CI)	Multivariable analysis HR (95% CI)	Univariable analysis HR (95% CI)	Multivariable analysis HR (95% CI)
Age ≥ 75 years (Ref, 65-74 years)	**3.88 (1.92, 7.86)**	**3.71 (1.81, 7.58)[a]**	**3.27 (1.94, 5.53)**	**2.98 (1.82, 4.88)[a]**
CFI				
Robust	REF	REF	**REF**	REF
Pre-frail	1.85 (0.44-7.80)	1.63 (0.38, 6.92)[b]	4.01 (0.56-28.72)	2.64 (0.63, 11.02)[b]
Frail	2.71 (0.63-11.72)	1.93 (0.44, 8.46)[b]	**19.39 (2.77-135.66)**	**8.62 (2.08, 35.66)[b]**

ESRD = end-stage renal disease, CFI = Claims-based frailty index,
[a]Adjusted for sex, frailty, pulmonary involvement, renal involvement, and BVAS/GPA.
[b]Adjusted for age, sex, pulmonary involvement, renal involvement, and BVAS/GPA.

Table 1. Factors associated with outcomes in older adults with AAV at 2 years.

PT-3B-52

Reduced levels of C5a Complement Receptor Antibodies are linked to Relapse in Eosinophilic Granulomatosis with Polyangiitis (EGPA)

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Background/ Objectives: Complement activation has been shown to play an important role in anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (AAV) [1,2]. Circulating proinflammatory anaphylatoxin C5a concentrations are increased and correlate with disease activity in AAV [3]. Binding of C5a to its corresponding G protein-coupled receptor (C5aR/CD88) enhances the influx of (neutrophilic) granulocytes and their activation, leading to ROS generation and severe necrotizing of vascular walls (3). Clinical use of the C5aR antagonist avacopan demonstrated a new potent glucocorticoid-sparing nephroprotective agent in GPA and MPA [4]. Recent studies identified reduced levels of endogenous antibodies against the C3a and C5a complement receptors (anti-C3aR- and anti-C5aR aabs) linked to disease activity and early relapse in GPA and MPA, indicating C5aR as a new immune checkpoint in AAV [5]. However, there is a lack of evidence in eosinophilic granulomatosis with polyangiitis (EGPA).

Methods: Concentrations of anti-C3aR and anti-C5aR aabs were determined in patients with EGPA (n=10), systemic lupus erythematosus as disease control (SLE, n=47) and healthy donors (HD, n=220). Clinical data were assessed at the time of serum sampling and during follow-up for 60 months.

Results: In EGPA, anti-C3aR and anti-C5aR antibodies were decreased compared to HD (anti-C3aR aabs: EGPA vs. HD: 4.82U/ml±2.43 vs. 6.49 U/ml±2.59, *P*=0.074, figure 1A; anti-C5aR aabs: 2.84U/ml±4.08 vs. 6.25U/ml±2.91, *P*=0.0001, figure 1B) and SLE (anti-C3aR aabs: EGPA vs. SLE: 4.82U/ml±2.43 vs. 11.92U/ml8.20, *P*<0.0001, figure 1A; anti-C5aR aabs: 2.84U/ml±4.08 vs. 3.01U/ml±10.05, *P*=0.743, figure 1B). In contrast to anti-C3aR aabs, reduced levels of anti-C5aR aabs were associated with major relapse in EGPA (HR:9.96, *P*=0.0494, figure 1C).

Conclusions: Low concentrations of circulating anti-C5aR aabs reflect an increased risk for relapse in EGPA, comparable to that reported in GPA and MPA [5].

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Disclosures: No conflict of interests.

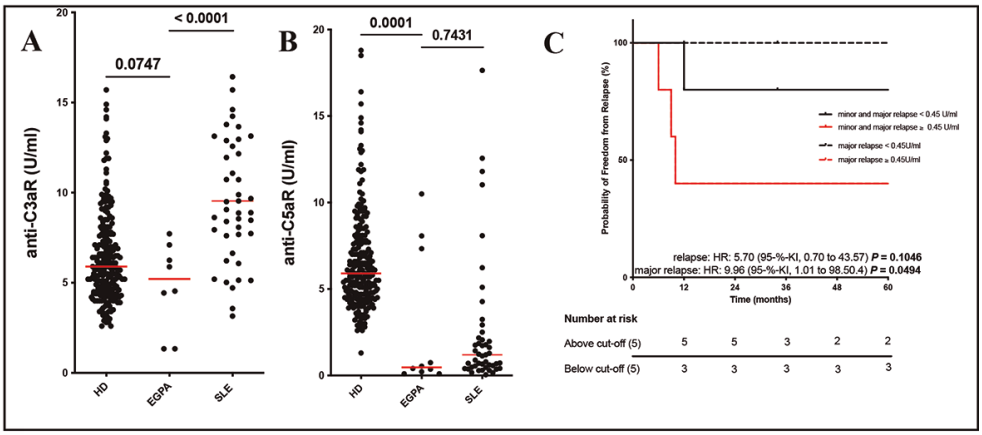

Figure 1 Anti-C3aR and anti-C5aR antibody concentrations in EGPA. **A:** Anti-C3aR antibody concentrations compared to HD and SLE. **B:** Anti-C5aR antibody concentrations compared to HD and SLE. **C:** Anti-C5aR antibody concentrations <0.45 U/l were associated with a higher relapse rate (major relapse) in EGPA.

PT-3B-53

Mortality Rate by Diagnosis in ANCA-Associated Vasculitis Across FAIRVASC Registries

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Background/ Objectives: Research into ANCA-associated vasculitis (AAV) is hampered by the rarity of the disease and the subsequent small sample sizes of observational cohorts. This is further aggravated by the observational cohorts being contained in fragmented data pools and lacking standardisation to allow for interoperability. FAIRVASC is a Europe-wide research project, which has developed an infrastructure linking 7 existing AAV registries into a single European dataset, to allow high-quality research on natural disease history and clinical outcomes.

This analysis highlights the capabilities of the FAIRVASC infrastructure to assess clinical outcome of AAV across the federated registries.

Methods: Within the FAIRVASC project, 7 national/regional AAV registries were harmonized using a semantic web approach, including the creation of a dedicated AAV ontology, to enable semantic interoperability. For this study, aggregated data regarding mortality rate (/100 person years, with related 95% Confidence Intervals) per diagnosis were retrieved through the FAIRVASC web interface, a tool that allows federated querying over linked registries. We defined mortality rate in the first and second year post diagnosis, and in years 3-5 and after 5 years.

Results: Mortality queries were posed over the FAIRVASC registries, namely RKD (Republic of Ireland, 677 patients), GFEV (France, 2814 pts), ANCA (Czech Republic, 377 pts), PolVas (Poland, 944 pts), Skane (Sweden, 374 pts), Italivas (Italy, 301 pts), GeVas (Germany, 169 pts). Mortality rates, stratified by diagnosis and registry, are reported in **Table 1.** The lowest mortality was reported for eosinophilic granulomatosis with polyangiitis (EGPA), with rates ranging from 0 to 2.5 cases/100 person-years depending on the post-diagnosis interval. Conversely, the highest mortality was found for microscopic polyangiitis (MPA), with mortality rates ranging from 6.7 to 22.3 across registries in the first year after diagnosis, and from 3.9 to 7.4 after >5 years from diagnosis. In patients with granulomatosis with polyangiitis (GPA), mortality rates ranged from 3.3 to 8.2 in the first year after diagnosis and from 0.7 to 4.5 after >5 years from diagnosis.

Conclusions: The FAIRVASC infrastructure is a reliable tool to query multiple AAV registries for assessing long-term clinical outcomes of AAV in a large number of patients, in a privacy-compliant manner.

Disclosures: None.

	EGPA				MPA				GPA			
Registries	**<1 y**	**1-2 y**	**2-5y**	**>5 y**	**<1 y**	**1-2 y**	**2-5y**	**>5 y**	**<1 y**	**1-2 y**	**2-5y**	**>5 y**
RKD (Rep. of Ireland)	0	0	0	2.5 (0.1-5.0)	8.1 (5.2-11.0)	5.3 (2.9-7.8)	7.2 (5.2-9.1)	7.4 (5.6-9.2)	3.8 (1.7-6.0)	0.7 (-0.3-1.6)	1.6 (0.7-2.5)	3.3 (2.5-4.1)
GFEV (France)	3.3 (1.6-5.0)	1.8 (0.5-3.2)	0.8 (0.2-1.4)	2.2 (1.4-3.0)	6.7 (4.3-9.2)	1.8 (0.5-3.6)	2.8 (1.7-3.9)	3.9 (2.8-5.0)	3.8 (2.6-5.0)	1.4 (0.6-2.1)	1.3 (0.9-1.7)	1.8 (1.4-2.2)
ANCA (Czech Rep.)	-	-	-	-	14.2 (8.4-20.0)	3.3 (0.1-6.5)	4.3 (1.5-7.1)	4.7 (1.0-8.5)	6.2 (1.9-10.4)	4.8 (0.6-9.0)	4.1 (0.8-7.4)	0.7 (-0.7-2.1)
PolVas (Poland)	0	1.0 (-0.9-2.8)	0	0	10.9 (5.6-16.2)	4.1 (0.5-7.8)	1.4 (-0.2-2.9)	4.4 (1.2-7.7)	3.3 (1.8-4.7)	2.0 (0.7-3.2)	1.3 (0.6-1.9)	1.4 (0.9-1.9)
Skane (Sweden)	0	0	0	2.2 (-0.3-4.8)	22.3 (14.5-30.2)	8.2 (3.1-13.3)	10.0 (6.3-13.7)	7.0 (4.6-9.3)	8.2 (4.1-12.4)	5.3 (1.8-8.8)	3.7 (1.9-5.5)	4.5 (3.1-5.8)
Italivas (Italy)	-	-	-	-	-	-	-	-	-	-	-	-
GeVas (Germany)	-	-	-	-	-	-	-	-	-	-	-	-

Table 1. Mortality rate (cases/100 person years with 95% CI) over FAIRVASC registries.

PT-3B-54

Incidence, Prevalence and Mortality of Eosinophilic Granulomatosis with Polyangiitis (EGPA) in England: A Retrospective Cohort Study

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Background/Objectives: Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare disorder associated with high mortality if untreated. We conducted a retrospective cohort analysis of EGPA epidemiology using linked electronic health records (EHR) databases in England.

Methods: The study period was 01 January 2006 to 28 February 2019, with follow up until 28 February 2020. The Clinical Practice Research Datalink (CPRD) Aurum database contains EHR collected during routine general practitioner (GP) primary care visits at 1489 practices, and is linked with Hospital Episode Statistics (HES; containing diagnoses, inpatient and outpatient visits, and procedures) and the Office for National Statistics death registration data (date, place and cause of death). Patients with a first EGPA diagnosis (index date [ID]) at any time during the study period (incidence cohort) and at any time (prevalence cohort) were identified from CPRD Aurum or HES records (2006–2019). Patients were required to have ≥1 year of medical records before the first EGPA diagnosis (ID). Follow up was from ID until death, deregistration or last data collection from the GP practice, or end of the study period, whichever occurred first. We assessed the incidence and prevalence of EGPA, and primary causes of death; standardised mortality ratios (SMR) were calculated using national mortality rates.

Results: There were 486 incident cases during the study period (3.04 [95% CI 2.77; 3.32] cases per million per year), with no considerable differences between sexes or over time. There were 729 prevalent cases during the study period, corresponding to 2.7 (95% CI 2.5, 2.9) cases per 100,000, steadily increasing from 1.9 (1.6, 2.1) in 2006 to 3.1 (2.8, 3.4) in 2015, and remaining at 3.1 through 2019; the increase over time was greater in women. Within the incident cohort, the mean (SD) age of patients at ID was 57.9 (15.2) years; 92.6% were ≥35 years old; 50.2% were women and 33.3% were from the lower quintiles of socioeconomic deprivation (Quintile 4 or 5; most deprived). Mean (SD) follow-up was 5.4 (3.7) years. During follow-up, 98 (20.2%) incident patients died. Patients with EGPA had a 2.3-times higher mortality rate than the age-adjusted national population (standardised mortality ratio: 2.3 [95% CI: 1.9, 2.8]; **Table**). The leading cause of death was circulatory/cardiovascular diseases (29.6%), with 2.6 times more deaths than the general population.

Table. Cause-specific standardised mortality ratio (95% CI)

Deaths	Total study period (2006–2020)			
	Observed deaths, n	Expected deaths, n	Standardized mortality ratio	95% CI
All-cause	98	42.2	2.3	1.9, 2.8
Diseases of the circulatory/ cardiovascular system	29	11.2	2.6	1.7, 3.7
Neoplasms	16	13.1	1.2	0.7, 2.0
Diseases of the respiratory system	15	5.3	2.8	1.6, 4.7
Diseases of the musculoskeletal system and connective tissue	13[a]	0.3	40.8	21.7, 69.8
Diseases of the digestive system	9	2.0	4.6	2.1, 8.7
Other	12	6.9	1.7	0.9, 3.0

[a]11 of these listed EGPA as cause of death
CI, confidence interval

Conclusions: Incidence and prevalence of EGPA in England were similar to published literature. In patients with EGPA, mortality was more than twice that of the general population; circulatory/cardiovascular diseases were the leading recorded cause of death, in line with previous studies. Although these data cannot ascertain that EGPA was the cause of circulatory/cardiovascular diseases, early evaluation of cardiac involvement and more effective treatments earlier in the patient pathway are needed to manage these conditions.

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PT-3B-55

Projecting the Impact of Standard, Reduced-Dose, and Minimal-Dose Glucocorticoid Regimens in the Treatment of ANCA-Associated Vasculitis using Simulation Modeling

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Background/ Objectives: Glucocorticoids (GCs) remain a cornerstone of treatment of ANCA-associated vasculitis (AAV) but predispose people to infectious, metabolic, and other toxicities. We projected the long-term clinical outcomes associated with different GC treatment strategies for AAV using AAV-Sim, a previously validated microsimulation model.

Methods: At model start, all individuals are in remission without diabetes. Each month, individuals in the model can transition between active (e.g., major/minor relapse) or inactive AAV states and are at risk of complications and death. Demographics, disease-specific characteristics, and monthly transition probabilities are derived from relevant literature and stratified by demographic, disease-specific (e.g., sex, ANCA type), and treatment characteristics. The GC regimen impacts risk of incident diabetes and severe infection; diabetes also directly increases the risk of severe infection, end-stage renal disease, and mortality (**Table**). In combination with fixed-dose rituximab (every 6 months), we evaluated 3 GC treatment strategies for major disease relapse: 1) **Standard**: prednisone 1 mg/kg daily, tapering to 10 mg daily by month 6, 2) **Reduced-dose**: prednisone 0.5 mg/kg daily, discontinuing by month 6, and 3) **Minimal** in conjunction with avacopan. We projected the outcomes of major and minor relapse, incident diabetes mellitus, ≥1 severe infection, end-stage renal disease, and death over 5 years.

Results: Over 5 years, among all individuals, the projected percentage with incident diabetes (5.9% vs. 4.8% vs. 4.1%) and ≥1 severe infection (34.5% vs. 34.2% vs. 34.2%) would be higher in the standard vs. reduced-dose vs. minimal GC strategies, respectively (**Table**). Cumulative incidence of death would be slightly higher in the standard GC group (9.2% vs. 9.0% with the other GC regimens). The GC-sparing benefits with regard to diabetes would be greater in PR3- vs. MPO-ANCA positive individuals (incident diabetes in 6.5% vs. 5.3% vs. 4.1% in PR3(+) versus 5.4% vs. 4.7% vs. 4.1% in MPO(+) individuals across GC regimens), owing largely to the greater probability of both major and minor relapse in those with PR3-ANCA positivity and subsequent increased GC exposure.

Conclusions: Over 5 years, an AAV treatment strategy that uses minimal GCs would be associated with lower cumulative incidence of diabetes and slightly reduced cumulative incidence of severe infection. The GC-sparing benefits would be most notable in people at highest risk of relapse (e.g., PR3-ANCA positivity). These findings highlight the importance of GC-sparing strategies and the need for studies that identify people most likely to benefit.

Input Parameter	Base-Case Monthly Transition Probability								
Major relapse	PR3-ANCA/MPO-ANCA			0.0017/0.0009					
Minor relapse	PR3-ANCA/MPO-ANCA			0.0029/0.0015					
	Standard GCs			Reduced-Dose GCs			Minimal GCs		
Diabetes*	0.0555			0.0229			0.0008		
Severe infection*	No Diabetes	Diabetes		No Diabetes	Diabetes		No Diabetes	Diabetes	
	0.0310	0.0459		0.0247	0.0365		0.0111	0.0166	
	Percentage with Model-Projected Outcome								
	Standard GCs			Reduced-Dose GCs			Minimal GCs		
Model-Projected Outcome	All	PR3-ANCA	MPO-ANCA	All	PR3-ANCA	MPO-ANCA	All	PR3-ANCA	MPO-ANCA
Minor Relapse	11.7	14.5	7.7	11.7	14.5	7.7	11.7	14.4	7.5
Major Relapse	7.2	8.9	4.6	7.1	9.1	4.6	7.1	8.9	4.5
Severe Infection	34.5	34.5	34.3	34.2	34.3	34.0	34.2	33.8	33.7
End-Stage Renal Disease	0.6	0.5	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Incident Diabetes	5.9	6.5	5.4	4.8	5.3	4.7	4.1	4.1	4.1
Death	9.2	8.9	9.1	9.0	8.9	9.2	9.0	8.9	9.1

*Risk based on age 45-64 with active disease with no end-stage renal disease

Table. Sample input parameters and 5-year model-projected outcomes by glucocorticoid tapering schedule for major relapse (standard vs. reduced-dose vs. minimal) and ANCA type.

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1. *Arthritis Care Res.* 2023;75(9):1976-1985.
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Poster Tour 4B: Mechanisms of Disease

PT-4B-56

Molecular and Immune Pathways in ANCA-associated Glomerulonephritis

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Background: ANCA-associated glomerulonephritis (AAGN) is a common manifestation of ANCA-associated vasculitis. Molecular characterization of kidney involvement in patients with AAGN has the potential of identifying unique molecular pathways associated with local tissue inflammation and injury. This study aimed to unravel the major molecular and cellular pathways associated with AAGN.

Methods: Whole-tissue RNA-sequencing was performed on kidney biopsy samples of 23 patients with AAGN, and 5 healthy kidney donors. After quality control, differential expression (DE) analysis was performed using generalized linear models correcting for number of genes and processing effects. To identify molecular pathways and immune cells associated with AAGN, Ingenuity Pathway Analysis and gene-set enrichment analysis (GSEA) were done, respectively. GSEA was performed using a single-cell RNAseq dataset generated from kidneys of patients with active lupus nephritis (LN).

Results: Patients' clinical and demographic characteristics are depicted in **Table 1**. Most patients were female (13/23), White (21/23), and had a median age of 58 years. Most patients had granulomatosis with polyangiitis.

DE analysis demonstrated 1917 upregulated and 1500 downregulated genes. Pathway analysis revealed multiple activated pathways including pathogen-induced cytokine storm signalling, macrophage classical activation signalling, T-helper 1, IL-8 signalling, and complement. Downregulated pathways included programmed death/ligand (PD-1/PDL-1) signalling, and macrophage-stimulating protein signaling. Predicted activated upstream regulators included tissue necrosis factor, interferon alpha, nuclear factor-κB, and interleukin-1B (IL1B). Predicted inhibited upstream regulators included IL-10 receptor, complement receptor 1 like, and IL1 receptor antagonist.

In AAGN, GSEA suggested expansion of most immune cell subsets encountered in LN kidneys including $CD56^{dim}$ natural killer cells, memory CD4+ T-cells, cytotoxic T lymphocytes, γδ T-cells, circulating CD16 monocytes, phagocytic and proinflammatory macrophages, dendritic cells, naïve B-cells, memory B-cells, and age-associated B-cells.

Conclusions: Analysis of mRNA expression in kidneys of patients with AAGN reveals many differentially expressed genes and upregulated immune cells. Taken together, these findings suggest a complex network of molecular pathways and immune cells in AAGN.

Disclosures: This work was supported by The Gilead Research Scholars in Rheumatology award.

Table 1. Patient and Disease Characteristics

Age at biopsy, median (IQR)	58 (41-68)
% Female	59%
% White	95%
Newly diagnosed	95%
ANCA ELISA	
anti-PR3	43% (10/22)
anti-MPO	43% (10/22)
both positive	5% (1/22)
negative	5% (1/22)
Phenotype	
GPA	52% (12/23)
MPA	35% (8/23)
EGPA	13% (3/23)
Serum Creatinine, average ±SD	3.6 ±2.9
Proteinuria median(g/day or g/g) (IQR)	0.58 (0.12-1.59)

Abbreviations: ANCA: antineutrophil cytoplasmic antibodies. PR3: proteinase 3. MPO: myeloperoxidase. c-ANCA: cytoplasmic ANCA. P-ANCA: perinuclear ANCA. GPA: granulomatosis with polyangiitis. MPA: microscopic polyangiititis. EGPA: eosinophilic GPA

PT-4B-57

Drug exposure and subsequent diagnosis with ANCA-associated vasculitis – A population-based case-control study

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Objective: To determine if prior exposure to certain drugs is associated with increased risk of ANCA associated vasculitis (AAV).

Patients and Method: We performed a population-based case–control study including patients with AAV diagnosed between 2006 and 2019 from a defined geographic area in southern Sweden. For each case, we identified 10 controls randomly sampled from the background general population, matched for age, sex and residential area. Using the unique personal identification numbers, data on drug exposure, for cases and controls, were retrieved from Swedish Prescribed Drug Register (SPDR). The SPDR includes all pharmaceutical prescription after July 2005 using the Anatomical Therapeutic Chemical codes. Exposure was defined as purchase of at least one prescription of corresponding drug during time prior to the date of diagnosis of AAV (and the index date for controls). A conditional logistic regression model was fitted. To reduce risk of reverse causality, a wash-out time of 6 months was applied (i.e., purchases within 6 months prior to date of diagnosis/index date were excluded).

Results: A total of 168 cases (females 77, 45.8%) and 1763 controls (females 808, 45.8%) were included. PR3 and MPO-ANCA were positive in 82 (48.8%) and 75 (44.6%) patients. All patients had a clinical diagnosis of small vessel vasculitis which was supported by histopathology, ANCA analysis and surrogate markers for vasculitis/granuloma. Patients were classified using the EMA algorithm into: GPA, MPA and EGPA in 86 (51.2%), 68 (40.5%) and 14 (8.3%), respectively.

ATC CODES	DRUG GROUPS	ALL PATIENTS (n=168)		MPO-AAV (n=75)		PR3-AAV (n=82)	
		OR	95% CI	OR	95% CI	OR	95% CI
A	Alimentary drugs and metabolism	1.02	[0.72, 1.45]	1.04	[0.62, 1.77]	0.97	[0.596, 1.578]
C	**Cardiovascular system**	**0.68**	**[0.47, 0.99]**	0.88	[0.5, 1.58]	**0.48**	**[0.28, 0.81]**
C10AA	**Statins**	0.75	[0.50, 1.12]	1.18	[0.7, 2.01]	**0.35**	**[0.17, 0.72]**
C03	**Diuretics**	**0.61**	**[0.40, 0.92]**	0.71	[0.41, 1.24]	**0.51**	**[0.27, 0.97]**
C07	Beta-blockers	0.68	[0.46, 1.11]	0.69	[0.41, 1.19]	0.69	[0.38, 1.23]
C08	Calcium antagonists	0.82	[0.53, 1.27]	1.14	[0.64, 2.03]	0.51	[0.24, 1.06]
C09	RAS blockers	0.78	[0.53, 1.16]	1.12	[0.66, 1.93]	**0.52**	**[0.28, 0.95]**
C09A	**ACE inhibitors**	0.7	[0.44, 1.1]	1.04	[0.58, 1.87]	**0.44**	**[0.21, 0.93]**
C09C	ARBs	0.96	[0.58, 1.59]	0.71	[0.33, 1.56]	1.25	[0.62, 2.51]
L	Antineoplastic and immunomodulator	1.11	[0.61, 2.02]	1.06	[0.47, 2.4]	1.06	[0.4, 2.76]
H	**Systemic hormone preparations**	**1.9**	**[1.35, 2.69]**	**2.22**	**[1.34, 3.68]**	1.3	[0.77, 2.2]
H02AB	**Glucocorticoids**	**2.02**	**[1.4, 2.9]**	**2.35**	**[1.39, 3.97]**	1.25	[0.7, 2.23]
H03A	**Thyroid hormones**	**1.96**	**[1.18, 3.24]**	**2.6**	**[1.33, 5.08]**	1.68	[0.75, 3.75]
H03B	Antithyroids	0.05	[0.001, 2.09]	0.043	N/A	0.04	N/A
J	**Antiinfectives**	0.97	[0.67, 1.4]	**1.95**	**[1, 3.83]**	**0.58**	**[0.36, 0.95]**
J01	**Antibacterials**	1.03	[0.72, 1.48]	**1.91**	**[1, 3.65]**	0.63	[0.39, 1.01]
J01C	**Tetracyclins**	1.3	[0.9, 1.88]	**1.84**	**[1.10, 3.06]**	0.62	[0.33, 1.02]
J01E	**Penicillins**	1.18	[0.84, 1.66]	**1.65**	**[0.96, 2.84]**	0.82	[0.51, 1.32]
J01M	Quinolones	*0.87*	*[0.54, 1.4]*	0.93	[0.48, 1.8]	0.9	[0.45, 1.81]
J05	**Antivirals**	**0.2**	**[0.05, 0.8]**	0.34	[0.08, 1.43]	**0.04**	N/A
J05AB	**Nucleosides and nucleotides**	**0.11**	**[0.02, 0.77]**	0.18	[0.03, 1.32]	**0.04**	N/A

Table. Odds ratios [95% confidence intervals] for the association between use of drugs and incidence of ANCA associated vasculitis (AAV). Estimates from conditional logistic regression models excluding any prescriptions within 6 months prior to AAV. ACE: Angiotensin converting enzyme, ARB: Angiotensin receptor blocker, RAS: Renin-angiotensin system.

With the 6-months wash-out period, the prior use of thyroid hormones was associated with increased risk of AAV (ORs 1.96 (95% CI 1.18-3.24) (Table). However, ORs of <1 were obtained for the exposure to cardiovascular (CV) drugs and antivirals (ORs 0.68 (95% CI 0.47-0.99) and 0.2 (95% CI 0.05-0.8), respectively. Exposure to certain drugs had different impact on subsequent development of MPO- vs. PR3-AAV. Glucocorticoid (GC) use prior to AAV had resulted in OR >1 but only in patients who later diagnosed with MPO-AAV. The exposure to anti-bacterial drugs and thyroid hormones was associated with increased risk of MPO-AAV only. On the contrary, exposure to CV drugs (statins, ACE inhibitors, diuretics) were only reducing risk of PR3-AAV. The prior use of antivirals was associated with reduced risk of AAV in the main analysis but not in antibody-specific analysis.

Discussion: This is the first pharmacoepidemiologic study investigating the association between development of AAV and prior drug exposure. The association of anti-bacterial agents with diagnosis of MPO-AAV is in line with our previous study on impact of infections on subsequent AAV diagnosis. The possible protective effect of CV drugs and antivirals is a novel finding for AAV. Patients with MPO-AAV may suffer a longer prodromal phase of disease or being treated for symptoms suggestive of a non-specific inflammatory disease and ORs in GC analysis are probably due to pre-diagnosis AAV manifestations rather than have a causative impact. Our study has a limitation of small sample size and limited power, further larger studies are needed to explore these associations.

PT-4B-58

The Relationship Between the Netosis Findings and Disease Activity in Behçet Disease

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Background/Objectives: Behçet disease (BD) has been classified among the variable vessel vasculitis, and neutrophil extracellular traps (NETs) have been claimed in the pathogenesis of BD [1]. We herein aimed to investigate the potential relationship between the NETosis findings and local and systemic disease activity in BD.

Methods: The study group was consisted of orally and/or systemically 30 active BD patients who met the ISG criteria and 10 healthy individuals. The patients with additional inflammatory conditions or using biologic agents were excluded. Serum and saliva samples were collected from the patients during their active (oral ulcer and/or systemic manifestations) and remission (no manifestations, normal acute phase reactants) periods cross-sectionally. Some of them were followed also longitudinally. Cell-free DNA (cf-DNA), neutrophil elastase (NE), myeloperoxidase (MPO) and citrullinated histon-3 (cit-H3) levels were measured as NETosis findings, and the results were adjusted according to the peripheral blood neutrophil counts (as the amount of biomarker per 1 million neutrophils). Unadjusted and adjusted levels were evaluated.

Results: Patient groups and control group were similar in terms of confounder factors. In active BD, serum cf-DNA and NE levels were found to be high ($p \leq 0.001$, $p < 0.05$), whereas adjusted serum MPO and cit-H3 levels were found to be low ($p \leq 0.001$, $p \leq 0.01$). In inactive BD, serum NE level were higher than controls ($p < 0.05$), while serum MPO, adjusted serum MPO and adjusted serum cit-H3 levels were lower than controls ($p < 0.05$, $p \leq 0.001$, $p < 0.05$, respectively). No difference was found in salivary NETosis findings between patient groups and control. Serum and saliva cf-DNA levels showed a decrease in longitudinal follow-up towards remission ($p \leq 0.01$, $p < 0.05$) (**Figure 1**). Similar results were also observed in vascular active patients. Serum and saliva cf-DNA positively correlated with C-reactive protein and erythrocyte sedimentation rate, while adjusted serum MPO and cit-H3 negatively corraleted ($p < 0.05$).

Conclusions: NETosis findings showed changes in association with systemic and/or local activity of BD patients in relation to the disease manifestations. Especially, cf-DNA levels potentially indicated the local and systemic disease activity, and NE level was high in both active and inactive periods. Changes of the findings after adjustment of the results according to the peripheral blood neutrophil counts may indicate that the NETosis findings detected in serum could be related to high neutrophil turnover in the active phase of the disease. Further studies are required to clarify the mechanism of the low adjusted serum MPO and cit-h3 levels, particularly in the active patients, and the biomarker potential of NETosis findings in BD.

References: 1. Le Joncour A et al. *Clin Immunol*. 2023;250:109318.

Disclosures: None.

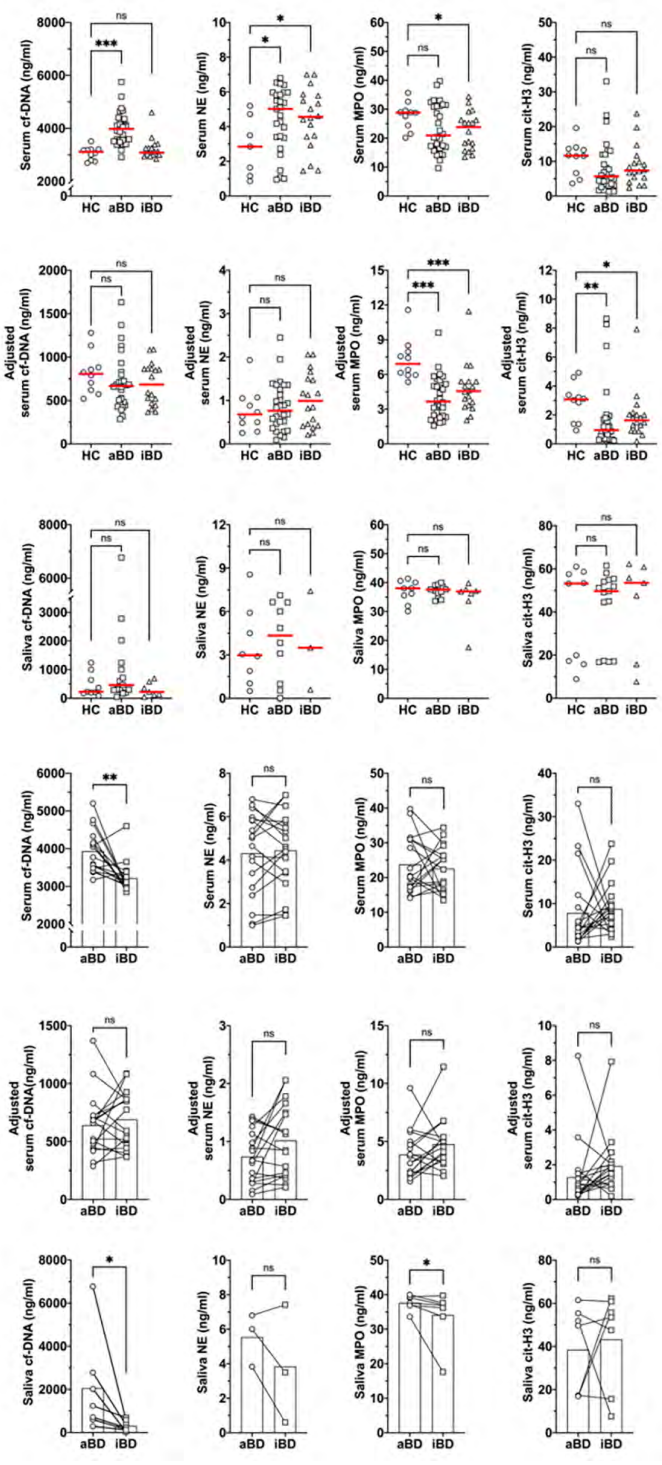

Figure 1. The levels of NETosis findings in groups and changing in longitudinally followed-up.

PT-4B-59

Hyperhomocysteinemia in takayasu arteritis - genetically defined or burden of the proinflammatory state?

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Background/objectives: Patients with Takayasu arteritis (TAK) present higher plasma homocysteine (Hcy) concentrations compared to controls, and elevated homocysteinemia has been shown to be a risk factor for ischemic arterial events (IAE) in TAK patients (1,2). This study aims to compare the frequency of single nucleotide polymorphisms (SNPs) of genes involved in the Hcy metabolism pathway between TAK patients and controls and to analyze associations with Hcy levels, TAK features and IAE.

Methods: This is a cross-sectional study including TAK patients and controls. We collected data about risk factors for hyperhomocysteinemia (HHcy), cardiovascular disease (CVD), and IAE in both groups. The following SNPs of the enzymes methylenetetrahydrofolate reductase (*MTHFR*) (e.g., C677T and A1298C), methionine synthase reductase (*MTRR*) (e.g., A66G), methionine synthetase (*MTR*) (e.g., A2756G) and reduced folate carrier (*RFC-1*) (e.g., G80A) were investigated by the Sanger sequencing technique, and plasma Hcy was measured by high-performance liquid chromatography.

Results: Seventy-three TAK patients and 71 controls with similar median age were included. TAK patients had a higher frequency of risk factors for CVD and HHCy, i.e., obesity, sedentarism, arterial hypertension, and proton pump inhibitor use ($p < 0.05$). However, they were also more frequently in use of folic acid, acetylsalicylic acid, and statins ($p < 0,0001$). IAE were observed in 31.5% of TA patients and only one control presented a previous cerebrovascular accident. There were no significant differences between both groups regarding the frequency of individual SNPs. Patients had higher Hcy levels than controls (13,85 ± 5,61 µmol/L vs. 8,61 ± 4,00 µmol/L; $p < 0,0001$); however, Hcy levels were neither associated with IAE in TAK patients nor with the carriage of any of the SNPs. Nevertheless, patients who presented both SNPs of the *MTHFR* gene in heterozygosis showed higher Hcy levels than those carrying the wildtype [19.03 ± 4.10 mmol/L vs. 13.39 ± 5.45 mmol/L; $p = 0.010$] while no difference was seen in controls ($p = 0.591$). In addition, no relations were observed between SNPs carriage and IAE in TAK, but there was a trend towards higher Hcy levels among patients in remission (11.53 ± 5.28 µmol/L vs. 14.62 ± 5.59 µmol/L; $p = 0.054$). Finally, TAK was an independent risk factor for HHcy [Odds ratio (OR) = 10.2; 95% confidence interval (CI): 4.162-25.002; $p < 0.0001$]. No continuous variables correlated with plasma Hyc concentration in the multivariate linear regression model.

Conclusions: This study confirms that TAK patients present a higher level of Hcy; however, HHyc is not due to a higher frequency of SNPs in genes encoding Hcy metabolism enzymes. HHcy found in TAK patients seems to be due to the TAK itself and not genetic factors. This study did not confirm the relation between higher Hcy levels and IAE in TA patients. The higher Hcy levels in TA might be due to the burden of chronic arterial inflammation in TAK. Further studies are needed to unravel the pathogenesis of HHyc in TAK.

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Disclosures: None.

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PT-4B-60

Induced pluripotent stem derived neutrophils from patients with ANCA vasculitis recapitulate genetic influence on *PRTN3* gene expression

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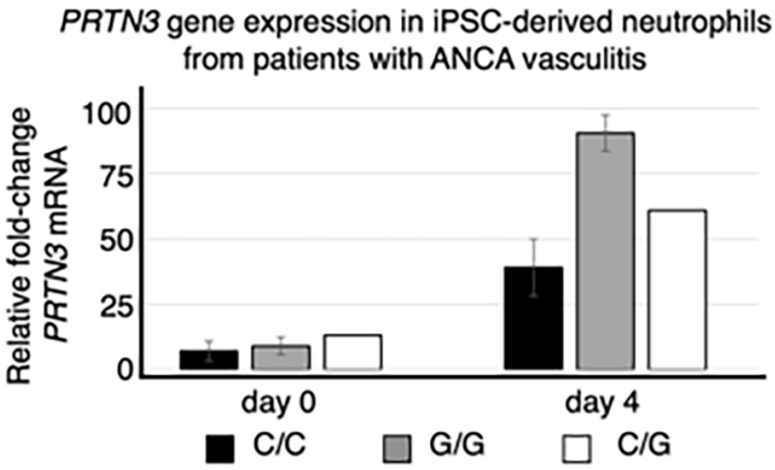
Background/ Objectives: A common characteristic of patients with ANCA vasculitis is elevated autoantigen gene expression. Elevated gene expression of *PRTN3* in patients is associated with a genetic variant (rs62132293) identified as a risk allele for PR3-ANCA (1) and risk allele for relapse among patients with PR3-ANCA disease (2). To test the hypothesis that the *PRTN3* risk allele directly impacts *PRTN3* gene expression we derived induced pluripotent stem cells (iPSCs) from patients with ANCA vasculitis who were homozygous for either the risk (G/G) or non-risk (C/C) allele or heterozygous (C/G).

Methods: Erythroblasts were expanded from peripheral blood mononuclear cells of 6 patients with ANCA vasculitis and reprogrammed into iPSCs using Sendai Virus encoding the Yamanaka reprogramming factors. Transduced cells were cultured on inactivated mouse embryonic fibroblast and after 2 weeks, colonies with typical stem cell morphology were expanded on Matrigel and chemically defined medium. Pluripotency was confirmed by immunofluorescent staining. Trilineage differentiation potential was evaluated with the TaqMan hPSC Scorecard Panel assay. For neutrophil differentiation, iPSC clones were differentiated into hematopoietic progenitor cells (HPCs) over 12 day culture in STEMdiff Hematopoietic medium. At day 12 HPCs were harvested and transferred to RPMI medium containing granulocyte colony stimulating factor (G-CSF) to induce neutrophil differentiation. Cells were collected on days 0-4 for cytospins, which were stained with Giemsa or used for immunofluorescence to detect MPO and PR3 protein. RNA was isolated on days 0-4, and *MPO* and *PRTN3* gene expression were measured by quantitative real time PCR (qRT-PCR).

Results: Six cell lines reprogrammed from patient erythroblasts expressed pluripotency markers indicating derivation of iPSCs. *In vitro* neutrophil differentiation of iPSCs resulted in neutrophil progenitors as early as day 1 of differentiation, and over 4 days of culture in G-CSF there was a progressive increase in cells with segmented nuclei, characteristic of mature neutrophils. MPO and PR3 protein and gene expression were detected starting at day 1 of neutrophil differentiation, and expression persisted over 4 days of culture. *PRTN3* gene expression was 2-fold greater in iPSC-derived neutrophils from patients homozygous for the risk variant (G/G) compared to expression in iPSC-derived neutrophils from patients homozygous for the non-risk variant (C/C). *PRTN3* gene expression was intermediate in heterozygous (C/G) iPSC-derived neutrophils (Figure).

Conclusions: Patient specific iPSCs that carry the *PRTN3* risk or non-risk variant recapitulate the pattern of *PRTN3* gene observed in patients. This supports a genetic basis for increased gene expression. These patient derived iPSCs will be valuable for testing strategies to suppress autoantigen gene expression.



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1. *Arthritis Rheumatol*. 2017;69(5):1054-1066.
2. *JCI Insight*. 2023;8(4):e166107.

Disclosures: None.

PT-4B-61

Transcriptomic and proteomic impact of blocking GM-CSF receptor with mavrilimumab versus blocking IL-6 receptor with tocilizumab on ex vivo-cultured arteries from patients with GCA

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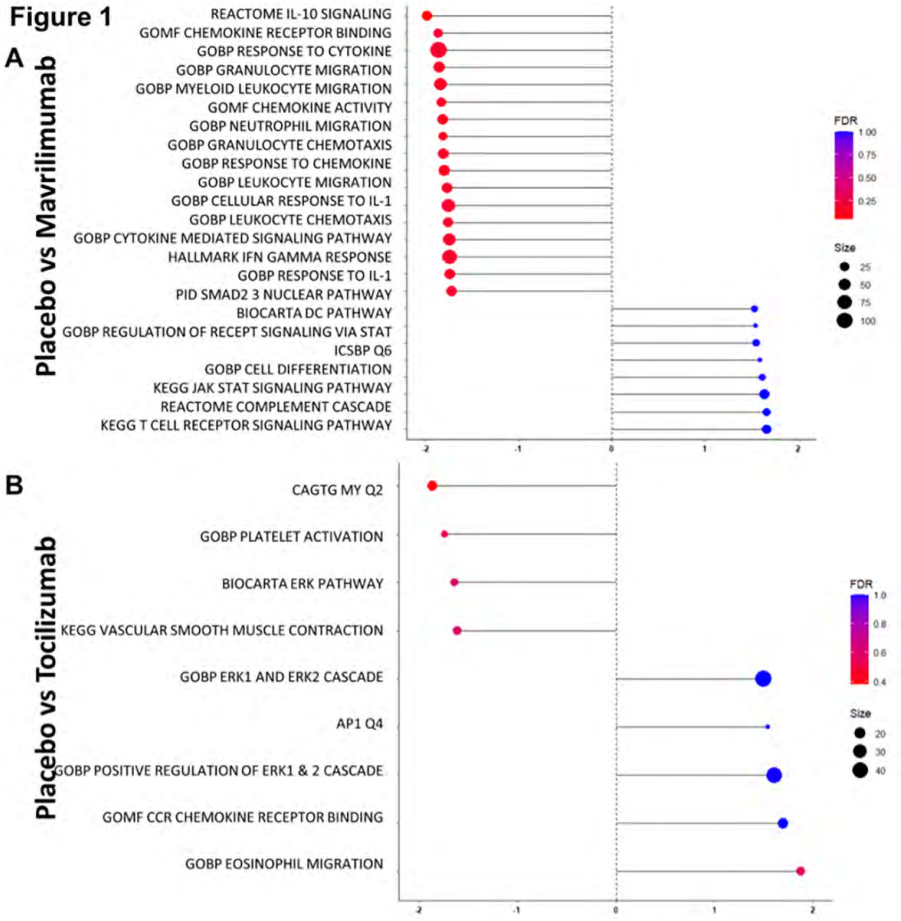
Background: After decades of glucocorticoid (GC) monotherapy and modest effect of adjuvants, TCZ has demonstrated efficacy in reducing relapses and sparing GC but complete discontinuation is successful in half of the patients only. Additional targeted therapies are emerging and are in advanced stages of development. Identifying the best treatment for patients requires a deeper understanding of the impact of targeted therapies on vascular inflammation.

Objectives: To investigate transcriptomic and proteomic changes induced by Mavrilimumab (MAV) or Tocilizumab (TCZ) in ex-vivo cultured arteries from patients with GCA.

Methods: Temporal artery sections obtained for diagnostic purposes from 27 patients with biopsy-proven GCA and 6 controls were cultured ex-vivo and exposed to placebo, MAV, or TCZ (both at 20 µg/mL) for 5 days. mRNA expression was analyzed with Nanostring Inflammation panel (250 transcripts) and validated by RT-PCR. Changes in tissue protein expression were determined by immunofluorescence and proteins in the supernatant were assessed with a human protein array (GS640, Raybiotech). Normalised data were analysed using R Studio 4.0.5, and paired Wilcoxon tests were applied to each comparison group. GSEAs were conducted with GSEA software (v4.3.2) using the pre-ranked modality and log2FC results as input data.

Figure 1



Results: 89 transcripts were differentially expressed between GCA-involved and control arteries. 21 transcripts were affected by MAV and 5 by TCZ. Differentially expressed genes were validated by RT-PCR with concordant results. Tissue expression of the proteins encoded by the transcripts more significantly affected by MAV (MRC1, CD40) showed similar differences. GSEA study revealed a potent effect of MAV on chemotaxis, IFNg, IL-6 and IL-10 dependent pathways (Fig1A) while TCZ impact was lower (Fig 1B). Proteomic analysis of the artery culture supernatants disclosed higher number of proteins regulated by MAV (111) compared to TCZ (21). Blocking GM-CSF receptor modulated proteins involved in chemotaxis, adhesion, and cytotoxicity, among others. Blocking IL6receptor mainly impacted proteins regulated by IL6 and IL12 pathways.

Conclusion: MAV and TCZ have different impact on cultured arteries from patients with GCA, with some overlapping effects. In our experimental conditions and with the transcript and protein sets analyzed, MAV has a more potent impact than TCZ downregulating inflammatory pathways. Investigating the impact of current and emerging targeted therapies on vascular inflammation may contribute to more tailored treatments for patients with GCA.

Disclosures: MCC: research grant from Kiniksa; consulting/educational fees from GSK, AstraZeneca, AbbVie and CSL-Vifor. JFP is employee/stockholder of Kiniksa Pharmaceuticals, and inventor on patent applications related to mavrilimumab. Funding: Kiniksa Pharmaceuticals, Ltd. MCC and MCB: AEI (PID2020-114909RB-I00); FK: ITN-HELICAL (MSC actions No813545).

PT-4B-62

Interleukin-6(IL-6)/IL-6 receptor and persistence of inflammation in Giant Cell Arteritis. Effects of IL-6 receptor blockade with tocilizumab

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Background/objectives: Blocking interleukin-6 (IL-6) receptor (IL-6R) with tocilizumab (TCZ) has demonstrated effectiveness in reducing Giant Cell Arteritis (GCA) flares and sparing glucocorticoids (GCs) but little is known about the functional role of IL-6 and the impact of TCZ on signalling pathways and cell responses in GCA vascular lesions. The impact of TCZ on imaging abnormalities is confounded by concomitant GC use and there is a concern about whether TCZ really modifies vascular inflammation or provides a valuable symptomatic relief only.

The aim of this study was to explore expression and functional roles of IL-6 and IL-6R in GCA and to assess effects of TCZ on GCA vascular lesions.

Methods: 29 GCA temporal artery biopsies (TABs) and 16 normal TABs were included. TAB sections were cultured with or without TCZ (10µg/mL, Roche) or with control IgG (10µg/mL, Sigma). mRNA encoding candidate molecules (n=40) according to the current pathogenesis model, which included transcription factors, cell markers, cytokines, chemokines, adhesion molecules, growth factors, metalloproteases, and matrix proteins, were explored by qRT-PCR and protein was assessed by immunofluorescence or western blot in tissue or ELISA in the supernatants. Adhesion and chemotaxis assays were also performed.

Results: IL-6 and IL-6 R expression by inflammatory cells and resident cells (vascular smooth muscle cells [VSMC] and endothelial cells) is increased in GCA tissue. TCZ treatment decreased expression/phosphorylation of STAT3 and reduced expression of STAT-3-dependent molecules including SOCS3, CCL-2, ICAM-1(Fig 1 A). Accordingly, TCZ reduced adhesion and chemotaxis of PBMC to primary VSMC and endothelial cells (HUVEC). In half of TABs, TCZ decreased and in the other half, increased STAT-1 (Fig 1 B-C) expression/phosphorylation and expression of STAT-1- dependent chemokines including CXCL9 and CXCL10.

A

Candidate molecule	TCZ/UNT	TCZ/IgG
CD163	0.83 *	0.74 **
STAT1	1.21	1.13
STAT3	0.81 *	0.98
CCL2	0.82	0.84 *
CXCL9	1.65 *	1.66
CXCL10	6.06 *	2.41
SOCS3	0.87 *	0.88 *
ICAM1	1.09	0.89 *
MMP3	1.05	0.88 *

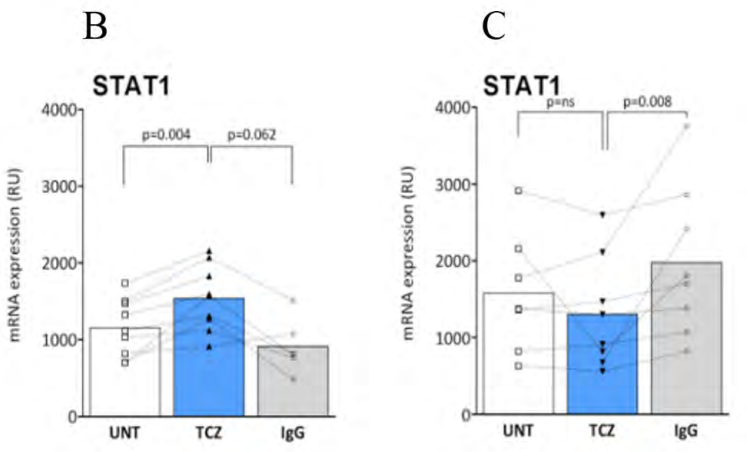

Figure 1. mRNA expression (ratio) of most relevant candidate molecules (A) and mRNA expression of STAT1 (B, C) in GCA cultured arteries treated with or without TCZ or non-immune IgG. STAT1 results are separated according to whether IL6 blockade increased (B) or decreased (C) STAT1 mRNA levels.

Conclusions: Our results indicate that TCZ has an impact on relevant inflammatory pathways in GCA tissue, probably resulting in decreased recruitment of inflammatory cells into lesions. Response was not homogeneous and about half of the patients are able to activate alternative inflammatory pathways in their lesions as a potential escape mechanism to TCZ.

Disclosures: MCC: research grant from Kiniksa; consulting/educational fees from GSK, AstraZenecaA AbbVie and CSL-Vifor. Funded by AEI (PID2020-114909RB-I00) and the Vasculitis Foundation; FK: ITN-HELICAL (MSCA No.813545).

Poster Tour 1C: Mechanisms of Disease

PT-1C-63

Complement activation in anti-GBM disease before and after treatment with imlifidase

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Background: The involvement of the complement system in anti-glomerular basement membrane (GBM) disease is well known, but in-completely characterized. The ability of autoantibodies to trigger the classical pathway is evident, but the lectin and alternative pathway also appears to be of importance (Tang et al., 2023). We studied complement activation in patients treated with imlifidase, which leads to rapid IgG depletion, using prospectively collected samples from a clinical trial, to elucidate the role of complement in anti-GBM disease.

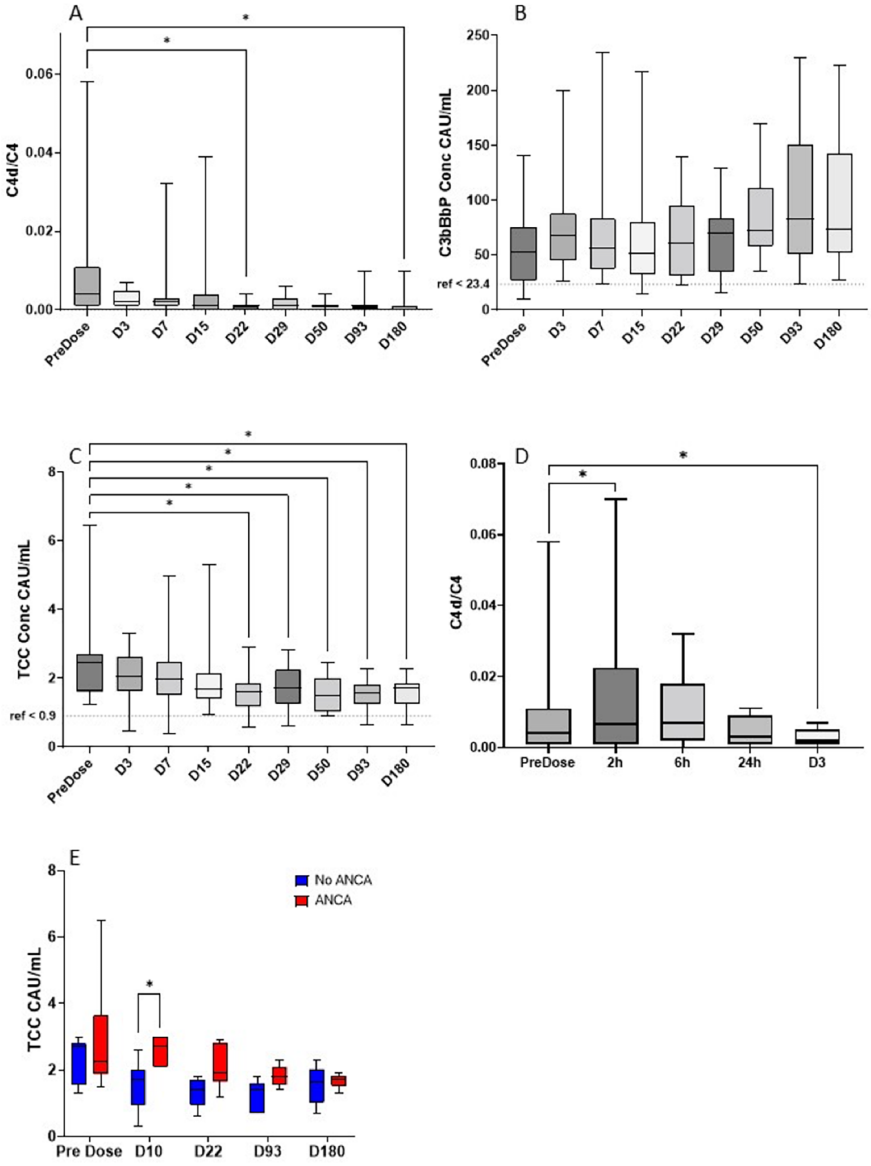

Figure 1 Products of complement activation (C4d/C4 (A), C3bBbP (B) and TCC (C)) in anti-GBM disease patients in the GOOD-IDES-01 trial. C4d/C4 before and immediately after treatment with Imlifidase for the entire group (D). TCC levels in patients double positive for ANCA (red) or single positive for anti-GBM (blue) (E). Significant differences ($p<0.05$) according to Friedmann's test (A-C), Wilcoxon's signed rank test (D) and Mann Whitney U-test (E) are indicated by *.

Methods: The GOOD-IDES-01 trial included 15 anti-GBM disease patients treated with one dose imlifidase in addition to standard therapy with 6 months follow-up (Uhlin et al., 2022). C4 and complement activation products (C4d, C3bBbP and terminal complement complex (TCC)) were measured using ELISA based on monoclonals reacting with neoepitopes formed during activation. A C4d/C4 ratio was calculated to correct for removal of C4d by plasmapheresis. Friedman's test, Wilcoxon's signed rank test and Mann-Whitney U-test were used for statistical analysis.

Results: The ratio of C4d/C4 decreased rapidly from its pre-dose level (Figure 1A). The level of TCC decreased more slowly and remained above the reference level throughout the trial (Figure 1B). C3bBbP was above the reference level before treatment and remained on similar levels throughout the trial (Figure 1C). Immediately following treatment with imlifidase an increase in C4d/C4 (0.004 vs 0.007, p=0.02), but not C3bBbP or TCC, was observed (Figure 1D). However, this increase was transient and on day 3 C4d/C4 was lower than before treatment with imlifidase (0.002 vs 0.004, p=0.03) (Figure 1D). Six patients in the GOOD-IDES-01 trial were double positive for ANCA and these patients showed a tendency to higher TCC levels compared to single positive anti-GBM patients (2.7 CAU/mL vs 1.7 CAU/mL day 10, *p*=0.005), but there were no differences in C4d/C4 or C3bBbP (Figure 1E).

Conclusions: Complement activation through the classical pathway ceased rapidly after imlifidase administration. Even though the activation of the total system decreased during the first 3 weeks of treatment, it remained elevated throughout the trial. The reason for this activation and its importance for disease progression and prognosis remain undetermined, but factors related to ANCA may be of importance in double positive patients.

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2. Uhlin, F., Szpirt, W., Kronbichler, A., Bruchfeld, A., Soveri, I., Rostaing, L., . . . Segelmark, M. (2022). Endopeptidase Cleavage of Anti-Glomerular Basement Membrane Antibodies in vivo in Severe Kidney Disease: An Open-Label Phase 2a Study. *J Am Soc Nephrol*. doi:10.1681/asn.2021111460

Disclosures: Linnéa Tyrberg: None.

Anna Blom: None.

Thomas Hellmark reports being a shareholder in Hansa Biopharma.

Mårten Segelmark reports being a consultant for Hansa Biopharma, Astra Zeneca and Viafor Pharma; and receiving research funding from Hansa Biopharma.

PT-1C-64

Increased miRNA-184 expression is linked to inflammatory cell death in Granulomatosis with Polyangiitis

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Background/ Objectives: Granulomatosis with polyangiitis (GPA) is characterized by extravascular necrotizing granulomatous inflammation and systemic anti-neutrophil cytoplasmic autoantibody (ANCA) – associated vasculitis[1]. Dysregulated cell death and tissue damage has major impact on perpetuating the chronic inflammation in GPA[2]. Preliminary work has shown that microRNA-184 (miR-184) is upregulated in GPA. In this study, we aimed to identify potential cellular sources of miRNA-184 in GPA. Furthermore, we investigated the role of miR-184 in the context of inflammatory cell death and potential regulation of the autoantigen proteinase 3 in granulocyte cell models.

Methods: NB4 cells were differentiated by all-trans retinoic acid for 24h. Granulocyte-like differentiation was analyzed by FACS, qPCR and western blot. Endogenous miR-184 expression was examined by qPCR. miR-184 and GPADH miRNA control was transfected using lipofection. Downregulation of target genes and proteins were analyzed by qPCR after 24h and by western blot after 48h. In U937 cells apoptosis and necroptosis was induced and miR-184 expression was analyzed by qPCR. Expression of cell death markers was confirmed by western blot. The effect of miR-184 inhibition on cell death was investigated by transfection of miRNA-184-inhibitor and confirmation of cell death marker expression by western blot.

Results: NB4 cells were differentiated into a CD11b+/CD14- granulocyte-like phenotype expressing PR3 mRNA and protein. Endogenous miR-184 expression was not found. Downregulation of GAPDH by control miRNA was validated on protein level. However, no downregulation of PR3 on mRNA level or protein level by miR-184 transfection was observed. In contrast, downregulation of AKT2 on mRNA and protein level by miR-184 was detected. We found expression of miR-184 in circulating mononuclear cells and granulocytes of the peripheral blood, but there was no significant difference between GPA and healthy controls. MiR-184 expression was increased in U937 cells after induction of necroptosis but not following apoptosis. In contrast, inhibition of miR-184 had no direct effect on cell death induction.

Conclusions: In this study we identified peripheral mononuclear cells and granulocytes as a source of miR-184. In addition, we showed that miR-184 regulates AKT2, but not PR3 mRNA in a granulocyte model. Moreover, we found a necroptosis-associated increase of miR-184 expression suggesting a potential link between up-regulated miR-184 and inflammatory cell death in GPA.

References:

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Disclosures: None.

PT-1C-65

Identification of Antibodies against Peroxidasin in Human and Experimental Glomerulonephritis

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Background / Objectives: Peroxidasin (Pxdn) is an extracellular matrix (ECM) haem peroxidase, primarily expressed in tissues undergoing active remodelling, such as during development, wound healing, and tissue repair. It functions by forming covalent crosslinks within type 4 collagen called sulfilimine bonds, contributing to the structural integrity and stability of the ECM whilst also providing immune privilege (1). Autoantibodies to peroxidasin have previously been identified in patients with anti-glomerular basement (GBM) disease and MPO-ANCA associated vasculitis (MPO-AAV) (2).

Methods: We utilized ELISA to quantify circulating anti-Pxdn IgG in patient sera (anti-GBM disease, AAV) and in an experimental autoimmune glomerulonephritis (EAG) rat model. Recombinant rat peroxidasin (expressed in HEK293 cells) and commercial human peroxidasin (Origene) were used for ELISA coating. Antibody specificity was validated via immunoblotting. Kidney tissue expreesion of Pxdn and smooth muscle actin (SMA) was assessed using indirect immunofluorescence (IF).

Results: Circulating anti-Pxdn IgG antibodies were detected in 29.4% of anti-GBM disease patients (15/51), 14.2% of active MPO-AAV patients (2/14), and no active PR3-AAV patients (0/6) (Fig 1A). In EAG rats, anti-Pxdn IgG was detected by day 28 (peak glomerular injury) in 86.7% (13/15) of rats (Fig 1B). Notably, anti-Pxdn antibodies emerged later than anti-α3(IV)NC1 antibodies, detectable from day 7. Immunofluorescence in EAG kidney tissue revealed Pxdn expression in areas of glomerular injury and crescent formation with increased expression as glomerular injury worsened. Pxdn partially co-localised with SMA (Fig 1C).

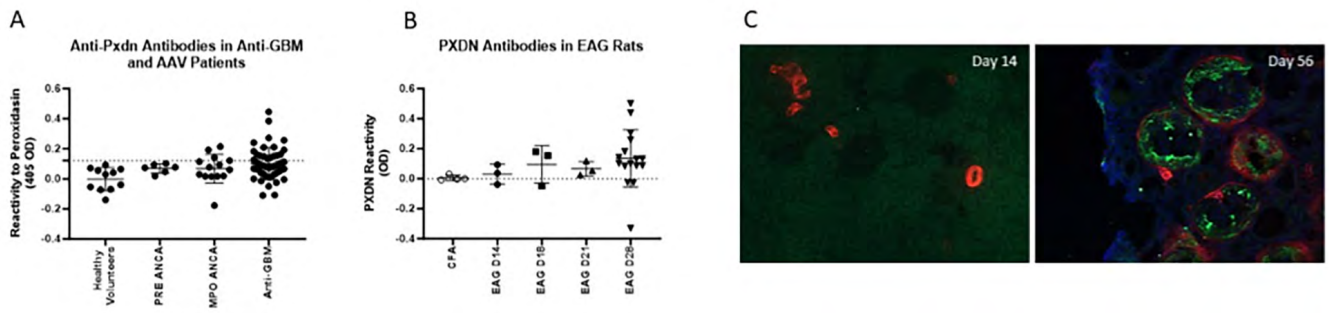

Figure 1. (A) Circulating anti-pxdn antibodies in patients with anti-GBM disease and AAV. (B) Circulating anti-pxdn antibodies in EAG rats. (C) Glomerular expression of pxdn and SMA 14 and 56 days after EAG induction. Original magnification 20x, Pxdn-green SMA-red

(A+B) Dotted line represents mean +2sd for HV and CFA respectively.

Conclusions: We confirm the presence of anti-Pxdn antibodies in patients with glomerular disease. In EAG, the emergence of anti-Pxdn antibodies followed α3(IV)NC1 antibodies, and glomerular Pxdn expression manifested only post-disease onset, thus, we suggest anti-Pxdn antibodies may arise by a process of inter-molecular epitope spreading in the diseased glomerulus.

References:

1. Bhave, G et al. Nat. Chem. Biol. 8:784–790.
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Disclosures: None.

PT-1C-66

Comparative analysis of phenotypic and functional properties of LDNs in AAV, sepsis and lung cancer patients

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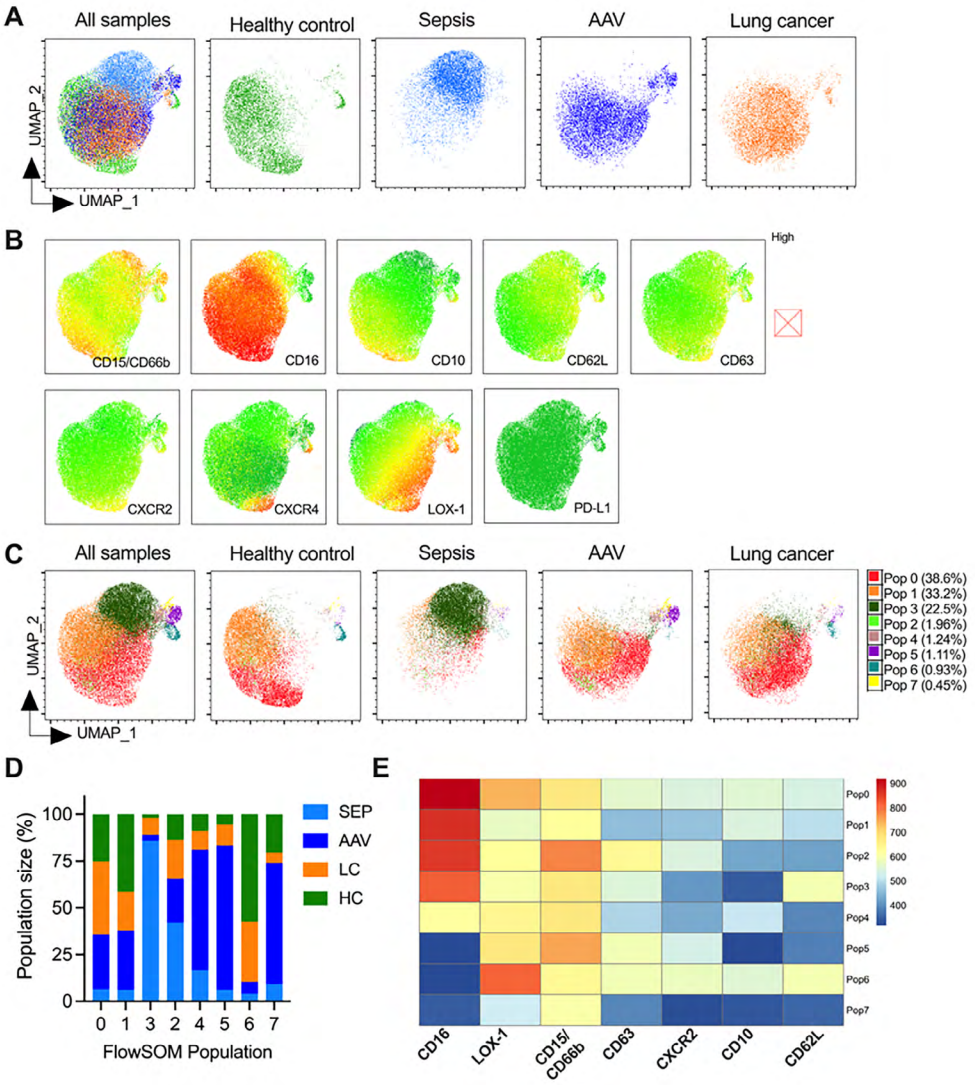
Background: Aberrant neutrophil activation is one of the key contributing factors in the ANCA vasculitis (AAV) immunopathology. A distinct subset of neutrophils is increased in AAV patients and associated with disease severity. This neutrophil subset is termed low-density neutrophils (LDNs), because they appear in the PBMC fraction of density-separated blood. LDNs have been reported in several conditions including sepsis, cancer and infection and are reported to perform distinct functions. However, it is yet unknown whether these populations are merely a response to emergency granulopoiesis or distinct neutrophil subsets within disease-specific adaptations. Therefore, we have applied a similar approach to isolating and studying these cells in different inflammatory conditions to understand whether LDN populations in AAV patients differ from those in sepsis and cancer patients. We hypothesized that these neutrophil subsets represent a disease-specific response and possess distinct phenotypic and functional characteristics depending on the disease context.

Methods: LDNs and normal-density neutrophils (NDNs) were isolated using density separation and analysed by multiparametric flow cytometry in patients with active AAV, sepsis, lung cancer and healthy controls. The phenotyping panel included CD15, CD66b, CD16, CD10, CD62L, CD63, PD-L1, LOX-1, CXCR2 and CXCR4. We used dimensionality reduction technique to identify altered neutrophil populations in whole blood within each cohort. We subsequently identified the relative composition of altered phenotypic signatures in LDN and NDN populations within each cohort. We then assessed the production of reactive oxygen species (ROS), neutrophil extracellular traps (NETs) and MPO degranulation in LDNs and NDNs following PMA and fMLP stimulation using dihydrorhodamine123 DNA dye-based NETosis assay, and MPO ELISA respectively.

Results: We found that the frequency of LDNs and composition significantly differed between AAV, sepsis and lung cancer patients. CD62L expression is significantly upregulated in sepsis LDNs compared to AAV and sepsis. LDNs upregulate CD15 and CD63 expression and downregulate CD62L expression across all patient cohorts. UMAP analysis of whole blood neutrophils resulted in distinct clusters suggesting heterogeneity between the patient groups. Distinct disease-associated populations were identified in AAV patients. Upon further examination, these altered neutrophil phenotypes were found to be enriched in LDNs from AAV patients. In addition to phenotypic differences, our findings also suggest that LDNs possess distinct functional abilities in this disease, with LDNs from cancer patients displaying higher ROS production and sepsis LDNs displaying enhanced MPO degranulation.

Conclusion: Our findings suggest that LDNs from AAV, sepsis and lung cancer display unique disease-specific phenotypic and functional features.

Disclosures: None.



PT-1C-67

FTY720 ameliorates experimental MPO-ANCA-associated vasculitis by regulating fatty acid oxidation via the neutrophil PPARα-CPT1a pathway

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Objectives: Increasing studies demonstrated the importance of C5a and anti-neutrophil cytoplasmic antibody (ANCA)-induced neutrophil activation in the pathogenesis of ANCAassociated vasculitis (AAV) [1]. Sphingosine-1-phosphate (S1P) acts as a downstream effector molecule of C5a and enhances neutrophil activation induced by C5a and ANCA [2]. The current study investigated the role of a S1P receptor modulator FTY720 in a model of experimental autoimmune vasculitis (EAV) and further explored the immunometabolism-related mechanisms of FTY720 in modulating ANCA-induced neutrophil activation.

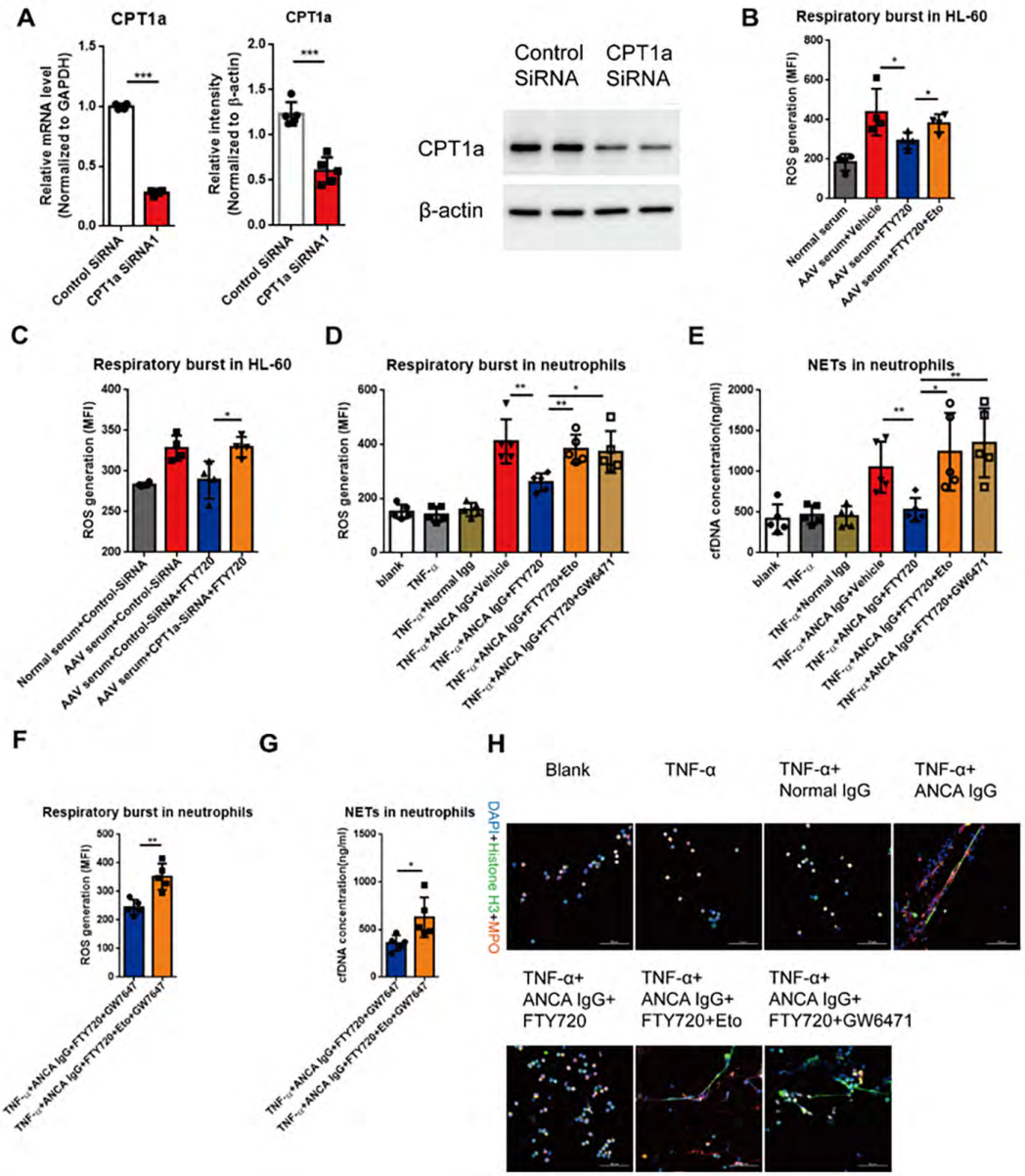

Fig 1: FTY720 exerted an inhibitory effect on ANCA-induced neutrophil activation via the PPARα-CPT1a pathway. (A) Determination of CPT1a knockdown efficiency by qPCR and Western blot. (B-C) The inhibitory effect of FTY720 on respiratory burst in differentiated HL-60 cells upon stimulation with 10% serum from AAV patients was reversed by CPT1 antagonist etomoxir (B) and CPT1a knockdown (C). (D-E) The effect of GW6471 (a PPARα antagonist) on the inhibition of FTY720 on respiratory burst (D) and NETs formation (E). (F-G) The effect of combination of GW7647 (a PPARα agonist) and etomoxir (a CPT1 inhibitor) on the inhibition of FTY720 on respiratory burst (F) and NETs formation (G). (H) Representative images of NETs formation with or without FTY720, etomoxir, GW6471 and GW7647 (Scale bar=50 μm).

Methods: The effects of FTY720 in EAV [3] were evaluated by quantifying hematuria, proteinuria, crescent formation and tubulointerstitial injury. RNA sequencing of renal cortex and gene enrichment analysis were performed. The proteins of key identified pathways were analyzed in neutrophils isolated from peripheral blood of patients with active AAV and normal controls. We assessed the effects of FTY720 on ANCA-induced neutrophil respiratory burst and neutrophil extracellular traps formation (NETosis) [4-5].

Results: FTY720 treatment significantly attenuated renal injury in EAV. RNA sequencing analysis of renal cortex demonstrated enhanced fatty acid oxidation (FAO) and peroxisome proliferators-activated receptors (PPAR) signaling in FTY720-treated rats. Compared with normal controls, patients with active AAV showed decreased FAO in neutrophils. FTY720-treated differentiated HL-60 cells showed increased expression of carnitine palmitoyltransferase 1A (CPT1a) and PPARα. Blocking or knockdown of CPT1a or PPARα in isolated human neutrophils and HL-60 cells reversed the inhibitory effect of FTY720 on ANCA-induced neutrophil respiratory burst and NETosis (Fig 1).

Conclusions: FTY720 attenuated renal injury in EAV through upregulating FAO via the PPARα-CPT1a pathway in neutrophils, offering potential immunometabolic targets in AAV treatment.

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5. Front Immunol. 2018;9:559.

Disclosures: None.

PT-1C-68

Dynamic alterations of non-classical and intermediate monocytes in patients with ANCA vasculitis

Dominic Ciavatta, Carolina A. Herrera, Eveline Y. Wu, Candace D. Henderson, Kristin B. Kennedy, Lauren Blazek, Yichun Hu, Susan L. Hogan, J. Charles Jennette, Meghan E. Free, Ronald Falk.

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Background/ Objectives: Monocyte subsets are key mediators of inflammation and implicated in the pathogenesis of ANCA vasculitis; however, it is unknown if the balance in monocyte subsets contributes to disease. We addressed whether alterations in circulating monocyte subset frequencies are accompanied by transcriptional changes that may implicate pro- or anti-inflammatory pathways during disease, and whether they are associated with renal disease.

Methods: Peripheral blood mononuclear cells (PBMC) were isolated from 53 patients with ANCA vasculitis and 31 healthy controls, according to IRB guidelines. Monocyte subsets (classical, intermediate, and non-classical) were isolated by fluorescence activated cell sorting based on surface expression of CD14 and CD16 from cryopreserved PBMCs of patients (4 active; 4 remission) and healthy controls (N=4). RNA was purified from isolated monocyte populations and analyzed by RNA sequencing. Peripheral blood and urinary monocyte subset frequencies and monocyte lymphocyte function-associated antigen (LFA-1; CD11a/CD18) surface protein expression were quantified by flow cytometry. Serum and urinary soluble intercellular adhesion molecule 1 (sICAM-1) levels were measured by ELISA.

Results: The frequency of classical monocytes was similar between patients and healthy controls. We confirmed, compared to healthy controls, the percentage of intermediate (pro-inflammatory) monocytes was increased during active disease (p=0.005) (1). We found a concomitant decrease in non-classical (anti-inflammatory) monocytes (p=0.009). RNA-seq analysis of purified populations of classical, intermediate, and non-classical monocytes revealed modest transcriptional differences between healthy controls and patients. However, gene set enrichment analysis of differentially expressed genes between intermediate and non-classical monocytes from active patients identified integrin signalling as the top significantly enriched pathway. We detected changes in integrin signaling by measuring surface expression of b2-integrin LFA-1 on monocyte subsets and found significantly less LFA-1 only on intermediate monocytes from patients with active disease compared to healthy controls (p=0.002). The ligand for LFA-1, sICAM-1, was significantly increased in the serum of ANCA vasculitis patients with active renal disease compared to healthy controls (p=0.0002). The increased sICAM-1 in active patients with renal disease prompted us to measure total CD14+ monocytes in urine. We found a striking increase in CD14+ monocytes in urine compared to peripheral blood of patients (p=0.001) but not in healthy controls. In patients, with active renal disease we observed elevated urinary sICAM-1 and the inflammatory marker soluble CD163.

Conclusions: The altered frequencies in monocyte subsets suggests the inflammatory state during active disease is promoted by alterations in pro- versus anti-inflammatory monocytes. Reduced LFA-1 on pro-inflammatory intermediate monocytes during active disease is consistent with an activated phenotype and is associated with renal inflammation.

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Disclosures: None.

PT-1C-69

PD-1, PD-L1 and PD-L2: performance of immune checkpoint molecules in ANCA vasculitis

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Background: The PD-1/PD-L1/PD-L2 axis known as the immune checkpoint (IC) pathway promotes immunotolerance [**1**]. Dysregulation of IC molecules has been described in several autoimmune diseases [**2**] [**3**], however, little is known about the role of ICs in anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). This study aims to assess the role of the IC pathway in the pathophysiology of AAV and to evaluate its potential as a biomarker of disease activity.

Methods: We recruited 88 AAV patients followed at our centre (42 acute and 46 remission phase). Then, we included 30 patients from another institution as an external validation cohort (16 acute and 14 remission stage). We collected serum and urine and separated peripheral blood mononuclear cells (PBMC) at the time of recruitment. We performed a lymphocyte stimulation test under 3 conditions: 1) without additional stimulation 2) stimulated with MPO or PR3 antigen 3) stimulated with phytohaematoglutinin. We obtained the cell culture supernatant by centrifugation. Using a multiplex assay, we measured the concentration of the soluble fraction of PD-1, PD-L1, and PD-L2 in serum(s), urine(u), and in the cell culture supernatant (SN) of AAV patients and healthy controls (HC). Finally, we analysed the expression of PD-1 and PD-L1 in kidney biopsies from 6 patients in the diagnostic phase by immunochemistry.

Results: The concentration of sPD-1 and sPD-L1 was significantly higher in AAV compared to HC ($p=0.007$ and $p<0.0001$). Regarding urine, we detected lower levels in uPD-1 and uPD-L2 in AAV compared to HC ($p<0.0001$ and $p=0.0075$). The serum and urine findings were confirmed in the validation cohort. Baseline (unstimulated) production of soluble PD1 by PBMCs from patients with AAV was lower compared to PBMCs from HC ($p= 0.0074$). In the same line, when stimulated with MPO or PR3, PBMCs from AAV patients produced less PD1 in comparison to HC ($p=0.04$). Regarding the histology, patients with more activity in the renal biopsy had fewer PD-1-positive interstitial cells and a lower staining intensity than patients with more chronic kidney biopsy lesions.

Conclusions: The alterations in the soluble components of the IC pathway described in this work suggest an alteration in the immunomodulation of the IC pathway in AAV. Moreover, the sPD-1/sPD-L1/sPDL-2 axis could be a good biomarker to detect active disease in ANCA vasculitis.

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Disclosures: None.

PT-1C-70

Overlapping macrophage profiles in PMR bursa and GCA temporal artery biopsies

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Background: Polymyalgia rheumatica (PMR), an inflammatory disease affecting the shoulder and hip girdles, co-occurs in 50% of giant cell arteritis (GCA) patients [1]. Glucocorticoids have remained the cornerstone treatment for GCA, although targeted therapies have emerged [2,3]. Nevertheless, relapses are still common, and half of the relapsing patients have PMR symptoms[4]. Ideally, novel therapies should treat both GCA and PMR. IL-6 targeted treatments for example, have been shown to be effective for both diseases [2,3].

Macrophages are major players in the immunopathology of GCA, whereas the immune pathology of PMR remains obscure. Here, we compared macrophage-related immune profiles in PMR- and GCA-affected tissues to identify shared therapeutic targets.

Methods: Subacromial bursa biopsies (SABB) from 12 patients with isolated PMR and temporal artery biopsies (TAB) from 10 patients with isolated GCA were included. To study macrophage phenotypes and functions, immunohistochemistry of SABB and TAB was focused on macrophage markers (CD68, CD86, CD64, CD206, folate receptor β(FRβ)) and cytokines (IL-1β, IL-6, IL-12, IL-23, TNF-α, GM-CSF, M-CSF), which were scored semi-quantitatively on a five-point scale (0–4) by two independent researchers: 0 = no positive cells, 1 = 0–1% estimated positive, 2 = > 1–20% positive, 3 = > 20–50% positive, 4 = > 50% positive. An average score was calculated. Statistical analysis was performed by the Mann Whitney U test. P values <0.05 were considered statistically significant.

Results: The number of CD68+ macrophages was comparable in TAB and PMR-affected bursa tissues. The distribution of M1/M2 markers and co-stimulatory molecules was similar in both types of tissue. Expression of GM-CSF, IL-1β, IL-23, M-CSF and TNF-α was comparable in GCA TAB and PMR SABB. Prominent expression of IL-6 and IL-12A was observed in GCA TAB, but these pro-inflammatory cytokines were even more intensely expressed in the PMR SABB (Fig.1).

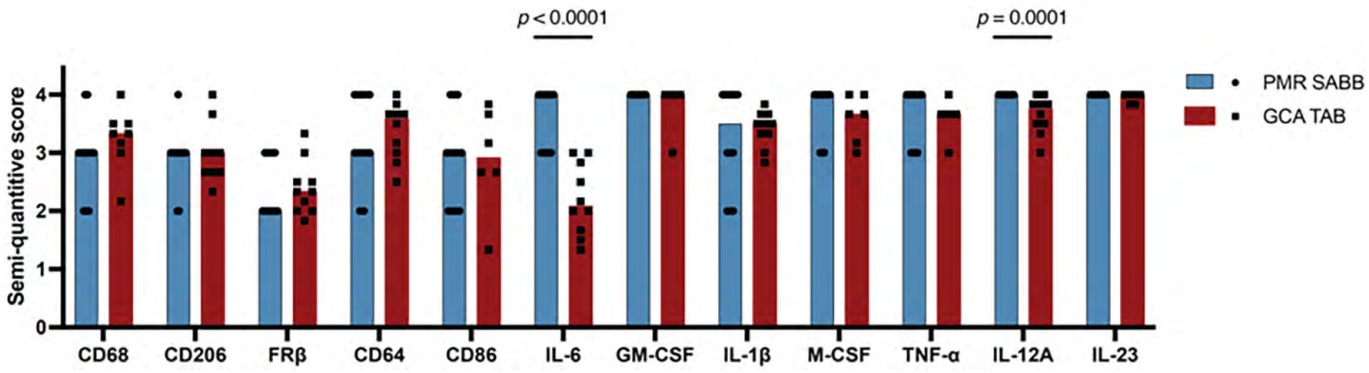

Fig.1 Semi-quantitative scores for macrophage markers and cytokines in PMR SABB and GCA TAB. PMR SABB: all markers and cytokines n=12. GCA TAB: CD68 n=7, CD206 n=8, CD86 n=6, CD64 n=10, FRβ n=10, IL-1β n=10, IL-6 n=10, IL-12 n=10, IL-23 n=10, TNF-α n=5, GM-CSF n=5, M-CSF n=5. SABB: subacromial bursa biopsy; TAB: temporal artery biopsy.

Conclusions: Macrophage immune profiles show substantial overlap in GCA and PMR tissue. Macrophage-related markers and cytokines may constitute therapeutic targets for both GCA and PMR.

Disclosures: K. van der Geest received research support from AbbVie.

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PT-1C-71

A macrophage-smooth muscle cells axis directs vascular remodeling via the activation of the EGFR pathway in giant cell arteritis

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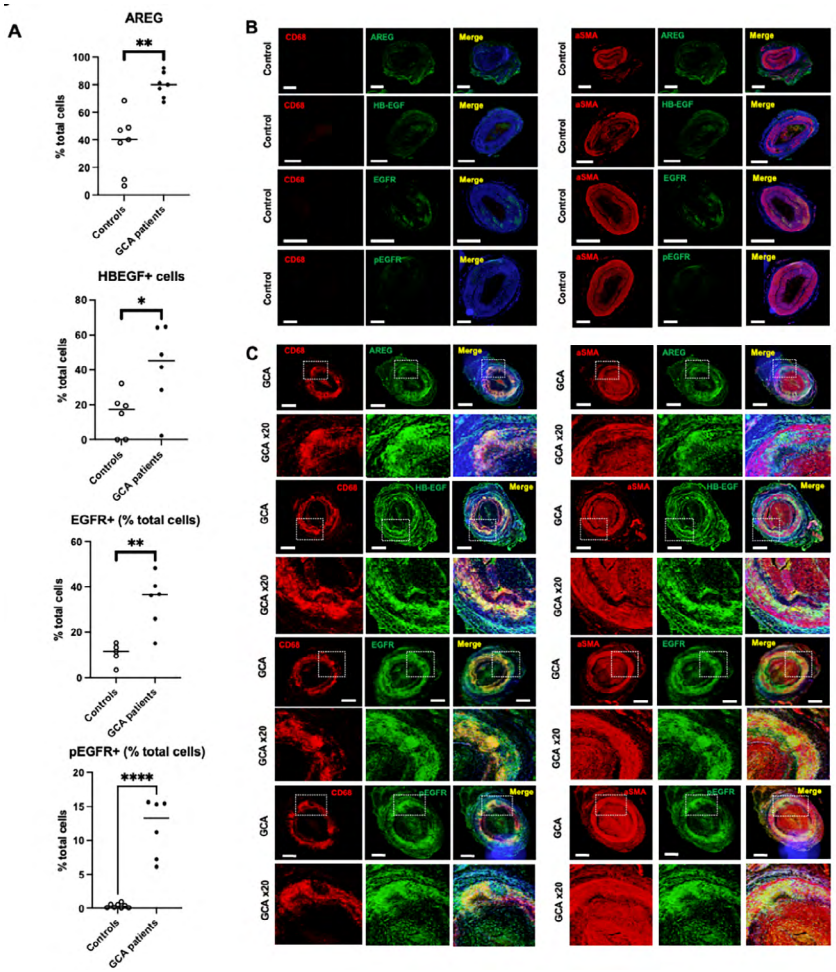
Introduction: Giant cell arteritis (GCA) is a granulomatous vasculitis affecting large vessels. The role of monocytes/macrophages and smooth muscle cells (SMC) appears to be prominent in the pathophysiology of the disease.

Standard treatment is based on glucocorticoids (GC), which are remarkably effective, but do not prevent further deterioration and major vascular damage. A better understanding of the pathophysiological mechanisms involved in GCA seems necessary for patient care.

The epidermal growth factor receptor (EGFR) signaling pathway may play a role in inflammatory diseases, SMC migration and proliferation. Heparin-binding epidermal growth factor (HBEGF) and amphiregulin (AREG) are the best known EGFR ligands and their role in human inflammatory diseases is emerging in the literature. The aim of this study was to investigate the role of the EGFR signaling pathway in the pathophysiology of GCA.



Material and methods: Human and cell line material was used in this study. Serum samples and temporal artery biopsies (TAB) were obtained from patients enrolled in the VASCO (VAScultitis COhort) study, a prospective cohort of patients with systemic vasculitis. Two cell lines were used: HAoSMC (human aortic SMC) and THP-1, human monocytes.

Results: Using multiplex immunohistochemical (IHC) technique and cellular quantification, we found that TAB from GCA patients expressed significantly higher levels of AREG, HBEGF, EGFR, and p-EGFR than controls. Colocalization images showed that AREG, HBEGF and EGFR were mainly expressed by infiltrating macrophages and HBEGF, EGFR and p-EGFR by SMC (Figure).

Using multiplex IHC technique and ELISA tests, we found that AREG, HBEGF, EGFR and pEGFR were significantly upregulated in macrophages than in THP-1, especially in pro-inflammatory M1-polarized macrophages. AREG and HBEGF levels were increased in the supernatant of M1-polarized macrophages and HBEGF in the supernatant of M2-polarized macrophages. AREG and HBEGF were not elevated in the serum of GCA patients, suggesting a paracrine and/or autocrine effect.

Stimulation of THP-1 cells with AREG or HBEGF induced p38 phosphorylation and activation of the MAPK pathway.

AREG and HBEGF did not increase inflammatory cytokine production by SMC but they increased SMC growth and migration in a live cell assay. AG1478, an EGFR inhibitor, completely stopped SMC migration and growth, suggesting a key role for the EGFR pathway in SMC proliferation and migration.

Conclusion: The EGFR pathway and its activation by AREG and HBEGF may play a key role in the pathophysiology of GCA, particularly in the vascular remodeling phase, which is responsible for late complications and is not well targeted by immunosuppressive therapies. A therapeutic strategy targeting the EGFR pathway or its ligands may lead to a GC-sparing effect and improved outcomes for GCA patients.

Disclosures: None.

PT-1C-72

Investigation of systemic Interferon type I responses in patients with giant cell arteritis and polymyalgia rheumatica

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Background/objectives: Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) are two inflammatory disorders within an overlapping spectrum. Interferon type I (IFN-I) plays a vital role in antiviral response and is involved in immunopathology of multiple auto-immune diseases such as systemic lupus erythematosus or systemic sclerosis (1). There is circumstantial evidence that IFN-I plays a role in GCA and/or PMR. This potentially can aid as a biomarker or personalized therapeutic target. This study investigates the presence of an IFN-I signature in patients with suspected GCA and PMR.

Methods: Patients with suspected GCA or PMR were included. Peripheral blood mononuclear cells (PMBCs) were isolated. Real-time quantitive PCR (qPCR) was performed to measure relative expression of five interferon stimulated genes (ISGs) identified by a literature study (*IFI44L, IFI44, IFIT1, MxA and RSAD2)*. A cumulative IFN-I score based on the ΔCT of the five genes was calculated for each patient, and patients were considered IFN-I positive if their score was one standard deviation higher than the mean score of the GCA negative group. Serum Luminex of IFN related protein markers CXCL10 and Galactin-9 will be performed to verify qPCR results (results available at time of conference).

Results: In total, 50 patients were included, of whom 11 were diagnosed with GCA (GCA+) and 9 were suspected of but not diagnosed with GCA (GCA-). Furthermore, 20 patients were diagnosed with PMR (PMR+) and 10 patients were diagnosed with PMR receiving glucocorticoids (GCs) at time of PMBC isolation (PMR-GC). Surprisingly, an IFN-I signature based on the IFN-I score was not found in any GCA+ or PMR+ patient, however two GCA- patients and one PMR-GC patient had a score higher than the mean +SD (9.96) of the GCA- group (Figure 1). Looking at individual genes, *MxA* was significantly decreased in the PMR-GC group when compared to the control group (p=0.041). For the other genes, no statistically significant differences were observed between GCA+, GCA-, PMR+ and PMR-GC groups.

Conclusions: An Interferon type I signature was not observed in GCA and PMR patients. The five selected ISGs do not appear to be increased in the circulation of GCA and/or PMR patients compared to patients who were suspected of but not diagnosed with GCA. Therefore, our findings imply that IFN-I might not play a role in systemic immunopathology.

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Disclosures: None.

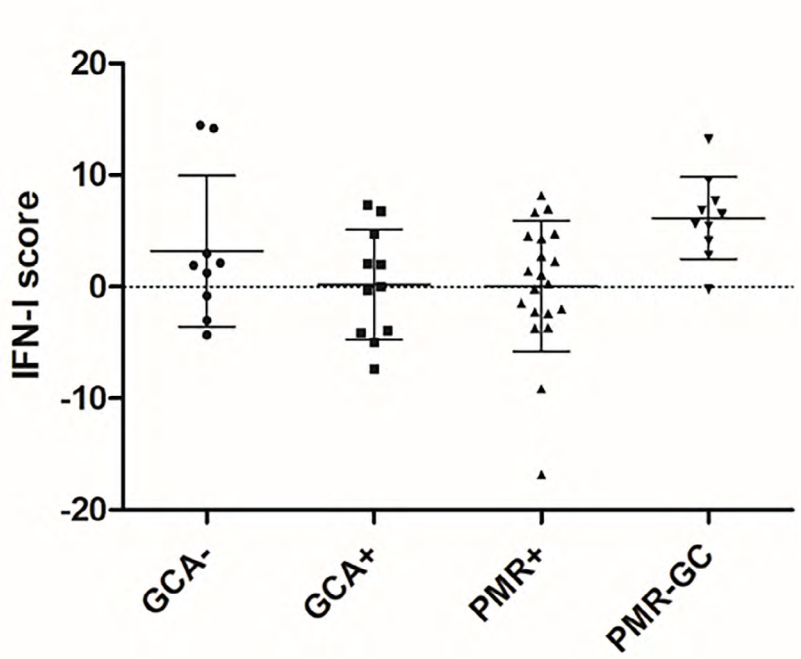

Figure 1 IFN-I scores of individual patients. Patients with a score higher than 9.96 (mean + SD of GCA- group) were considered IFN-I positive.

Poster Tour 2C: Mechanisms of Disease

PT-2C-73

A novel cathepsin C inhibitor suppressed development of MPO-ANCA-associated vasculitis in rat model

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Background/ Objectives: MPO-ANCA-associated vasculitis (MPO-AAV) is a systemic small vessel vasculitis with the production of MPO-ANCA in the serum. Recent studies have revealed that neutrophil extracellular traps (NETs) induced by MPO-ANCA are critically involved in its pathogenesis [1], and that neutrophil elastase (NE) plays an essential role in NET formation [2]. Cathepsin C (CatC) functions as a key enzyme in the activation process of several serine proteases (NSPs) in granulocytes, such as NE, proteinase 3 and cathepsin G [3] by converting the inactive forms of the NSPs to the active forms. Although glucocorticoids and immunosuppressive drugs used as the standard of cares can lead remission in MPO-AAV patients, there are remaining unmet medical needs such as severe side effects, resistance to the treatment and relapse. Therefore, development of new therapeutic strategies is awaited. The aim of this study is to demonstrate the efficacy of MOD06051, a novel CatC inhibitor, against MPO-AAV, using an MPO-AAV rat model established previously [4].

Methods: 4-week-old Wistar Kyoto (WKY) rats were immunized with human MPO according to Little's protocol [4]. The rats were divided into three groups (n=8 per group), and vehicle (0.5% methylcellulose) or MOD06051 (0.3 or 3 mg/kg bid) was orally administered every day for 42 days. All rats were euthanized at the end of the study for serological and histological evaluations.

Results: MPO-ANCA was induced in all groups at the same level. The percentage of affected glomeruli including those with necrotizing and crescentic glomerulonephritis (NCGN), NET-forming neutrophils in the peripheral blood and tissues, and glomerular neutrophil counts were significantly suppressed by MOD06051 treatment in a dose-dependent manner. Furthermore, hematuria score, urinary NGAL (Neutrophil Gelatinase-Associated Lipocalin), tubular erythrocyte cast counts, and pulmonary hemorrhage foci were significantly decreased in the 3 mg/kg of MOD06051 treated group with the similar trends in 0.3 mg/kg group.

Conclusions: A novel CatC inhibitor MOD06051 suppressed NET formation in the MPO-AAV model rats, resulting in amelioration of MPO-ANCA-induced tissue destruction, including NCGN and tubular interstitial damage in the kidneys and disorder of alveolar septal capillaries in the lungs. MOD06051 appears to be a promising agent for treatment of MPO-AAV patients.

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Disclosures: Modulus Discovery, Inc.

PT-2C-74

Expansion of TCRβ clonotypes contributing to recognition of viral peptides in nasal tissue indicates active granulomatosis with polyangiitis

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Background / Objective: In ANCA vasculitis antigen-specific T lymphocytes recognizing exogenous (e.g. infectious agents) or endogenous [e.g. myeloperoxidase (MPO) and proteinase 3 (PR3) peptides] molecules mediate disease mechanisms.[1] Sequencing of the TCR repertoire has been used to identify TCRaβ binding regions of MPO- and PR3-reactive T cells in ANCA disease.[2,3] To search for potential antigen-specific T cells in granulomatosis with polyangiitis (GPA), the TCRβ repertoire of PBMC and nasal tissue samples was analysed, using next generation sequencing (NGS).

Methods: Epidemiological (age, gender) and clinical (BVAS3.0, PR3-ANCA, organ involvement, medication) data of GPA patients (n=7) at the time of sampling were recorded. Both, paired and unpaired PBMC and nasal tissue samples derived from GPA patients were subjected to RNA isolation followed by NGS protocols as described[4] and bioinformatic analysis of TCRβ gene sequences. Immunohistochemical staining of nasal tissue sections was performed as described.[5]

Results: In total, 308.334 unique TCRβ clonotypes were obtained from peripheral blood and nasal tissue T cells. The TRBV and TRBJ gene segment composition was similar among the nasal tissue samples. TRBV20-1 and TRB28 belonged to the most frequently used gene segments in both compartments. While some TCRβ clonotypes were shared among the peripheral blood T cells, none were common among the nasal tissue T cells. The majority of high abundant tissue- or blood-derived TCRβ clonotypes have not been described before, apart from two previously identified TCRβ chains. Detailed analysis revealed a high overlap with EBV- and CMV-specific CDR3β sequences. The frequency distribution of the CDR3 length showed an increase of longer TCRβ CDR3 chains (14 – 20 aa) in nasal tissue when compared to peripheral blood. This proposes a local antigenic exposure such as numerous PR3-expressing cells found in close vicinity to $CD3^+$ T cells in nasal tissue.

Conclusion: Abundant TCRβ clonotypes in peripheral blood and nasal tissue comprise unknown and two known TCRβ molecules. The latter contribute to recognition of viral peptides, supposedly by $CD8^+$ T cells, and their high frequency in combination with corresponding clinical data suggests that EBV and CMV infections can trigger GPA activity.

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Disclosures: None.

PT-2C-75

Phenotypic and functional alteration of unconventional T cells in adult IgA vasculitis

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IgA vasculitis (IgAV) affects small vessels and often occurs after a mucosal infection. Patients with IgAV present with purpura associated with joint, gastrointestinal and renal involvement. Diagnosis is based on invasive procedures such as biopsies of the tissue injured. Unconventional T cells (UTC) represent a heterogeneous family of T cells characterised by hybrid properties of both innate and adaptive immunity. They comprise three main lineages including mucosal-associated invariant T cells (MAIT), invariant Natural Killer T cells (iNKT), and certain subsets of γδ T cells (γδT). The role of UTC in the field of autoimmune diseases has already been supported by numerous experimental and clinical studies. However, their involvement in the pathophysiology of vasculitis, and more specifically in IgA vasculitis has been poorly studied.

To investigate a potential involvement of these cells, we studied peripheral blood mononuclear cells (PBMCs) of adult patients from the University Tours Hospital (France) with histologically proven IgA vasculitis prior any corticosteroid treatment. Control patients with ANCA-associated vasculitis (AAV) and giant cell arteritis (GCA), as well as healthy donors (HC), were also enrolled.

Ten patients with IgAV have been included (Fig 1.A), half of them were women (57%) with a median age of 62 years. Regarding the frequencies of circulating UTC, no differences were observed in iNKT cells while the frequency of γδT and MAIT cells were both significantly decreased in IgAV patients (Fig 1.B). Interesting, MAIT cells from IgAV patients displayed a clear phenotype of activated cells as demonstrated by increased CD69 and PD-1 expression (Fig 1.C). A decreasing trend in MAIT cells during the course of two others vasculitis, ACG and ANCA associated vasculitis has was also observed. In addition, a higher proportion of $CD4^+$ MAIT in IgAV patients compared with HC was founded (Fig 1.D). Among a large panel of integrins and/or chemokine receptors potentially expressed by MAIT, a decrease of the expression of CCR6 on the circulating MAIT in patients with IgAV compared to HC was observed. MAIT cells of IgAV patients were also more prone to produce interferon-γ compared to HC. In parallel, no difference was noted regarding IL-17A secretion (Fig 1.E). Finally, we observed, one month after the vasculitis diagnosis, a trend towards an increase in the percentage of circulating MAIT cells (Fig 1.F).

We described for the first time a numerical and phenotypic alteration in circulating UTC MAIT cells in IgAV patients. This latter phenomenon is also observed in others vasculitis such as ACG and ANCA associated vasculitis. The next step is to localise MAITs in the tissues affected by vasculitis in order to support their role in IgA vasculitis.

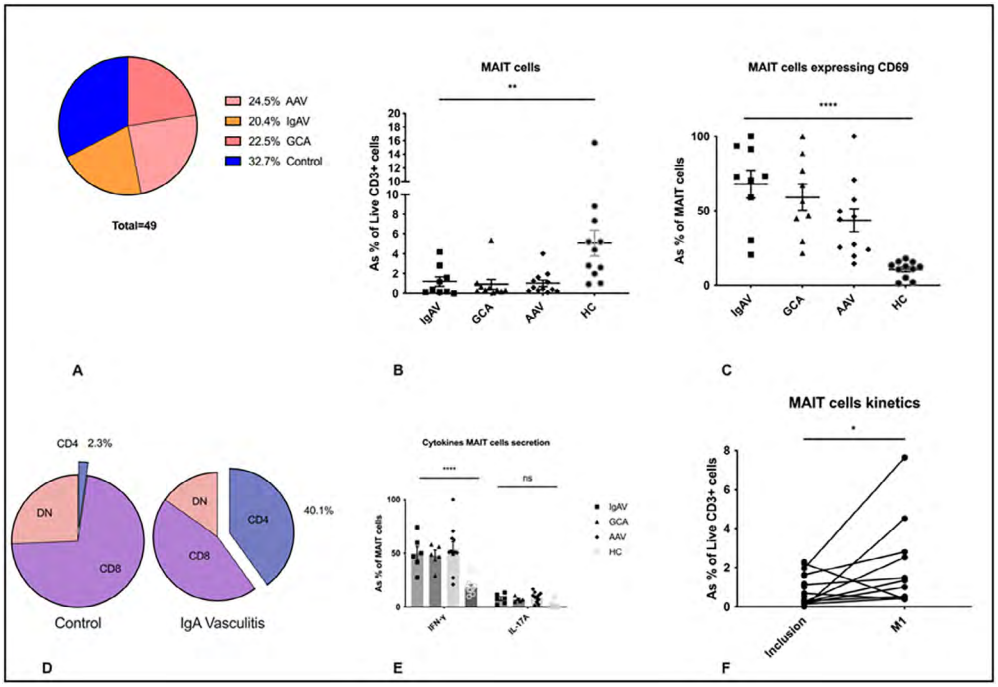

Figure 1: A: Frequency of populations included ; B, C: Frequency and phenotype of MAIT cells in HC, in patients with IgAV, AAV and GCA; D: MAIT population subtypes at baseline ; E: Intracellular staining for IFN-γ and IL-17A of PMA/ionomycin-activated PBMCs.; F: Kinetics of MAIT cell frequency at whale and one-month follow-up. Kruskal–Wallis test followed by a Dunn's multiple comparisons test. *, P < 0.05; **, P < 0.01; ***, P < 0.001. ns, not significant.

PT-2C-76

ANCA induced changes in neutrophil cytoskeleton and biomechanics are modulated by hypoxia, and associate with disease phenotype in AAV

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Background: ANCA associated vasculitis (AAV) is characterised by neutrophil mediated vascular inflammation. Neutrophils are uniquely deformable enabling them to squeeze through microvasculature. Although *in vitro*, cells are exposed to 21% O_2, this is supra-normal oxygen tension; 5% O_2 is representative of *in vivo* physiological normoxia. Tissue inflammation such as sites of active vasculitis are profoundly hypoxic with oxygen tension ≤1%. How biomechanical properties of neutrophils, and hypoxia contribute to the pathogenesis of AAV is unknown.

Methods: Biomechanical properties of neutrophils were analysed using real time deformability cytometry including from patients with active AAV (aAAV), AAV in remission (rAAV) or healthy controls (HC). Isolated neutrophils (HC or aAAV) were primed (TNF) and stimulated with MPO or PR3 ANCA IgG or control IgG (CIgG) in 'normoxia' (21% O_2), physiological normoxia (5% O_2) or hypoxia (1% O_2). Actin polymerisation was assessed by staining with AF488-Phalloidin (F-actin). NETosis was visualised by staining for H3Cit. Neutrophils were cocultured with glomerular endothelial cells (gEC) to assess EC injury and neutrophil transmigration.

Results: aAAV neutrophils were stiffer (less deformable) than rAAV or HC (**Fig 1A**). Deformability was lowest in those with kidney or lung involvement with strong inverse correlation with BVAS (r=-0.60, p=0.0002). Stimulation of HC neutrophils with ANCA decreased deformability (median 0.086, 0.084, 0.082 au for unstim, CIgG, ANCA, p=0.01) and increased actin polymerisation with filopodia formation (median area F-actin/cell 62.3, 71.9, 85.5, 93.8μm^2 for unstim, CIgG, MPO-ANCA, and PR3-ANCA, p<0.0001). ANCA induced changes in neutrophil deformability & actin polymerisation were inhibited at 5% O_2 but enhanced at 1% O_2 (**Fig 1B**). Oxygen tension also impacted neutrophil function. ANCA induced NETosis was completely abolished at 5% O_2 but enhanced at 1% O_2 (**Fig 1C**). gEC injury following incubation with ANCA stimulated neutrophils was enhanced (**Fig 1D**) and there was 40% increase in neutrophil transmigration across a gEC monolayer at 1% O_2 compared to 21% O_2. aAAV neutrophils expressed greater hypoxia inducible transcripts than rAAV or HC (**Fig 1E**) When aAAV neutrophils were stimulated with ANCA there was enhanced actin polymerisation and gEC injury compared to HC. In contrast to HC this was not inhibited by incubation at 5% O_2.

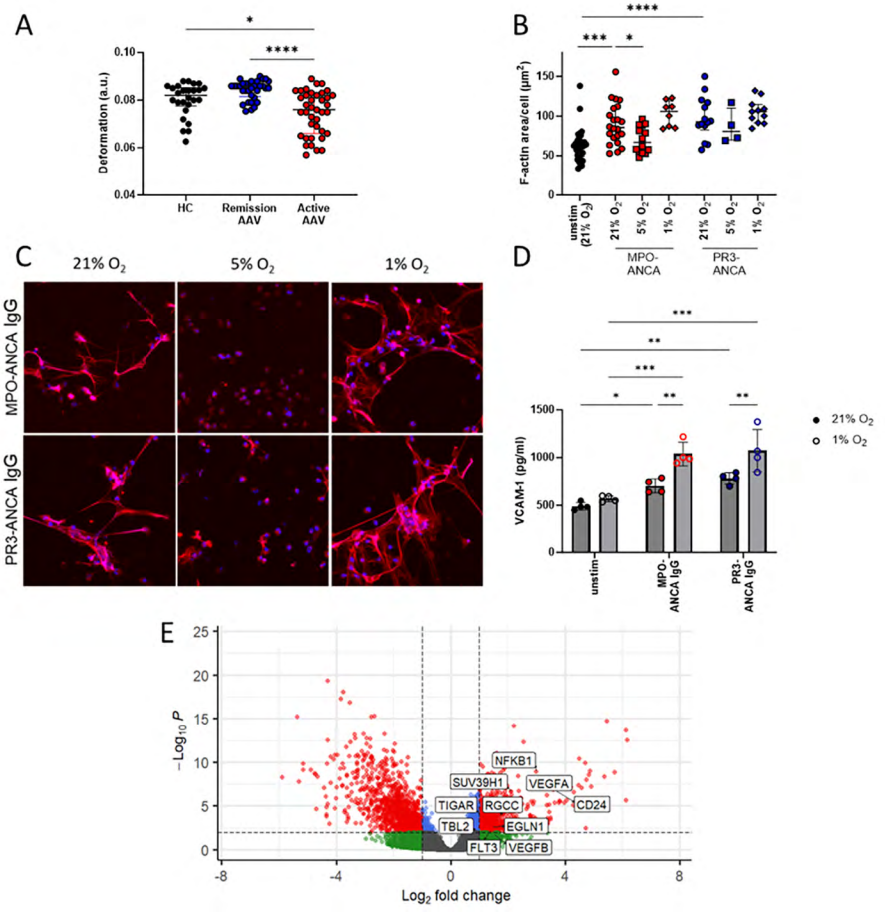

Figure 1 (A) Neutrophil deformability in patients with AAV (B) ANCA IgG induced actin polymerisation (C) ANCA IgG induced NETosis (H3Cit-red DAPI-blue) (D) VCAM-1 release following gEC/neutrophil co-culture (E) Differentially expressed genes in aAAV vs rAAV neutrophils with genes in the GO BP term 'response to hypoxia' highlighted.

Conclusions: Increased neutrophil stiffness in AAV may lead to retention in pulmonary and renal microvasculature, increasing potential for neutrophil-EC interactions and microvascular damage. Incubation at physiological normoxia diminished ANCA induced responses in HC, but not AAV neutrophils, whereas pathological hypoxia enhanced ANCA responses. Hypoxia at sites of inflamed vasculature may therefore enhance neutrophil induced endothelial injury.

PT-2C-77

Activation of endothelial cells and priming of circulating PMN by high serum IgA are required to elicit IgA vasculitis

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Background: Perivascular deposition of IgA1 immune-complexes (IgA-IC) was thought to be the decisive trigger for neutrophil (PMN)-mediated damage In IgA vasculitis (IgAV). Since we have demonstrated that perivascular deposition of IgA1 also occurred in clinically uninvolved skin during remission and that in lesional skin IgA was detected also on intravascular neutrophils, we have proposed that for elicitation of vessel damage perivascular IgA-IC must be complemented by pre-activation of circulating neutrophils and of endothelial cells.

Objectives: We want to analyze if flares of IgAV correlate with higher serum levels IgA-IC, binding of IgA to PMN in circulation and simultaneous activation of endothelial cells.

Methods: Activation of endothelial cells was analyzed by means of expression of adhesion molecules. Serum IgA-IC levels and IgA-IC binding to PMNs were quantified in IgAV patients and controls. Activation of PMN was evaluated by NET release, adherence and cytotoxicity assays and in a flow-system to mirror conditions at postcapillary venules. *In vitro* results were related to findings in biopsies and a mouse vasculitis model.

Results: In lesional skin with perivascular IgA1 deposition, but not in non-lesional skin with perivascular IgA1 deposition we detected endothelial expression of E-selection and IgA-positive neutrophils. During acute IgAV flares we found that increased binding of IgA-IC to circulating PMNs was associated with elevated serum levels of IgA-IC: Both decreased during resolution of IgAV. IgA-IC binding lowered the threshold of PMN for NETosis. Blocking of FcαRI abolished these effects. In the flow system intensive NETosis only occurred after PMN had adhered to activated E-selectin expressing or IgA-biiding endothelial cells. Binding of IgA-IC enhanced tethering of PMN, NET release and NET-mediated injury of endothelial cells. Reflecting these *in vitro* findings we visualized NETs in close proximity to endothelial cells and IgA-coated PMN in tissue sections of IgAV patients.

Conclusion: Endothelial expression of E-selectin increased serum levels of IgA-IC as well as binding of IgA to circulating PMN combine with perivascular deposition of IgA to result in increased adhesion of PMN to endothelium, vigorous NETosis.and ensuing vessel damage.

PT-2C-78

Exploring Biological Ageing in ANCA-Associated Vasculitis

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Background/ Objectives: Unusually for an autoimmune disease, ANCA-associated vasculitis (AAV) develops later-in-life. Despite chronological age being a well-known risk factor for AAV, biological age, a measure of the cellular processes associated with ageing and superior predictor of age-related morbidity/mortality, has yet to be investigated in the context of AAV. DNA methylation (DNAm) clocks are considered the most accurate predictors of this measure.

Accelerated biological ageing is associated with chronic, low-grade inflammation called “inflammageing”. A key early step in AAV development is the activation of innate immune cells by anti-MPO and anti-PR3 autoantibodies (ANCAs). The effect that age has on cellular responses to ANCAs is unclear.

Hypothesis.

AAV patients experience accelerated biological ageing and the immunological changes associated with this drive AAV pathogenesis.

Aims

- To measure biological ageing in AAV patients using an *ELOVL2* DNAm clock.
- To explore the effects of age on innate immune cell function following ANCA stimulation.

Methods: Blood samples were collected from untreated AAV patients (n=97) and age-matched healthy controls (HC; n=24). DNA was extracted, bisulfite converted and the *ELOVL2* sequence amplified using PCR. Pyrosequencing was used to measure methylation at 7 CpG probe sites to estimate DNAm age. PBMCs and neutrophils were isolated from younger (<35 years) and older (>60 years) healthy donors and stimulated with ANCAs. We measured supernatant cytokines by ELISA, gene expression in cell pellets by qPCR and NETosis and reactive oxygen species (ROS) production by flow cytometry.

Results: AAV patients experience accelerated biological age compared to HC when measured using an *ELOVL2* DNAm clock (Figure 1 A). PBMCs isolated from older individuals show increased inflammatory gene expression (Figure 1 B) and cytokine production in response to anti-MPO compared to younger individuals. No significant differences in NETosis by ANCA stimulated neutrophils were seen. Increased ROS production in response to anti-PR3 was noted in neutrophils isolated from older compared to younger donors but no differences in ROS production with age were shown in response to ANCA stimulation in monocytes.

Conclusions: AAV patients experience accelerated biological ageing. Age-related changes to the immune system may promote AAV pathogenesis. The relationship between biological ageing and AAV warrants further investigation.

Disclosures: None.

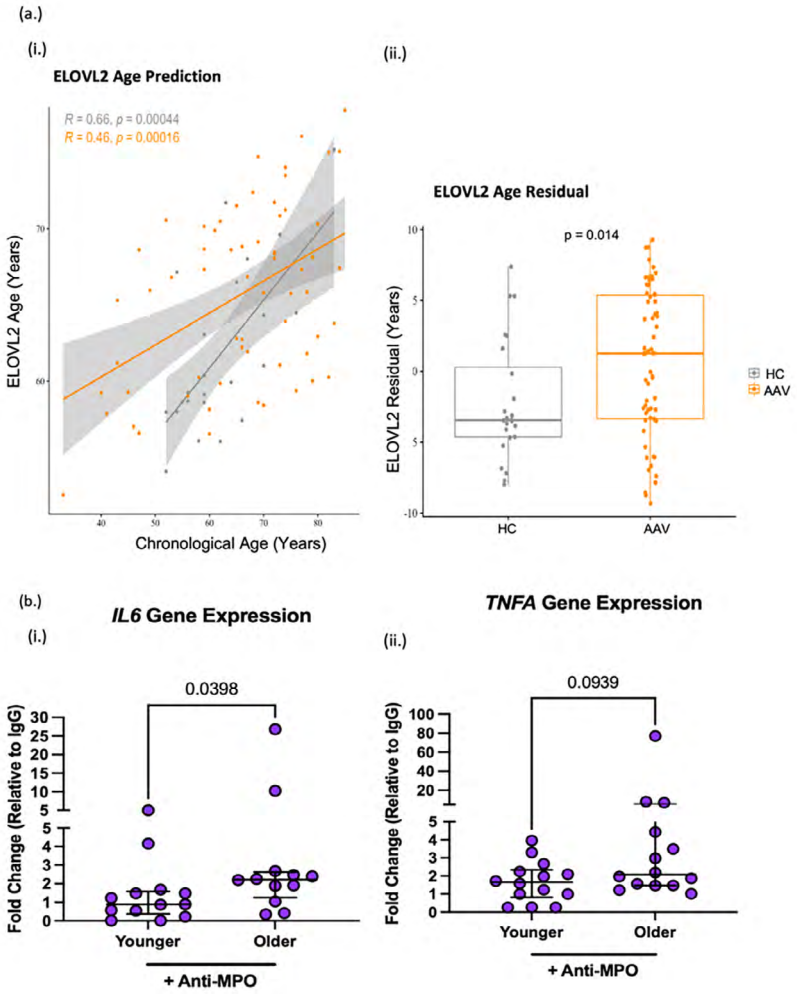

Figure 1. Biological Ageing in AAV. (a.) Methylation surrounding *ELOVL2* was measured and multi-linear regression models used to estimate DNAm age in AAV patients (n=97) and HC (n=24). (i) Correlation between DNAm age and chronological age. (ii) Difference in DNAm age acceleration between cohorts measured by the residual. (b.) qPCR was used to quantify (i.) *IL-6* and (ii.) *TNFA* gene expression from anti-MPO stimulated PBMCs isolated from younger (n=14) and older (n=14) healthy donors. qPCR data is made relative to the housekeeping gene *RPL27* and normalized to IgG controls (2^{-DDCT}). Spearman correlation analysis and unpaired t tests were used to test the correlation coefficients and statistical significance.

PT-2C-79

Cytomegalovirus reactivation and renal damage in active ANCA-associated vasculitis

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Background: Cytomegalovirus (CMV) is a widely prevalent herpesvirus, present in over half the population by middle age. Following primary infection, CMV remains latent but can intermittently reactivate. We have previously shown that asymptomatic CMV reactivation occurs in 25% of CMV seropositive patients with ANCA-associated vasculitis (AAV) in remission, and that CMV specific immune signatures driven by CMV reactivation are associated with clinically important outcomes such as increased infection, increased arterial stiffness and reduced kidney function.

We hypothesised that asymptomatic CMV reactivation may amplify kidney damage in active AAV. To investigate this, we are undertaking a prospective observational study in newly diagnosed or relapsed AAV to determine the frequency of CMV reactivation in active AAV and its association with clinical outcomes and CMV driven immune signatures in peripheral blood and kidney tissue. We report here our findings of an interim analysis.

Methods: Patients were recruited within 14 days of disease presentation. Quantitative CMV PCR of blood and urine samples was performed at baseline, fortnightly until month 1, monthly until month 6, then 3 monthly until month 12. Clinical data were collected at each visit. Peripheral blood mononuclear cells are collected at 3 monthly intervals and kidney tissue at diagnosis.

Results: This analysis includes 47 CMV seropositive patients and 20 CMV seronegative patients followed up for a median duration of 198 days (IQR 99-308). There was no difference in renal involvement or degree of kidney injury between CMV seropositive and CMV seronegative patients. 49% of the CMV seropositive patients had evidence of asymptomatic CMV reactivation in blood or urine, with 96% occurring in the first 3 months. Those with CMV reactivation were more likely to have renal involvement (87 vs. 54%; p=0.014) and had significantly worse kidney function at baseline compared to those without CMV reactivation (median creatinine 277umol/L, IQR 185-564 vs. 99, IQR 79-219; p=0.002) [Figure 1]. Patients with CMV reactivation had more proteinuria compared to those with no reactivation (uACR 99.2 mg/mmol, IQR 33.5-325.3 vs. 42.2, IQR 3.8-232.7; p=0.023). Patients with evidence of CMV reactivation continued to have worse kidney function at 12 months [Figure 1]. A higher cumulative steroid burden at the time of recruitment was associated with CMV reactivation (p=0.004).

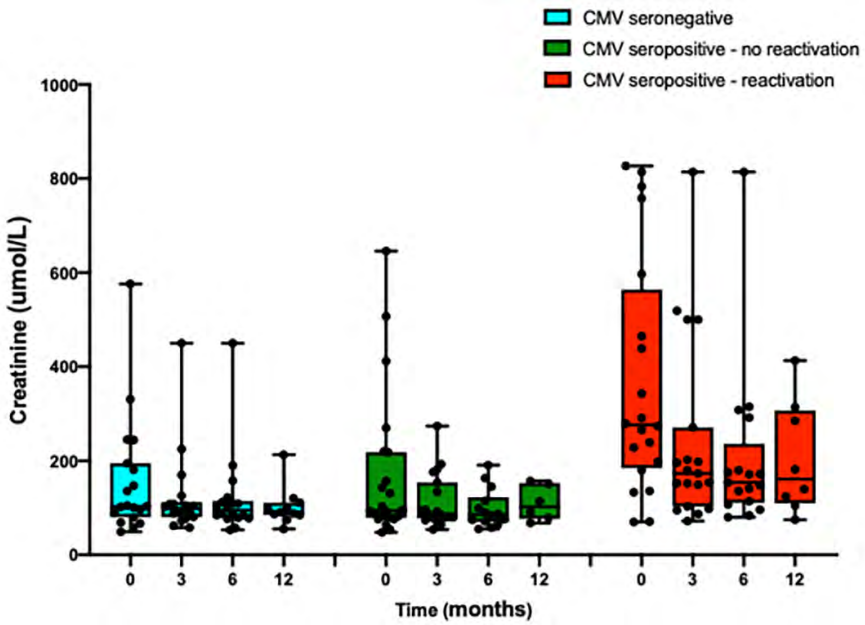

Figure 1: Longitudinal renal function following acute diagnosis of AAV according to CMV serostatus and reactivation:

Conclusions: Asymptomatic CMV reactivation has occurred in half of CMV seropositive patients with acute AAV during the first 12 months and is associated with worse renal outcomes in these preliminary results. We are currently investigating the potential mechanisms whereby CMV infection may amplify kidney injury in AAV by assessing CMV driven immune signatures in peripheral blood and kidney tissue.

Disclosures: This study is partly supported from an Investigator-Initiated Program of Merck Sharp & Dohme Corp (MSD). The opinions expressed are those of the authors and do not necessarily represent those of MSD.

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Poster Tour 3C: Biomarkers of Clinical Relevance

PT-3C-80

Identification of Giant Cell Arteritis Using Plasma Proteome Profiles Integrated with Machine Learning

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Background/Objectives: The availability of diagnostic laboratory tests and specific biomarkers of disease activity for giant cell arteritis (GCA) remains an unmet need. The purpose of this study was to identify plasma proteins that 1) differentiate patients with GCA from controls; and 2) associate with disease activity in GCA by utilizing a high-throughput protein screening array.

Methods: This study included patients with GCA (n = 30) from a multi-institutional prospective longitudinal cohort study and 30 age-/sex-/race-matched healthy controls (**Fig. 1A**). Plasma samples were collected from patients with GCA at two separate time points: 1) during active disease and 2) during inactive disease. An aptamer-based, multiplex microarray platform (SomaScan® Assay, SomaLogic) measured semi-quantitative abundances of 7,289 proteins in relative fluorescence units. Linear regression models identified differentially abundant proteins (*P*-value of the corresponding regression coefficient < 0.01) between patients with GCA (at either active or inactive disease state) compared with controls while adjusting for potential confounders.

Results: 537 and 781 differentially abundant proteins were identified between active GCA and controls and inactive GCA and controls, respectively. Among these, 202 and 331 proteins had significantly higher abundances in active GCA and inactive GCA, respectively (**Fig. 1B**). In addition, 16 proteins were found to be correlated with physician global assessment (PGA) of disease activity in active GCA patients (**Fig. 1C**). A random forest classifier correctly predicted active GCA vs. controls with an accuracy of 95.0% in 5-fold cross-validation (**Fig. 1D**). Similarly, in the case of inactive GCA vs. controls, a random forest classifier distinguished these two groups at 93.3% accuracy.

Conclusions: Plasma proteome profiling in two different disease states of GCA produced highly accurate classification for distinguishing active and inactive disease states from controls. Future studies will include validating these findings in a larger independent cohort and with non-GCA disease controls.

Disclosures: None.

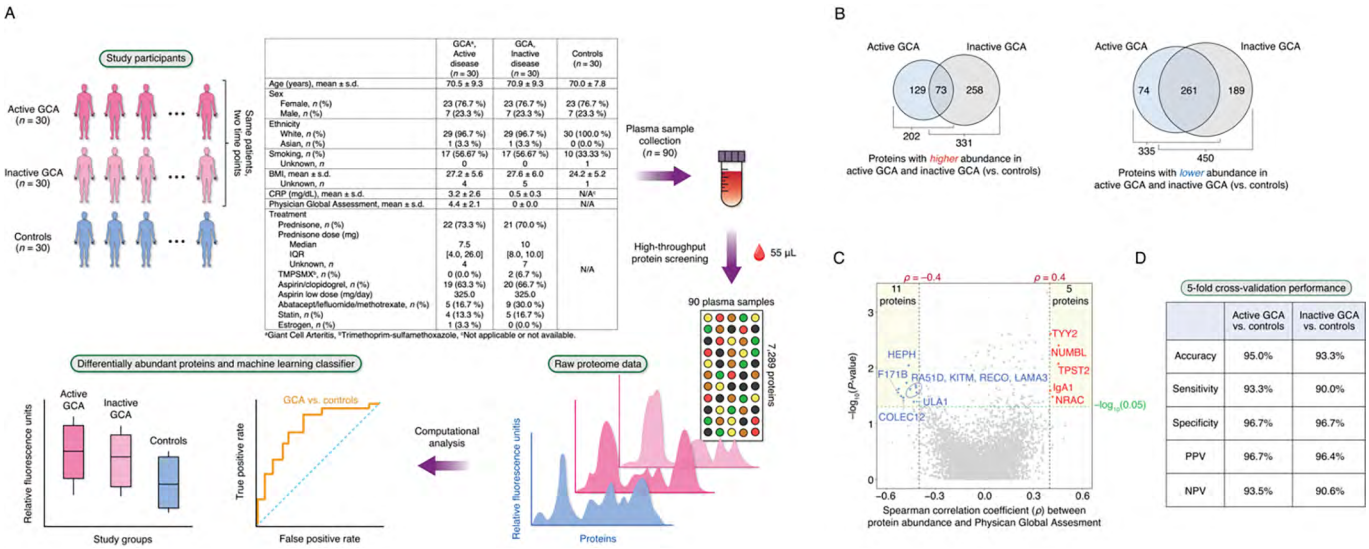

Figure 1. (A) Study design overview. **(B)** Plasma proteins found to have significantly higher or lower abundance in active GCA and inactive GCA compared with controls ($P < 0.01$). (**C**) 16 proteins were significantly associated with PGA in active GCA. **(D)** Random forest classifiers could differentiate patients with GCA from controls with high accuracy in 5-fold cross-validation.

PT-3C-81

Gut Dysbiosis with Oral-derived Campylobacter as a Potential Predictor for Aortic Aneurysm Formation and Progression in Takayasu Arteritis

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Background: Takayasu arteritis (TAK) is an autoimmune large vessel vasculitis that affects the aorta and its major branches, eventually leading to the development of aortic aneurysm and vascular stenosis or occlusion. The current retrospective and prospective study aimed to investigate whether the gut dysbiosis exists in patients with TAK and to identify specific gut microorganisms related to aortic aneurysm formation/progression in TAK.

Methods and Materials: We analysed the faecal microbiome of 76 patients with TAK and 56 healthy controls (HCs) using 16S ribosomal RNA sequencing. We examined the relationship between the composition of the gut microbiota and clinical parameters.

Results: The patients with TAK showed an altered gut microbiota with a higher abundance of oral-derived bacteria, such as *Streptococcus* and *Campylobacter*, regardless of the disease activity, than HCs. This increase was significantly associated with the administration of a proton pump inhibitor used for preventing gastric ulcers in patients treated with aspirin and glucocorticoids. Among patients taking a proton pump inhibitor, *Campylobacter* was more frequently detected in those who underwent vascular surgeries and endovascular therapy for aortic dilatation than in those who did not. Among the genus of *Campylobacter*, *Campylobacter gracilis* in the gut microbiome was significantly associated with clinical events related to aortic aneurysm formation/worsening in patients with TAK. In a prospective analysis, patients with a gut microbiome positive for *Campylobacter* were significantly more likely to require interventions for aortic dilatation than those who were negative for *Campylobacter*. Furthermore, patients with TAK who were positive for *C. gracilis* by polymerase chain reaction showed a tendency to have severe aortic aneurysms.

Conclusion and Perspective: A specific increase in oral-derived *Campylobacter* in the gut may be a novel biomarker of aortic aneurysm formation/progression in patients with TAK. Since a multi-centre analysis should be warranted for validation of the above findings, we are now launching a multi-centre study collecting and analysing the faecal and salivary samples of the patients with TAK from the 20 medical institutes in Japan.

Disclosure: All authors have no conflict of interests to disclose related to this study.

PT-3C-82

Association of urinary adhesion molecules derived from endothelial cells and kidney pathology in ANCA-associated glomerulonephritis

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Background/ Objectives: Although kidney pathology provides valuable information including diagnosis, severity of kidney damage and prognosis, kidney biopsy is an invasive procedure carrying a bleeding risk in patients with ANCA-associated glomerulonephritis (ANCA-GN). Therefore, biopsy is often avoided in some cases with critical condition, and the examination is unsuitable for frequent follow-up. Thus, non-invasive urinary biomarkers reflecting kidney pathology are highly desirable. Intracellular adhesion molecule-1 (ICAM-1) constitutively present and vascular cell adhesion molecule-1 (VCAM-1) expressed at low levels on vascular endothelial cells belong to the immunoglobulin superfamily serving as cell adhesion molecules. Of note, expressions of both adhesion molecules on the cell surface are induced in response to inflammatory stimuli. The aim of our study is to evaluate the clinical significance of ICAM-1 and VCAM-1 as urinary biomarkers for ANCA-GN in relation to the pathological findings.

Methods: ANCA-GN patients who underwent kidney biopsy from nationwide Remission Induction Therapy in Japanese Patients with ANCA-associated Vasculitis and Rapidly Progressive Glomerulonephritis cohort (RemIT-JAV-RPGN, n = 44) and from Fujita Health University cohort (FHU, n = 76) were subjected to the current study. Urinary concentrations of soluble ICAM-1 and VCAM-1 measured by enzyme-linked immunosorbent assay (ELISA) were standardized with urinary creatinine (urine ICAM-1 or VCAM-1 to creatinine ratio; UICR or UVCR), and urine VCAM-1 to ICAM-1 ratio (UVIR) were also obtained. We investigated the association of both biomarkers with kidney pathology.

Results: In RemIT-JAV-RPGN cohort, UVCR was significantly elevated in ANCA-GN cases with interstitial arteriolitis, and UVIR correlated with the severity of interstitial fibrosis and tubular atrophy (IF/TA). When validated using FHU cohort, similar associations were observed as UVCR with arterial lesions and as both UVCR and UVIR with the severity of IF/TA. Furthermore, UVIR was a superior indicator for the assessment of the IF/TA severity to UVCR. In FHU cohort, when categorizing interstitial damages to interstitial inflammatory cell infiltration (ICI) and interstitial fibrosis (IF), UVIR were consistently increased according to ICI severity, but not to IF severity. Association of urine ICAM-1 or VCAM-1 with cellular crescents was not observed in either cohort. ROC analysis demonstrated superior prediction ability of UVIR for IF/TA ≥25%, with AUC values of 0.872 (95% CI 0.615 – 0.902) in RemIT-JAV-RPGN cohort and of 0.758 (95% CI 0.793 – 0.950) in FHU cohort, compared to UICR and UVCR. The prediction ability of UVIR for IF/TA ≥25% was comparable to that of urine α1-microglobulin to creatinine ratio (Uα1MGCR) which is an existing marker of interstitial injury, but multivariate ROC analysis of UVIR combined with Uα1MGCR improved the prediction ability compared to Uα1MGCR alone.

Conclusions: The urinary VCAM-1 is a reliable biomarker that reflects renal disease activity related to acute interstitial inflammation in ANCA-GN.

Disclosures: None.

PT-3C-83

Discovery and Validation of Novel Circulating Protein Biomarkers in ANCA-Associated Vasculitis

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Background: Currently used biomarkers of disease activity in ANCA-associated vasculitis (AAV), including ANCA titers and inflammatory markers, are often insufficient to guide clinical decision making. Identifying novel biomarkers could improve outcomes in AAV, in part by individualizing treatment decisions. Prior studies have examined a limited number of potential circulating protein biomarkers but not been validated. Our objective was to identify circulating protein biomarkers of disease activity in AAV using a high-throughput platform and to validate these findings.

Methods: Blood samples from patients with AAV were identified from the Mass General Brigham (MGB) Biobank as well as the MGB prospective registry. Samples from 78 patients were included in the "Discovery" cohort and samples from 65 patients were included in the "Validation" cohort. We classified disease activity as "Active" or "Remission" at sample collection; details of their demographics and medical history were manually extracted from the electronic health record (EHR). The Olink high-throughput inflammation proteomic assay was used to measure 92 circulating protein levels. Measurements of ESR, CRP, white blood cell (WBC) count, and platelets collected for clinical purposes were extracted from the EHR. Protein levels were normalized and levels were compared among those with active disease vs remission, adjusted for age, sex, ANCA-type, and steroid use. The false discovery rate adjusted p-value was assessed using the Benjamini-Hochberg procedure (threshold < 0.05). We used area under the receiver operating curves (AUCs) and logistic regression (odds ratio, OR) to assess the association of protein levels with disease activity.

Results: The Discovery cohort mean age was 57.3 years, 55% were female, and 28% had active disease. The Validation cohort mean age was 60.5 years, 61.5% were female, and 35% had active disease. Five of 92 proteins were statistically significantly different between active disease and remission in the Discovery cohort: monocyte chemoattractant protein-3 (MCP-3), tumor necrosis factor superfamily member 14 (TNFSF-14), oncostatin M (OSM), FMS-like tyrosine kinase 3 ligand (Flt3L), and stem cell factor (SCF). In both the Discovery and Validation cohorts, OSM and TNFSF-14 consistently differentiated active disease from remission well when comparing AUCs and ORs (Table). These biomarkers performed better than conventional circulating biomarkers. Five protein biomarkers reported in prior cohorts using different platforms did not differentiate disease activity well.

Conclusion: Using a high-throughput approach, we investigated circulating proteins as potential biomarkers of disease activity. OSM and TNFSF-14 performed particularly well in both cohorts. These proteins outperformed conventional inflammatory markers. Study limitations include a small sample size and cross-sectional design. The target specificity of affinity based proteomics will need to be validated and these findings can be investigated further using longitudinally collected samples. These biomarkers may also identify novel therapeutic targets.

Disclosures: None.

Figure: Performance of Candidate Novel vs Conventional Biomarkers in Discovery and Validation Cohorts

Biomarker	Discovery Cohort Odds Ratio (CI, p value)	Validation Cohort Odds Ratio (CI, p value)
OSM	**5.10 (1.64-15.85, 0.01)**	**9.50 (2.71- 33.31, <0.001)**
TNFSF14	**3.71 (1.26-10.93, 0.02)**	**6.48 (2.00-20.98, 0.002)**
WBC	2.86 (1.01-8.10, <0.05)	4.27 (1.37-13.32, 0.01)
Platelets	2.86 (1.01-8.10, <0.05)	3.08 (1.02- 9.26, 0.05)
CRP	1.68 (0.53-5.37, 0.38)	1.09 (0.38-3.11, 0.87)
ESR	1.4 (0.45-4.35 ,0.56)	5.01 (1.58-15.87, 0.01)
MCP3	1.24 (0.46-3.36, 0.67)	1.30 (0.47-3.61, 0.62)
Flt3L	0.13 (0.04-0.43, 0.001)	0.48 (0.17-1.36, 0.17)
SCF	0.34 (0.12- 0.95, 0.04)	0.64 (0.23-1.77, 0.39)
Biomarker	**Discovery Cohort AUC (CI)**	**Validation Cohort AUC (CI)**
OSM	**0.75 (0.62-0.87)**	**0.80 (0.67-0.92)**
TNFSF14	**0.73 (0.60-0.86)**	**0.76 (0.64-0.88)**
WBC	0.70 (0.57-0.84)	0.73 (0.60-0.87)
Platelets	0.68 (0.55-0.81)	0.70 (0.55-0.85)
CRP	0.55 (0.38-0.72)	0.58 (0.42-0.74)
ESR	0.55 (0.37-0.72)	0.75 (0.61-0.88)
MCP3	0.63 (0.49-0.77)	0.59 (0.44-0.74)
Flt3L	0.76 (0.64-0.87)	0.64 (0.49-0.78)
SCF	0.70 (0.57-0.83)	0.56 (0.40-0.72)

PT-3C-84

Clustering model of 23 antibodies against G protein-coupled receptors (GPCR) identifies two different subsets of ANCA-associated vasculitis (AAV) with different prognoses

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Background/ Objectives: In vivo signatures of antibodies targeting G protein-coupled receptors (GPCR) have been described as a novel immunological feature in healthy individuals and in different diseases [1]. For instance, decreased antibody concentrations against complement-receptors C5a and C3a are detected in ANCA-associated vasculitis (AAV) and associated with relapse [2]. So far, clustering models of a wide range of antibodies targeting GPCRs have not been determined in AAV.

Methods: To determine circulating antibodies against GPCR (specifically antibodies against receptors for angiotensin AT1 & AT2, ACE-II, endothelin ETA & ETB, PAR1, adrenaline a1-A, a2-AD, b1-A & b2-A, muscarin M1, M2, M3, M4 & M5, nicotine N1& N2, chemokines CXC3, CX1, C3a & C5a, and cannabinoid CB1& CB2) and analyze their diagnostic and/or prognostic value using a Kmeans clustering-model, sera of patients with AAV (granulomatosis with polyangiitis [GPA], n=59; microscopic polyangiitis [MPA], n=9) were analyzed by ELISA. Clinical data including vasculitis activity and damage scores BVAS V3.0 and VDI, respectively, inflammatory markers (ESR, C-reactive protein), creatinine, PR3-ANCA, MPO-ANCA, and treatment were assessed at the time of serum sampling and during follow-up for 60 months.

Results: Using Kmeans clustering model, we identified two subtypes of patients with AAV mainly defined by the correlation with antibody levels of anti-ETAR/anti-C3aR (cluster 1: r=-0.6844, *P*=0.0006 vs. cluster 2: r=-0.0991, *P* =0.5430), anti-AT2R/anti-ETBR (cluster 1: r=0.8047, *P*<0.0001 vs. cluster 2: r=0.5728, *P*=0.0001), and anti-M2R/anti-a1-AR (cluster 1: r=0.8554, *P*<0.0001 vs. cluster 2: r=0.5529, *P*=0.0002). There were no differences between both clusters according to inflammatory markers or clinical findings at baseline. However, patients of cluster 2 were characterized by an increased risk for major relapse (HR: 6.53, *P*=0.0372; Figure 1) and need for intensified immunosuppressive therapy (rituximab, cyclophosphamide) during follow-up at 36 and 60 months.

Conclusions: The findings of our study suggest segregation of different AAV-subtypes related to clustering of anti-GPCR antibodies and may help to identify patients with an increased risk of relapse.

References:

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2. Klapa S. et al. Low Concentrations of C5a Complement Receptor Antibodies Are Linked to Disease Activity and Relapse in Antineutrophil Cytoplasmic Autoantibody-Associated Vasculitis. Arthritis Rheumatol. 2023 May;75(5):760-767

Disclosures: No conflict of interests.

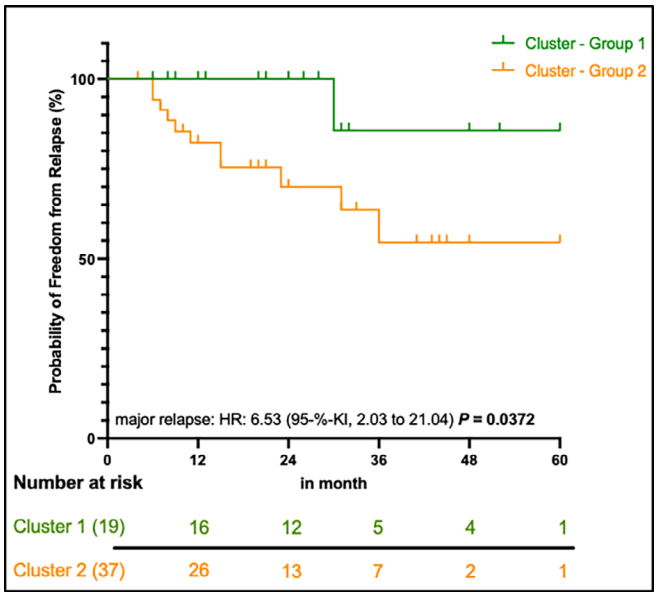

Figure 1. Kaplan-Meier analysis. Using Kmeans clustering model, two distinct groups of AAV were identified related to anti-GPCR antibody signature. Whereas no clinical differences were found at baseline, patients of cluster group 2 presented an elevated risk of relapse with major organ involvement.

PT-3C-85

Identification of kidney transcripts associated with prognosis in ANCA-associated glomerulonephritis

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Background/ Objectives: Kidney involvement in ANCA-associated vasculitis (AAV-GN) predicts poor patient and kidney survival. Deciphering the transcriptomic landscape in AAV-GN may provide insights into pathogenic mechanisms or identify biomarkers for refining diagnosis and/or prognosis, which would help stratify risk and tailor therapeutic management. We aimed to investigate the potential prognostic value of kidney transcripts associated with kidney survival.

Methods: This study included adult patients with AAV-GN from the French Maine-Anjou Registry. Immune gene transcript analysis was performed on RNA extracted from 97 AAV-GN kidney biopsies using NanoString technology. Transcripts of interest were selected, and their prognostic performance was assessed with respect to current histological-based classifications. Following the identification of a possible role for clusterin (CLU), the relationship between serum CLU and prognosis was assessed.

Results: Among the 750 evaluated transcripts, we identified a 4-gene signature (XRCC6, PRKCD, TEK, and CLU) that was strongly associated with kidney survival (**Figure 1A**). This signature predicted kidney survival better than histological-based classifications (global C-Index 0.87 vs. 0.65 for Berden classification or 0.81 for Renal Risk Score, with better time-dependent AUC and Brier scores, especially beyond 1 year after diagnosis) (**Figure 1B**). Among these 4 transcripts, the expression level of the CLU transcript had the highest correlation with glomerular involvement, kidney function at diagnosis, and kidney survival. Serum CLU levels were associated with kidney survival, especially when assessed at 6 months from diagnosis (**Figure 1C**, p = 0.023).

Conclusions: Transcriptomic analysis of kidney biopsies of AAV-GN identified potential transcripts that may improve prediction of kidney survival. This transcriptomic signature may help us gain a deeper understanding of the AAV-GN pathogenesis and provide insights for developing new therapeutic options.

References: None.

Disclosures: None.

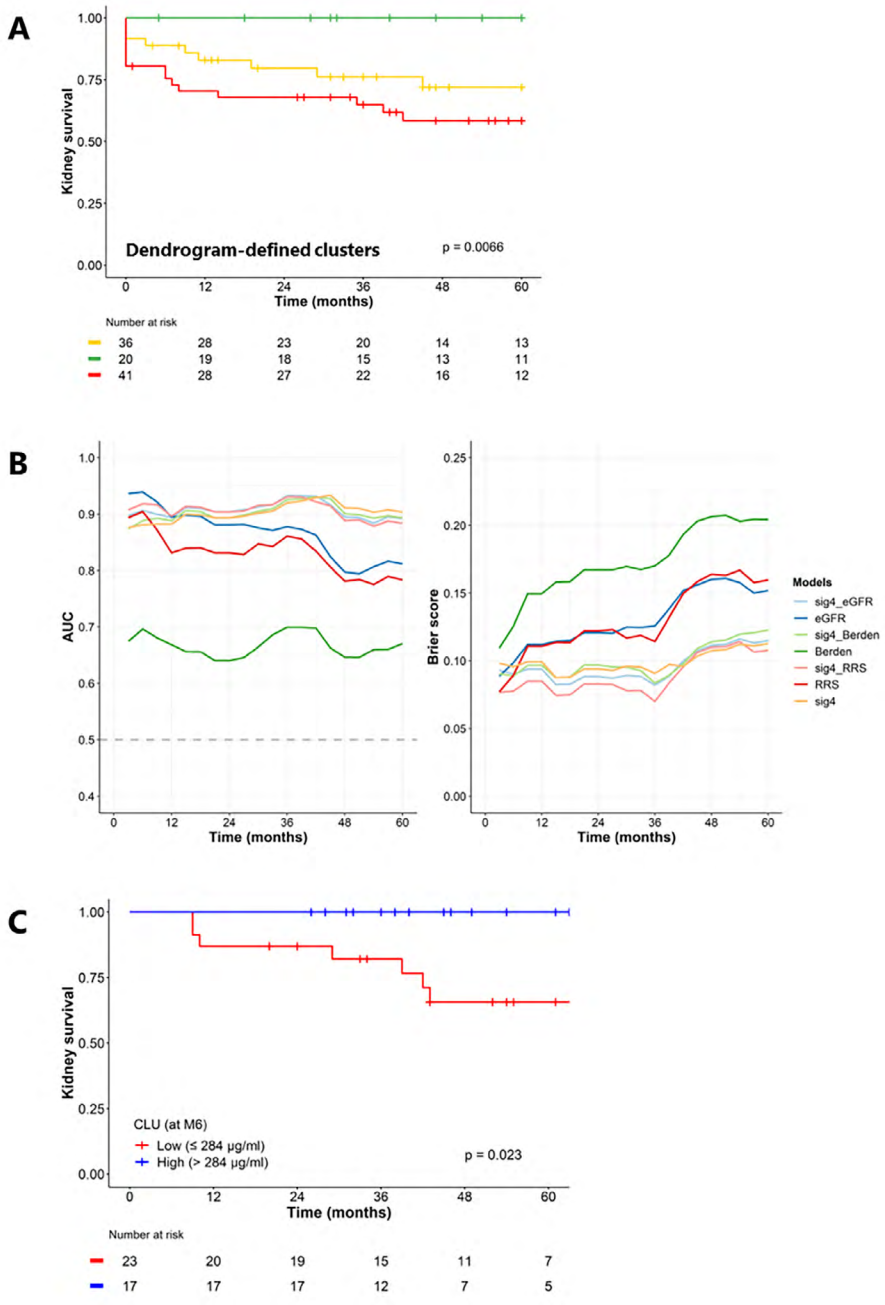

Figure 1. A: Association between kidney survival and a 3 clusters classification (dendrogram-hierarchical classification defined clusters) based on the 4-gene expression signature (Sig4). B: Prognosis performance of Sig4, whether alone or associated with other clinico-pathological classification. C: Association between Clusterin (CLU) levels assessed in plasma after 6 months from diagnosis and kidney survival.

PT-3C-86

Fibrosis and CD-163+ macrophages: making a difference between MPO-AAV and PR3-AAV

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Background/Objectives: Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a necrotizing vasculitis characterised by inflammation of small blood vessels, with the kidney being one of the most affected organs. Its pathogenesis is a complex, multifactorial process involving inflammation and fibrosis in which macrophages play a crucial role. Macrophages are plastic cells that can change their phenotype in response to their environment. Infiltration of CD163+ macrophages (anti-inflammatory) in the interstitium and glomeruli is observed in AAV patients. Clinical and demographic differences between PR3-AAV and MPO-AAV were observed. We observed that interstitial fibrosis (IFTA) is more pronounced in MPO-AAV than in PR3-AAV.

We aimed to investigate the differences in CD163+ macrophage infiltration and interstitial fibrosis between PR3-AAV and MPO-AAV.

Methods: Retrospective single-center study of 80 AAV patients (66 MPO-AAV and 14 PR3-AAV) diagnosed by renal biopsy with at least 1 year of follow-up. Clinical and laboratory variables, ANCA type and renal/patient survival were evaluated. 26 human kidney tissue samples (13 MPO-AAV and 13 PR3-AAV) were stained for CD163+ by immunohistochemistry and immunofluorescence, and trichrome-stained biopsy slides were used to measure the degree of fibrosis. Histomorphometric quantification was performed using MetaMorph® software in both cases (Figure 1A). Data analysis was performed under standard conditions. Statistical significance was defined as P values less than 0.05. All P values were 2-sided.

Results: CD163+ macrophages infiltration in the interstitial space was greater in MPO-AAV than PR3-AAV with statistical significance ($p<0.001$), observing an average infiltration area of 0.333% in MPO-AAV than 0.116% in PR3-AAV. Furthermore, IFTA was higher at diagnosis in MPO-AAV (35.35%) than in PR3-AAV (31,21%) at the diagnosis with a $p=0.03$ (Figure 1B). However, a correlation between IF and CD163+ macrophages infiltration was not possible to stablish.

Conclusions: We have observed an increased macrophage infiltrate with an anti-inflammatory and reparative phenotype that is higher at diagnosis in ANCAS-MPO compared to ANCAS-PR3, the same difference occurs with respect to interstitial fibrosis. Since the study population is small, no correlations between fibrosis and CD163 macrophage infiltration have yet been found.

Disclosures: None.

Figure 1

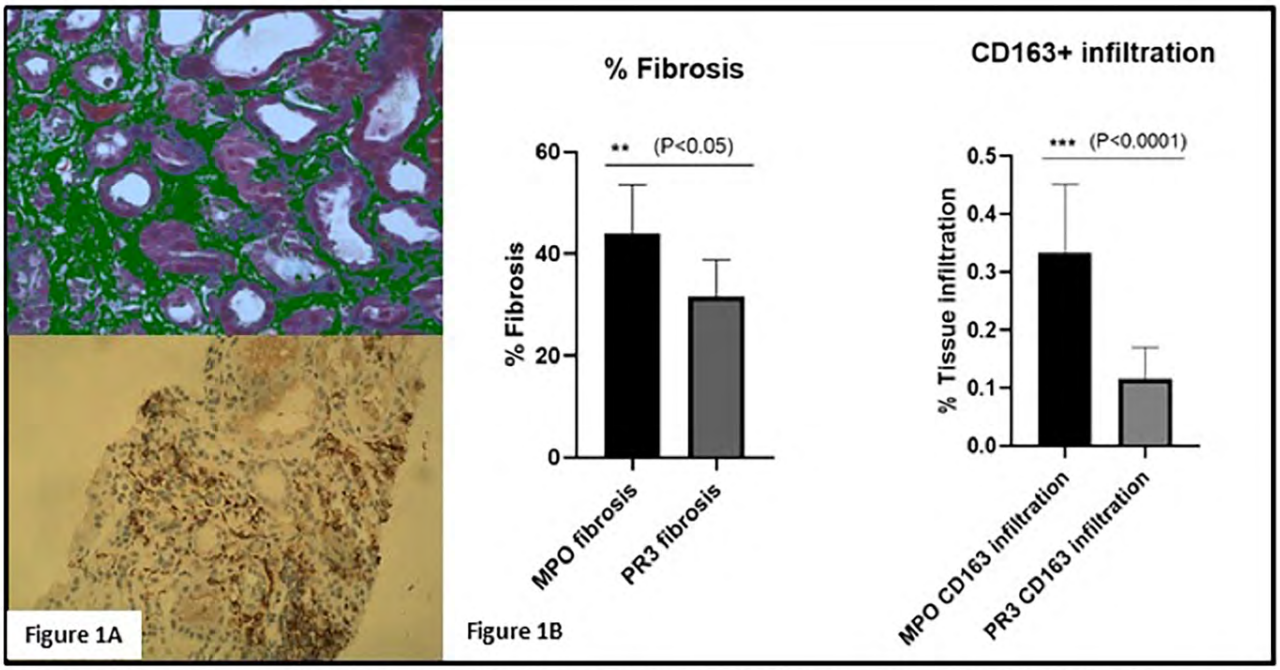

Figure 1A. Histomorphometric quantification of Interstitial Fibrosis using MetaMorph® software on trichrome-stained biopsies slides(up) and a sample stained for CD163+ using immunohistochemistry and immunofluorescence (down). **Figure 1B.** Graphics showing a greater % of fibrosis and CD163+ infiltration in MPO-AAV than in PR3-AAV (statistical significance in both cases).

Poster Tour 4C: Diagnosis and classification

PT-4C-87

Superb microvascular imaging and high frequency ultrasound for vessel wall evaluation in giant cell arteritis

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Background: Ultrasound is a useful tool for diagnose of large vessel vasculitis. New technology, including superb microvascular imaging (SMI), can visualise neovascularisation in the arterial wall, as well as giving more morphological details of the inflamed arterial wall. The aim was to evaluate the value of this technique in patients with suspected giant cell arteritis (GCA).

Methods: US of carotid and central arteries, as well as temporal arteries, was evaluated in 120 consecutive patients with suspected GCA (median age 74 years). Thirteen of these patients had a previous GCA diagnosis, and were investigated for relapse. A Canon Aplio i800 US system with linear transducer i11LX3 and hockeystick transducer i22LH8 were used. Intima media thickness (IMT) and vessel wall echogenicity were assessed in all investigated arteries. Temporal arteries were also investigated regarding compression test, occurrence of neovascularization, and medium echogenic swelling outside the vessel wall (interpreted as inflammatory oedema).

At least 6 months after US, an experienced rheumatologist assessed the final clinical diagnosis. The diagnosis was based on both US and clinical parameters.

Results: US revealed inflammatory findings in 33 out of 107 new patients. Two patient had inflammatory findings restricted to carotid/central arteries. Cranial involvement was observed in 64%. Thirty percent had a combined pattern with ultrasound inflammatory findings in both cranial and extra cranial vessels. Compression test was positive in all affected temporal arteries. A low-medium echogenic homogenous wall thickening was seen in all affected temporal arteries (Figure 1a). However, 14 patients (45 %) depicted a combination with areas of a higher echogenic pattern (Figure 1b).

With SMI, neovascularization was detected in 14 patients (45 %), (Figure 1c).These patients had a more extended inflammation including an increased number of affected cranial vessels. Medium echogenic areas outside the vessel were seen in 35% (Figure 1d). All patients with positive results at US received a clinical diagnosis of GCA >6 months after US.

In the group with previous established GCA, a medium-high echogenic vessel wall pattern was often seen. However, 3 of these patients showed signs of active disease (neovascularization and low-medium echogenic walls) interpreted as GCA relapse and one of these also had neovascularisation.

Conclusion: Modern US equipment, including SMI, can give more morphologic details of the arterial wall and facilitate the evaluation of inflammatory activity in GCA. Further prospective studies regarding vessel wall appearance during the course of GCA disease are warranted.

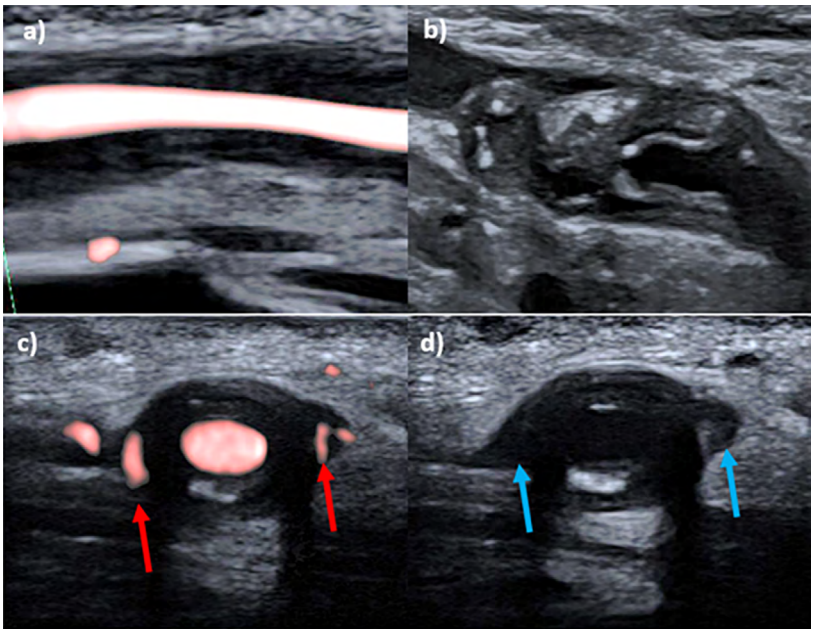

Figure 1. Ultrasound images of GCA affected temporal arteries. a) Low-medium echogenic walls b) Mixed echogenic walls c) Neovascularization (red arrows) d) Swelling outside the vessel walls (blue arrows).

Disclosures: None.

PT-4C-88

Optic nerve sheath enhancement on orbital MRI in giant cell arteritis versus non-arteritic anterior ischemic optic neuropathy

Rebka Ephrem[1], Ryan Rebello[2], Suyash Mohan[1], Robert Kurtz[1], Rui Liang[1], Jae Song[1], Madhura Tamhankar[1], Rennie Rhee[1].
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Background/Objectives: Differentiating giant cell arteritis (GCA)-related anterior ischemic optic neuropathy (GCA-AION) from non-arteritic anterior ischemic optic neuropathy (NA-AION) is challenging, particularly since some patients with GCA lack extra-ocular symptoms. Several case reports describe MRI enhancement of the optic nerve sheath (ONS) in GCA-AION but studies comparing orbital MRI enhancement between GCA-AION and NA-AION are lacking. This study aimed to assess the utility of ONS enhancement on dedicated orbital MRI in distinguishing GCA-AION from NA-AION.

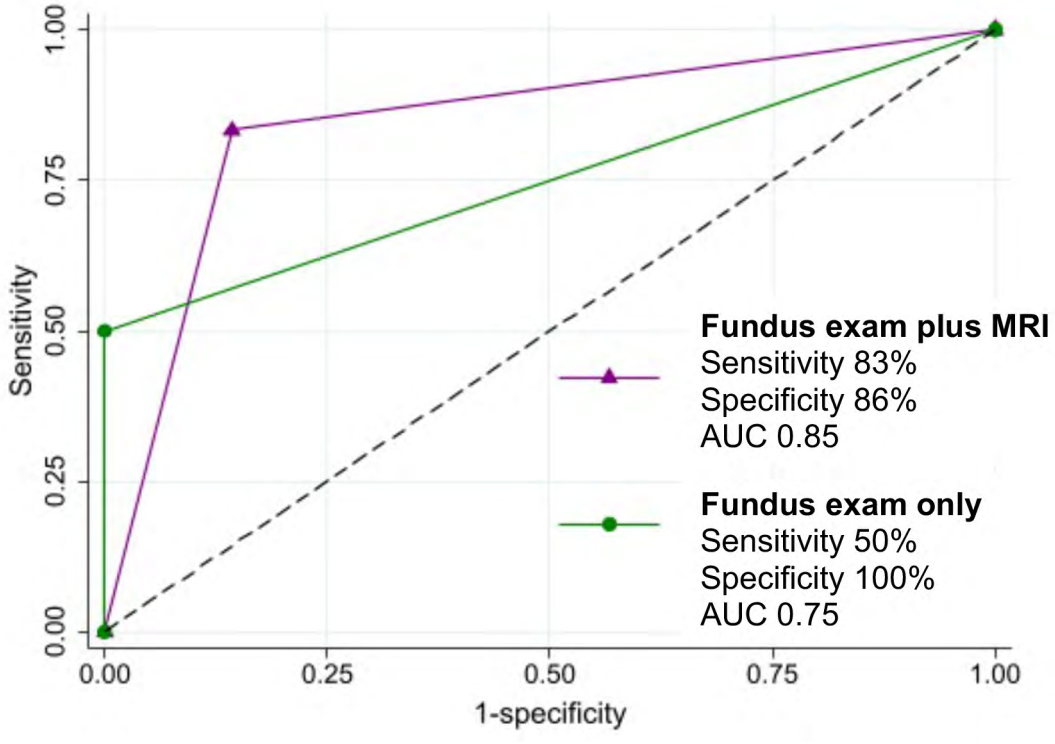
Methods: This case-control study included 26 patients (12 GCA-AION, 14 NA-AION) who underwent contrast-enhanced orbital MRIs within 3 months of symptom onset. Diagnosis of GCA was determined by temporal artery biopsy and/or ACR-EULAR classification criteria. Two radiologists blinded to clinical data independently evaluated MRIs for ONS enhancement; discrepancies were resolved during a consensus reading session with remaining disagreements resolved by a third reader. Groups were compared using Fisher's exact or McNemar's test.

Results: Compared to NA-AION, patients with GCA-AION were significantly older, had more extra-ocular cranial symptoms, but had no difference in visual acuity. On orbital MRI, ONS enhancement was more common in GCA-AION than in NA-AION (67% vs. 14%, P = 0.01). GCA-associated ophthalmologic exam findings of pallid disc edema or retinal ischemia were seen in 50% of GCA-AION vs 0% in NA-AION (P < 0.01). Among 6 GCA-AION patients without pallid disc edema or retinal ischemia, ONS enhancement was seen in 4 (67%) patients. Compared to ophthalmologic exam alone, adding orbital MRI to ophthalmologic exam significantly increased the sensitivity for GCA-AION (50% vs 83%, P = 0.04) and numerically increased the area under ROC curve (AUC) although the difference was not statistically significant (AUC 0.75 vs 0.85, P = 0.27) (**Figure 1**).

Conclusions: Optic nerve sheath enhancement on MRI is more likely to occur in GCA-AION vs NA-AION and was also observed among GCA-AION patients who lacked typical ophthalmologic exam findings, highlighting the potential additive value of orbital MRI in detecting GCA-AION. Future studies are needed to validate these results and demonstrate that orbital MRI improves diagnostic accuracy and patient outcomes.

Disclosures: None.

A. Diagnostic performance of ophthalmologic exam with or without orbital MRI for giant cell arteritis-related anterior ischemic optic neuropathy.



B. Example image of optic nerve sheath enhancement on orbital MRI in patient with giant cell arteritis-related anterior ischemic optic neuropathy.

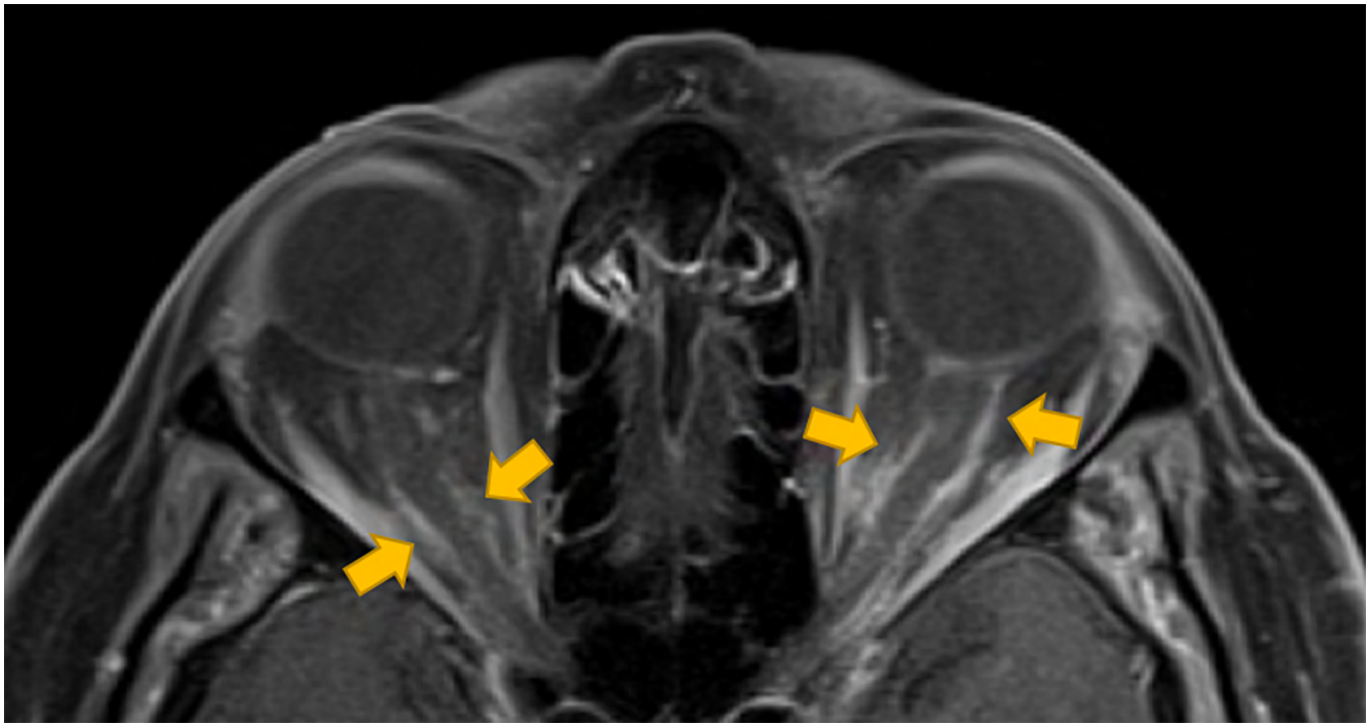


Figure 1. Optic nerve sheath enhancement on MRI distinguishes GCA-related from non-arteritic anterior ischemic optic neuropathy. (A) Diagnostic performance of fundus exam with vs without orbital MRI. Sensitivity for GCA-AION significantly increased upon adding orbital MRI to ophthalmologic examination (P = 0.04). (B) Example of optic nerve sheath enhancement (arrows) in biopsy-confirmed patient with GCA-AION. Image is axial post-contrast T1-weighed fat-suppressed MR image.

PT-4C-89

Validating the 2022 ACR/EULAR ANCA-associated vasculitis Classification Criteria in a Japanese Cohort Study; the Japan Collaborative registry of ANca-associated VAsculitis (J-CANVAS)

Mabuchi Nakako[1], Takashi Kida[2], Yoshiaki Kobayashi[1], Shunichiro Hanai[1], Toshiko Ito - Ihara[3], Takashi Kawaguchi[4], Nobuyuki Yajima[5], Yutaka Kawahito[2], Daiki Nakagomi[1].

[1]Department of Rheumatology, University of Yamanashi Hospital,, Yamanashi, Japan; [2]Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan; [3]The Clinical and Translational Research Center, University Hospital, Kyoto Prefectural University of Medicine, Kyoto, Japan; [4]Department of Practical Pharmacy, Tokyo University of Pharmacy and Life Sciences, Tokyo, Japan; [5]Division of Rheumatology, Department of Medicine, Showa University School of Medicine, Tokyo, Japan.

Background/Objectives: The American College of Rheumatology/European Alliance of Associations for Rheumatology (ACR/EULAR) developed novel classification criteria for ANCA-associated vasculitis (AAV) in 2022[1-3]. This is the first study to validate these criteria in the Japanese population, featuring J-CANVAS, a cohort of AAV patients from multiple institutions and medical departments in Japan.

Methods: The study included 558 patients diagnosed with Microscopic Polyangiitis (MPA), Granulomatosis with polyangiitis (GPA), or Eosinophilic Granulomatosis with Polyangiitis (EGPA) based on the 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides (CHCC2012). We investigated the sensitivity and specificity of each criterion, patients diagnosed with the other two disease subtypes served as the control group.

Results: 335 MPA, 99 GPA, and 104 EGPA patients were enrolled in J-CANVAS. The mean age of patients was 74, 70, 61 years, and the male-to-female ratio was 193(54.4%),54(54.5%),57(54.8%) females, respectively. The sensitivity and specificity of the novel criteria were as follows; MPA 96.1% ・70.0%、GPA 48.5% ・95.8%、 EGPA 84.6 ・98.0%. For the J-CANVAS data, the specificity of MPA and the sensitivity of GPA are particularly low. Therefore, we re-evaluated the new weighting for Japanese people using multivariate analysis. The sensitivity and specificity increased by modifying the items as follows; MPA 90.7% ・86.1%、GPA 83.7% ・99%、EGPA 96.2 ・95.8%.

Conclusions: The 2022 ACR/EULAR ANCA-associated vasculitis Classification Criteria were established referring to the worldwide cohort study, Diagnostic and Classification Criteria in Vasculitis Study (DCVAS). The sensitivity/specificity of this criteria is said to be MPA 91%/94%、GPA 93%/94%、EGPA 85%/99%. However, in a Japanese cohort, the sensitivity of GPA, EGPA and the specificity of MPA seemed to be lower than is described in DCVAS. There may be phenotypic differences between races.

References:

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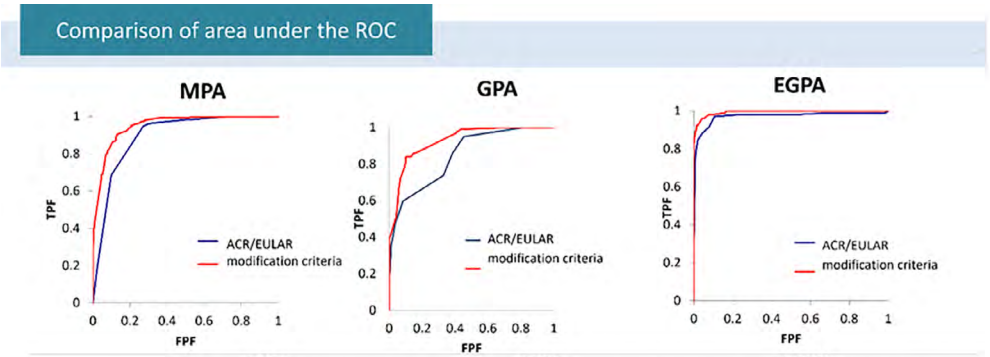
Disclosures: None.



	MPA			GPA			EGPA		
	ACR/EULAR	modification criteria	p値	ACR/EULAR	modification criteria	p値	ACR/EULAR	modification criteria	p値
Sensitivity	96.1	90.7		48.48	→ 83.8		84.62	96.2	
Specificity	70	→ 86.7		95.86	99		98.02	95.8	
Area Under the ROC Curve	0.8962	0.951	<0.001	0.8462	0.9269	<0.001	0.972	0.9942	0.0293
Cut off	5	1.23		5	1.22		6	1.85	

PT-4C-90

Defining Clinical Subgroups of Patients with Relapsing Polychondritis: A Latent Class and Decision Tree Analysis in Two Independent Prospective Cohorts

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[1]University of Maryland, Baltimore, United States; [2]University of Pennsylvania, Pennsylvania, United States; [3]NIH, Bethesda, United States.

Background/ Objectives: Multiple factors contribute to diagnostic delay in patients with relapsing polychondritis (RP), including lack of awareness among healthcare providers, rarity, and disease heterogeneity. Using latent class analysis (LAC), phenotypic subgroups have been identified in a prospective cohort of patients with RP. [1] Identifying these subgroups can help clinicians to recognize patterns of organ involvement, facilitating prompt diagnosis and treatment. This study aimed to validate previously identified clinical subgroups using LAC and develop a decision tree algorithm to accurately predict assignment of individual patients to these subgroups.

Methods: Patients ≥ 18 years old who met diagnostic criteria for RP. All patients had a dynamic chest computerized tomography (CT) and audiometry. LAC was conducted in two independent prospective cohorts of patients with RP using the following variables: arthritis, tracheomalacia, bronchomalacia, subglottic stenosis, ear damage, nose damage, eye inflammation, and sensorineural hearing loss. Ear damage was defined by thickening of the cartilage or cauliflower ear. Nose damage was defined by saddle nose deformity or nasal septal perforation. Tracheomalacia and bronchomalacia were defined as ≥ 50% airway collapse on dynamic chest CT. Optimization of latent class models was performed using Bayesian information criterion (BIC) and Akaike information criterion (AIC). Decision tree analysis was performed to predict latent class group status.

Results: 162 patients with RP were included in this study. Cohort #1 included 102 patients: 92 (90%) females; 93 (91%) Caucasians; median age 48 years (IQR= 38-59). Cohort #2 included 60 patients: 52 (86%) females; 52 (86 %) Caucasians; median age 44 years (IQR=38-52).

Three clinical subgroups were identified by LAC in each cohort: Type 1 was characterized by ear damage, nose damage and subglottic stenosis, Type 2 was characterized by tracheomalacia and bronchomalacia, and Type 3 was characterized by absence of tracheomalacia.

Tracheomalacia and ear damage were the two critical variables found on the decision tree that predicted latent class assignment in both cohorts. In cohort #1, the accuracy was 98% (R-square = 0.91) and in cohort #2 the accuracy was 100% (R-square=0.95). **Figure 1.**

Conclusions: This study corroborates the existence of previously identified clinical subtypes of RP. Tracheomalacia and ear damage effectively categorize patients into these subgroups. These findings support the potential use of this subgrouping in clinical practice and clinical research design.

References:

1. Ferrada M, Rimland CA, et al. Defining Clinical Subgroups in Relapsing Polychondritis: A Prospective Observational Cohort Study. *Arthritis Rheumatol*. Aug 2020;72(8):1396-1402. doi:10.1002/art.41270

Disclosures: Consulting and Research Support: AbbVie, Amgen, AstraZeneca, Boeringher-Ingelheim, Bristol-Myers Squibb, GlaxoSmithKline, InflaRx, Takeda.

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Research support only: Eicos, Electra, Forbius, Genentech/Roche, Genzyme/Sanofi, Neutrolis.

Consulting and stock options: Kyverna, Q32, Sparrow

Royalties: UpToDate.

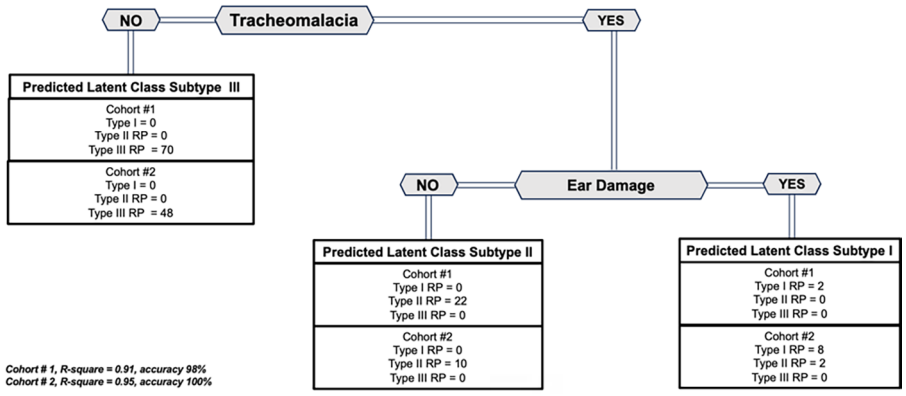

Figure 1. Decision tree analysis to classify patients with relapsing polychondritis into three subgroups defined by latent class analysis.

PT-4C-91

*HLA-B*51* and its subtypes as diagnostic tools for Behçet's Disease – where do we stand?

Erika Biegelmeyer[1], Frederico A. G. Pinheiro[1], Sarah A. C. Neaime[1], Joao Gabriel A. O. Dantas[1], Faustino Peron[1], Joice M. F. M. Belém[1], Luis Eduardo C. Andrade[2], Alexandre W. S. De Souza[1].

[1]UNIFESP-EPM, São Paulo, Brazil; [2]Fleury Group, São Paulo, Brazil.

Background/ Objectives: To evaluate the diagnostic properties of *HLA-B*51, HLA-B*51:01,* and *HLA-B*51:08* subtypes as a diagnostic tool for Behçet's disease (BD).

Methods: In this cross-sectional study, we included 73 BD patients who met the 1990 International Study Group Criteria and healthy controls (n=253)[1]. Study participants underwent the *HLA-B*51* genotyping by the PCR-SSP technique and the presence of *HLA-B*51:01* and *HLA-B*51:08* subtypes was determined by the Sanger sequencing method.

Results: Most of the participants were female (54.8% in BD and 61.6% in HC). The median age at study was significantly lower in BD patients than in HC [44.0 years (33.0-53.0) vs. 55.0 years (43.0-65.2); $p < 0.0001$], as we intentionally aimed to include HC older than the median age at BD onset. There were no other significant demographic differences between groups. The calculated prevalence of BD in this study population was 22%. *HLA-B*51, HLA-B*51:01* and *HLA-B*51:08* subtypes had an overall low sensitivity (32.8%, 20.5%, and 5.5%, respectively), but high specificity (84.5%, 87.9% and 99.8%) and good diagnostic accuracy (73.1%, 73.1% and 79%, respectively) for BD. Intriguingly, the *HLA-B*51:08* subtype had very high specificity (99.8%) and it was the only test with a high positive predictive value (PPV = 88.8%), as well as an elevated positive posttest probability (88.9%), represented in Fagan`s nomogram in Figure 1. In addition, *HLA-B*51:08* had the highest diagnostic odds ratio (DOR = 29.00) when compared to *HLA-B*51* (DOR = 2.66) and *HLA-B*51:01* (DOR = 1.89). All alleles had a moderately low negative likelihood ratio (LR-) (0.79, 0.90, and 0.94), but only *HLA-B*51:01* had a high positive likelihood ratio (LR+ = 28.32) compared to *HLA-B*51* and *HLA-B*51:01* (2.12 and 1.71 respectively) for BD diagnosis. Notably, *HLA-B*51:08* was *also exclusively positive in BD patients in this cohort.*

Conclusions: *HLA-B*51:08* carriage was associated with higher diagnostic parameters than the other *HLA-B*51* subtypes. *HLA-B*51:08* was associated with higher specificity, PPV, LR+, and post-test probability for diagnosis of BD. However, it had a very low sensitivity for BD. To date, there is no data to support *HLA-B*51* testing for BD diagnosis.

References:

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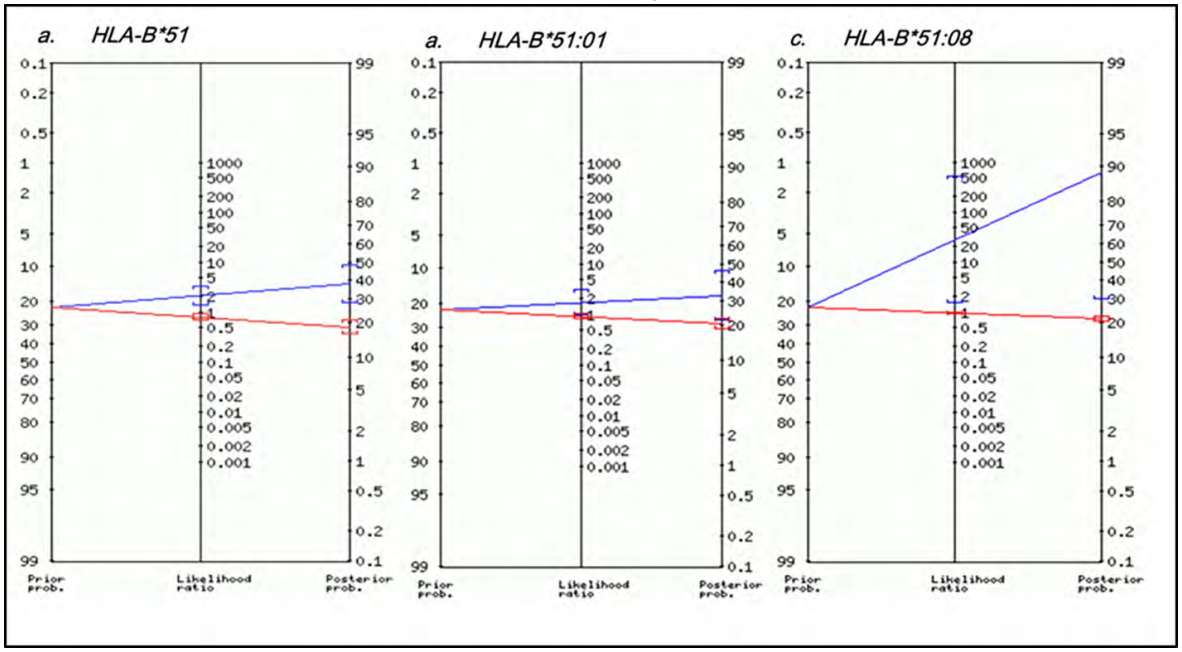
Disclosures: None.

Keywords: Behçet's syndrome, HLA-B51, B51:08, Diagnostic test.

Figure 1 – Fagan`s nomogram for the diagnostic performance of *HLA-B*51, HLA-B*51:01* and *HLA-B*51:08* subtypes in Behçet's disease



Legend: Fagan's nomogram illustrates that the *HLA-B*51:08* subtype achieves the highest positive post-test probability (88.9%) for Behçet's disease when compared to *HLA-B*51* (a) and *HLA-B*51:01* (b) (31.5% and 32.6%, respectively).

PT-4C-92

The role of miRNAs in classifying ANCA-associated vasculitis: epigenetics versus serology

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Background/ Objectives: Comprehensive data on expression of microRNAs (miRNAs) in renal tissue affected by ANCA-associated vasculitis (AAV) is lacking despite recent advances that have implicated miRNAs in AAV[1]. Currently, ANCAs are still considered the best standard diagnostic classifier and activity marker in AAV despite several limitations they bear. Since miRNAs have been touted as promising biomarkers in other autoimmune diseases, we have analysed and compared tissue samples of AAV patients stratified by ANCA serology studies into either MPO-AAV or PR3-AAV as to compare their miRNA expression profiles.

Methods: Comprehensive miRNA expression profiling was performed using panels with 752 miRNAs by means of qPCR on formalin-fixed, paraffin-embedded renal biopsy tissue samples from 26 patients. Both MPO-AAV and PR3-AAV groups comprised 13 treatment-naive AAV patients with histological verification of florid renal involvement in the form of pauci-immune crescentic glomerulonephritis and no significant renal (glomerular) co-pathology. RNA isolates from renal biopsy material were randomly pooled into two pools for each MPO-AAV and PR3-AAV and each pool contained different patients. The expression of individual miRNAs (ΔCt) was normalized by global mean averaging. Differences in normalized individual miRNA expression values ($\Delta\Delta$Ct) were then tested for statistical significance between the pooled samples using a t-test.

Additionally, we strove to match both study groups (MPO-AAV and PR3-AAV) by age, gender, eGFR, daily proteinuria values and the degree of interstitial fibrosis/tubular atrophy to the maximum extent possible as to minimize the potential effect of these variables on our results.

Results: The screening revealed 14 miRNA that differentiated MPO-AAV from PR3-AAV-PR3. Interestingly, three of 14 identified miRNAs belong to *miR-181* family, which is known to be involved in different stages of T-cell activation/differentiation[2]. However, a validation study of these differentially expressed miRNAs in an independent, larger sample cohort is needed to establish their potential diagnostic utility.

Conclusions: Specific expression alterations of miRNAs could be considered candidate diagnostic and activity biomarkers of AAV. Moreover, given that MPO- and PR3-AAV are increasingly considered distinct entities and that ANCAs suffer from several limitations as AAV biomarkers, we hypothesize that differential expression of selected miRNAs is superior to ANCA serology studies in classifying and reflecting activity of AAV. However, a validation study is warranted to establish the putative utility of miRNA expression profile as a reliable and accurate AAV biomarker.

References:

1. Bošnjak, M.; Večerić-Haler, Ž.; Boštjančcič, E.; Kojc, N. Renal Tissue miRNA Expression Profiles in ANCA-Associated Vasculitis—A Comparative Analysis. *Int. J. Mol. Sci.* 2022, 23, 105. https://doi.org/10.3390/ijms23010105
2. Bell-Hensley, A., Das, S., & McAlinden, A. (2023). The miR-181 family: Wide-ranging pathophysiological effects on cell fate and function. *J. Cell. Physiol.* 238, 698–713. https://doi.org/10.1002/jcp.30969

Disclosures: None.

PT-4C-93

Evaluation of the 2022 ACR/EULAR Classification Criteria for GPA and MPA in a European Cohort

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Background and Purpose: In 2022, ACR and EULAR proposed new classification criteria for granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) based on a numerical item scoring system for different manifestations in ANCA-associated vasculitis (AAV) emphasizing the role of laboratory findings. We (i) retrospectively re-classified patients from our multicentric AAV cohort according to the 2022 ACR/EULAR criteria for GPA and MPA using a computational algorithm that involved existing clinical, laboratory and histological data, (ii) compared these results to prior clinical diagnoses and (iii) investigated the predictive power of organ manifestations for classification.

Methods: Data of AAV patients, diagnosed between 2000 and 2021 in four tertiary referral centers (Germany and Switzerland), were collected. Cases without conclusive ANCA status were excluded from computed analysis. The 2022 ACR/EULAR criteria were applied by algorithmically analyzing BVAS entries for organ manifestation, laboratory results for ANCA/ELISA testing and histological data for detection of granuloma and/or pauci-immune glomerulonephritis. Results were compared to previously reported diagnoses and clinical manifestations were analyzed by their odds ratio (OR) to be either diagnosed or classified as GPA or MPA.

Results: The dataset included a total of 358 cases, 168 females (46.9%), mean age 59.2 years (range 16-87). Based on the 2022 ACR/EULAR criteria, 342 (95.5%) cases could be unambiguously classified. 203 patients classified as GPA, 136 as MPA, 3 fulfilled GPA and MPA criteria and 16 remained unclassified. The overall accuracy was found to be higher in GPA with 94,8% (vs. 87,3% in MPA). Within all cases classified as MPA, the ACR/EULAR itemized score sums up to a median of 9 points (range 5-9) in MPA cases. Classification as GPA sums up to a median score of 6 points (range 5-12). All 14 patients who switched from GPA to MPA were MPO-ANCA/pANCA positive. Among those, 9 patients had ENT-manifestations and 8 had lung manifestations. All 3 patients who fulfilled both criteria were double positive for MPO-ANCA/pANCA and PR3-ANCA/cANCA. Mucous membranes-eyes-, and ENT manifestations were indicative for classification as GPA. Within the patients who classified as MPA, only renal manifestation favored MPA, while mucous membranes- /eyes- and ENT manifestations, along with nervous system manifestation, were associated not to classify as MPA (fig1).

Conclusion: The computational algorithm performed well to categorize 95.5% of all cases. Our findings demonstrated accuracy rates above 87,3% and suggest a higher specificity for GPA, but higher sensitivity for MPA classification criteria as well as better selectivity in MPA. Reclassification shifted typical risk factors for relapse into MPA subtype, which might impact relapse rates in MPA.

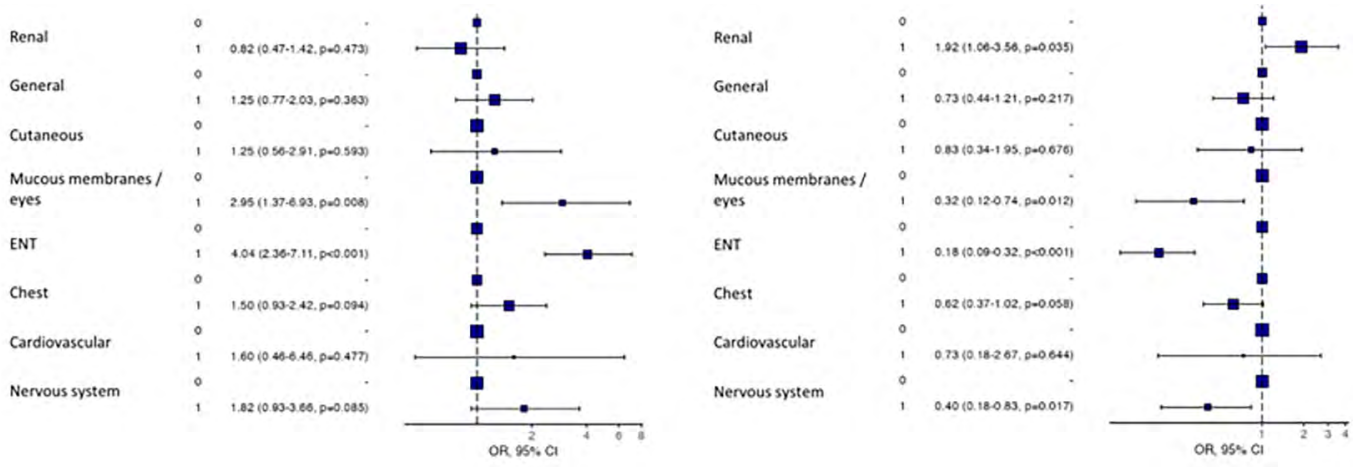

Figure 1. *Distribution of organ manifestation, indicated by box size and probability, represented by odds ratio, of being classified as GPA (left) or MPA (right) according to ACR/EULAR 2022 criteria.*

Disclosures: Study funding from Vifor Fresenius Medical Care Renal Pharma Ltd.

POSTERS

21ST INTERNATIONAL

VASCULITIS

WORKSHOP

BARCELONA

7 - 10 APRIL **2024**

1. CLINICAL SCIENCE
1.01. Diagnosis and classification: imaging (role in diagnosis, new tracers); pathology...

P-001

Histopathological diagnostic markers of otitis media with ANCA associated vasculitis

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Background/ Objectives: ANCA-associated vasculitis (AAV), such as GPA, manifest necrotic granulomatous lesions in the upper respiratory tract. Among refractory otitis media in adults, there exhibit otitis media with ANCA associated vasculitis (OMAAV), which develops by the same mechanism, and its difference from GPA has been debated. OMAAV is difficult to diagnose early and can cause serious complications and even be fatal. However, the histological characteristics and diagnostic criteria for OMAAV have not yet been established. Therefore, we extracted the histological parameters of OMAAV and validated them to formulate diagnostic criteria.

Methods: A total of 206 slides from 81 cases including 34 cases of OMAAV, as well as 32 cases of chronic sinusitis, 5 cases of non-specific chronic otitis media, and 10 cases of laryngeal granuloma as control cases were analysed. As a preliminary analysis, histological parameters were qualitatively or semi-quantitatively evaluated in a double-blind manner. Histological parameters included: (1) erosion, (2) edema, (3) fibrosis, (4) any inflammatory cell infiltration, (5) lymphocyte infiltration, (6) neutrophil infiltration, (7) eosinophil infiltration, (8) plasma cell infiltration, (9) macrophage infiltration, (10) superficial necrosis, (11) inflammatory cell infiltration in small vessel walls, (12) cell anchoring to vascular endothelium, (13) granuloma formation, (14) occlusion of muscular arteries/veins, (15) qualitative evaluation of muscular arteriovenous vasculitis, (16) small vessel hyperplasia, (17) irregular vascular thickening, (18) granulation, (19) thickness of the mucosa with Belag, (20) Russell's body number per high-power field as well as description regarding (21) the pattern of fibrosis, (22) the type of covering epithelium, and (23) the main infiltrating cells. As the next step, in order to verify the validity of candidate parameters revealed in the preliminary study, we divide the above cases into a Training Set and a Testing Set, then share the whole slide images with the research collaborators.

Results: In the preliminary analyses, significant differences were found in: 1) manifestation of arteritis/phlebitis; 2) arterial/venous occlusion as positive findings in OMAAV, on the other hand, 3) edema; 4) eosinophil infiltration and 5) plasma cell infiltration were found to be negatively correlated candidate histological parameters. In order to verify the validity of each of these parameters, the cases were divided into a training set and a testing set. The male to female ratio was almost the same, and the average age was within ±2 years. Using this set, we conducted the validity of extracted parameters.

Conclusions: We successfully obtained effective histological biomarker of OMAAV with statistical validity. We expected those parameters will be established as the diagnostic criterion.

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3. Tabei A. et al. Mod Rheumatol.; 32(5), 923-929, 2023.

Disclosures: None.

P-002

Dual MPO/PR3 ANCA Positivity and Vasculitis: Insights from a 7-Cases Study and an AI-Powered Systematic Literature Review

Eléonore Bettacchioli[1], Jean-Baptiste Foulquier[2], Baptiste Chevet[1], Emilie Cornec-Le Gall[1], Catherine Hanrotel[1], Luca Lanfranco[1], Claire De Moreuil[1], Yannick Lambert[2], Maryvonne Dueymes[1], Nathan Foulquier[1], Divi Cornec[1].

[1]CHU de Brest, Brest, France; [2]CH de Morlaix, Morlaix, France.

Background: Anti-neutrophil cytoplasm antibodies (ANCA)-associated vasculitides (AAV) are rare conditions characterized by inflammatory cell infiltration in small blood vessels, leading to tissue necrosis. While the majority of patients with AAV present antibodies against either myeloperoxidase (MPO) or proteinase 3 (PR3), rare cases of dual positivity for both antibodies have been reported, and their impact on the clinical picture remains unclear.

Methods: We conducted a retrospective screening for dual positive (DP)-ANCA cases, analyzing ANCA results from March 2013 to March 2022 in our University Hospital. Detailed clinical, biological, imaging, and histological data were collected for each DP-ANCA case. Additionally, a literature review on DP-ANCA cases was performed using an artificial intelligence (AI)-based search with the BIBOT software combined to a manual search in PUBMED database.

Results: The report of our cases over the last 9 years and those from the literature allowed us to analyze 103 described cases of patients with DP-ANCA. We identified four distinct phenotypic profiles: (i) idiopathic AAV (~30%), (ii) drug-induced AAV (~25%), (iii) autoimmune disease associated with a low risk of developing vasculitis (~20%), and (iv) immune-disrupting comorbidities (infections, cancers, etc.) not associated with AAV (~25%).

Conclusion: This study presents a comprehensive analysis of over a hundred DP-ANCA cases, revealing distinct phenotypic profiles. Continued reporting of these rare DP-ANCA cases is necessary to validate and further enhance our understanding of this rare presentation.

Conflict of interest: None.

P-003

Evaluation of takayasu arteritis 1990 and 2022 classification criteria: age of onset of symptoms may be important for maintaining specificity

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Background: Takayasu Arteritis (TA) is a rare large vessel vasculitis affecting aorta and its major branches. Diagnosis and classification are often challenging due to low prevalence of TA and increased rate of atherosclerotic vascular disease (AVD) which is also the frequent problem in differential diagnosis. In 2022, a new criteria set has been developed by ACR/EULAR as a replacement for historical 1990 classification criteria. We aimed to evaluate both criteria and factors that may predict final TA diagnosis in our cohort with long term follow-up, which includes patients with a preliminary diagnosis of TA.

Methods: Data of 142 patients who followed-up at least six months with a clinical diagnosis of TA between 1990-2020 in a single referral centre was included into the study. ACR 1990 and ACR/EULAR 2022 classification criteria were retrospectively implemented and evaluated for performance and agreement. Clinical, laboratory and imaging findings of patients with a final diagnosis of TA were compared to the patients who were not considered as TA and excluded from follow-up.

Results: Mean age of the TA patients at diagnosis was 33.4±12.7 (7-70) and 127 (89.4%) was female. Median time between diagnosis and time of onset of complaints was 14 (6-50) months. Eight (5.6%) patients who met the ACR 1990 CC were decided to have AVD after a mean follow up time of 9.4±4.1 (6-12) months and excluded from follow-up. In the initial cohort of 142 patients, 138 (97.2%) fulfilled the ACR 1990 criteria (sensitivity was 97%) and 129 (90.8%) fulfilled the ACR/EULAR 2022 CC (sensitivity was 93.2%). Eight patients with a final diagnosis of TA did not meet the absolute requirements, five of them were over 60 years old at diagnosis and three patients did not have structural arterial changes but vessel wall enhancement compatible with inflammation in angiography. Four of eight patients with a final diagnosis of AVD were met ACR/EULAR 2022 Criteria. Kappa statistics between two criteria sets was statistically significant (p=0.004) but agreement was low (0.21). Comparison of patients with a final diagnosis of TA and AVD revealed that, patients with a final diagnosis of TA were significantly younger; had abnormal CRP and ESR at diagnosis, significant history of smoking and increased thoracic aorta involvement compared to AVD (table 1).

Conclusions: In our cohort, both criteria showed sufficient sensitivity. Premature AVD has been the most common mimic of TA and despite an improvement in ACR/EULAR 2022 criteria which reduced false positivity rate, both criteria failed to distinguish between these two diseases. Similar clinical findings and angiographic involvement of TA may be confused with AVD, and younger age of onset and high acute phase reactants should lead clinicians towards a diagnosis of TA. Agreement between criteria sets was low possibly due to absolute requirements in the 2022 criteria. Vessel wall enhancement in imaging studies may be a useful early detectable sign of inflammation. We suggest further studies with sufficient number of controls with AVD are needed to solve this potential specificity issue.

Disclosures: None.

	TA (n=134)		AVD (n=8)		P	OR	95% CI
	N	%	N	%			
Age of onset of complaints<40 years	**114**	**85.1**	**2**	**25**	**<0.001**	**17.1**	**3.2-90.8**
Age of onset of complaints	**32.3±12**		**51±11.9**		**<0.001**		
Sex (female)	121	90.3	6	75	0.17		
Smoking	**21**	**18.8**	**5**	**62.5**	**0.004**	**0.14**	**0.03-0.6**
Hypercholesterolemia	10	7.5	2	25	0.08		
Clinical findings							
Carotydinia	48	35.8	2	25	0.53		
Decreased pulse on brachial artery	100	74.6	4	50	0.13		
Systolic BP difference> 10mmHg between arms	87	64.9	4	50	0.4		
Laboratory at diagnosis							
CRP,mg/dl, med (IQR)	**26 (52)**		**6 (6)**		**0.005**		
ESR,mm/h, mean±SD	**63.4±35.5**		**29±22**		**0.006**		
Platelets x10^9/L, mean±SD	**337±110**		**229±46**		**0.02**		
Involved arteries							
Thoracic aorta	**82**	**61.2**	**2**	**25**	**0.04**	**4.7**	**1.05-24.3**
Pulmonary artery	14	10.4	0	0	0.33		
Abdominal aorta	78	58.2	5	62.5	0.8		
Carotid arteries	97	72.4	5	62.5	0.55		
Subclavian arteries	118	88.1	8	100	0.3		
Renal arteries	84	62.7	1	12.5	0.16		
Mesenteric artery	39	29.1	0	0	0.07		
Iliac arteries	18	13.4	2	25	0.36		

Table 1: Comparison of patients with a final diagnosis of TA and AVD. AVD: Atherosclerotic vascular disease, BP: Blood pressure, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate.

P-004

The Real World Performance of Combined Cranial and Large Vessel FDG-PET/CT as a First-Line Investigation for Giant Cell Arteritis

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Background/ Objectives: GCA is a systemic medium-large vessel vasculitis (M-LVV) that is increasingly being diagnosed with advanced imaging rather than biopsy. Studies conducted in research settings have shown that PET/CT including the cranial and large vessels offers high diagnostic accuracy for GCA(1). Little is known, however, about its performance as first line test for GCA in real-world settings where patient selection and pre-scanning treatment cannot be controlled. At our institution in Sydney, Australia, PET/CT is the first-line investigation for GCA, and we aimed to assess its diagnostic performance in this “all comer” setting.

Methods: We audited all inpatients and outpatients investigated with PET/CT for suspected new onset GCA between July 2019 and March 2022. Patients were scanned from vertex to thighs with arms by their side, 90 minutes post-fluorodeoxyglucose (FDG) administration. Patients completed a self-reported questionnaire at the time of scan. Scans were reported by the experienced nuclear medicine physician of the day as overall positive, equivocal or negative for M-LVV. FDG uptake by vascular region was also reported. The gold standard comparator was the treating clinician’s diagnosis of active M-LVV at a minimum of 6 months after the scan. Active M-LVV included diagnoses of GCA, large vessel vasculitis and aortitis. Temporal artery biopsy (TAB) and vascular US results conducted within 4 weeks of scan were recorded.

Results: 135 patients underwent PET/CT for suspected new onset GCA, with a median age of 73 years (range 48-98), 70% were female. 86 (63.7%) patients were taking glucocorticoids at the time of scan including 50 (37%) on doses of 40 mg or higher. 44 (32.6%) patients had a final clinical diagnosis of active M-LVV. 35 (25.9%) scans were reported as positive, 27 (20%) equivocal and 73 (54.1%) negative for M-LVV. The likelihood ratio for a diagnosis of active M-LVV with a positive scan was 70.3, equivocal scan 0.59, and a negative scan 0.12. Sensitivity (Sn) and specificity (Sp) of PET/CT was dependent on treatment of equivocal scans in the binary analysis. If equivocal scans were excluded, Sn was 89.5% and Sp 98.6%. If equivocal scans were considered positive, Sn was 90.9% and Sp 75.8%. If equivocal scans were considered negative, Sn was 77.3% and Sp 98.9%. Half of those with an equivocal scan underwent second line testing with either temporal artery biopsy (TAB) or ultrasound (US) and ultimately 6/27 (22%) were diagnosed with M-LVV.

Conclusions: This is the largest real-world study of combined cranial and large vessel PET/CT as a first-line test for GCA. PET/CT had good diagnostic performance with sensitivity ranging from 77.3 to 90.9%, and specificity 75.8 to 98.9% for a clinician diagnosis of active M-LVV, depending on treatment of equivocal scans. This performance is similar to that reported for TAB and US performed in expert centres and supports its use as a first-line investigation.

References:

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Disclosures: Nil.

P-005

Addressing Obliterative Endarteritis: Unveiling Neuropathic Pain through POCUS and Managing Recurrent Leg Pain with Ultrasound-Guided Dry Needling

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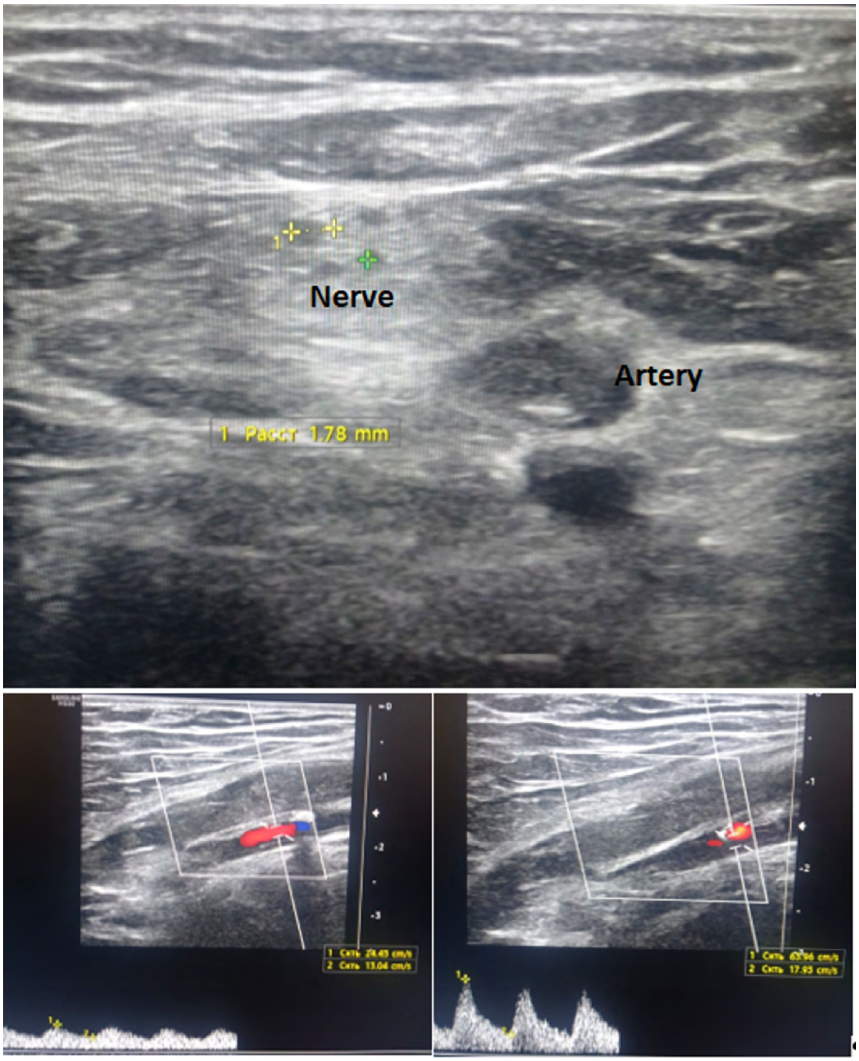
Introduction: Leg pain poses diagnostic challenges, necessitating innovative approaches. This case explores a 62-year-old male mechanic (exposure to cold and long standing) with leg pain, initially suspected to be sciatic neuropathy. Diabetes, smoking excluded Point-of-care neuromuscular ultrasound (POCUS) played a pivotal role in uncovering a vascular component to the pain.

Methods: Neurophysiological exams indicated sciatic neuropathy, confirmed by multiple EMG tests. The ultrasound examination revealed specific findings of moderate sciatic neuropathy: echoscopy of the sciatic nerves displayed tibial and peroneal fascicles measuring 1.3-2.2 mm and 2.6 mm, respectively, on both sides (Figure). Notably, there was occlusion of the right popliteal and femoral arteries, with right tibialis posterior showing narrowing due to hypoechoic layers on the walls. The left posterior tibial artery exhibited almost total obliteration, emphasizing obliterative endarteritis.



Treatment Approach: Ultrasound-guided dry needling (DN-US) addressed myofascial and neuropathic components. Following R. Bubnov's protocol [1], myofascial trigger points were identified and treated with a single fine needle (28G) under US guidance. This approach resulted in a significant reduction in pain levels.

Results: Pre-treatment observations included arterial occlusions, muscle hypotrophy, and altered blood flow. DN-US led to improved blood flow, increased mean systolic velocity (MSV), and reduced pain (VAS score 6-7 to 1-2). Collateral arteries showed enhanced blood flow with new vessels appearing, emphasizing the unexpected efficacy of DN-US in addressing vascular issues.

Discussion: The neurophysiological diagnosis initially considered neuropathy as the primary cause of pain. However, ultrasound findings suggested a more moderate neuropathic involvement and indicated a vascular cause. Despite this, the patient underwent US-guided dry needling (DN-US) as initially directed, and remarkably, it proved effective in addressing both neuropathic and unexpectedly, vascular issues contributing to the pain. Relevant ultrasound parameters were recorded to document the observed improvements. This case is notable for the rarity and complexity of its components. Challenges in achieving a conclusive neurophysiological diagnosis prompted consideration of alternative diagnostic methods, emphasizing the importance of a comprehensive diagnostic approach in complex pain scenarios.

Conclusion: The positive response to DN-US emphasizes the interconnected nature of neuropathic and vascular pain components. This case underscores the potential efficacy of innovative interventions in managing complex pain scenarios, even when the primary cause is not immediately evident.

Keywords: Obliterative endarteritis, Ultrasound-Guided Dry Needling, Recurrent Low Back Pain, Myofascial Trigger Points, Non-Invasive Management, Clinical Guidelines.

Reference:

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P-006

The angiographic and echocardiographic characteristics of pulmonary artery involvement in Takayasu arteritis

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Background/Objectives: The frequency of pulmonary arterial involvement (PAI) in Takayasu arteritis (TAK) has been reported to range between 5.7-20.0%.[1,2] PAI may be related to a worse prognosis, and early detection and treatment of PAI may lead to a better disease course. Diagnosis of PAI is mainly based on computed tomographic pulmonary angiography (CTPA) with high iodinated contrast and radiation exposure. It was reported that echocardiography could provide evidence of characteristic changes in pulmonary arteries (PA) in TAK patients.[3] In this study, we investigated the characteristics of PAI and echocardiographic findings of PA in TAK patients.

Methods: This study included 72 TAK patients (62 female/10 male) who underwent CTPA to investigate PAI between January 2021 and July 2023. An echocardiographic evaluation was done, and two cardiologists measured PA wall thickness. An experienced radiologist reviewed CTPA images, and pulmonary vasculitis (PV) is characterized by increased PA wall thickness, stenosis, and/or thrombosis. Disease characteristics of the patients were collected from patient files.

Results: The mean age of the patients was 46.4±13.0 years, and nine patients had active disease. The median CRP and ESR values were 3.1 (3.7)mg/L and 14.5 (21.0)mm/hr. The treatments for TAK were csDMARD in 62 (86.1%), bDMARD in 25 (34.7%), glucocorticoids (GC) in 30 (41.7%) and acetylsalicylic acid (ASA) in 50 (69.4%) patients.

Twenty-two (30.6%) patients had a pulmonary symptom, most commonly dyspnea and chest pain when CTPA was performed.

PV was detected in 13 (18.1%) patients. Additionally, in 5 (6.9%) patients PA thrombosis unrelated to vasculitis was present. (Figure 1) Among 13 PV patients, csDMARD or bDMARD was changed in 9 (69.2%), GC was started, or the dose was increased in 8 (61.5%) and anticoagulants were started in 7 (53.8%).

The presence of pulmonary symptoms, CRP and ESR values were significantly higher in patients with PV ($p<0.001$, $p=0.001$, and $p=0.008$). In addition, PV was significantly lower in patients using ASA ($p=0.002$).

Echocardiographic evaluation of the PA wall thickness could be done in 48 (66.7%) patients. The mean PA wall thickness was 0.45±0.10 cm. There was no significant difference regarding PA wall thickness between patients with and without PV ($p=0.50$). Additionally, no significant difference was found between PA wall thickness and age, pulmonary symptoms, GC or csDMARD use, ESR and CRP values.($p>0.05$ for all).

Conclusions: In this study, PV was present in 18.1% of TAK patients, and pulmonary symptoms, higher ESR and CRP values, and lower ASA use were significantly associated with PV. We found no relationship between PAI and PA wall thickness measured by echocardiography. Further studies are required to understand the role of echocardiography in evaluating PAI in TAK patients.

Disclosures: None.

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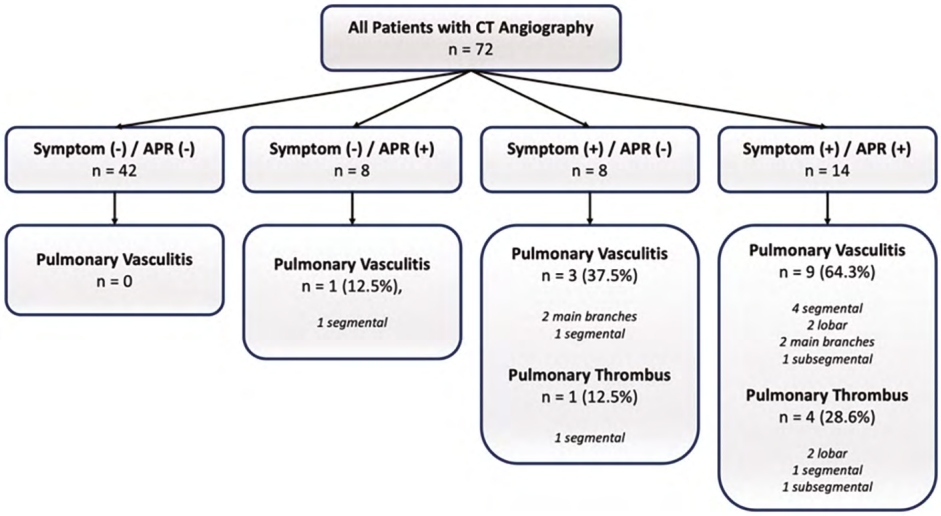

Figure 1. The distribution of CT angiography findings according to the presence of symptoms and high acute phase reactants.

P-008

Eosinophilic Granulomatosis with Polyangiitis: Clinical Suspicion Red Flags Identification by a Systematic Literature Review and Multidisciplinary Expert Consensus

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Background/Purpose: Eosinophilic Granulomatosis with Polyangiitis (EGPA) is a rare ANCA-associated vasculitis, characterized histologically by eosinophilic tissue infiltration, necrotizing vasculitis, and eosinophil-rich granulomatous inflammation.

The diagnosis of EGPA is often challenging due to its rarity, heterogeneous and multiorgan clinical presentation, and the overlapping with other vasculitis or eosinophilic disorders. The identification of suspicion signals of EGPA addresses a fundamental practical barrier in achieving timely diagnosis for patients with this rare but potentially devastating disease.

Our purpose was to identify a comprehensive and evidence-based checklist of signs, symptoms and laboratory parameters reported to precede the diagnosis of EGPA that can be used as red flags, raising the suspicion and prompt the performance of appropriate confirmatory tests.

Methods: A systematic literature search strategy was developed to identify signs, symptoms and laboratory abnormalities that should raise the suspicion of a possible EGPA patient. GRADE (Grading of Recommendations, Assessment, Development and Evaluations) methodology was used to assess the quality of the scientific evidence supporting each criterion.

A multidisciplinary nominal group consensus approach (including rheumatologists, internal medicine specialists, pulmonologists, and allergists) was established for the development of the expert consensus.

Red flags identified as suspicion signals for EGPA were categorized by organ system, manifestation, and laboratory test to facilitate rational, evidence-based clinical review of patients presenting with eosinophilia.

Results: A total of 382 records were identified and reviewed, and 85 studies were included in the literature review (Figure 1). From these 85 publications a total of 214 items were assessed and 40 red flags were identified as relevant to raise a suspicion of EGPA. As the publications were derived from observational studies the GRADE level of evidence was low.

Using these 40 red flags, an evidence-based clinical checklist tool was developed for use in routine practice to raise EGPA suspicion in patients with eosinophilia (peripheral blood eosinophil count >1 x 10^9/L, with no treatment that could explain an alteration of this value) (Table 1).

Conclusion: Systematic literature review, multidisciplinary expert consensus rating and GRADE methodology has enabled, for the first time, the identification of a comprehensive set of red flags that could be used to raise a suspicion for EGPA, providing clinicians with an evidence-based checklist tool that can be integrated into their routine practice.

Funded by GSK.

Blood eosinophil count: • levels of > 1000 cells /μL (>1 x 109/L) with no pharmacological treatment that could explain an alteration of this value • levels of > 500 cells /μL with a treatment that could decrease this value (such as glucocorticoids)			
	Red flag		**Red flag**
Respiratory		ENT	
	Asthma		Nasal polyps
	Lung infiltrates / nodules / alveolitis		Chronic media otitis
	Eosinophilic pleural effusion	Dermatological	
	Alveolar haemorrhage / haemoptysis		Palpable purpura
	Chronic cough over 8 weeks / wheezing (not explained by another cause)		Skin lesions such as ulcers, urticaria, nodules and papules (cannot be explained by another cause)
Histopathological		Neurological	
	Vasculitis on biopsy		Mononeuritis multiplex/polyneuropathy
	Biopsy with inflammatory infiltrate predominantly eosinophilic		Paraesthesia
Analytical marker-related			Cerebrovascular disease, other pathologies ruled out
	ANCA positive	Renal	
	Elevated creatinine (together with sediment alteration)		Glomerulonephritis
	Proteinuria (>500 mg)		Glomerular extra-capillary proliferation in renal biopsy
	Elevated troponin (cannot be explained by another cause)		Renal infarction
	High BNP (without any other apparent cause)	Gastrointestinal	
	Positive rheumatoid factor		Ischaemic injuries including intestinal ischaemia and perforation (gastric, oesophageal, and small intestine, unexplained by any other cause)
	High IgE		Recurrent abdominal pain ischemic in nature (cannot be explained by another cause)
Cardiac			Chronic diarrhoea, melena (not explained by another cause)
	Pericardial effusion / pericarditis	Musculoskeletal	
	Cardiomyopathy		Polyarthritis (no alternative explanation)
	Ischaemic heart disease /arterial occlusion / infarction in a patient under 45 years of age		Myositis / myopathy
	Cardiomegaly	Ophthalmological	
Vascular			Retinal vasculitis
	Digital ischaemia		Episcleritis / scleritis
	Venous thrombosis (without any other factors)		Orbital inflammatory disease/ orbital pseudotumour
			Red eye (including conjunctivitis and keratitis)
Constitutional syndrome and/or fever (not attributable to any other cause)			
If a patient has the indicated levels of eosinophilia, the detection of any of the listed factors, with no other apparent cause, should alert to the possibility of EGPA. The presence of more than one factor will reinforce the suspicion of EGPA.			

TABLE. EGPA suspicion red flags.

P-009

Something Doesn't Add Up: Lung Cancer Risk Calculators and Radiomics Applied to Granulomatosis with Polyangiitis

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Background/Objective: Granulomatosis with polyangiitis (GPA) often presents with pulmonary nodules or masses.[1] Such lesions often raise concern for malignancy. Non-invasive models exist to guide management of the indeterminant pulmonary nodules in clinical practice, yet the the external validity of these tools is likely limited in those with ANCA-associated vasculitis[2]. Clinical risk calculators are commonly utilized. Additionally, several radiomic models have been developed to guide management of pulmonary nodules[3]. We sought highlight potential limitations of these modalities in those with GPA.

Methods: We retrospectively analyzed patients at Mayo Clinic sites with GPA and pulmonary nodules at time of diagnosis between 1/1/2009 and 9/1/2022. Inclusion criteria were age over 18 years, meeting Chapel Hill and ACR/EULAR consensus definitions of GPA, with CT chest at initial presentation. The Mayo Clinic model and Brock model were calculated for the dominant nodule to stratify probability of malignancy. Radiomic analysis and nodule segmentation yielded the BRODERS classifier (Benign *versus* aggRessive nODule Evaluation using Radiomic Stratification) stratifying risk of malignancy.

Results: A total 45 patients, with a mean of age 55 ±15 at GPA diagnosis were included. Patients were predominantly male (N=24) and 48% (N= 22) were former smokers. Nodule characteristics are illustrated in Figure 1. Using the Brock and Mayo models, the median probability of malignancy was 9.8% (IQR 3.4, 20.0) and 15.4% (IQR 9.8, 36.8), respectively. The median probability of malignancy according to the BRODERS radiomics model was 0.935 (IQR 0.833-0.989), classifying 41 (82%) of the nodules as malignant.[3]

Conclusions: Pulmonary nodules identified at initial presentation of GPA were most often classified as intermediate or high risk for malignancy using validated clinical risk calculators or radiomic tools**.** Broad application of these models in clinical practice while failing to consider GPA in the differential may result in unnecessary diagnostics as well as delay diagnosis and treatment for GPA.

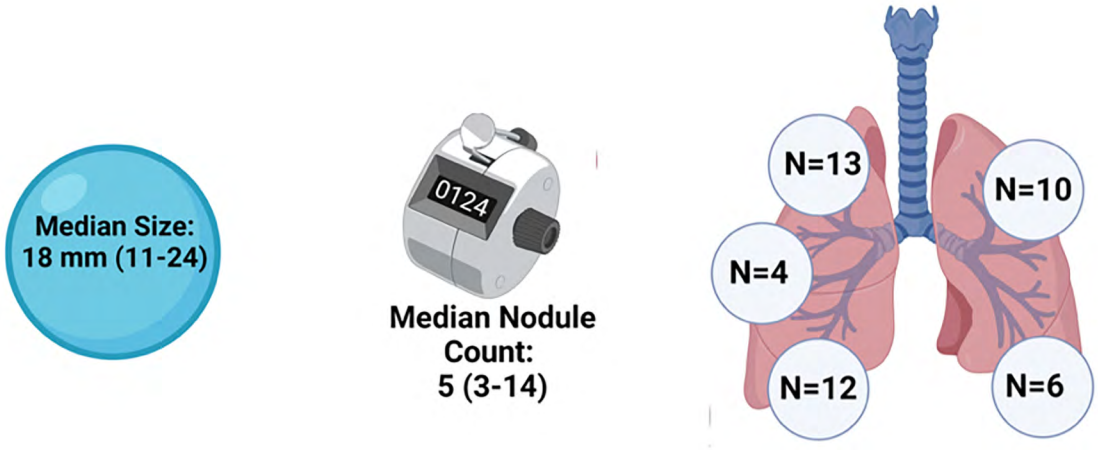

Figure 1: Characteristics of nodules included including in risk calcuation and radiomic analysis.

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P-010

Organ manifestations and overlaps in GPA vs. MPA - Insights from a large European ANCA-associated Vasculitis (AAV) cohort

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Background and objectives: Multiple organ involvement is a typical feature of vasculitis per se and especially in ANCA-associated vasculitis (AAV). Distinct manifestations within organ involvement served as criteria in the 2022 ACR/EULAR classification, differentiating granulomatosis and polyangiitis (GPA) from microscopic polyangiitis (MPA). This study aimed to explore differences between GPA and MPA in terms of single organ involvement and overlaps in organ manifestations.

Methods: Data of AAV patients from four tertiary referral centers (Germany and Switzerland) were collected between 2000 and 2022, classification was performed in accordance with the 2022 ACR/EULAR criteria for GPA and MPA. Organ involvement was identified by BVAS entries. Most important manifestation, regarding kidney, lung, ENT, and nervous system were compared in relation to classification by Pearson's Chi²-test and their combinations illustrated graphically.

Results: The dataset included 358 patients, of whom 168 (46.9%) were females, with a median age of 61 years (25-75 percentile: 50-70). According to the 2022 ACR/EULAR criteria, 203 (58.1%) were classified as GPA, 139 (38.8%) as MPA, and 16 cases (4.5%) could not be categorized unambiguously. The mean age differed between GPA (56.3 ± 15) and MPA (63.6 ± 13.4). Renal involvement was dominant in MPA (84.9%) compared to GPA (68.3%), while pulmonary affection was found in 59.6% in GPA vs. 38.8% in MPA. ENT involvement was present in 50% of all GPA cases but only in 11.5% of MPA cases, with all differences found to be significant ($p < .001$). Isolated ENT involvement was completely uncommon in MPA (0%), whereas a combination with kidney and lung was documented in 8 cases, exclusively with kidney in 4, with lung in 4 cases, and a combination of nervous, renal, and pulmonary manifestations was documented once (fig.1).

Conclusion: Even in our renal-dominated cohort, a wider spectrum of organ involvement is present in GPA, while MPA showed an increased frequency of mono-organic manifestation. GPA and MPA differed in age and most prominent in ENT involvement in accordance with recently introduced classification criteria.

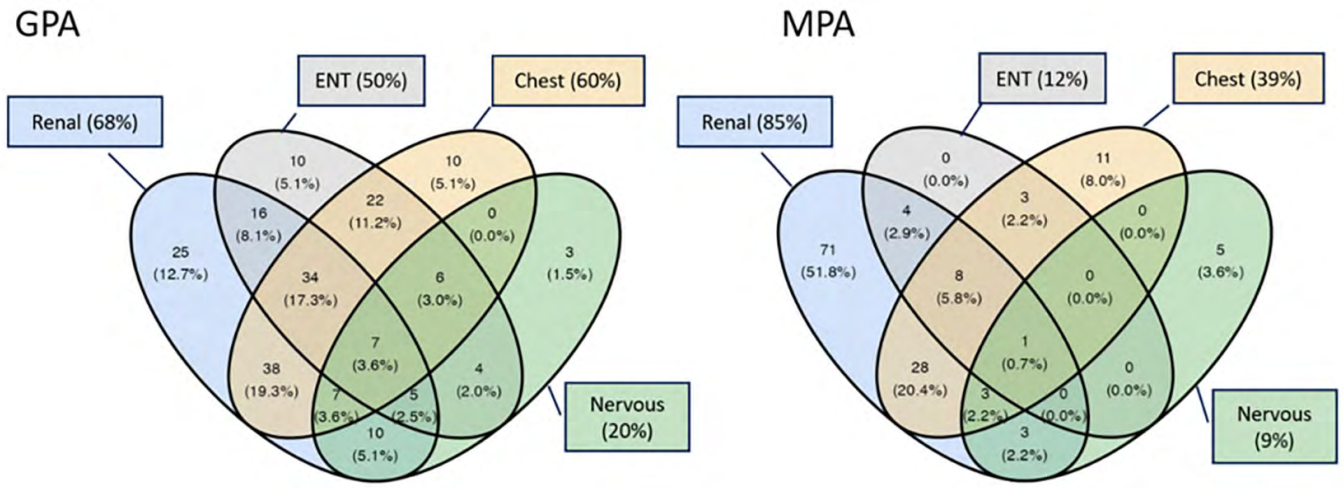

Figure 1: Organ involvement and overlaps between GPA and MPA in a European cohort.

Disclosures: Study funding from Vifor Fresenius Medical Care Renal Pharma Ltd.

P-011

Clinical characteristics of EGPA patients in comparison to GPA subgroup with increased blood eosinophilia from POLVAS registry

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Objective: To characterize the eosinophilic granulomatosis with polyangiitis (EGPA) population from the POLVAS registry[1] depending on ANCA status and diagnosis onset, including their comparison with the granulomatosis with polyangiitis (GPA) subset with elevated blood eosinophilia (min. 400/ml)(GPA HE) to develop a differentiating strategy.

Methods: A retrospective analysis of the POLVAS registry.

Results: The EGPA group comprised 111 patients. The ANCA-positive subset (n=45 [40.54%]) did not differ from the ANCA-negative one in clinics. However, those with anti-myeloperoxidase (MPO) antibodies (n=26 [23.42%]) had 20% higher prevalence of cardiovascular manifestations than the ANCA-negative subtype (46.97% vs. 26.92%, p=0.045). Patients diagnosed before 2012 (n=73 [62.93%]) were younger (median 41 vs. 49 years, p<0.01), had higher blood eosinophilia at diagnosis (median 4946 vs. 3200/µl, p<0.01), and more often ear/nose/throat (ENT) and cardiovascular symptoms.

GPA HE comprised 42 (13.00%) out of 323 cases with reported blood eosinophil count. Both GPA subsets had less prevalent respiratory and cardiovascular manifestations and more prevalent renal, ocular, and neurologic involvement than EGPA. EGPA also had cutaneous and gastrointestinal signs more often than GPA NE but not GPA HE. The model differentiating EGPA from GPA HE, using ANCA status and clinical manifestations, had an AUC of 0.92, sensitivity of 96%, and specificity of 95%.

Conclusion: Cardiovascular symptoms were more prevalent in the ANCA-negative subset than in the anti-MPO-positive one. ENT and cardiovascular symptoms were less common in patients diagnosed after the 2012 Revised Chapel Hill Consensus[2]. EGPA and GPE HE could be efficiently distinguished based on ANCA status and clinics.

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Disclosures: None.

P-012

Validity of the 2022 ACR/EULAR classification criteria for antineutrophil cytoplasmic antibody-associated vasculitis in Japan

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Background/ Objectives: The 2007 European Medicines Agency (EMA) algorithm has been widely accepted as a conventional method to diagnose antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). In 2022, ACR/EULAR proposed new classification criteria for AAV, microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), and eosinophilic granulomatosis with polyangiitis (EGPA). Epidemiological studies revealed that myeloperoxidase (MPO)-ANCA-positive GPA patients are more common in Asia than in northern Europe[1]. This study aimed to evaluate the validity of the new criteria when targeting AAV patients in Japan.

Methods: This study included a total of 432 AAV patients diagnosed by the conventional method at three medical institutions in Japan between 2000 and 2023. All patients were Asian and composed of 147, 141, and 144 patients conventionally diagnosed with MPA, GPA, and EGPA, respectively. The distribution of AAV subtypes and ANCA serotypes and the difference in the proportion of organ involvement in each AAV subtype were examined before and after reclassification according to the new criteria.

Results: The patients conventionally diagnosed with MPA or EGPA were reclassified into the same AAV subtype at a very high rate (144 out of 147 and 130 out of 144 patients, respectively). On the other hand, the patients conventionally diagnosed with GPA were less likely to be reclassified as the same AAV subtype (74 out of 141 patients) (Figure A). In the conventionally-diagnosed GPA population, those who presented with pulmonary nodules, sinusitis, chronic otitis media, and interstitial lung disease were partially reclassified as MPA, and most of them were MPO-ANCA-positive. However, those who presented with orbital and intracranial nodules were all reclassified as GPA as ever, and those were proteinase 3 (PR3)-ANCA positive. In the conventionally-diagnosed MPA population, those who presented with alveolar hemorrhage and pauci-immune glomerulonephritis were mostly reclassified as MPA as ever, and most of them were MPO-ANCA-positive (Figure B1, B2).

Conclusions: In this study, even in the presence of findings suggesting granulomatous inflammation, the MPO-ANCA-positive patients conventionally diagnosed with GPA were partially reclassified as MPA according to the new criteria. PR3-ANCA-positive patients conventionally diagnosed with GPA were more likely to present with recurrent or severe organ involvements, and the new criteria also reclassified these patients as GPA.

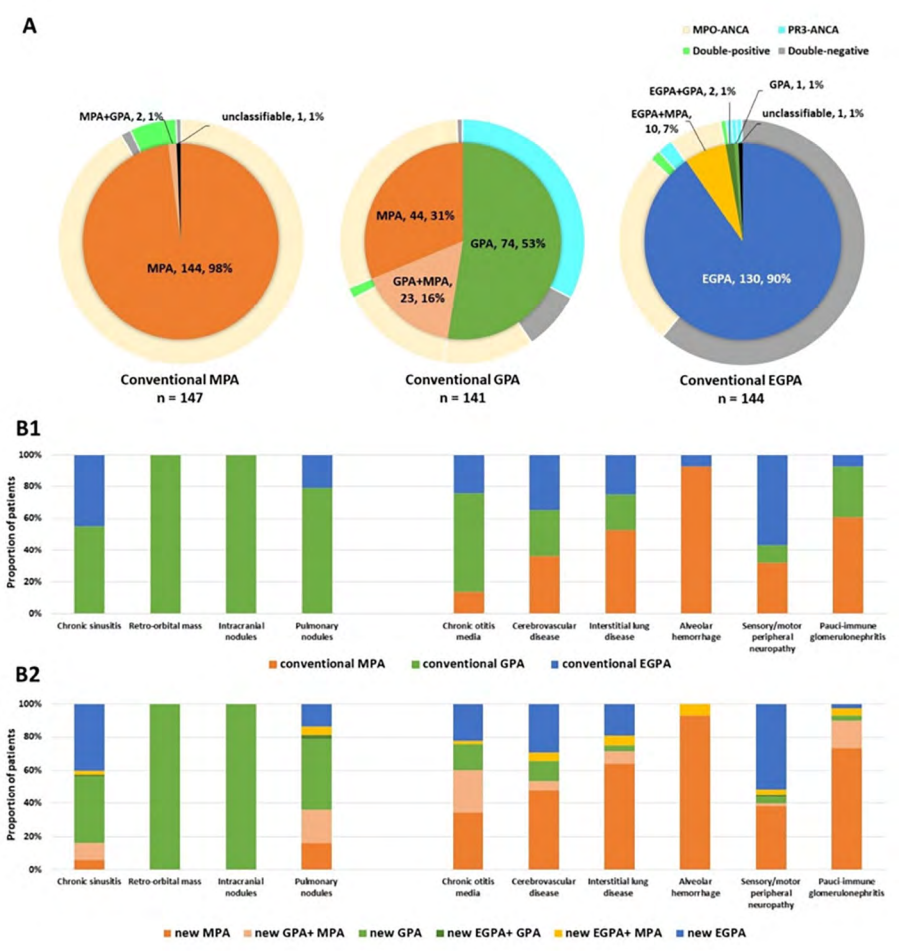

Figure. A) The distribution of AAV subtypes and ANCA serotypes after applying the new criteria to the patients conventionally diagnosed with MPA, GPA, and EGPA. B) The proportion of AAV subtype per phenotype of organ involvement before and after applying the new criteria among the AAV patients diagnosed by the conventional method (B1 and B2, respectively).

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Disclosures: None.

P-013

A comparison of different methods and strategies of ANCA testing in the past decade. A single-centre experience in a large teaching hospital in the Netherlands

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Background/ Objectives: The 1999 consensus for antineutrophil cytoplasmic antibody (ANCA) testing recommended indirect immunofluorescence (IIF) followed by an antigen-specific myeloperoxidase (MPO)/ proteinase 3 (PR3) assay if IIF was positive. The 2017 consensus proposed starting with an MPO/PR3 immuno-assay and considering a second immuno-assay and/or IIF if the test was negative. This change was based on multi-centre data from tertiary referral centres for ANCA-associated vasculitis (AAV). We analysed the test characteristics of different ANCA testing strategies throughout time in a large teaching hospital in The Netherlands.

Table 1. Clinical characteristics of ANCA-positive patients with and without ANCA-associated vasculitis (AAV).

	Total (n=286)	No AAV (n=179)	AAV (n=107)	P-value
Female, n (%)	144 (50.3)	94 (52.5)	50 (46.7)	0.410[c]
ANCA, n (%)				0.065[f]
MPO-Anca	156 (54.5)	104 (58.1)	52 (48.6)	
PR3-Anca	126 (44.1)	71 (39.7)	55 (51.4)	
Double positive	4 (1.4)	4 (2.2)	0 (0.0)	
Age, mean (SD)	60.5 (17.7)	59.7 (18.6)	62.0 (16.1)	0.275[t]
Malignancy, n (%)	48 (16.8)	30 (16.8)	18 (16.8)	1.000[c]
Carcinoma, n (%)	35 (12.2)	22 (12.3)	13 (12.1)	1.000[c]
Melanoma, n (%)	1 (0.3)	0 (0.0)	1 (0.9)	0.374[f]
Hematological malignancy, n (%)	15 (5.2)	10 (5.6)	5 (4.7)	0.951[c]
Sarcoma, n (%)	1 (0.3)	1 (0.6)	0 (0.0)	1.000[f]
Glioma, n (%)	1 (0.3)	1 (0.6)	0 (0.0)	1.000[f]
Infectious diseases, n (%)	63 (22.0)	54 (30.2)	9 (8.4)	<0.001[c]
Hepatitis B, n (%)	5 (1.7)	4 (2.2)	1 (0.9)	0.654[f]
Hepatitis C, n (%)	1 (0.3)	1 (0.6)	0 (0.0)	1.000[f]
Lues/syphilis, n (%)	5 (1.7)	4 (2.2)	1 (0.9)	0.654[f]
Tuberculosis, n (%)	2 (0.7)	1 (0.6)	1 (0.9)	1.000[f]
HIV, n (%)	2 (0.7)	2 (1.1)	0 (0.0)	0.530[f]
Other infections, n (%)	6 (2.1)	6 (3.4)	0 (0.0)	0.087[f]
Infective endocarditis, n (%)	1 (0.3)	1 (0.6)	0 (0.0)	1.000[f]
Autoimmune disease, n (%)	57 (19.9)	51 (28.5)	6 (5.6)	<0.001[c]
RA, n (%)	23 (8.0)	18 (10.1)	5 (4.7)	0.163[c]
SLE, n (%)	7 (2.4)	7 (3.9)	0 (0.0)	0.048[f]
Sarcoidosis, n (%)	4 (1.4)	4 (2.2)	0 (0.0)	0.301[f]
IBD, n (%)	23 (8.0)	22 (12.3)	1 (0.9)	0.001[c]
Other autoimmune disease, n (%)	11 (3.8)	11 (6.1)	0 (0.0)	0.008[f]
Drugs usage, n (%)	103 (36.0)	60 (33.5)	43 (40.2)	0.313[c]
Minocyclin, n (%)	1 (0.3)	1 (0.6)	0 (0.0)	1.000[f]
Thyroid medication, n (%)	1 (0.3)	1 (0.6)	0 (0.0)	1.000[f]
Hydralazine, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	NA
Immune suppressants, n (%)	96 (33.6)	55 (30.7)	41 (38.3)	0.236[c]
Cocaine, n (%)	7 (2.4)	5 (2.8)	2 (1.9)	1.000[f]

[c] Pearson's chi-squared test
[f] Fisher's exact test
[t] Student's t-test

Methods: All patients screened for ANCA between 2012 and 2023 were included; clinical data were retrospectively collected. ANCA IIF was performed using EUROPLUS™ Granulocyte Mosaic 25 IIF (Euroimmun). MPO/PR3 was detected by ImmunoCAP®250, ELiA method (Thermo Fisher Scientific). Statistical analyses were performed in *R*.

Results: A total of 5518 patients were tested for ANCA and 286 (5.2%) were positive. Of these, 107 patients (37%) were diagnosed with AAV; a prevalence of 1.9%. However, the majority of ANCA positive patients (63%) did not have AAV. *Table 1* summarizes clinical characteristics of patients without AAV, who have conditions including other autoimmune diseases, malignancy, infection or specific drug usage. Both IIF and ELISA as a first test have good negative predictive values (NPV), but positive predictive values (PPV) are limited. IIF as first test showed a sensitivity of 90%, specificity of 97%, PPV of 37% and NPV of 99.8%. IIF followed by ELISA led to an increase in PPV to 76% with an NPV of 99.7%. ELISA as first test showed a sensitivity of 100%, specificity of 99%, PPV of 64% and NPV of 100%. Regarding ELISA, titres were higher for ANCA positive patients with AAV compared to without. Median MPO and PR3 titres for patients with AAV were 63 (interquartile range (IQR) 25-210) and 49 (IQR 19-129) respectively, compared to 9 (IQR 5.5-21) and 8.4 (IQR 4.8-15) for non-AAV patients.

Conclusions: In a period of >10 years, 5.2% of ANCA tests in our hospital was positive. Of those patients, the majority did not have AAV (63%), but another autoimmune disease such as inflammatory bowel disease, malignancy, infection, or usage of specific drugs. High titres were associated with AAV. Both IIF and ELISA are good screening tests to rule out AAV, but positive predictive values are limited. Therefore, ANCA test results should be integrated with comprehensive clinical evaluation to ensure accurate diagnosis, emphasizing the essential role of collaborative interpretation between clinicians and laboratory experts.

Disclosures: None.

P-014

Drug-Associated ANCA Vasculitis: A Case-Control Study

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Introduction: There have been reported associations between certain drugs and anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis; primarily hydralazine, propylthiouracil, methimazole, cocaine (including levamisole-adulterated cocaine), minocycline, and allopurinol. (ref: Choi, H.K. et al, Arthritis & Rheumatism 2000, 43(2), pp.405-413; McGrath et al. CJASN. 2011 Dec;6(12):2799-805). Large studies confirming these associations are lacking.

Methods: We conducted the largest retrospective case-control study to date comparing drug exposure in newly diagnosed ANCA-positive (+) patients to ANCA-negative individuals (control group) between 2015 and 2022 within the Mass General Brigham healthcare system. The control group were subjects with a negative ANCA test and were selected at random. Medication exposure to drugs previously associated with positive ANCA tests (hydralazine, propylthiouracil, methimazole, cocaine/levamisole, minocycline, and allopurinol) and negative control medications (levothyroxine, atorvastatin, omeprazole, citalopram, metformin, and amlodipine) prior to initial ANCA test was determined by manual chart review. We examined the difference in exposure to suspected culprit medications and control medications between ANCA+ and ANCA-negative subjects using univariable and multivariable logistic regression models. We also compared ANCA titers between ANCA+ individuals who had exposure to suspected culprit medications and those who did not.

Results: We identified 572 ANCA+ subjects, including 377 myeloperoxidase [MPO], 186 proteinase 3 [PR3], and 9 double-positive MPO & PR3 ANCA, and 1128 ANCA-negative controls. The prevalence of medication exposure in each group is shown in **Fig. 1A**. In univariate analyses, MPO-ANCA+ individuals were more likely to have used hydralazine, cocaine/levamisole, minocycline, propylthiouracil/methimazole, and one negative control medication (levothyroxine) compared to the control group ($P < 0.05$ for all, **Fig. 1B**). There was no difference in the association of allopurinol with ANCA test status. The findings persisted after adjusting for age, sex, and all control medications **(Fig. 1C)**. In PR3-ANCA+ individuals, exposure to propylthiouracil/methimazole and cocaine/levamisole was higher compared to the control group in univariable analysis ($P < 0.05$ for both**, Fig. 1D**). The number of PR3-ANCA+ individuals was insufficient to perform a multivariable analysis. Compared to PR3-ANCA+ individuals, MPO-ANCA+ individuals were more likely to have been exposed to hydralazine and levothyroxine ($P < 0.05$ for both) but none of the other medications. MPO ANCA titers were significantly higher in individuals who had received hydralazine compared to those who had no known exposure to any of the suspected culprit drugs ($P < 0.001$, **Fig. 1E**). PR3 ANCA titers in comparison, did not differ significantly between both groups **(Fig 1F)**.

Conclusion: We confirmed the association of exposure to multiple suspected culprit medications with ANCA positivity. Additional studies are needed to elucidate the potential mechanisms of pathogenesis of drug-associated ANCA vasculitis.

Disclosures: None.

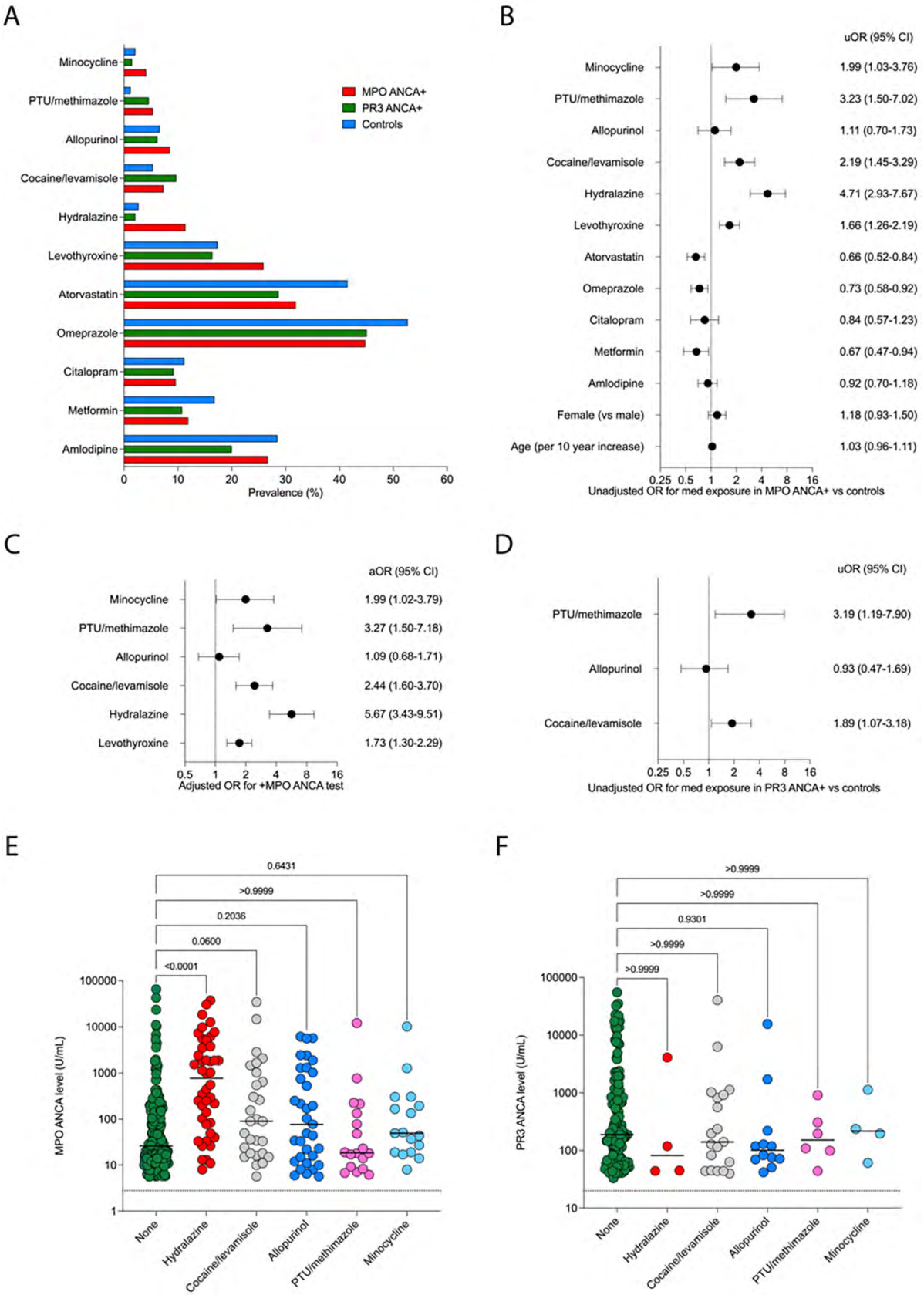

Figure 1. Medication associations with ANCA-associated vasculitis. **(A)** Medication exposure prevalence in ANCA+ and ANCA-negative groups. **(B)** Univariable and **(C)** multivariable analysis for the association between medication exposure in the MPO-ANCA+ vs control groups. **(D)** Univariable analysis for the association between medication exposure in the PR3-ANCA+ vs control groups. **(E)** MPO ANCA and **(F)** PR3 ANCA level in the ANCA+ group stratified by medication exposure history. Statistics by (B, D) univariable and (C) multivariable logistic regression, and (E,F) Kruskal-Wallis test with Dunn's correction for multiple pairwise comparisons.

P-015

Identifying Heterogeneity in Temporal Artery Biopsy Positivity Criteria for the Diagnosis of Giant Cell Arteritis: An Umbrella Review

Luka Newton[1], Sagar Patel[2], Nader Khalidi[2], Mats Junek[2].

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Objectives: The frequency that information concerning processing and interpretation of temporal artery biopsies (TAB) in the literature is reported is unknown. This umbrella review sought to demonstrate this and how reporting practices may impact diagnoses of giant cell arteritis (GCA).

Methods: We performed an umbrella review of studies that diagnosed GCA that were found through three strategies: a systematic search of randomized controlled trials, a systematic search of systematic reviews on the diagnosis of GCA, and four systematic reviews highlighting TAB sensitivity. Studies included for analysis diagnosed GCA, included TAB in diagnostic assessments for GCA, and reported TAB positivity criteria.

Results: 426 publications were screened; of these 90 (25.4%) reported on preparation and/or interpretation of TABs and were included. Median TAB positivity was 30.5%, the overall prevalence of GCA was 28.5%. Reporting of procedures and criteria used to interpret TABs was heterogeneous (Table 1). Where histopathological positivity criteria were listed, it was poorly defined and inconsistent between studies. The criteria most often used for determining TAB positivity were the presence of an inflammatory infiltrate (88 or 97.8% of studies), granulomas (74 or 82.2%), and/or giant cells (64 or 71.1%). Pre-published criteria for TAB positivity were used in 30% of studies; the use of these criteria did not impact TAB yield or rate of GCA diagnosis (p = 0.83 and 0.91 respectively) compared to studies that did not use pre-published criteria.

Conclusions: Reporting of TAB positivity criteria was infrequent and of poor quality. There was no evidence if this impacted the rate of GCA diagnoses. Standardized reporting of TAB positivity criteria in the literature would improve the integrity of reporting.

Disclosures of interest: LN – none. SP – none. MJ – Unrestricted educational funding from Roche. NK – BMS: support of investigator initiated clinical trial; AbbVie: clinical trial funding; Sanofi: clinical trial funding; Roche: Educational & operational grant support. Astra Zeneca, Kataka Medical, Otsuka, GSK, Mallinckrodt: honoraria paid to McMaster.

	All Studies N=90 (%)	Studies without pre-published criteria N=63 (%)	Studies with pre-published criteria N=27 (%)
Histopathological criteria for positive biopsy			
Granulomatous inflammation	74 (82.2)	49 (77.7)	25 (92.6)
Location of granulomatous inflammation	7 (7.8)	6 (9.5)	1 (3.7)
Inflammatory infiltrate	88 (97.8)	61 (96.8)	27 (100)
Mononuclear cells	46 (51.1)	24 (38.1)	22 (81.5)
Lymphocytes	17 (18.8)	16 (25.4)	1 (3.7)
Histiocytes	10 (11.1)	9 (14.3)	1 (3.7)
Epithelioid histiocytes	7 (7.8)	7 (11.1)	0 (0)
Eosinophils	2 (2.2)	2 (3.2)	0 (0)
Location of inflammatory infiltrate	18 (20)	17 (26.9)	1 (3.7)
Giant cells present	64 (71.1)	41 (65.1)	23 (85.2)
Tunica media disruption	5 (5.6)	5 (7.9)	0 (0)
Tunica intima hyperplasia	12 (13.3)	12 (19.1)	0 (0)
Tunica intima fibrosis	2 (2.2)	2 (3.2)	0 (0)
Luminal occlusion	4 (4.4)	4 (6.3)	0 (0)
Neoangiogenesis	1 (1.1)	1 (1.6)	0 (0)
Disruption of internal elastic lamina	36 (40)	34 (53.9)	2 (7.4)
Medial/adventitial scarring	8 (8.9)	8 (12.7)	0 (0)
Standards of biopsy preparation			
Bilateral biopsies used	23 (25.6)	18 (28.6)	5 (18.5)
Pathologist blinded to clinical data	20 (22.2)	15 (23.8)	5 (18.5)
Pathologist re-review of histopathology	13 (14.4)	7 (11.1)	6 (22.2)
Stain used reported	22 (24.4)	19 (30.2)	3 (13.6)
Fixation procedure reported	21 (23.3)	15 (23.8)	6 (22.2)
Specimen sectioning reported	18 (20)*	15 (23.8)	3 (11.1)

*range 3-5 um

P-016

The nature and incidence of cutaneous vasculitis in the adult population of Norfolk, UK between 2011 to 2020

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Background/ Objectives: Cutaneous vasculitis may be primary or a feature of an underlying systemic condition. There are limited data on the incidence of cutaneous vasculitis. This UK based single centre retrospective cohort study aimed to provide clarity on the incidence and nature of cutaneous vasculitis.

Methods: Individuals attending a secondary care hospital with histologically confirmed cutaneous vasculitis diagnosed between 2011 and 2020, who lived within the NR postcode districts of Norfolk country borders were included. 2011 census population data from the Office of National Statistics were used as the denominator. The 95% confidence intervals were calculated using Byar approximation.

Results: 161 individuals presented with biopsy proven cutaneous vasculitis during the study period. Median age at diagnosis was 54 years (IQR 34.75-65.25). 57% were female (92/161). 154/161 (96%) self-identified as white British. During the study period, the at-risk population was 4,698,862 people over the age of 18. 94.7% self-identified as 'white'. The annual incidence of cutaneous vasculitis was 34.3/million (95% CI 29.2-40.0). Primary leukocytoclastic vasculitis was the most common diagnosis (45/161) with an annual incidence 9.6/million (95% CI 7.0-12.8). Adult IgA vasculitis was diagnosed in 28/161 with an annual incidence of 6.0/million (95% CI 4.0-8.6). The other conditions are as described in Table 1.

Conclusions: This is the first comprehensive report of the incidence of objectively diagnosed cutaneous vasculitis from a large stable population. A broad range of conditions present as cutaneous vasculitis. These conditions affect patients of all ages. It is important to have high quality epidemiological data to better understand this uncommon but potentially life-threatening disease.

Disclosures: None.

	No. cases
ANCA associated vasculitis	3
Polyarteritis nodosa	3
Cutaneous arteritis	3
IgA vasculitis	28
Leukocytoclastic vasculitis	45
Erythema elevatum diutinum	3
Urticarial vasculitis	9
Adult-onset Still's disease	1
Behçet's disease	6
Cutaneous t-cell lymphoma	2
Dermatitis herpetiformis	1
Erythema nodosum	2
Granulomatous panniculitis compatible with erythema induratum	1
Lymphocytic vasculitis	6
Perniosis	2
Pityriasis lichenoides	1
Rheumatoid vasculitis	1
SLE	2
Sweet's syndrome	2
Urticaria	6
Miscellaneous causes	34

Table 1 – list of conditions diagnosed during study period and number of cases identified.

P-017

Ultrasonographic evaluation of temporal artery frontal branch intima-media thickness as a diagnostic tool for giant cell arteritis

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Background/ Objectives: Different clinical (probability score for giant cell arteritis (PSGCA)) (1) and ultrasonographic (US) score (UHS) (2) have been proposed to identify patients with giant cell arteritis (GCA). We propose a simplified US score to correctly identify GCA patients in the setting of GCA fast track clinic.

Methods: All patients with suspected GCA seen at our rheumatological centre are evaluated according to a clinical, laboratory and US protocol before execution of superficial temporal artery biopsy (TAB). Bilateral US examination of all the temporal branches were done with an Esaote MyLabClassC machine equipped with a 22MHz linear probe. Images of all arterial segments were stored and reviewed for subsequent measurement of right frontal branch intima media thickness (FBIMT) by a rheumatologist blind to the final clinical diagnosis and to the results of TAB histological examination. The validity of the FBIMT was assessed using the area under the curve (AUC) of the receiver operating characteristic curve (ROC) for discrimination and was compared to the AUC of PSGCA and UHS. Sensitivity and specificity were calculated for each sum score of the FBIMT. Correlation coefficients (Spearman rho) was calculated between each score and ESR and CRP values at baseline.

Results: Table 1 shows comparisons between GCA vs non GCA patients (clinical diagnosis) and GCA biopsy positive vs GCA biopsy negative patients.

Correlation coefficients between the different scores were FBIMT/PSGCA 0.479 (p<0.001), FBIMT/UHS 0.806 (p<0.001) and between scores and ESR and CRP levels were FBIMT/ESR 0.306 (p<0.001), FBIMT/CRP 0.394 (p<0.001), PSGCA/ESR 0.443 (p<0.001), PSGCA/CRP 0.468 (p<0.001), UHS/ESR 0.333 (P<0.001) and UHS/CRP 0.389 (P<0.001).

FBIMT AUC to discriminate GCA vs non GCA patients (clinical diagnosis) was 0.863 (95%CI=0.803-0.923), similar to PSGCA AUC (0.823;95%CI= 0.752-0.893) or UHS AUC (0.840;95%CI=0.771-0.910).

FBIMT AUC to discriminate TAB positive vs TAB negative patients was 0.849 (95%CI=0.791-0.916), without differences with PSGCA AUC (0.791;95%CI= 0.715-0.867) or UHS AUC (0.848;95%CI=0.780-0.916).

A right frontal US IMT cut off value of 0.24 had a sensitivity of 0.70 (95%CI 0.59-0.79), a specificity of 0.94 (95%CI 0.83-0.99), a LHR+ of 11.63 (95%CI=3.85-35.14), a LHR- of 0.32 (95%CI=0.23-0.45), a PPV of 0.72 (95%CI 0.74-0.79), a NPV of 0.87 (95%CI 0.76-0.93), and a OR of 36.1 (95%CI 10.3-126.8) for correctly classify GCA at first visit.

A right frontal US IMT cut off value of 0.24 had a sensitivity of 0.72 (95%CI 0.61-0.82), a specificity of 0.91 (95%CI 0.79-0.97), a LHR+ of 7.65 (95%CI=3.28-17.81). a LHR- of 0.31 (95%CI=0.21-0.44), a PPV of 0.92 (95%CI 0.83-0.96), a NPV of 0.69 (95%CI 0.60-0.76), and a OR of 24.9 (95%CI 8.8-70.7) for correctly classify TAB positive patients at first visit.

Conclusions: IMT of the frontal TA branch has high LHR+, sensitivity, specificity, PPV and NPV to correctly classify GCA patients at first visit in a GCA fast track clinic.

References:

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Disclosures: None.

	GCA clin (86 PTS)	NO GCA clin (50 PTS)	P
ESR	66.7 + 31.6	42.9 + 26.1	< 0.001
CRP	7.54 + 5.72	3.33 + 6.57	< 0.001
AGE	73.2 + 8.02	72.2 + 10.2	0.528
PSGCA	15.4 + 4.06	10.9 + 2.93	< 0.001
UHS	13.9 + 8.7	4.4 + 4.73	< 0.001
FBIMT	0.43 + 0.23	0.19 + 0.05	< 0.001
	TAB positive (79 PTS)	TAB negative (53 PTS)	P
ESR	68.3 + 32.1	44.1 + 25.5	< 0.001
CRP	7.63 + 5.72	3.78 + 6.55	< 0.001
AGE	72.8 + 7.97	73.1 + 9.9	0.870
PSGCA	15.5 + 4.16	11.5 + 2.89	< 0.001
UHS	14.3 + 8.8	4.6 + 4.9	< 0.001
FBIMT	0.43 + 0.23	0.21 + 0.09	< 0.001

Table 1. Comparison between clinical GCA vs No GCA and TAB positive vs TAB negative patients.

P-018

Replication of the 23-Valent Polysaccharide Pneumococcal Vaccine-Induced Skin Pathergy Test in an Independent Cohort of Patients with Behçet Disease

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Background/Objective: The skin pathergy test (SPT) is an important tool in the diagnosis of Behçet Disease (BD), but its decreasing sensitivity over the years has limited its use(1, 2). In our previous study, we showed a dramatic improvement in the sensitivity of SPT with the additional stimulation by the 23-valent polysaccharide pneumococcal vaccine (PS-23) antigens, especially in BD patients with active disease manifestations (aBD) as high as 80.3% with preserved specificity of 100%(3). The current study aimed to replicate our previous findings and improve its methodology by increasing the number of PS-23-induced pricks.

Methods: This study was performed between March 2022 and November 2023. Information related to demographics, clinical findings, disease activity, and treatment were collected. BD patients, patients with other inflammatory diseases, and recurrent aphthous stomatitis comprised the study group. Standard SPT was done by pricking the forearm with a 3-5mm deep oblique insertion at a 30-45° angle and using 20G hypodermic needles (20G-SPT). PS-23-induced SPT (PS23-SPT) was applied by dropping a total volume of 10ml PS-23 (Pneumovax) additionally before pricking by 20G needle. In total four pricks were applied to each arm(2 20G-SPT, 2 PS23-SPT). Development of erythema and induration at 48h were evaluated by the same observer. Induration (³2 mm) with erythema at 48h was accepted as positive. Patients with at least one active disease manifestation were grouped as aBD.

Results: Stimulation of forearm skin by PS23-SPT showed 79.6% sensitivity and 100% specificity in the analysis of all patients with BD, and 91.3% sensitivity and 100% specificity in aBD patients, compared to the sensitivity of 8.6% in all and 10% in aBD using the 20G-SPT method. Both erythema and induration results with PS23-SPT showed a significant correlation between the first and second prick sites of the arms, and between the right and left arms ($p<0.0001$, and $r=0.7$-0.85 for all comparisons). In aBD group, 28.6% of the PS23-SPT negative and 6.3% of PS23-SPT positive patients were under at least one immunosuppressive. Fifty out of 73 PS-SPT-positive aBD patients (68.5%) developed pustule in at least one of the prick sites.

Conclusions: The current study replicated the results of the previous findings of increased sensitivity of PS23-SPT especially in active patients and in those not using immunosuppressives, and doubling of the prick numbers increased further the sensitivity of PS23-SPT. The PS23-SPT is being considered a promising tool for the diagnosis of BD, and an international replication study in different ethnic groups is underway.

References:

1. Davatchi F, et al. Clin Rheumatol.2011;30(9):1151-5.
2. Dilsen N, et al. Ann Rheum Dis.1993;52(11):823-5.
3. Deniz R, et al. Rheumatology (Oxford).2023;62(5):1903-9.

Disclosure: None. No funding was received. This study was approved by the Institutional Research Ethics Committee(Project number2022/826), and all patients gave a written informed consent.

Table 1: Sensitivity, Specificity and Area Under the Curve (AUC) Results of SPT Methods.

SPT Method	Active BD				Whole BD			
Method	**Sensitivity (%)**	**Specificity (%)**	**AUC (95%)**	**p value**	**Sensitivity (%)**	**Specificity (%)**	**AUC (95%)**	**p value**
US 20G needle	6.1	100	0.530 (0.448-0.613)	0.459	4.8	100	0.524 (0.448-0.559)	0.530
PS-23+ 20Gneedle	**91.3**	**100**	**0.954 (0.918-0.991)**	**0.0001**	**79.6**	**100**	**0.898 (0.848-0.947)**	**0.0001**

P-019

The value of ANCA testing in renal disease – is the current consensus statement evidence based?

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Background/ Objectives: The 2017 international consensus document on ANCA testing includes a gating strategy for when to request an ANCA-test. For patients with kidney related symptoms the text is vague and reads “Glomerulonephritis, especially rapidly progressive glomerulonephritis (RPGN)” (1). As this text provide little guidance on when to perform ANCA testing in patients with different combinations of proteinuria, hematuria and elevated creatinine we calculated the likelihood ratio, pretest- and posttest probability for AAV in a large renal biopsy material.

Methods: All patients entered in the Swedish Renal Biopsy registry between 2015 and 2020 were screened for ANCA tests. The result of ANCA testing was compared with the final diagnosis set by the nephrologist using the ERA (Eurpoean Renal Association) codes for primary renal disease and the indication to perform the biopsy. In this registry the clinician has to provide the indication for the biopsy by ticking one of five boxes: early chronic kidney disease (CKD1-2), late chronic kidney disease (CKD3-5), massive proteinuria (nephrosis), acute/subacute nephritis (RPGN) and other acute kidney injury (AKI).

Results: ANCA test were ordered for 2705 patients out of 3165 (85%) undergoing renal biopsy (Table 1). 13% of those were diagnosed as AAV. The overall likelihood ratio was 22.3 which with a pretest-probability of 13 % gives a posttest-probability of 77%. The lowest likelihood ration was found for RPGN 9.8 while the highest was found for nephrosis 73. The corresponding values for CKD1-2, CKD3-5 and AKI was 19, 26 and 27.

Conclusions: A likelihood ration of 10 is often used as a cut-off for when a diagnostic test is considered to be clinically useful. In patients undergoing renal biopsy this cut-off level is exceeded in all different clinical situations except for RPGN, which is the only setting strongly suggested by current consensus statement. More liberal ANCA testing is warranted in renal disease of unclear origin.

References:

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Disclosures: None.

Table 1.

	Total ANCA test	AAV yes	ANCA+	Likelihood ratio	pre-test prob	posttest prob
CKD 1-2	390	19	36	19,53	4,9%	50,0%
CKD3-5	745	57	76	26,15	7,7%	68,4%
AKI	339	35	45	26,85	10,3%	75,6%
RPGN	583	215	248	9,76	36,9%	85,1%
Nephrosis	648	12	19	72,88	1,9%	57,9%
Totalt	2705	353	424	22,31	13,0%	77,0%

P-020

Utilizing Machine Learning with Claims Data to Diagnose and Quantify the Prevalence of Eosinophilic Granulomatosis with Polyangiitis

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Background/ Objectives: Eosinophilic granulomatosis with polyangiitis (EGPA) is a vasculitis that can present indolently. This can lead to a delay in diagnosis and treatment. This study used machine learning to identify pre-diagnostic attributes of EGPA, estimate the prevalence of EGPA, and create a clinical decision screening tool (CDST) to reduce time to diagnose EGPA.

Methods: Leveraging IQVIA's U.S. medical and pharmacy claims data and laboratory results, ≈2,800-4,000 patients were split into positive and negative cohorts. All patients were required to have a history of asthma or oral glucocorticoid use. Two cohort designs and decision tree models are being developed to create a CDST.

Results: The positive predictive value of all models exceeded the baseline prevalence and incidence rates in the dataset. The RCS model estimated approximately 9,644-11,793 cases of EGPA. Key determinants within the models showed that eosinophilia, asthma, arteritis, chronic sinusitis, multiple chest x-rays, skin biopsies, multiple prescriptions of oral glucocorticoids, and rheumatology visits were most predictive of a diagnosis of EGPA. The first decision tree model uncovered four possible decision pathways for use within the CDST.

Conclusions: These results demonstrate that leveraging machine learning and claims data can improve the estimation of prevalence of EGPA in the US and aid in arriving at an earlier diagnosis of EGPA. Up to 100 key events were identified by the model as playing a pivotal role in identifying patients with EGPA. The decision tree models may offer an avenue for health systems to improve the care of patients with EGPA.

Disclosures: This study was funded by AstraZeneca.

PAM: Consulting: AbbVie, AstraZeneca, Boeringher-Ingelheim, Bristol-Myers Squibb, ChemoCentryx, CSL Behring, Dynacure, EMDSerono, Genentech/Roche, Genzyme/Sanofi, GlaxoSmithKline, Immagene, InflaRx, Jannsen, Kiniksa, Kyverna, Mitsubishi, Neutrolis, Novartis, NS Pharma, Pfizer, Regeneron, Sparrow, and Takeda; Research Support: AbbVie, AstraZeneca, Boeringher-Ingelheim, Bristol-Myers Squibb, ChemoCentryx, Eicos, Electra, Forbius, Genentech/Roche, Genzyme/Sanofi, GlaxoSmithKline, InflaRx, Sanofi, and Takeda: Stock options: Kyverna; Royalties: UpToDate

PB and DC: employees of AstraZeneca and may own stock/stock options.

BN, MD, SR, HM: Employees of IQVIA, which received funding from AstraZeneca to conduct this study.

GLC: GlaxoSmithKline, Boehringer Ingelheim Pharmaceuticals, Genentech, AstraZeneca, Sanofi Genzyme, Regeneron, Circassia, Teva, Boston Scientific.

P-021

Clustered Insights: Unraveling Patterns in ANCA Associated Vasculitis from a Turkish Multicenter Cohort

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Background/ Objectives: Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a complex and heterogeneous disease requiring a comprehensive understanding of its diverse manifestations. Identifying distinct AAV subphenotypes based on the distribution of organ involvement and ANCA types may help illuminate our knowledge of the pathogenesis, predict prognosis, and guide management. This study aimed to elucidate the intricate patterns within AAV by performing latent class analysis (LCA) on the Turkish Vasculitis Study Group (TRVaS) registry.

Methods: In this nationwide study, we included 496 patients with granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and unclassified AAV (uAAV) according to the European Medicines Agency algorithm from TRVaS, multicenter, and e-database of Turkey. Clustering analysis was conducted using LCA to identify subgroups with distinct patterns of organ involvement at disease diagnosis and ANCA status. Determining the optimal number of latent classes was guided by statistical criteria, specifically the Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC). The clusters were presented and characterized by demographics, baseline characteristics, and mortality.

Results: The analyses included data for 401 (80.8%), 77 (15.5%), and 18 (3.6%) patients with GPA, MPA, and uAAV, respectively. Of the 496 AAV cases, the mean age was 51.2 ± 16.4 years, and 54.6% were male. Our clustering analysis revealed three distinct clusters within the Turkish AAV population, each characterized by a different pattern. Cluster 1 (“Pulmonary+/PR3+”) included half of the patients (51.4%). Cluster 2 (“Pulmonary+/MPO+”) and Cluster 3 (“Non-Pulmonary/PR3+”) contained 29.8% and 18.7% of the AAV cases, respectively. The largest cluster (“Pulmonary+/PR3+”) had predominantly anti-PR3 positive patients with pulmonary, renal, and ear-nose-throat (ENT) involvement. According to the classical classification, a cluster of “Pulmonary+/MPO+” corresponded to all patients with MPA and other MPO+ patients with pulmonary and renal involvement. Mortality rates were 10.6%, 14.9%, and 7.5% for Clusters 1, 2, and 3, respectively. The descriptive characteristics of prior classifications and the new 3 clusters are shown in the table.

Conclusions: This comprehensive analysis provided valuable insights into the intricate patterns of AAV, shedding light on potential subphenotypes based on organ involvement and ANCA types. Further research is warranted to validate and extend these findings. The identified clusters may contribute to a better understanding of AAV pathogenesis, prognosis prediction, and tailored management strategies.

Keywords: ANCA associated vasculitis, clustering analysis, cohort study, personalized medicine.

Disclosures: None.

	All Patients n =496	GPA n=401 80.8%	MPA n=77 15.6%	uAAV n=18 3.6%	Cluster1 (n=255; 51.4%) (Pulmonary+/PR3+)	Cluster2 (n=148; 29.8%) (Pulmonary+/MPO+)	Cluster3 (n=93; 18.7%) (Non-Pulmonary/PR3+)	p
Age at Diagnosis, year, mean ± SD	51.2 ± 16.4	48.6 ± 15.7	63.4 ± 11.8	55.4 ± 22.8	48.7 ± 15.9	58.9 ± 15.4	45.6 ± 14.8	<0.001
Follow-up time, month, Median (IQR)	35 (63)	38 (68)	25 (41)	28.5 (50.0)	37 (67.0)	26.5 (51.0)	40 (64.0)	<0.001
Male, n (%)	271 (54.6)	219 (54.6)	42 (54.5)	10 (55.6)	146 (57.3)	75 (50.7)	50 (53.8)	0.434
GPA, n (%)	401 (80.8)	401 (100)	-	-	254 (99.6)	57 (38.5)	90 (96.8)	<0.001
MPA, n (%)	77 (15.5)	-	77 (100)	-	0 (0)	77 (52.0)	0 (0)	
uAAV, n (%)	18 (3.6)	-	-	18 (100)	1 (0.4)	14 (9.5)	3 (3.2)	
PR3+, n (%)	332 (66.9)	329 (82.0)	0 (0)	3 (16.7)	246 (96.5)	1 (0.7)	85 (91.4)	<0.001
MPO+, n (%)	127 (25.6)	47 (11.7)	68 (88.3)	12 (66.7)	0 (0)	127 (85.8)	0 (0)	<0.001
Constitutional Symptoms, n (%)	259 (52.2)	209 (52.1)	45 (58.4)	5 (.27.8)	156 (61.2)	75 (50.7)	28 (30.1)	<0.001
Musculoskeletal Findings, n (%)	275 (55.4)	237 (59.1)	30 (39.0)	8 (44.4)	161 (63.1)	65 (43.9)	49 (52.7)	0.001
Skin Involvement, n (%)	68 (13.7)	57 (14.2)	7 (9.1)	4 (22.2)	42 (16.5)	13 (8.8)	13 (14.0)	0.096
Ophthalmological Involvement, n (%)	90 (18.1)	81 (20.2)	5 (6.5)	4 (22.2)	49 (19.2)	15 (10.1)	26 (28.0)	0.002
ENT Involvement, n (%)	252 (50.8)	242 (60.3)	5 (6.5)	5 (27.8)	177 (69.4)	30 (20.3)	45 (48.4)	<0.001
Pulmonary Involvement, n (%)	355 (71.6)	293 (73.1)	54 (70.1)	8 (44.4)	255 (100)	100 (67.6)	0 (0)	<0.001
Cardiac Involvement, n (%)	10 (2.0)	9 (2.2)	1 (1.3)	0 (0)	4 (1.6)	2 (1.4)	4 (4.3)	0.218
GI Involvement, n (%)	18 (3.6)	17 (4.2)	0 (0)	1 (5.6)	9 (3.5)	3 (2.0)	6 (6.5)	0.201
Kidney Involvement, n (%)	323 (65.1)	251 (62.6)	63 (81.8)	9 (50.0)	168 (65.9)	112 (75.7)	43 (46.2)	<0.001
Neurological Involvement, n (%)	63 (12.7)	51 (12.7)	11 (14.3)	1 (5.6)	30 (11.8)	19 (12.8)	14 (151)	0.716
Death, n (%)	56 (11.3)	43 (10.7)	12(156)	1 (5.6)	27 (10.6)	22 (14.9)	7 (7.5)	0.189

Table: Baseline characteristics and outcome of 496 patients with AAV by diagnosis and after clustering.

P-022

Survey results on the utility of the Renal Risk Score and Histopathological Classification of ANCA-glomerulonephritis

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Background/Objectives: The importance of kidney biopsy in ANCA-associated glomerulonephritis (AAV) is widely recognized: both the Berden classification[1] and the ANCA renal risk score (ARRS)[2] are widely used and reliable predictors of prognosis. AAV phenotypes, outcomes and treatment have changed over the last decades: whether and how the existing classification and ARRS need to be updated is a matter of discussion. A survey to assess the current use of the classification and ARRS in clinical practice was conducted on behalf of the newly formed "Working Group on classifications and risk scores".

Methods: An online survey was sent to the active members of the European Vasculitis Society (EUVAS) between September 13th and September 27th, 2023. The survey used an internet platform, contained 12 multiple-choice and 2 open questions and results were analyzed anonymously.

Results: 76 of 295 EUVAS members replied to the questionnaire: 40 (52.6%) were nephrologists, 25 (32.9%) rheumatologists, 4 (5.3%) pathologists and 7 (9.3%) "others". Their level of expertise was high, with 61 (80.3%) physicians encountering more than 10 new-diagnosed AAV patients per year. A total of 64 (84.2%) responders usually performed a kidney biopsy in suspected AAV patients, considering the pathological examination a useful tool for prognosis (89.5%), diagnosis (85.5%) and treatment (81.6%). More than 90% of responders indicated they discuss kidney biopsy results in a multidisciplinary meeting involving both clinicians and pathologists. Both the Berden classification and the ARRS are known by around 70% of experts in the field; the first being commonly used by clinicians in everyday practice (70.1% vs 52.5%, p=0.08). Both systems were considered useful on a scale from 0 to 10, with a median grade of 7 [(IQR 5-8) vs (IQR 6-8), p=0.21].

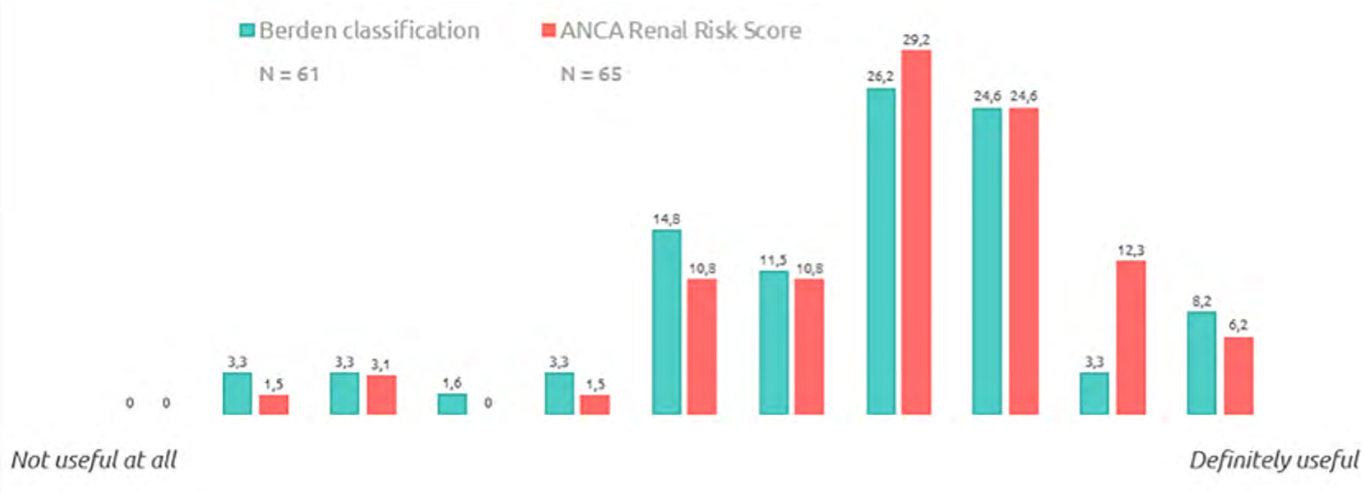
Suggested improvements were further standardizations and simplicity. New parameters (e.g., extraglomerular involvement, laboratory and clinical features) and biomarkers should be considered for future inclusion.

Conclusions: A survey assessing the current use of the Berden classification and ARRS in clinical practice showed that both systems are widely used among vasculitis clinicians and that the ideal system should be able to guide treatment decisions. The validation of pathological systems for targeted treatment decisions is an unmet need.

References:

1. Berden et al., J Am Soc Nephrol, vol. 21, no. 10, pp. 1628-36 (2010)
2. Brix et al., Kidney Int, vol. 94, no. 6, pp. 1177-1188 (2018)

Disclosures: None.



P-023

Diagnostic yield of biopsies in Eosinophilic Granulomatosis With Polyangiitis

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Background: Recently published classification criteria for eosinophilic granulomatosis with polyangiitis (EGPA)[1] require, to be applied, a diagnosis of small- or medium-vessel vasculitis, without specifying how that diagnosis should be made. Histologically, EGPA is characterized by eosinophil-rich and necrotizing granulomatous inflammation together with necrotizing vasculitis, predominantly affecting small to medium vessels. Some of these features are not specific for EGPA and may be seen in other forms of ANCA associated vasculitis (AAV). Current guidelines on the management of AAV recommend biopsies to assist in establishing a new diagnosis and for further evaluation of patients with suspected relapse[2]. Therefore, biopsies are essential tools for the diagnosis, classification and management of these diseases.

Objectives: To describe the histopathological findings, diagnostic yield and the most common localizations of biopsies performed to assist in the diagnosis and follow-up of patients with EGPA.

Methods: Medical charts of patients with EGPA regularly followed at our department were reviewed to retrieve the number and localization of biopsies, as well as biopsy findings including proportion of a) eosinophil-rich extravascular inflammation, b) granulomas and/or c) necrotizing vasculitis. Biopsies were performed if patients presented symptoms in any given and most accessible localization (at diagnosis) or if they were necessary to confirm active disease (during follow-up).

Results: Among 59 EGPA patients regularly controlled at our department, a total of 163 biopsies were performed on 54 of them. In 44 patients (81.5%), 89 biopsies were performed at diagnosis and in 27 (50%), 74 biopsies were performed during follow-up. A total of 37 biopsies in 26 patients (48.1%) had proven vasculitis. A total of 7 biopsies in 5 patients (9.3%) had proven granuloma. A total of 87 biopsies in 42 patients (77.8%) had proven eosinophil-rich extravascular inflammation. The main localizations were: ear, nose and throat (ENT, 49 biopsies), respiratory (31), skin (25), gastrointestinal (GI, 18), muscular (14), nerve (12), bone marrow (8), renal (4) and temporal artery biopsy (TAB, 2). Among them, at least 1 typical histological feature detailed above was found in: ENT 38/49 biopsies (sensitivity of 77.6%), respiratory 15/31 (48.4%), skin 23/25 (92%), GI 10/18 (55.6%), muscular 4/14 (28.6%), nerve 5/12 (41.7%), bone marrow 6/8 (75%), renal 4/4 (100%) and TAB 1/2 (50%). A total of 57 biopsies performed in 29 patients (53.7%) showed none of the typical findings described above, although only 6 patients had all their biopsies without abnormal findings. These results are summarized in Table 1.

Biopsies in the EGPA cohort (N=59)			
Patients with biopsy: 54 (91.5%) At diagnosis: 44 (81.5%); 89 biopsies During follow-up: 27 (50%); 74 biopsies			
Histological findings			
Vasculitis			
Patients with vasculitis: 26 (48.1%) At diagnosis: 22 (40.7%) During follow-up: 5 (9.3%)			
Granuloma			
Patients with granuloma: 5 (9.3%) At diagnosis: 3 (5.6%) During follow-up: 2 (3.7%)			
Eosinophil-rich inflammation			
Patients with eosinophil-rich inflammation: 42 (77.8%) At diagnosis: 31 (57.4%) During follow-up: 23 (42.6%)			
Main localizations of biopsies, n (with at least 1 histological finding, n)			
	At diagnosis	During follow-up	Total
ENT	21 (16)	28 (22)	49 (38)
Respiratory	13 (6)	18 (9)	31 (15)
Skin	15 (14)	10 (9)	25 (23)
Gastrointestinal	3 (3)	15 (7)	18 (10)
Muscular	13 (4)	1 (0)	14 (4)
Nerve	12 (5)	0 (0)	12 (5)
Bone marrow	6 (5)	2 (1)	8 (6)
Renal	4 (4)	0 (0)	4 (4)
Vascular (temporal artery biopsy)	2 (1)	0 (0)	2 (1)

Conclusion: Multiple tissues are biopsied in clinical practice to assist in the diagnosis and evaluation of patients with EGPA, according to the multi-organ nature of this disease. Biopsies are more frequently obtained from accessible sites such as ENT or skin and usually dictated by clinical manifestations. In our cohort, the highest sensitivity was obtained from kidney, skin, ENT, bone marrow? and GI tract.

References:

1. Grayson et al, Ann Rheum Dis 2022.
2. Yates et al, Ann Rheum Dis 2016.

P-024

Eosinophilic giant cell arteritis: a different subset of disease?

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Background/Objectives: Temporal artery biopsy (TAB) still represents the gold standard for giant cell arteritis (GCA) diagnosis. The eosinophilic infiltrate at TAB has been described in 8% of 274 TAB with transmural inflammation[1]. Whether it is part of the GCA spectrum or other conditions remain controversial. The aim of our study was to describe the clinical findings, disease course and treatment response of GCA patients with transmural eosinophilic infiltration at TAB.

Methods: All biopsies with evidence of transmural inflammation obtained between January 1986 and December 2013 at the IRCCS in Reggio Emilia were reviewed by a single pathologist. The eosinophilic infiltrate was defined according to the severity as mild [≥20 and <40/high-power-field (hpf)], moderate (≥40 and <60/hpf), or severe (≥60/hpf). Patients with histological evidence of eosinophilic infiltration were compared with patients without for demographic, clinical and histological features. To compare the presence of eosinophil-related manifestations (namely asthma, allergic rhinitis, and nasal polyposis), patients with eosinophilic infiltrate were matched 1:2 for age, sex, and duration of follow-up (+/-5 years) with patients without.

Results: 254 TAB were included, 22 (8.7%) showed evidence of eosinophilic infiltrate. GCA patients with eosinophilic infiltrate were more likely females (p = 0.055). At diagnosis, they presented more frequently cranial symptoms (p = 0.052), particularly headache (p = 0.005), systemic manifestations (p = 0.016), and showed higher C-reactive protein levels (p = 0.001) (Table1). Regarding histological lesions, a severe transmural inflammation, laminar necrosis, and intraluminal acute thrombosis were more frequently observed in patients with eosinophilic infiltration (p = 0.066, p < 0.001, and p = 0.010, respectively). Almost no differences were observed in the two groups regarding frequencies of relapses, long-term remission, duration of glucocorticoid therapy and its cumulative dose. When the 22 patients were matched with 44 without eosinophilic infiltrate, no differences in the eosinophil levels or in the development of eosinophil-related manifestations were detected. Furthermore, no patient developed signs of systemic necrotizing vasculitis during follow up.

Conclusions: Patients with transmural eosinophilic infiltration represent a subset of GCA patients with cranial manifestations and more severe inflammation, both at clinical and histological levels.

Disclosures: None.

Reference:

1. Cavazza A, et al. Am J Surg Pathol. 2014 Oct;38:1360-70.

Table 1 Findings at diagnosis of the cohorts.

Findings	All (N=254)	Eosinophils in TAB (N=22)	No eosinophils in TAB (N=232)	P-value
Age of onset, years (mean ± SD)	74.2±7.4	74.9±5.8	74.2±7.6	0.632
Female, n (%)	198 (78)	21 (95)	177 (76.2)	0.055
Clinical manifestations				
Cranial symptoms, n (%)	219 (86.2)	22 (100%)	197 (84.9)	0.052
Headache, n (%)	198(78.0)	22 (100%)	176 (75.9)	0.005
Carotidodynia, n (%)	26 (10.2)	4 (18.2)	22 (9.5)	0.258
Visual manifestations, n (%)	73 (28.7)	6 (27.3)	67 (28.9)	1.000
Severe ischemic events, n (%)	52 (20.5)	4 (18.2)	48 (20.7)	1.000
Systemic manifestations, n (%)	170 (66.9)	20 (90.9)	150 (64.7)	0.016
Polymyalgia rheumatica, n (%)	109 (42.9)	11 (50.0)	98 (42.2)	0.506
ESR, mm/hour (mean ± SD)	86.2±30.4	97.2±29.3	85.1±30.3	0.081
CRP, mg/dl (mean ± SD)	8.8±6.1	13.3±5.3	8.3±5.9	0.001
Initial prednisone dose mg/day (mean ± SD)	50.0±31.1	46.9±10.5	50.3±32.4	0.621

P-025

From systemic vasculitis to other conditions: the broad spectrum of ANCA-positivity

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Background and Objective: Anti-neutrophil cytoplasmic antibodies (ANCA), specific autoantibodies for ANCA-associated vasculitis (AAV), may have clinical, pathogenic and diagnostic significance in a broad spectrum of diseases[1].

Our aim is to determine whether patients with a positive ANCA test have AAV or not. We report the indications, diagnoses and laboratory results of the included patients.

Methods: We retrospectively analyzed 169 ANCA-positive tests between March 2021 and June 2023. Excluded were repeated samples or those without adequate clinical data available.

ANCA-positivity was defined as p-ANCA, c-ANCA, atypical or unspecified patterns by indirect immunofluorescence (IIF) staining and/or an elevated anti-MPO or anti-PR3 levels by CLIA.

Cases were reviewed to establish if patients had AAV (granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), eosinophilic granulomatosis with polyangiitis (EGPA), renal-limited associated vasculitis (RLV) and cocaine-levamisole induced vasculitis (CLIV)), or alternative diagnoses according to their underlying organic pathology.

Results: The majority of patients (72%, n=121) had some type of autoimmune disease. Also, 25% (n=43) had an established or new diagnosis of AAV.

In AAV-newly diagnosed patients (n=21), ANCA screening primarily targeted suspicion of rapidly progressive glomerulonephritis (66%), followed by otorhinolaryngological disorders (20%) and lung disease (14%).

In established AAV patients (n=22), testing indicated routine monitoring, clinical changes (possible relapse/flare), or suspicion of a new vasculitic condition.

Non -AAV patients (n=126) were frequently tested for suspicion of liver or gastrointestinal disorders (25%), followed by lung disease (17%), arthritis (12%), renal disease (9%) or routine monitoring (9%).

The most common AAV was GPA (30%), followed by RLV (26%), EGPA (16%), MPA (14%) and CLIV (14%); and the more prevalent non-AAV conditions included inflammatory bowel disease (IBD) (13%), non-autoimmune liver diseases (17%), demyelinating diseases (6%), autoimmune liver diseases (5%) and idiopathic pulmonary fibrosis (4%).

Screening the 169 ANCA-positive samples through IIF revealed patterns as follows: 64 p-ANCA, 47 c-ANCA, 7 doubly positive (c-ANCA, p-ANCA), 4 atypical x-ANCA, 3 unspecified, and 44 negative. Additionally, 26 p-ANCA cases (41%) and 12 c-ANCA patients (25%) had clinical diagnoses of AAV.

In CLIA screening, 38% of MPO patients and 26% of PR3 patients had AAV.

Conclusions: In our cohort, the majority of patients had an autoimmune disease, and 25% of the total had AAV. p-ANCA and MPO-ANCA were more frequent than c-ANCA and PR3-ANCA for AAV diagnosis. The most common ANCA-positive condition in the non-AAV group was IBD. Clinical correlation is essential in interpreting ANCA tests.

Reference:

Moiseev S, et al. 2020 international consensus on ANCA testing beyond systemic vasculitis. Autoimmun Rev 2020; 19:102618.

Disclosures: None.

P-026

ANCA utility during interstitial lung disease diagnosis: a retrospective 5-year analysis from an ILD clinic

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Background/ Objectives: To determine the diagnostic yield of anti-neutrophil cytoplasmic antibodies (ANCA) as part of the diagnostic evaluation of patients with an interstitial lung disease (ILD). To describe the characteristics of patients showing pANCA and cANCA.

Methods: Observational retrospective study that reviewed all patients submitted for evaluation at an Interstitial Lung Diseases Clinic between 01/2016 and 12/2020 with a positive ANCA test. Final diagnosis was set according to clinical judgement and review of the electronic health records. Data were described as proportions, mean ± standard deviation or median (quartile 1 – quartile 3). Analysis was performed using StataBE17.

Results: We evaluated 586 possible candidates being ANCA positive in 50 (8.5%). Twenty-six (52%) were woman with a mean age of 66.0±11.8 years. Thirty-one (62%) had been smokers (27 pack-year). Symptoms at diagnosis were heartburn in 20 (40%), shortness of breath in 30 (60%), cough in 24 (48.9%), arthralgia in 10 (20.8%), Raynaud in 3 (6.3%), xerophthalmia in 9 (18.8%) and xerostomia in 8 (16.7%). Physical exam showed crackles in 27 (54%) and digital clubbing in 4 (8.0%).

Blood tests evidenced a normal haemoglobin (mean concentration 13.9±1.9mg/dL), an eosinophil blood count of 222±289x10E9/L and a preserved kidney function (creatinine 0.94±0.4mg/dL). Myeloperoxidase (MPO) levels were 72.3 (20.6-129.4) U/mL and proteinase-3 (PR3) 14.5 (8.1-37.0)U/mL. Ten (20.0%) patients had a positive rheumatoid factor, anti-citrullinated peptide antibodies were present in 7 (14%), Ro60 in 2 (4.1%) and Ro52 in 1 (2.0%). Urine analysis showed glomerular activity in 2.

Age	Gender	ANCA IFI	MPO	PR3	Diagnosis
40	M	pANCA	8.3	51.3	No final diagnosis
75	M	pANCA	104.9	253	Ulcerative colitis
82	W	pANCA	129.4	N	Interstitital Usual Pneumonia
51	M	pANCA	213	N	Microscopic polyangiitis
37	M	pANCA	20.6	N	Microscopic polyangiitis
66	M	pANCA	53.8	N	Non-specific interstitial pneumonia
71	W	pANCA	90.8	N	Microscopic polyangiitis
75	W	pANCA	N	N	Interstitial pneumonia with autoimmune features
80	W	pANCA	186.9	N	Microscopic polyangiitis
50	W	pANCA	49.9	N	Sjogren's syndrome
78	W	pANCA	N	22.7	Ulcerative colitis
71	M	pANCA	7.3	N	Rheumatoid arthritis
56	M	cANCA	N	16.8	Granulomatosis with polyangiitis
76	W	cANCA	N	N	Idiopathic pulmonary fibrosis
58	W	cANCA	N	9.3	Chronic Obstructive Pulmonary Disease
73	W	cANCA	N	N	Unclassifiable interstitial pneumonia
71	M	cANCA	N	N	Possible hypersensitivity pneumònia
76	M	xANCA	N	6.7	Organizing pneumonia
71	M	p/cANCA	N	6.9	Interstitial pneumonia with autoimmune features
64	W	ND	N	12.2	Sarcoidosis

Figure 1. Correlation between gender (Man/Woman) ANCA immunofluorescence (IFI) status, myeloperoxidase (MPO), proteinase-3 (PR3) and diagnosis. N = negative, ND = not determined.

ANCA immunofluorescence (IFI) patterns showed a pANCA in 12 (24.5%), cANCA in 5 (10.2%) and xANCA in 31 (62.3%). One patient alternatively exhibited pANCA and cANCA. According to MPO/PR3 status, 10 patients with pANCA showed a positive MPO test and 3 a PR3 test. Two pANCA positive patients showed MPO and PR3 at the same time and one pANCA patient was negative for both MPO and PR3. Two cANCA patients showed positive PR3. MPO was not present in any patient with cANCA. A patient with xANCA showed positive PR3 but the remaining 30 were negative for both MPO and PR3. The patient alternating p/cANCA had positive PR3 antibodies. IFI was not performed in one patient who had positive PR3.

Regarding clinical diagnosis, 4 patients were diagnosed as having a microscopic polyangiitis and 1 as a granulomatosis with polyangiitis. Other diagnosis and its serological correlation are reported in figure 1.

Conclusions: ANCA IFI, pANCA and cANCA should always be performed during an ILD evaluation, as it appears that its combination increases diagnostic yield. These results in an appropriate clinical context, including lung and extrapulmonary findings can help to reach a proper diagnosis. Multidisciplinary evaluation is essential.

References: None.

Disclosures: None.

P-027

Axial Spondyloarthritis in Patients with Gastrointestinal Involvement of Behçet Syndrome

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Background/ Objectives: Controlled studies have shown that radiographic sacroiliitis was not increased in Behçet syndrome (BS), compared to other inflammatory diseases. However, gastrointestinal involvement of Behçet syndrome (GIBS) shares common features with inflammatory bowel disease which, in turn, can be associated with spondyloarthritis (SpA). We wanted to see whether GIBS patients have an increased frequency of radiographic sacroiliitis or non-radiographic axial spondyloarthropathy (nr-AxSpA) compared to BS patients with only mucocutaneous and/or joint involvement with no major organ involvement.

Methods: We included 71 GIBS patients and 76 consecutive BS patients without major organ involvement. Patients were screened for axial spondyloarthritis (axSpA) using the Assessment of Spondyloarthritis International Society (ASAS) criteria. First they were questioned for chronic back pain, defined by ASAS as the presence of chronic back pain for more than 3 months and an age at onset of <45 years. Patients with chronic back pain were questioned for other spondyloarthritis features and tested for HLA-B27 status, CRP levels and X-ray and magnetic resonance imaging of the sacroiliac joints. All radiologic images were evaluated independently and blind by two radiologists.

Results: Chronic back pain was reported by 30 (42%) GIBS patients and 25 (33%) BS patients with only mucocutaneous and/or joint involvement (p=0.24). Five (7%) GIBS patients and 4 (5%) controls met ASAS criteria for axSpA (p=0.74). Only 1 GIBS patient had radiographic axSpA (also termed ankylosing spondylitis), whereas 4 GIBS patients and 4 patients among the controls had nr-AxSpA. HLA B27 was positive in 3 (4%) of the GIBS patients and in 5 (7%) of the controls (p=0.72). There were no significant differences between the groups regarding other SpA features of the ASAS criteria (Table).

Conclusions: The frequency of axSpA in GIBS patients was not found to be higher than that in BS patients who have only mucocutaneous and/or joint involvement. This finding further suggests that, despite certain clinical similarities between GIBS and Crohn's disease, different disease mechanisms may be involved

References: None.

Disclosures: GH has received research grant, lecture fees and fees for serving on an advisory board from Celgene, receiving consulting fees from UCB Pharma, Bayer, Johnson & Johnson, lecture fees from Novartis, Abbvie, Amgen, and UCB Pharma.

	GIBS (n=71)	BS with only mucocutaneous and/or joint involvement (n=76)
Male	38 (53.5%)	23 (30%)
Mean (SD) age, years	45 ±12	42 ± 13
AxSpA according to ASAS criteria	5 (7%)	4 (5%)
Clinical arm	2	2
Imaging arm	3	2
Chronic back pain	30 (42%)	25 (33%)
Inflammatory back pain	17 (24%)	13 (17%)
SpA features among patients with chronic back pain		
Inflammatory back pain	17 (57%)	13 (52%)
HLA-B27	2 (7%)	3 (12%)
Arthritis	14 (47%)	11 (44%)
Enthesitis	11 (37%)	7 (28%)
Dactylitis	2	0
Psoriasis	1	1
Good response to NSAID	21 (70%)	16 (64%)
Family history for SpA	10 (33%)	6 (24%)
Elevated CRP	7 (23%)	3 (12%)

P-028

Venous Wall Inflammation Detected with Superb Microvascular Imaging in Behçet Syndrome

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Background/ Objectives: Superb microvascular imaging (SMI) is a novel technique that provides a more sensitive assessment of small vessels compared to color Doppler US (CDUS), by distinction of low-speed flow signals from motion artifacts. Superficial thrombophlebitis (STM) is a common manifestation in patients with Behçet syndrome (BS) and is thought to be associated with inflammation of the vessel wall rather than a procoagulant state. We aimed to assess STM lesions of patients with BS, together with controls, using SMI.

Methods: We studied 51 BS (16F/35M, mean age:40.6±12.8) patients and 28 non-BS (21F/7M mean age:44.9±11.7) patients with nodular lesions on physical examination. B-mode US, CDUS, PDUS and SMI were performed and recorded by the same radiologist and images were then evaluated by 2 radiologists. Both radiologists were blinded to the diagnoses and to each other's assessments. First, presence/absence of vessel was assessed with CDUS to differentiate STM from erythema nodosum (EN). Then STM lesions were evaluated for the presence/absence of thrombus, vessel wall color-coded signal intensity, and thickness using the imaging modalities defined above. Vessel wall signal intensity was graded into 4 groups according to the percentages of the effected vessel wall area (Grade 0= no signal, Grade 1= < 25%, Grade 2= 25-50%, Grade 3= 50-75%, Grade 4= >75%). CDUS was the gold standard in the final diagnosis of STM. Interobserver reliability was assessed by kappa statistic.

Results: The nodular lesions of 26 BS and 17 non-BS patients were diagnosed as STM. The diagnosis was EN in the remaining 25 BS and 11 non-BS patients. SMI showed increased color-coded signal intensity in the vessel wall in patients with STM. We did not observe increased signal intensity in any of the patients with EN. According to the grading system, at least grade 1 or higher vessel-wall signals were detected in 22 BS (84.6%) patients with STM, in contrast to only 3 (17.6%) non-BS patients with STM (Table). Sixteen of 26 BS patients (61.5%) had at least grade 2 signal, and 4 of them had halo shaped signals all around the vessel-wall (Figure). On the other hand, 2 of 3 non-BS patients (75%) had only grade 1 signal and none of them had grade 4 signal. The interobserver reliability was good (κ=0.87, p<0.001).

Conclusions: A high-grade color-coded signal suggesting inflammation of the vessel wall was detected with SMI, in the majority of BS patients with STM. This finding needs to be studied in different vascular lesions of a large number of BS patients together with controls, in order to understand its specificity for BS and its significance.

References: None.

Disclosures: GH has received research grant, lecture fees and fees for serving on an advisory board from Celgene, receiving consulting fees from UCB Pharma, Bayer, Johnson & Johnson, lecture fees from Novartis, Abbvie, Amgen, and UCB Pharma.

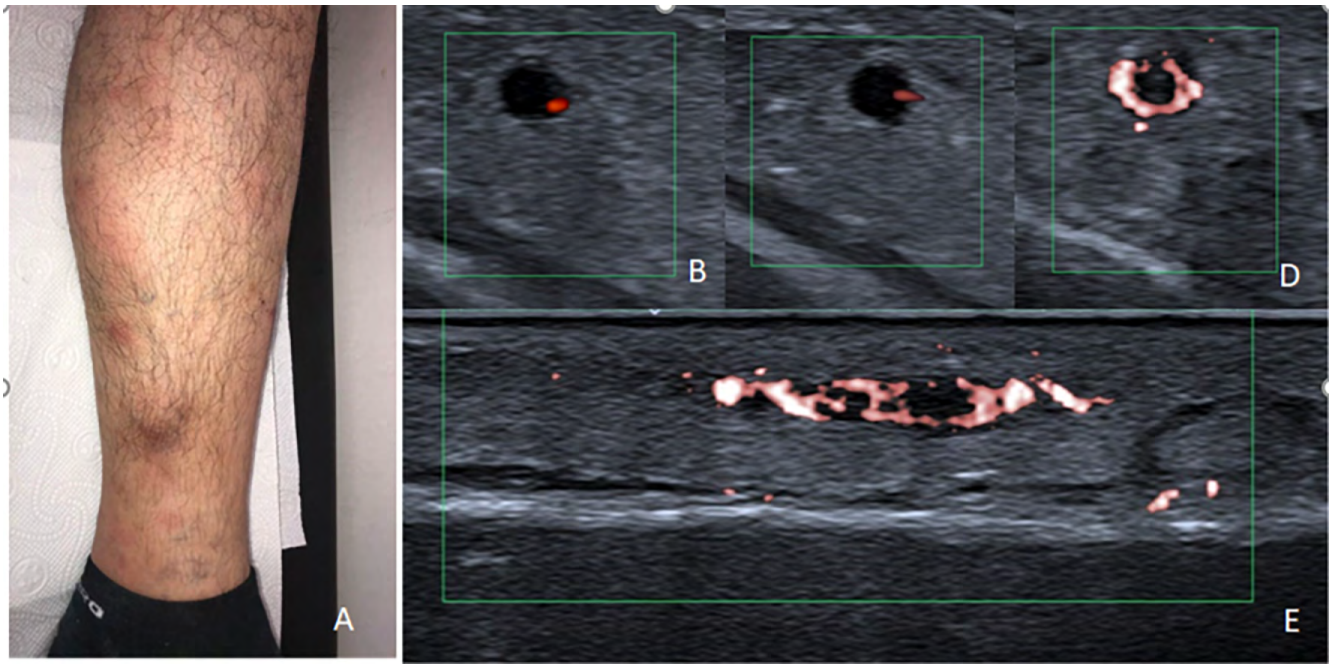

Figure. A-Nodul-like lesion on the posterior side of the cruris, B-Color Doppler US, C- Power Doppler US, D- Venous halo sign in axial plane SMI, and E-Venous wall inflammation in longitudinal plane SMI

P-029

ANCAs beyond anti-MPO and anti-PR3

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Background/ Objectives: According to international consensus on ANCA testing statement issued in 1999[1], indirect immunofluorescence assay (IFA) is the initial screening method to detect the presence of ANCAs. However, due to the recent international consensus and the improvement of antigen-specific immunoassays sensitivity and specificity, the two-stage diagnostic strategy for ANCA detection is being questioned[2, 3].

The objective of this study is to evaluate the ANCA testing in our clinical laboratory practice in a tertiary referral hospital.

Methods: A retrospective review was carried out over 5 years of patients admitted to the Vall d'Hebron Hospital who underwent ANCA tests. IFA was performed on a composite slide that included: human neutrophils fixed with ethanol, human neutrophils fixed with formalin and HEP2 cells with neutrophils fixed with ethanol. Antibodies against myeloperoxidase (MPO) and proteinase 3 (PR3) were tested by a commercial Chemiluminescent Immuno-Assay (CLIA).

Results: Out of 10281 patients with ANCA tested, 1131 (11%) gave a positive result. Out of these 10281 ANCA analysed, 1738 (16.9%) were ordered from primary care and 8543 (83.1%) were hospital cases. The positivity rate for tests ordered from primary care practices was 6%, whereas it was 11.9% from those ordered from hospital.

Atypical pattern (X-ANCA) was the most frequent (64.5%) followed by perinuclear (P-ANCA) (19.3%) and cytoplasmatic (C-ANCA) (15.5%). Fifty-one percent (51.2%) of P-ANCA and 36.2% of C-ANCA were positive for MPO-ANCA and PR3-ANCA respectively, whereas 98% of X-ANCA tested were negative by CLIA.

Conclusions: These findings suggest that IFA is not only useful to detect atypical X-ANCA but also to identify the high percentage of classical P-ANCA (48.8%) and C-ANCA (63.8%) negative for MPO or PR3. In such cases, known and unknown granulocyte related antigens could be implicated. Thus, the current diagnostic strategy for ANCA in a tertiary referral hospital should start by IFA method.

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Disclosures: None.

P-030

The role of 18F FDG-PET imaging in the diagnosis of large vessel vasculitis: outcome predictors and impact of prior glucocorticoid therapy

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Background: 18F-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) is one of the most important imaging modalities for diagnosing large vessel vasculitis (LVV). However, the sensitivity and specificity of PET/CT may be affected by several factors, including disease phenotype and the use and duration of treatment with glucocorticoids (GCs). Therefore, proper selection of patients and timing of examination concerning treatment should be considered. This study aims to describe the characteristics of patients with LVV diagnosed using PET/CT and to identify factors that predict findings of LVV on PET/CT.

Methods: This retrospective study includes patients from the southernmost region of Sweden, Skåne, who were assigned a diagnosis code of LVV or aortitis between 1998 and 2019 and underwent PET/CT for any reason between 1998 and 2019. Information on demographics and laboratory data, as well as treatment data and doses, were collected from patients' medical records. Analyses were then performed on all patients with the referral letter for PET/CT with a question of vasculitis. A multiple logistic regression model was fitted to identify predictors of finding LVV on PET/CT.

Results: Three hundred forty-one patients underwent PET/CT between 1998 and 2019. Of them, 220 patients were referred for PET/CT with a suspicion of "vasculitis", 142 (65%) of which were female. Mean age at PET/CT was 71 (SD 10.8) years. One hundred thirty-four (61%) patients were on GC at time of PET/CT. Eighty (36%) patients had signs of LVV on PET/CT, 33 had received GC treatment before the examination. In comparison to individuals without LVV on PET/CT scans, patients exhibiting LVV findings on PET/CT were younger (mean age 68 vs. 73 years, p=0.001) and displayed a notably elevated inflammatory response, as evidenced by higher levels of erythrocyte sedimentation rate (ESR) (mean 66 vs. 51 mm/h, p<0.001), C-reactive protein (CRP) (median 39 vs. 18 mg/L, p=0.02), and platelet count (mean 393 vs. 329 x10^9/L, p<0.001). Additionally, this group had a lower body weight (68 vs. 73 kg, p=0.049). Patients with LVV on PET/CT were also less likely to receive GC treatment before the PET/CT examination. In univariate analysis, several factors predict LVV; however, the most important one is being on GC before or at the time of PET/CT. In a multiple regression analysis, the following factors are potential predictors for LVV on PET/CT: Not taking GCs before PET/CT, lower age, and higher platelet count (Table 1).

Conclusions: Younger patients and those with high platelet counts were more likely to have findings on PET/CT indicating LVV.To improve the sensitivity of PET/CT, the examination needs to be performed, if feasible, before starting treatment with GC.

Disclosures: None.

Table 1: Predictors of LVV in PET/CT.

	Univariate Regression			Multiple Regression		
Predictors	*OR*	*95% CI*	*P*	*OR*	*95% CI*	***P***
Age at diagnosis*	0.66	0.49-0.85	0.002	0.66	0.47-0.88	**0.008**
Gender (Male)	1.46	0.82-2.66	0.2	1.63	0.83-3.26	**0.1**
GC treatment before PET/CT	0.27	0.15-0.48	<0.0001	0.42	0.19-0.91	**0.02**
GC dose >10mg at PET/CT**	0.32	0.15-0.64	0.001	0.57	0.17-2.12	**0.4**
Platelet count***	1.23	1.09-1.39	0.0007	1.17	1.02-1.35	**0.02**
CRP******	1.06	1.00-1.12	0.02	1.00	0.95-1.07	**0.8**

OR: Odds ratio of positive LVV findings on PET/CT. CI: confidence interval, GC: glucocorticoids, CRP: C-reactive protein.

*Age at diagnosis increased by 10 years, **Patient on >10 mg of prednisolone at day of PET/CT ***Platelet count increased by 50, ****CRP increased by 10. Note: Only potential predictors with significant effects are reported.

P-031

Systemic vasculitides in Portugal and Brazil: preliminary results from the Reuma.pt/vasculitis registry

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Background/objectives: The epidemiology of vasculitis varies widely across different areas of the world which may be due to different ethnic and environmental factors. Brazil has a heterogeneous population with influences from Indigenous, African, Asian, and European countries, while Portugal has a very ethnically homogeneous background. This study aims to assess differences in the profile of systemic vasculitides between Portugal and Brazil.

Methods: Collaborative project between the Portuguese and the Brazilian Societies of Rheumatology in which centres from both countries were invited to register data in the vasculitis module of the Rheumatic Diseases Portuguese Register, Reuma.pt/vasculitis. A cross-sectional analysis was performed comparing demographic, ethnic and diagnostic information between Brazilian and Portuguese centres.

Results: A total of 1,955 patients were analysed: 74.2% from 30 Portuguese centres and 25.8% from 7 Brazilian centres. Portuguese patients were predominantly European White (89.2%) and in Brazil the most common ethnic groups with vasculitis were the non-European White (48.3%) and Mestizos (40.1%); 5.4% of all participants were born in other countries. Brazilian patients were younger at the onset of symptoms [35.2 (24.1-46.6) vs. 48.1 (27.4-70.1) years; $p<0.05$] and diagnosis of vasculitis [37.0 (27.6-48.3) vs. 50.8 (32.7-70.4) years; $p<0.05$] than Portuguese patients, respectively. When analysing individual forms of vasculitis, Brazilian patients with giant cell arteritis (GCA), Takayasu arteritis (TAK), polyarteritis nodosa (PAN) and granulomatosis with polyangiitis (GPA) were significantly younger than Portuguese patients at diagnosis ($p<0.05$). The proportion of females was higher in Portuguese patients with Behçet's disease (BD) than in Brazilian patients ($p=0.03$). No differences regarding the proportion of females were observed for other vasculitides (Table 1). The most common form of vasculitis in both countries was BD followed by GCA in Portugal and by TAK in Brazil. Regarding ANCA-associated vasculitis, GPA was more common in Brazil and microscopic polyangiitis (MPA) in Portugal. Both countries had similar proportions of patients with PAN and eosinophilic granulomatosis with polyangiitis (EGPA). Time elapsed between the onset of symptoms and the diagnosis of GCA was higher in Brazil than in Portugal ($p=0.014$) while Portugal had a longer interval between the onset of BD symptoms and its diagnosis compared to Brazil ($p<0.05$) (Table 1).

Conclusions: In this large multicentre binational study, Portugal and Brazil had a different profile of systemic vasculitis concerning the proportion of GCA and TAK patients, as well as GPA and MPA patients. In addition, both countries had differences in the age of onset, female gender, and ethnicity of patients with systemic vasculitis.

Disclosures: None.

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Table 1. Demographic features of patients with vasculitis in Portugal and Brazil.

Variables	Portugal	Brazil	*p*
Behçet's disease			
Females, %	75.5	67.2	0.033*
Age at diagnosis, years	33.3 (25.0-42.3)	33.3 (27.0-40.7)	0.878
Time between symptoms and diagnosis, years	4.00 (1.00-12.00)	0.99 (0.32-4.00)	< 0.0001*
Giant cell arteritis			
Females, %	66.0	80.6	0.076
Age at diagnosis, years	75.3 (69.4-80.4)	68.6 (61.7-75.4)	< 0.0001*
Time between symptoms and diagnosis, years	0.16 (0.05-0.37)	0.43 (0.08-1.83)	0.014*
Takayasu arteritis			
Females, %	85.2	93.9	0.066
Age at diagnosis, years	37.0 (24.3-49.6)	30.3 (23.3-40.4)	0.020*
Time elapsed between symptoms and diagnosis, years	1.16 (0.58-4.61)	1.08 (0.41-4.37)	0.692
Polyarteritis nodosa			
Females, %	56.8	70.0	0.316
Age at diagnosis, years	43.1 ± 17.1	32.3 ± 14.4	0.027*
Time between symptoms and diagnosis, years	1.00 (0.49-2.87)	0.48 (0.29-3.83)	0.463
Granulomatosis with polyangiitis			
Females, %	58.6	60.2	0.818
Age at diagnosis, years	51.5 ± 15.8	43.9 ± 14.2	0,001*
Time elapsed between symptoms and diagnosis, years	0.67 (0.24-3.00)	0.99 (0.29-2.08)	0.600
Microscopic polyangiitis			
Females, %	57.3	75.0	0.239
Age at diagnosis, years	64.3 (54.8-74.1)	58.2 (38.2-74.5)	0.352
Time elapsed between symptoms and diagnosis, years	0.42 (0.10-0.91)	0.33 (0.23-1.58)	0.738
Eosinophilic granulomatosis with polyangiitis			
Females, %	61.0	54.5	0.598
Age at diagnosis, years	54.7 ± 15.8	49.6 ± 11.1	0.176
Time elapsed between symptoms and diagnosis, years	1.56 (0.26-6.50)	2.00 (0.83-4.00)	0.480

Continuous data are presented as median and interquartile range or as mean and standard deviation; * - Flags significant results.

P-032

IgA vasculitis in Tunisia: The experience of an internal medicine department

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Introduction: IgA vasculitis usually affects children. Adult presentations are less frequent and usually more severe.

The aim of our study was to describe the clinical and histological characteristics of IgA vasculitis in adults in an internal medicine department.

Patients and methods: A retrospective monocentric descriptive study carried out at the Internal Medicine Department of the interior forces hospital. It included data of patients IgA vasculitis between January 2001 and November 2023.

Results: 11 patients were included. The mean age of our patients was 40,45 years [24-64]. Gender ratio (M/F) was 10.

Systemic lesions were as follows: cutaneous involvement (n=11); digestive (n=5); renal (n=), articular (n=2).

Cutaneous involvement with purpuric lesions was the initial presentation of all our patients. with the following localisations: lower limbs (n=11); upper limbs (n=8); abdomen (7); face (n=1). Skin biopsy was performed in all patients. It revealed leukocytoclastic vasculitis with IgA deposits on the vascular walls on direct immunofluorescence (DIF) in 9 among them.

Kidney biopsy was performed for 7 patients and showed an IgA nephropathy in 6 among them.

A biological inflammatory syndrome (BIS) was observed in 5 patients. Antinuclear antibodies (ANA), antineutrophil cytoplasmic antibodies (ANCA) and cryoglobulinemia were negative.

All patients were started on corticosteroid therapy. Complete remission was obtained for 8 patients while 2 patients progressed to chronic renal failure. One patient died following small bowel ischemia complicated by perforation.

Conclusion: Digestive damage during IgA vasculitis is life-threatening in the short term, while renal damage affects the long-term prognosis due to the renal failure it can cause.

1. CLINICAL SCIENCE

1.02. Treatment: clinical trials (new trials, post-hoc analysis, long-term follow-up); real world data with new therapies; observational studies; emerging therapies (i.e. CAR-T, multi-target molecules); classical and new treatment optimization for special situations (frailty, advanced age...)

P-033

Annual rituximab dosing as a remission maintenance strategy in ANCA associated vasculitis

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Background/ Objectives: Rituximab is an established remission maintenance therapy in ANCA associated vasculitis (AAV).[1,2] In the RITAZAREM trial, despite the administration of 5g maintenance rituximab in the first 24 months, 50% experienced a relapse by month 48.[2] The MAINRITSAN 3 trial extended rituximab maintenance for 18 months beyond the standard maintenance period, and 96% were in remission at month 28.[3]

Relapse after cessation of maintenance therapy occurs in the majority of AAV patients, but continuation of therapy reduces relapse risk. However, with prolonged immunosuppression, there is increasing risk of adverse effects, particularly infections and the development of hypogammaglobulinaemia and poor vaccine responses. The optimal duration and exact nature of long term remission maintenance strategies in AAV is unclear.

In our centre, selected patients have received prolonged maintenance annual rituximab therapy generally for an additional 3-5 years after a standard 2 year (typically 6g cumulative dose) maintenance course. Here we describe this cohort and our experience with this strategy aimed at reducing longer term immunosuppression burden.

Methods: In this single centre, retrospective study, we identified all patients who had received annual rituximab therapy as a longer term AAV maintenance strategy by reviewing drug administration and electronic medical records.

Results: Between March 2010 and November 2023, 78 patients (37 (47%) male) received annual doses of 1g rituximab as extended maintenance therapy. Mean age at AAV diagnosis was 49.3 years (SD 16.9) and at start of annual rituximab treatment 60.0 years (SD 15.9). Mean disease duration prior to annual rituximab dosing was 10 years (SD 7.8). Historical ANCA status was as follows: PR3 59 (76%), MPO (14%) 11, ANCA negative 8 (10%). Previous immunosuppression included cyclophosphamide 60 (77%) of patients, rituximab 73 (94%) (mean cumulative rituximab dose prior to annual dosing was 6.1g (SD 3.4)), azathioprine 46 (59%), mycophenolate mofetil 28 (36%) and methotrexate 17 (22%).

The majority of patients commenced annual rituximab when in remission (Disease Extent Index (DEI) 0 (range 0-8). For those patients where reason for annual rituximab dosing was documented, 30/77 (39%) had experienced a relapse, whereas the remainder (47/77 (61%)) were started to maintain remission in view of high perceived risk of relapse. Of 78 patients, 33 patients stopped annual rituximab during the follow up period. Median follow up time was 39 months (range 5–134).

During follow up, 16/78 (21%) of patients suffered a relapse. Ten relapses occurred within a year of last dose, and were managed by earlier rituximab dosing, and 6 occurred in those who had stopped annual rituximab therapy at a mean of 14.5 months after last dose.

Conclusions: This AAV cohort is characterised by a long duration of disease prior to starting annual rituximab dosing, with the majority following a relapsing disease course. Although relapses occurred, rates were lower than observed following cessation of immunosuppression.[2,3] Further data on infections, glucocorticoid exposure, hypogammaglobulinaemia and CD19 B cells counts will be available in 2024.

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P-034

Variation in the Acute Management of ANCA-Associated Vasculitis in Australia and New Zealand

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Background/Objectives: Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a rare autoimmune disease which is managed by a range of specialities. There is limited data on treatment practices in Australia and New Zealand.[1] The aim of the study is to understand current patterns of acute AAV treatment in Australia and New Zealand.

Methods: An online survey was conducted between July and October 2022 investigating physicians' views on the management of AAV, focusing on induction therapy. The survey contained questions pertaining to ease of access to treatment and responses to clinical management scenarios. Eosinophilic granulomatosis with polyangiitis was not included.

Results: From a total of 55 responses, plasma exchange was difficult to access for 44% of respondents, more so in rural centres, which also had difficulty accessing infusion centres. New Zealand clinicians had more difficulty accessing rituximab, with only 44% reporting easy access to this medication compared with Australian clinicians (93%). With clinical management scenarios, there was variation in the dosing regimen of glucocorticoids and whether plasma exchange is initiated, with 42% of respondents prescribing a different glucocorticoid regimen from the standard of care, 'reduced-dose' arm of the PEXIVAS trial.[2] The choice of cyclophosphamide or rituximab for induction therapy was based on patient characteristics and medical history.

Conclusions: There is substantial variation in approaches to the acute management of AAV in Australia and New Zealand, including differences in resource availability. This variation in care demonstrates the need to implement current practice guidelines, and institute contemporary monitoring of AAV management to achieve best patient outcomes.[1]

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P-035

Design of AVACOSTAR: A real-world study of avacopan in ANCA-associated vasculitis (AAV)

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Background/Objectives: Avacopan, a first-in-class oral C5aR antagonist, was shown to be superior to a prednisone taper in sustaining remission, and was associated with improved estimated glomerular filtration rate after 12 months in patients with severe active granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA)[1]. Avacopan was approved for the treatment of adult patients with severe active GPA and MPA in combination with rituximab or cyclophosphamide by the European Commission in January 2022. The assessment of the EU Marketing Authorization Application for avacopan was based on data available from the clinical development program; however, long term data beyond the 12-month pivotal phase 3 ADVOCATE study period is lacking. AVACOSTAR is a post-authorization safety study designed to evaluate the incidence of safety events of interest during long-term follow up in a real-world cohort of participants with GPA and MPA treated with avacopan (NCT05897684) in EU.

Methods: AVACOSTAR is a non-interventional, multi-national, prospective cohort study that will enroll participants with severe active GPA/MPA into two cohorts: those treated with avacopan, and a second cohort treated with a cyclophosphamide or rituximab-based induction regimen without avacopan. Participants will be followed until the last patient last visit milestone, 4 years after the last participant is enrolled. All decisions on therapeutic or diagnostic procedures, treatments, disease management, timing of visits, or resource utilization will follow the investigator's usual clinical practice (figure 1).

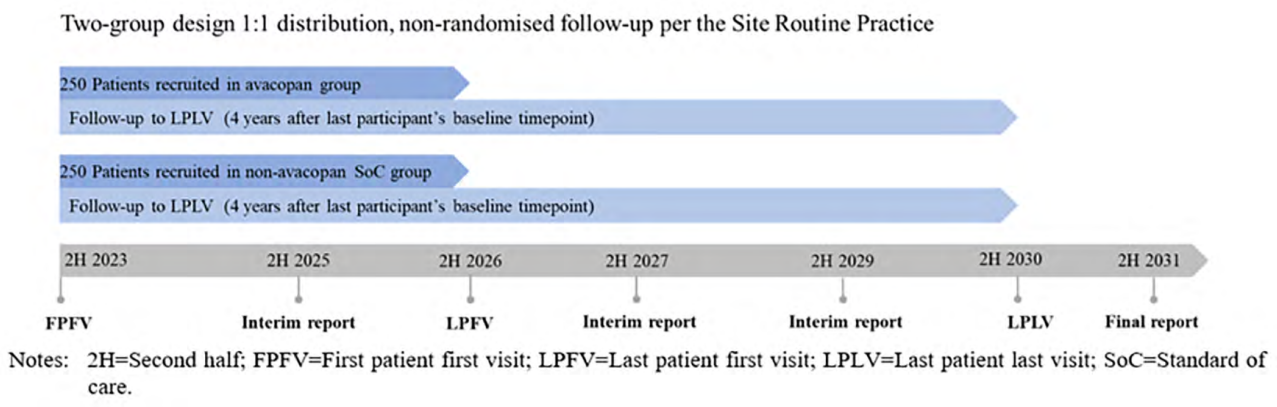

Figure 1: Study Flowchart.

The primary objective of the study is to evaluate the incidence of defined medical events of special interest (MESIs) in both cohorts. Secondary objectives include evaluating adverse events (AEs), AEs leading to discontinuation of therapy, serious adverse events, adverse drug reactions, serious adverse drug reactions, selected laboratory abnormalities, disease flares, organ damage, and patterns of immunosuppression and glucocorticoid use.

Results: The study has been approved in UK and Germany and plans to enroll 500 participants, 250 in each arm, the first of which enrolled in September 2023.

Conclusions: The AVACOSTAR study will be the largest real world evidence study conducted to date that evaluates long-term safety of novel therapeutics in GPA/MPA and is expected to yield important insights on the use of avacopan in GPA/MPA in a real-world setting, including continuation beyond 12 months.

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Disclosures:

DJ Consulting Alentis, Amgen, AstraZeneca, Aurinia, Boehringer, Chinook, GSK, Novartis, Otsuka, Roche/Genentech, Takeda, CSL Vifor. Lecture Fee Amgen, GSK, CSL Vifor. Stocks Alentis, Aurinia.

RL Grants BMS, Celgene, CSL Vifor. Consulting GSK, Roche, CSL Vifor. Lecture Fee GSK, CSL Vifor; Advisory board GSK.

BT Lecture Fee - Advisory Board CSL Vifor.

AO, CP, MB, MB Employees CSL Vifor.

BH Lecture Fee - Advisory board CSL Vifor.

P-036

Efficacy of avacopan for ANCA-associated vasculitis: a single center experience in Japan

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Background/ Objectives: Although avacopan (AVA) has recently become available for AAV in Japan, its usefulness with or without corticosteroids remains to be established. Therefore, we conducted a retrospective analysis of clinical database of the AAV patients treated with AVA and a reduced regimen of corticosteroids.

Methods: All patients met the Chapel Hill Consensus Conference classification criteria for microscopic polyangiitis (MPA) or granulomatosis with polyangiitis (GPA). Nineteen patients [9(47%) females)] treated with AVA that could be followed more than 6 months were analyzed for the clinical data and therapeutic response including remission rates. Remission was defined as Birmingham Vasculitis Activity Score (BVAS) 0. GC Pulse, RTX, and AVA were used as induction therapy. PSL was begun at a dose of 0.4-1.0 mg/kg/day depending on the patient conditions and then tapered off at 12 weeks (Table 1.).

Results: There were 19 patients of AAV (10 MPO-MPA, 7 MPO-GPA, 1 PR3-GPA and 1 MPO/GPA double positive-GPA), with the mean age of 72.2±11.5 years, including 12 newly diagnosed, 4 relapsing cases and 3 at the maintenance phases. Rapidly progressive glomerulonephritis was seen in 58% (11/19 cases), pulmonary lesions in 53% (10/19 cases). Rituximab was used in 74% (14/19 cases). At the start of AVA, BVAS 12.2±8.1(median14), CRP was 0.95±1.99 mg/dL, Cr 1.8±1.0 mg/dl, eGFR 36.9±22.7 ml/min/1.73m2, and the initial dose of PSL was 32.2±20.7 mg/day. At week 12, 24 and 48, the remission rates were 84%, 83%, 86%, respectively. The percentages of patients who could have reduced PSL below 5 mg/day were 58%, 75%, 86% and those who could have tapered off PSL were 26%, 42%, 57% at week 12, 24 and 48. One patient died from pneumonia, and no patients required maintenance dialysis.

Conclusions: These results showed that AVA may be effective with the reduced PSL regimen and have acceptable safety profiles in relatively older AAV patients in Japan.

References: Jayne DRW et al.:N Eng J Med 384:599, 2021.

Disclosures: None.

weeks	BW 40kg	BW 50kg	BW 60kg	BW Over 75kg
1	40mg	50	60mg	75mg
2	20mg	25	30mg	40mg
3	15mg	20mg	20mg	30mg
4	10mg	15mg	15mg	20mg
5	7.5mg	10mg	10mg	15mg
6	5mg	7.5mg	7.5mg	10mg
7	5mg	5mg	5mg	7.5mg
8	5mg EOD	5mg	5mg	5mg
9	5mg EOD	5mg EOD	5mg EOD	5mg
10	OFF	5mg EOD	5mg EOD	5mg EOD
11		OFF	OFF	5mg EOD
12				OFF
Total	752.5mg	997.5mg	1102.5mg	1452.5mg

Table 1. Our hospital's GC reduction regimen.
PSL dose after GC pulse: Start PSL 1mg/kg and then off by 12wks. EOD: every other day

Figure.

P-037

The usefulness of serum monitoring of mizoribine in patients with myeloperoxidase anti-neutrophil cytoplasmic antibody-associated vasculitis

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Background/ Objectives: The prognosis of myeloperoxidase anti-neutrophil cytoplasmic antibody-associated vasculitis (MPO-AAV) is improving with the combination of steroids and immunosuppressive agents (IAs) such as rituximab, but there are still unresolved issues such as infections related to treatment. Mizoribine (MZR) has an established reputation for safety, and the ability to measure serum concentrations may allow its use in patients who have difficulty using the above IAs.

Methods: From the participants of a previous study [Clin Exp Nephrol. 2022;26:1092-1099] evaluating the efficacy and safety of MZR with MPO-AAV in the maintenance phase of remission, 22 patients who received MZR and whose serum levels were measured were enrolled. The relationship between the maximum serum concentration (Cmax) of MZR and relapse, laboratory values, or adverse events was evaluated.

Results: 5 patients relapsed during the observation period. There was no significant relationship between Cmax and relapse. However, there was a significant negative correlation between Cmax and final CRP level (r=-0.23, P=0.03). Two patients with adverse events suspected to be related to MZR had significantly higher serum creatinine at the start of MZR (P=0.64) and significantly higher Cmax (P=0.01).

Conclusions: The results suggest that monitoring serum concentrations may be useful for effective and safe use of MZR in patients with MPO-AAV.

Disclosures: NH (Takeda), KY (Chugai, Daiichi-Sankyo, Kyowakirin, Tanabe-Mitsubishi, Astrazeneca, Bayer), YY (Baxter, Bayer, Chugai, Japan Tobacco, Kyowakirin, Ono, Otsuka, Sanofi, Sumitomo Dainippon, Torii).

P-038

Effect of Vitamin D Treatment in ANCA-Associated Vasculitis: Results from an Exploratory Pragmatic Study

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Background/Objectives: There is a paucity of data on vitamin D status and the potential impact on ANCA-associated vasculitis (AAV). In an exploratory, pragmatic study, we looked at the association between disease activity and 25-hydroxyvitamin D levels [25(OH)D] at enrollment and month 12.

Methods: The study aimed to enroll >100 patients with AAV at the Vasculitis Clinic, in Toronto, Ontario from January to July 2021. 25(OH)D was measured (by ELISA) at baseline; low vitamin D levels were defined as 25(OH)D < 75 nmol/L. Patients with low 25(OH)D at baseline were asked to increase vitamin D supplementation by 1000 (to a maximum of 2000 IU/day). 25(OH)D levels were measured again at month 12. The primary endpoint was relapse during the 12-month study period. Clinical and serological disease characteristics in addition to medications were collected at diagnosis, at enrollment, potential relapse occurrences during study period, and at month 12.

Results: Due to the COVID-19 pandemic, the enrollment period was extended to December 2021. Of the 103 patients who consented and enrolled, one patient was excluded due to a history of hyperparathyroidism. Mean age of the remaining 102 patients at enrollment was 54.7±20 years and 59 (58%) were female. Fifty had granulomatosis with polyangiitis, 28 microscopic polyangiitis and 24 eosinophilic granulomatosis with polyangiitis; lungs were involved in 79 (77%) patients, kidneys in 63 (62%), and peripheral nerves in 25 (24.5%). A history of positive ANCA status was recorded in 87 (85.3%) patients. At enrollment, 89 patients were in remission; 52 were on prednisone, and 45 on rituximab. At month 12, 14 patients did not proceed with their month 12 vitamin D level measurement, and two patients died during the study period (one from sepsis, one from cancer).

A total of 41 (40.2%) patients had low vitamin D at baseline. Of the 86 patients with a month 12 follow-up, 14 (16.3%) had low vitamin D at month 12. Over the study period, 7 (8.1%) patients had a relapse: 3 (7.3%) of the patients with low vitamin D at baseline vs. 4 (6.6%) of the patients with sufficient vitamin D levels at baseline; 1 (7.1%) of those patients with low vitamin D levels at month 12 vs. 6 (8.3%) of those with sufficient levels at month 12 (p=0.999 for both comparisons). None of the patients whose vitamin D levels increased from low at baseline to sufficient levels at month 12 experienced a relapse over the study period.

Conclusions: Over a third of the patients with AAV had low vitamin D levels at baseline, and a sixth at month 12. Low vitamin D levels were not associated with disease activity or relapse at the group level. However, patients whose vitamin D levels increased from low at baseline to sufficient at month 12, following study intervention, had no relapses. Given the limited sample size of this exploratory study, larger studies may still be considered to further investigate the effect of vitamin D in AAV at the individual patient level.

Disclosures: None.

P-039

Rituximab and infection-related risk in anti-neutrophil cytoplasmic antibody-associated vasculitis: a systematic review and pairwise and network meta-analysis

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Background: Anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV), which includes granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic GPA (EGPA), may have life-threatening complications. The 2022 EULAR recommendations for the management of AAV advocated induction therapy with rituximab (RTX) or cyclophosphamide (CYC) for patients with severe GPA or MPA. RTX affects CD20-expressing B-cells and may induce B-cell depletion for 6–9 months. This raises concerns about increased infection risks, although existing reports are conflicting. This study aimed to validate this inconsistency.

Methods: We conducted a focused literature search in PubMed, ClinicalTrials.gov, and Embase from January 1998 to April 2023 to identify relevant studies. The search strategy used specific keywords related to our research topic.

Results: Eight and five RCTs involving 800 and 623 participants were used for network and pairwise meta-analyses, respectively. Pairwise meta-analysis revealed a relative risk (RR) of 0.31 (95% CI: 0.648–1.337) for RTX-associated serious infections. Sensitivity analysis of induction (RR: 0.993, 95% CI: 0.434–2.274) and maintenance (RR: 0.917, 95% CI: 0.613–1.372) therapies did not show significantly different serious infection risks. AZA (RR: 1.11, 95% CI: 0.75–1.64), CYC (RR: 1.04, 95% CI: 0.49–2.17), CYC-AZA (RR: 1.00, 95% CI: 0.24–4.25), and placebo (RR: 0.93, 95% CI: 0.51–1.67), relative to RTX, did not demonstrate increased serious infection risks. Pairwise (RR: 1.368, 95% CI: 0.54–3.51) and network (AZA RR: 0.58, 95% CI: 0.13–2.60; CYC-AZA RR: 1.00, 95% CI: 0.11–9.00) meta-analyses did not indicate increased serious infection risks for AZA or CYC-AZA relative to RTX.

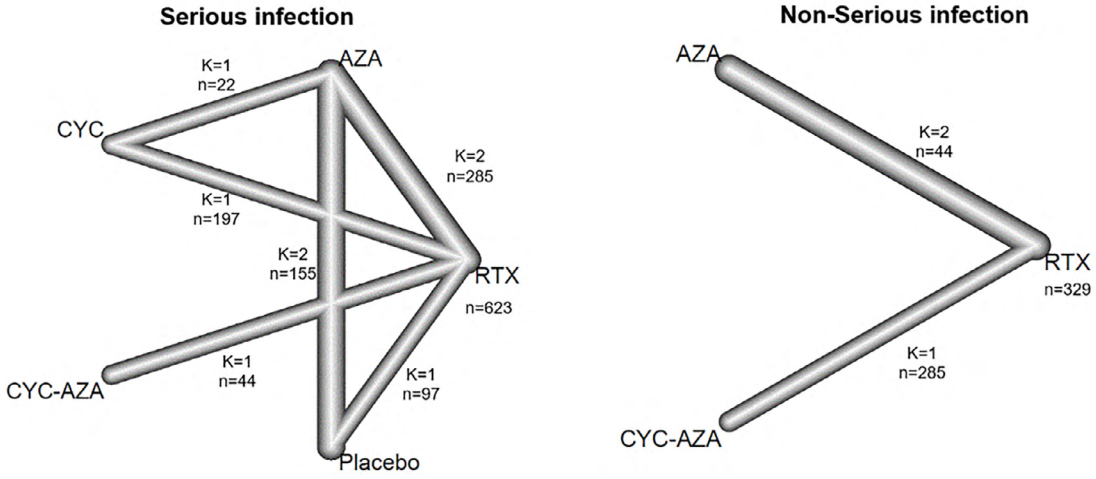

Fig. 1 Network graphs for the comparison of rituximab (RTX), azathioprine (AZA), cyclophosphamide (CYC), CYC-AZA, and placebo.

Conclusion: RTX does not demonstrate a heightened risk of infection relative to AZA, CYC, CYC-AZA, and placebo and making it a safe option for AAV management.

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Disclosures: Portions of this abstract were previously presented at the 2023 annual meeting of the Taiwan College of Rheumatology.

P-040

Revisiting Bioequivalence and Dose-dependent Effects of Prednisolone and Dexamethasone on Circulating Immune Cells in Healthy Volunteers

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Background/Objectives: Corticosteroids are an important pillar in the treatment of many inflammatory and autoimmune diseases. Prednisolone and dexamethasone, common synthetic glucocorticoids, are often used interchangeably in clinical practice but their equivalent doses are based on outdated data. Furthermore, the role of different corticosteroids in modulating the immune system is not fully understood. To address these issues, the CORE (COrticosteroids Revised) study, a double-blind, randomized, cross-over clinical trial, was designed to re-examine the clinical bioequivalence and dose-dependent effects of corticosteroids on various physiological systems, including the immune system.

Methods: To investigate the impact of glucocorticoid dosage on immune cell counts, distribution, and function, we recruited 24 healthy volunteers (both male and female, aged 18-75). In a randomized crossover study design, participants received either a daily dose of 7.5 mg prednisolone for one week followed by 30 mg for another week (N=12), or they began with 1.125 mg dexamethasone followed by 4.5 mg (N=12), with a 4-8 week washout period between treatments. We collected early morning fasting blood samples at baseline and after each treatment allowing whole blood quantification of leukocyte counts and isolation of peripheral blood mononuclear cells (PBMC). A 40-color optimized multicolor immunofluorescence panel (OMIP-69) was employed to deep phenotype PBMC populations. Additionally, functional studies of immune cell cytokine production were performed.

Results: Prednisolone and dexamethasone treatment induced significant alterations in the absolute counts and frequencies of major circulating immune cell populations including an increase of neutrophils, lymphocytes, monocytes, T cells, and B cells, and a decrease of eosinophils and basophils compared to baseline. Higher doses had a more pronounced effect on immune cell subsets. Notably, dexamethasone treatment showed a greater impact on the composition of circulating immune cells than the assumed equipotent doses of prednisolone. Preliminary functional studies indicated a trend towards the suppression of inflammatory cytokines in T cells.

Conclusions: Our study revealed discrepancies between presumed clinical bioequivalent doses of prednisolone and dexamethasone, suggesting the need for revised dose calculations. In addition, the effects of both glucocorticoids on the immune system are dose-dependent. Our results may serve as a reference for understanding immune cell responses to corticosteroid treatment, providing guidance to clinicians for tailoring doses and treatments to individual patient needs.

References: Stam, S. P., et al. (2022).

Disclosures: None.

Immune cell subsets	Pred $LD_{(7.5\ mg)}$ - Baseline % Median (25^{th}, 75^{th} percentile)	Dex $LD_{(1.125\ mg)}$ - Baseline % Median (25^{th}, 75^{th} percentile)	P-value (Wilcoxon matched-pairs signed rank test)
Leukocytes	**14.7** (3.1, 27.7)	**30.4** (14.8, 43.68)	*, 0.0149
Neutrophils	**11.6** (-19.0, 41.4)	**12.8** (2.34, 64.8)	ns
Monocytes	**5.5** (-4.7, 11.7)	**28.1** (12.2, 41.2)	**, 0.0016
Lymphocytes	**29.2** (21.0, 51.4)	**49.2** (35.3, 66.5)	****, <0.0001
Basophils	**8.34** (-19.2, 45.8)	**0** (-25.0, 40.0)	ns
Eosinophils	**-17.4** (-47.8, 9.52)	**-34.8** (-50.0, -22.2)	*, 0.0229
Total T cells	**34.9** (20.2, 50.0)	**60.8** (49.1, 84.4)	****, <0.0001
Total B cells	**55.5** (25.9, 95.9)	**102** (59.1, 142)	***, 0.0007
NK cells	**-6.8** (-24.3, 19.9)	**-12.0** (-36.2, 14.6)	ns
Total ILCs	**6.4** (-13.2, 25.0)	**10.5** (0.0, 30.0)	*, 0.0368
$CD4^+$ T cells	**44.5** (26.9, 60.7)	**62.6** (47.7, 109)	****, <0.0001
$CD8^+$ T cells	**26.8** (5.44, 45.5)	**46.6** (31.1, 69.2)	****, <0.0001

Study population (N=24; male = 12, female = 12). Significant *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001

Table 1 Comparative effects of low doses of prednisolone and dexamethasone on circulating immune cell distributions.

P-041

Efficacy and safety of subcutaneous infliximab [CT-P13] in Behçet's disease: a monocentric case series

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Background/ Objectives: Behçet's disease (BD) is a rare systemic inflammatory disease with a chronic relapsing course. In case of severe clinical manifestations, the use of conventional immunosuppressive drugs (cDMARDs) or biological drugs such as TNF-α inhibitors is necessary. Recently, a new formulation of infliximab (CT-P13) administered subcutaneously demonstrated its efficacy in maintaining remission in patients with rheumatoid arthritis, seronegative spondyloarthritis and inflammatory bowel disease. The aim of the study was to demonstrate the efficacy and safety of infliximab subcutaneously in a group of BD patients.

Methods: We prospectively enrolled BD patients (classified according to International Criteria for Behçet's disease), treated with infliximab CT-P13 administered subcutaneously (120mg every 14 days), either for maintenance of remission after switch from intravenous formulation or for induction of remission. Clinical and laboratory data were collected at baseline and during follow-up. Remission was defined according to BDCAF 2006 (Behçet's disease current activity form) and Japan's criteria of activity, associated with negativity of acute phase reactants and clinical judgement. Safety of the drug was defined as the absence of adverse drug reactions (local and systemic), serious infections and liver toxicity.

Results: Between January 2022 and May 2023, 7 patients (28.5% female, mean age 50.1 years) affected with BD were included. At the time of CT-P13 initiation, the disease was in remission in 5 (71.4%) patients, while 2 had an active disease. Median disease duration was 172 [IQR 48-190] months. Six (85.7%) patients failed at least one cDMARD and 4 (57.1%) had also failed a biologic drug (both anti TNF-alpha and anti-interleukin-6). The median follow-up with infliximab therapy was 8 [IQR 5-10] months. Therapy with CT-P13 resulted in a significant decrease in BDCAF 2006 score (2[0-2] vs 0[0-1], p=0.037) and absence of Japan's criteria for active disease. Treatment resulted in remission of oral ulcers, folliculitis, inflammatory arthritis/arthralgias, superficial thrombophlebitis, and uveitis. In patients switched from intravenous infliximab, no significant changes in activity indices or acute phase reactants were observed. No local or systemic adverse drug reactions or liver toxicity were registered. A single episode of Herpes Zoster ophthalmicus was observed, which was successfully treated with acyclovir. Of note, 75% of patients discontinued oral glucocorticoid permanently.

Conclusions: Subcutaneous infliximab [CT-P13] appears to be an effective and safe treatment in patients with BD, including those who are refractory to several lines of therapy. Future prospective studies on larger cohorts are needed.

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Disclosures: None.

P-042

Annual rituximab therapy as an extended remission maintenance strategy in ANCA associated vasculitis (AAV)

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Background/ Objectives: Rituximab is an established remission maintenance therapy in ANCA associated vasculitis (AAV).[1,2] In the RITAZAREM trial, despite the administration of 5g maintenance rituximab in the first 24 months, 50% experienced a relapse by month 48.[2] The MAINRITSAN 3 trial extended rituximab maintenance for 18 months beyond the standard maintenance period, and 96% were in remission at month 28.[3]

Relapse after cessation of maintenance therapy occurs in the majority of AAV patients, but continuation of therapy reduces relapse risk. However, with prolonged immunosuppression, there is increasing risk of adverse effects, particularly infections and the development of hypogammaglobulinaemia and poor vaccine responses. The optimal duration and exact nature of long term remission maintenance strategies in AAV is unclear.

In our centre, selected patients have received prolonged maintenance annual rituximab therapy generally for an additional 3-5 years after a standard 2 year (typically 6g cumulative dose) maintenance course. Here we describe this cohort and our experience with this strategy aimed at reducing longer term immunosuppression burden.

Methods: In this single centre, retrospective study, we identified all patients who had received annual rituximab therapy as a longer term AAV maintenance strategy by reviewing drug administration and electronic medical records.

Results: Between March 2010 and November 2023, 78 patients (37 (47%) male) received annual doses of 1g rituximab as extended maintenance therapy. Mean age at AAV diagnosis was 49.3 years (SD 16.9) and at start of annual rituximab treatment 60.0 years (SD 15.9). Mean disease duration prior to annual rituximab dosing was 10 years (SD 7.8). Historical ANCA status was as follows: PR3 59 (76%), MPO (14%) 11, ANCA negative 8 (10%). Previous immunosuppression included cyclophosphamide 60 (77%) of patients, rituximab 73 (94%) (mean cumulative rituximab dose prior to annual dosing was 6.1g (SD 3.4)), azathioprine 46 (59%), mycophenolate mofetil 28 (36%) and methotrexate 17 (22%).

The majority of patients commenced annual rituximab when in remission (Disease Extent Index (DEI) 0 (range 0-8). For those patients where reason for annual rituximab dosing was documented, 30/77 (39%) had experienced a relapse, whereas the remainder (47/77 (61%)) were started to maintain remission in view of high perceived risk of relapse. Of 78 patients, 33 patients stopped annual rituximab during the follow up period. Median follow up time was 39 months (range 5–134).

During follow up, 16/78 (21%) of patients suffered a relapse. Ten relapses occurred within a year of last dose, and were managed by earlier rituximab dosing, and 6 occurred in those who had stopped annual rituximab therapy at a mean of 14.5 months after last dose.

Conclusions: This AAV cohort is characterised by a long duration of disease prior to starting annual rituximab dosing, with the majority following a relapsing disease course. Although relapses occurred, rates were lower than observed following cessation of immunosuppression.[2,3] Further data on infections, glucocorticoid exposure, hypogammaglobulinaemia and CD19 B cells counts will be available in 2024.

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P-043

Multi-Center Study on the Safety of Tocilizumab Use for Giant Cell Arteritis in Japan

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Objective: Japanese patients did not participate in the GiACTA trial[1)], a phase 3 trial of tocilizumab(TCZ) in giant cell arteritis (GCA), and therefore, only limited data were available for its safety. Hence, this study aims to reveal the real-world safety of TCZ in Japanese GCA patients.

Methods: This multicenter, retrospective study targeted GCA patients treated with TCZ at seven hospitals in Japan. The data on adverse events and subsequent TCZ discontinuation were recorded up to 24 months after the initiation of TCZ. Adverse events of special interest included death, severe infections (death/hospitalization/intravenous antibiotic administration), non-severe infections (oral antibiotic administration), injection site reactions, neutropenia (<500/μL), and hyperlipidemia (LDL-C >160 mg/dL). Other adverse events were also documented.

Results: A total of 62 cases with a follow-up of 95.5 person-years were included. The median age was 74±5 years, and 40(65%) were female. There were a total of 29 adverse events occurring in 23(37%) patients. Severe and non-severe infections were common adverse events. Eight adverse events (13%) led to TCZ discontinuation: two severe infections, one non-severe infection, one injection site reaction, and four other adverse events(Table 1). The TCZ discontinuation due to adverse events occurred within 6 months in four cases and, between 6 and 12 months in four cases. Patients who tolerated TCZ for 12 months did not discontinue TCZ due to adverse events thereafter. The administration methods for discontinued cases were subcutaneous injection every week in four cases, subcutaneous injection at intervals of two weeks or more in three cases, and intravenous injection in one case.

Table 1.Results and Compared with GiACTA trial[1)]

	This research(n=62)	GiACTA Weekly(n=100)	GiACTA Every Other Week (n=49)
Age -Yr	74±5	69.5±8.5	69.4±8.2
Female sex -no.(%)	40(65)	78(78)	35(70)
Duration in trial -patient-yr	95.5	92.9	45.6
Patients with ≥1 Adverse event -no.(%)	23(37) -Death 0(0) -Neutropenia 0(0) -Hyperlipidemia 0(0) -Others 14(23): 3 cases exacerbation of diabetes, aortic dissection, elevated liver enzymes, syndrome of inappropriate antidiuretic hormone secretion, herpes esophagitis, adrenal insufficiency, elevated creatinine, worsening heart failure, gastrocnemius pain, elevated liver enzymes, general fatigue, decreased platelet count	98(98)	47(96)
Patients with ≥1 infection -no.(%)	11(19) -Severe infection 7(11):influenza pneumonia, viral gastritis, infective endocarditis, acute laryngitis, bacterial pneumonia, fecal lleus, cellulitis -Non-Severe infection 6(10):3 cases of herpes zoster, viral upper respiratory tract infection, subcutaneous abscess, simple herpes	75(75)	36(73)
Patients with injection site reaction -no.(%)	1(2)	7(7)	7(14)
Patients who withdrew from the using/trial because of adverse events -no.(%)	8(13) --Severe infection 2(3):infective endocarditis, bacterial pneumonia -Non-Severe infection 1(2): herpes zoster -Injection site reaction 1(2) -Others 4(6):gastrocnemius pain, elevated liver enzymes, general fatigue, and decreased platelet count	6(6)	3(6)

Conclusion: In the real-world Japanese setting, TCZ was used in more elderly patients, and a larger number of patients discontinued TCZ due to adverse events compared to the GiACTA trial. However, TCZ was well-tolerated and safely use in the majority of patients. Similar to the GiACTA trial, infections were the most common adverse events, yet reports of injection site reactions were relatively infrequent.

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Disclosures: None.

P-044

Changes in Treatment of ANCA-Associated Vasculitis with the Emergence of Avacopan

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Background/ Objectives: Avacopan was launched in Japan in June 2022 for the treatment of ANCA-associated vasculitis. In the ADVOCATE study[1], avacopan showed non-inferiority to prednisone, it is expected to be a trump card to break away from the current glucocorticoid-dependent treatment of ANCA-associated vasculitis. As real-world data, we examined changes in the treatment of ANCA-associated vasculitis complicating renal dysfunction before and after the launch of avacopan at our hospital.

Methods: Thirteen cases treated with avacopan of 60 mg/day (A group) were compared with 16 cases most recently treated before the launch of avacopan (non-A group) at our hospital.

Results: The mean age was 73.5 years in A group and 75.1 years in non-A group. The mean eGFR was 20.0 mL/min/1.73 m^2 in A group and 15.0 mL/min/1.73 m^2 in non-A group. Most cases were MPO-ANCA positive, with a PR3-ANCA positivity rate of 23.1% in A group and 18.8% in non-A group. The complication rate of extrarenal lesions was 46.2% in A group and 50.0% in non-A group. The mean starting dose of predonisolone (PSL) was significantly lower in A group (A group: non-A group = 9.2 mg: 25.9 mg), and methylpredonisolone pulse therapy was administered less frequently in A group (A group: non-A group = 23.1%: 75.0%). On the other hand, rituximab was administered more frequently in A group (A group: non-A group = 92.3%: 31.3%). MPO-ANCA titers before, 1 month, 3 months, and 6 months of treatment were 180.8, 46.8, 28.6, and 24.4 in A group and 336.2, 95.7, 58.1, and 50.6 in non-A group, respectively. The changes in eGFR before, 1 month, 3 months, and 6 months of treatment were 20.0, 24.8, 25.7, and 29.9 in A group and 15.0, 23.7, 24.3, and 24.1 in non-A group, respectively. Renal death was 1 case (7.7%) in A group and 5 cases (31.3%) in non-A group. Death was 0 case in A group and 3 cases (18.8%) in non-A group. Liver dysfunction due to avacopan was observed in 7 of 13 patients (53.8%), a higher rate than in the ADVOCATE study. It occurred on mean 32 days after the start of treatment and was more common in females than in males (male: female = 37.5%: 80%).

Conclusions: There were no significant differences between A group and non-A group, although comparisons were made during the first 6 months of treatment; the A group had a lower PSL dose and rituximab was available in more patients. A relatively high rate of liver dysfunction was observed in Japanese patients.

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Disclosures: None.

P-045

Changing spectrum of systemic therapies for eosinophilic granulomatosis with polyangiitis from 2006-2023

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Background/Objectives: The emergence of biologic therapies targeting interleukin (IL)-5 and its receptor (IL-5R) provided new treatment options in eosinophilic granulomatosis with polyangiitis (EGPA). This study evaluated the landscape of systemic therapies utilized for EGPA before and after introduction of these agents in North America.

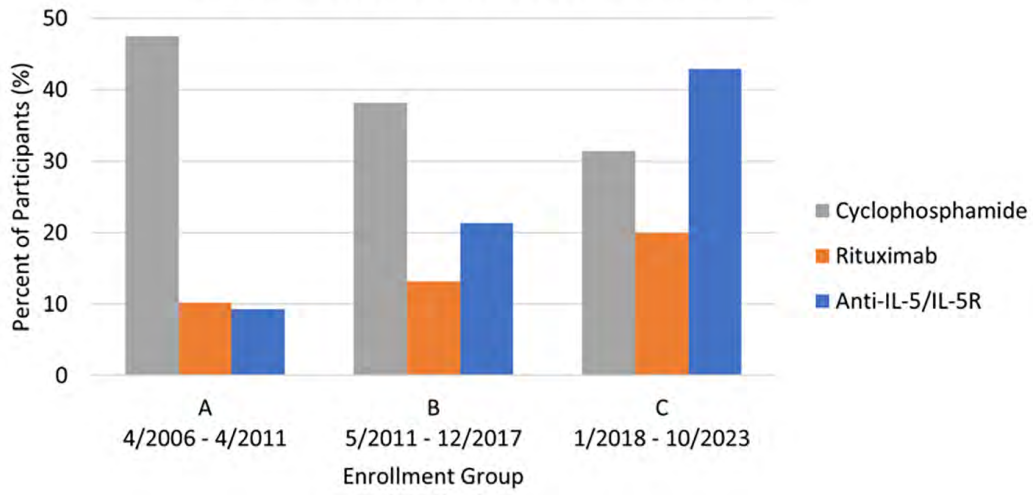
Methods: Clinical data were examined from 326 participants in a longitudinal cohort at 11 academic centers in the USA and Canada. Participants were grouped based on the timing of their enrollment in the cohort, using three separate periods: (A) April 2006 -- April 2011; (B) May 2011 (first full month after FDA approval of rituximab for use in other forms of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis) -- December 2017; (C) January 2018 (first full month after FDA approval of mepolizumab for use in EGPA) -- October 2023. Results were analyzed across these three enrollment groups, followed over time.

Results: Enrollment per period: A-118 participants; B-136; C-72. Sex and age distribution were similar across all time periods, with female participants comprising 187 (57.4%) of the total group, and an overall mean ± SD age of 53.4 ± 14.2 years at enrollment. Mean disease duration at enrollment was 3.2 ± 4.7 years, and 127/326 (40.0%) were ANCA positive. Cyclophosphamide (intravenous or oral) was used at some point during the treatment course of 56 (47.5%) participants enrolled during A, 52 (38.2%) from B, and 22 (31.4%) from C (p=0.0792) (**Figure 1**). Rituximab was used in 12 (10.2%) of patients enrolled in period A, as compared to 18 (13.2%) from B, and 14 (20.0%) from C (p=0.1762). A total of 70 (21.6%) among all enrolled participants received an anti-IL-5 or anti-IL5R agent (mepolizumab, benralizumab, or reslizumab) during their course, with mepolizumab used most commonly among these, in 53 (16.4%) participants. Use of these three agents increased over time, with eleven (9.3%) participants enrolled during period A ultimately receiving one of these agents during follow-up, versus 29 (21.3%) among those in group B, and 30 (42.9%) among group C (p<0.0001). Two participants were concurrently treated with both mepolizumab and rituximab, including 1 each from groups B and C. One participant, who had enrolled during period B, received concurrent cyclophosphamide and mepolizumab.

Conclusions: Treatment regimens for EGPA have evolved over time. Further analyses are warranted to investigate the relationship with disease severity and the efficacy of agents and regimens for management of specific disease features in EGPA.

Disclosures: This analysis was supported in part by AstraZeneca and GlaxoSmithKline.

Figure 1. Medication use for EGPA over time



EGPA, eosinophilic granulomatosis with polyangiitis; IL-5, interleukin-5; IL-5R, IL-5 receptor.

P-046

Biosimilars of Rituximab in ANCA-associated Vasculitis compared to the Originator (BRAVO): baseline characteristics of a Canadian multicentre study

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Background/Objectives: Rituximab (RTX) is a first-line induction and maintenance treatment in granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA). Starting in 2020, reimbursement for RTX across Canada became increasingly restricted to biosimilars (including mandatory switching for prevalent users), despite little data on their comparative safety and effectiveness to the originator in AAV. We report baseline characteristics of a Canadian multi-centre AAV cohort starting RTX originator or biosimilars for induction or maintenance of remission between 2018-2023.

Methods: We included adults with GPA or MPA who started RTX originator or biosimilar induction or maintenance 1) in the 6 months prior to enrollment, or 2) after January 2018 if followed within an existing prospective vasculitis cohort. We also recruited patients who switched from originator to biosimilar RTX in the prior 6 months. We collected baseline demographic and disease characteristics (i.e., at the time of starting RTX induction, maintenance, or switching), including disease activity (measured with the Birmingham Vasculitis Activity Score, BVAS), damage (measured with the Vasculitis Damage Index, VDI), prior RTX or cyclophosphamide use, and current vasculitis medications. We examined baseline differences between originator and biosimilar subgroups using the 95% confidence interval (CI) for the difference in mean or proportion, as applicable.

Results: We recruited 201 participants from 9 centres: 127 who received RTX induction (52 originator; 75 biosimilar), 57 who received maintenance (23 originator, 35 biosimilar), and 17 who switched from originator to biosimilar maintenance at cohort entry (Table 1). Mean age was 57.2 (SD 17.4), 52% were female, and 79% were White. The majority had GPA (69%) and were PR3-ANCA+ (64%) at diagnosis. Common vasculitis manifestations at last flare were ear/nose/throat (54%), pulmonary (58%), glomerulonephritis (53%), and musculoskeletal (39%). Originator induction recipients were similar to biosimilar induction recipients, except that the former group was younger (mean age 50.3 vs 59.8, difference 9.5 [95%CI 3-16]). Among maintenance recipients, the originator group had longer disease duration compared to the biosimilar group (mean 7.5 vs 2.4 years; difference 5.1 [95% CI 1.4-8.9]), and a greater proportion had PR3-ANCA (87% vs 56%; difference 31% [95%CI 7-50%]), had suffered ≥1 prior relapse (57% vs 12%; difference 45% [95%CI 20-64%]), and had previously received RTX induction (57% vs 26%; difference 30% [95%CI, 4-51%]).

Conclusions: This multi-centre cohort will evaluate real-world outcomes following treatment with RTX originator and biosimilars in AAV. Baseline differences between induction groups (i.e., biosimilar recipients having older age) and maintenance groups (i.e., biosimilar recipients having shorter disease duration/less relapsing disease) might suggest less restricted access to RTX for AAV in Canada coinciding with the availability of biosimilars.

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Table 1. Characteristics of the BRAVO cohort at time of starting rituximab originator, biosimilar, or switching from originator to biosimilar (N=201, 2018-2023)[1].

Characteristic	Induction		Maintenance		Switch (maintenance) n=17
	Originator n=52	Biosimilar n=75	Originator n=23	Biosimilar n=34	
Age, mean (SD)	**50.3 (19.5)**	**59.8 (17.1)**	56.1 (16.1)	59.3 (14.0)	63.4 (14.9)
Female sex, n (%)	29 (56)	43 (57)	11 (48)	14 (41)	8 (47)
Race/ethnicity, n (%)					
White	40 (76)	59 (79)	20 (87)	25 (74)	14 (82)

Asian	8 (15)	8 (11)	<5 (9)	6 (18)	<5 (6)
Hispanic	<5 (2)	<5 (1)	0	<5 (6)	<5 (12)
Indigenous	<5 (4)	<5 (1)	0	<5 (3)	0
Black	0	<5 (1)	<5 (4)	0	0
Other or unknown	<5 (2)	5 (7)	0	0	0
Highest education, n (%)					
High school or less	16 (31)	18 (24)	6 (26)	8 (26)	8 (47)
Post-secondary	32 (62)	43 (57)	14 (61)	22 (65)	8 (47)
Unknown	<5 (8)	14 (19)	<5 (13)	<5 (12)	<5 (6)
Diagnosis (n, %)					
GPA	36 (69)	53 (71)	19 (83)	20 (59)	11 (65)
MPA	16 (31)	22 (29)	<5 (17)	14 (41)	6 (35)
ANCA type, n (%)					
Anti-PR3	31 (60)	47 (63)	**20 (87)**	**19 (56)**	11 (65)
Anti-MPO	21 (40)	23 (31)	**<5 (13)**	**15 (44)**	6 (35)
ANCA negative	0	<5 (5)	0	0	0
Disease duration (years), mean (SD)	4.2 (6.7)	4.4 (6.5)	**7.5 (10.0)**	**2.4 (3.7)**	3.1 (2.5-6.9)
≥1 prior relapse, n (%)	31 (60)	37 (49)	**13 (57)**	**<5 (12)**	7 (41)
Manifestations at last flare, n (%)					
Mucocutaneous	11 (21)	20 (27)	<5 (13)	6 (18)	5 (29)
Ocular	14 (27)	14 (19)	6 (26)	<5 (9)	<5 (12)
Ear, nose, or throat	29 (56)	41 (55)	10 (44)	18 (53)	11 (65)
Pulmonary	29 (56)	38 (51)	15 (65)	22 (65)	12 (71)
Glomerulonephritis	26 (50)	37 (49)	11 (48)	23 (68)	10 (59)
Musculoskeletal	21 (40)	28 (37)	9 (39)	10 (29)	10 (59)
Neurologic	6 (12)	14 (19)	0	7 (21)	<5 (12)
Cardiovascular	<5 (4)	<5 (1)	0	<5 (3)	0
Gastrointestinal	<5 (2)	<5 (1)	0	0	0
BVAS, mean (SD)	12.5 (7.0)	13.4 (8.2)	1.0 (2.3)	0.7 (2.5)	0
VDI, mean (SD)	1.9 (1.8)	1.5 (2.0)	3.0 (2.8)	2.4 (1.8)	3.3 (2.1)
Prior treatment (ever), n (%)					
Cyclophosphamide (IV or PO)	24 (46)	25 (33)	14 (61)	21 (62)	10 (59)
RTX induction (originator)	8 (15)	11 (11)	**13 (57)**	**5 (14)**	13 (76)
RTX induction (biosimilar)	0	<5 (1)	0	<5 (12)	0
RTX maintenance (originator)	<5 (8)	<5 (5)	<5 (4)	0	17 (100)
RTX payor (n, %)					
Public insurance plan	21 (40)	28 (37)	16 (70)	15 (44)	13 (76)
Hospital (public payor)	11 (21)	25 (33)	0	0	0
Private insurance plan	11 (21)	13 (17)	6 (26)	17 (50)	<5 (24)
Other/combination	5 (10)	7 (9)	<5 (4)	<5 (3)	0
Unknown	<5 (8)	<5 (3)	-	<5 (3)	-
Time to RTX application approval, median days (IQR)[2]	11 (3-25)	4.5 (0-21)	14 (6-26)	14 (6-36)	42 (16-54)
Treatment (at Month 0), n (%)					
Prednisone	49 (94)	70 (93)	18 (78)	26 (76)	<5 (24)
mg/day, mean (SD)	40.7 (24.0)	49.9 (117.1)	**10.6 (5.2)**	**6.0 (2.3)**	6.3 (2.5)
Other immunosuppressant[3]	7 (13)	16 (21)	<5 (9)	<5 (6)	0
Antibiotic prophylaxis	42 (81)	61 (81)	18 (78)	27 (79)	6 (35)

Abbreviations: SD, standard deviation; IQR, interquartile range; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; ANCA, antineutrophil cytoplasm antibody; RTX, rituximab; BVAS, Birmingham Vasculitis Activity Score; VDI, Vasculitis Damage Index; mg, milligrams, IV, intravenous, PO, per os.

[1] **bold** denotes that the 95% CI for difference in mean or proportion between originator and biosimilar subgroups excludes the null; no comparisons made between 'Switch' group and other groups.

[2] data unavailable for 20 (38%) induction originator, 32 (43%) induction biosimilar, 11 (48%) maintenance originator, 13 (35%) maintenance biosimilar, 3 (18%) 'Switch' group

[3] Azathioprine (n=8), methotrexate (n=7), mycophenolate (n=6), leflunomide (n=1), avacopan (n=2) cyclophosphamide (n=3)

P-047

Plasma Exchange treatment in ANCA associated vasculitis patients in Croatian refferal center

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Background/ Objectives: Plasma exchange treatment (PLEX) in ANCA associated vasculitis (AAV) is still recomended for some patients in KDIGO[1] guidelines regarding renal and lung involvement. We analysed data from Croatian referral center regarding PLEX use.

Methods: Study included 108 patients (55,6% females; median age of 61) with AAV. Data regarding PLEX treatment were analysed and compared in patients grouped by phenotypes: clinical (microscopic polyangiitis = MPA, granulomatosis with polyangiitis = GPA and renal limited vasculitis = RLV), serological (MPO-ANCA, PR3-ANCA, MPO and PR3- ANCA positive, ANCA negative) and histopathological (Berden[2] classification). Survival analysis was performed for clinical outcomes: composite outcome end-stage renal disease(ESRD)/death(D), ESRD, death, and relaps rate.

Results: In our cohort there were 66 (61,1%) patients with MPA, 20 (18,5%) with GPA, 20 (18,5%) with RLV and 2(1,9%) with EGPA which were excluded from analysis due to small number. Median serum creatinine (SCr) were 316.5 umol/l (IQR= 207-548.5). Patients treated with PLEX included more often: MPA (p=0.002), MPO-ANCA AAVs (p=0.042), histologicaly crescentic class (p=<0.001). Univariant analysis found PLEX to be significant positive predictor for ESRD/D (p=0.068, HR 1.85; CI 0.956-3.592), ESRD (p=0.039, HR 2.3; CI 1.04.-5.114) and relapse rate (p=0.038; HR 4.2; CI 1.082-16.353). Multivariant analysis showed PLEX not to be significant predictor for any of the outcomes. We then divided patients into 4 groups based on SCr quartiles (Q1 SCr min-208 umol/l; Q2 SCr 209-319 umol/l; Q3 320-563 umol/l; Q4 SCr 564-max). Distribution per quartile was: Q1 N(PLEX)= 3, N(nonPLEX)= 23; Q2 N(PLEX)= 6, N(nonPLEX) =21; Q3 N(PLEX)= 14, N(nonPLEX)= 14 and Q4 N(PLEX)= 24, N(nonPLEX)= 1. PLEX not to be significant predictor for any outcome in our patient cohort in Q1-Q3 and significance was found in Q4 group, but there was only one patient in that group not being treated with PLEX.

Conclusions: The usefullness of PLEX remains variable depending on the indications, disease severity as well as probably standard of care in individual hospitals. In our cohort PLEX was more often used for patients with more severe disease at presentation and it is therefore expected that these patients would have had less favorable outcomes independent of the PLEX treatment. Also in our cohort MPA and MPO-ANCA positive patients and those with crescentic histological class were more likely to be treated with PLEX.

References:

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Disclosures: None.

P-048

Persistent B cell depletion after Rituximab for autoimmune diseases: a retrospective cohort study

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Introduction: Rituximab, an anti-CD20 monoclonal antibody, depletes peripheral B cells and usually lasts for 6-12 months. Seldomly, B cells remain persistently depleted; however, the frequency and risk factors for this complication are unknown. We assessed the frequency and clinical features of patients with persistent B cell depletion following rituximab infusions for autoimmune diseases.

Methods: This is a single-center retrospective cohort of patients with autoimmune disease who have persistent B cell depletion after receiving rituximab at the Vasculitis and Glomerulonephritis Center at Massachusetts General Hospital, between 2003-2021. We defined B cell depletion as a total $CD19^{+}CD20^{+}$ cell count of < 5 cells/µl. Persistent is defined as a duration of B cell depletion lasting >2 years from the last rituximab infusion. Patients were included if they were > 18 years old, received at least one infusion of rituximab for the treatment of an autoimmune disease, and met criteria for persistent B cell depletion. The primary outcome measure was the duration of B cell depletion, calculated as the time from the date of last rituximab infusion through the last documented date of B cell depletion prior to B cell return. The evaluated risk factors and associations included underlying disease, age, ANCA levels (in ANCA-associated vasculitis (AAV)), cumulative rituximab dose, other immunosuppressants, and selected adverse events. ANOVA was used for ≥3 group comparisons.

Results: Among 1527 patients who received rituximab, 2% (n=31) had persistent B cell depletion. The median (IQR) age was 63 (44 - 77) years. 74% (23 / 31) had AAV. The median time from diagnosis to last rituximab was 5.2 years (3.1 – 8.9). The cumulative rituximab dose was 10,000 mg (8,000 - 12,000), given over 3.4 years (2.5 – 5.1). All except one patient had exposure to preceding or concurrent cytotoxic agents, often high cumulative doses, and 70% (22 / 31) received maintenance steroids for adrenal insufficiency or disease control. After the last rituximab infusion, 47.5% had B cell return at 4 years (6 years total) by Kaplan Meier (**Fig.1A-1B**). Even when B cells recovered, B cell count remained very low, at a median of only 7 cells/µl (6 - 15) at last follow-up. In patients with AAV, serum ANCA titers were low at last follow-up compared to pre-rituximab (**Fig.1C**). Total IgG levels were lower at last follow-up compared to pre-rituximab or the first available post-rituximab levels in patients who did not receive Ig replacement (**Fig.1D**). Recurrent, prolonged, or severe infectious episodes occurred in 55% (n=17), late-onset neutropenia in 23% (n=7), and vaginitis in 16% (n=5). In total, 23% (n=7) required Ig replacement and 23% (n=7) died. Four of the deaths were associated with infection, but only one was solely posed by infection. Disease relapse was very rare.

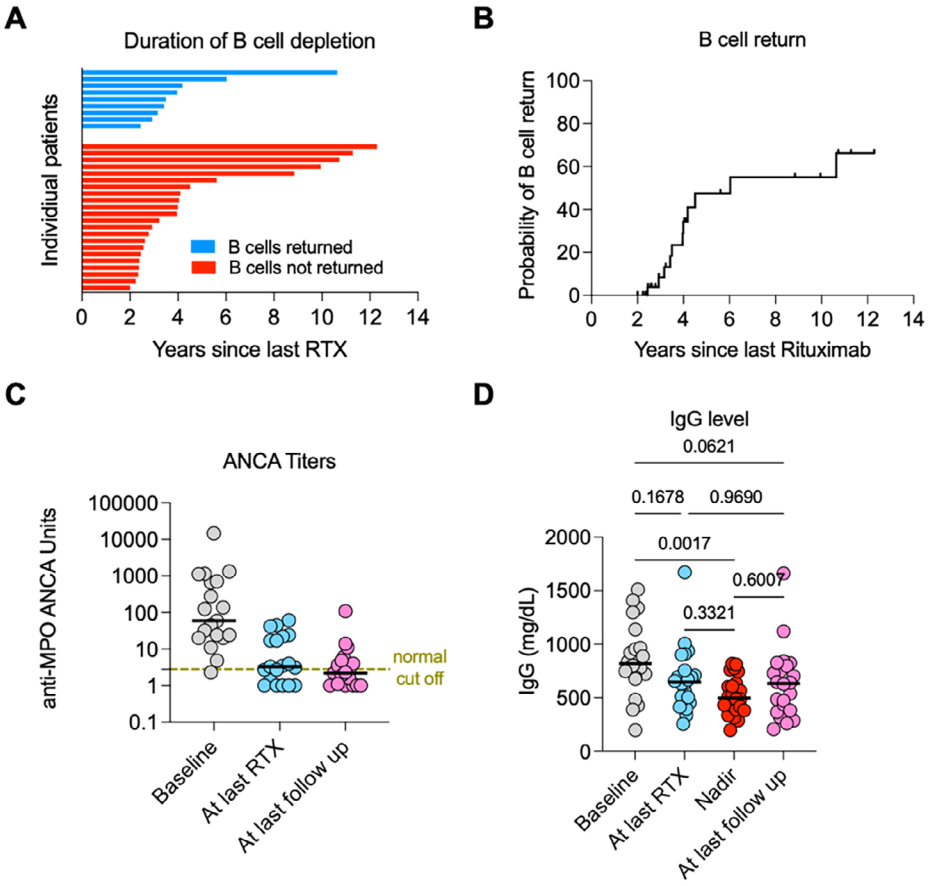

Figure 1. Outcomes in patients with persistent B cell depletion after Rituximab.

Discussion: Persistent B cell depletion is a rare complication of rituximab infusion, mostly affecting patients with high exposure to cytotoxic therapies for extended disease considerations. It is associated with a quiescent disease course but also the adverse effects of B cell depletion.

Disclosures: None.

P-049

Receipt of Antimicrobial Prophylaxis in United States Medicare Beneficiaries Initiating Immunosuppressive Medications for ANCA Vasculitis

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Background/Objectives: Infections are the leading cause of hospitalization and mortality in anti-neutrophil cytoplasmic autoantibody (ANCA) vasculitis (AV). Multiple guidelines recommend antimicrobial prophylaxis during treatment with corticosteroids and rituximab (RTX) or cyclophosphamide (CYC) to prevent *Pneumocystis jirovecii* pneumonia (PJP) but vary in recommendations for patients on other immunosuppressants (IS). Providers may also initiate other antimicrobials to prevent non-PJP infections. To address a knowledge gap regarding real-world prophylaxis patterns, we characterized receipt, type, and duration of antimicrobial prophylaxis in United States Medicare beneficiaries with AV initiating IS medication over 2016-2018.

Methods: Using Medicare claims and a 90-day washout, we identified a national cohort of new IS treatment episodes in 2016-2018, including RTX, CYC, methotrexate, azathioprine, mycophenolate, leflunomide, mepolizumab, reslizumab, benralizumab, dupilumab, and/or corticosteroids (CS) at >10 mg/day prednisone equivalents. We restricted to adults with ≥1 diagnosis code for granulomatosis with polyangiitis, microscopic polyangiitis, or eosinophilic granulomatosis with polyangiitis in the prior year. IS regimens were classified as having a strong indication for prophylaxis (regimens containing RTX, CYC, or CS of >20 mg/day in combination with another IS) or weaker indication (all other regimens). Prophylaxis was defined as ≥14 days' supply of a qualifying antimicrobial overlapping the first 30 days of IS treatment. Antimicrobials included PJP prevention (trimethoprim-sulfamethoxazole, pentamidine, dapsone, atovaquone), other antibacterials (azithromycin, doxycycline, fluoroquinolones), and antifungals. We calculated descriptive statistics overall and by IS regimen. We estimated cumulative incidence of prophylaxis discontinuation over one year of follow-up, with death as a competing risk.

Results: In 14,798 new AV IS treatment episodes, 35% involved regimens with a stronger indication for prophylaxis. Overall, 21% received prophylaxis in the 30 days following IS initiation. PJP prophylaxis was used in 16%, other antibacterials in 7%) and antifungals in 2%. IS regimens with a stronger vs. weaker indication for prophylaxis more often involved any prophylaxis (29% vs. 16%) and PJP prophylaxis (26% vs. 11%), but less often involved other antibacterials (5.5% vs. 7.4%). Cumulative incidence of antimicrobial discontinuation was 51.3% (95% CI=49.1, 53.7) at 180 days after IS initiation and 65.1% (95% CI=62.6-67.5) at 360 days, and was higher for regimens with a weaker indication (360-day RD=5.6%, 95% CI=0.9-9.9).

Conclusions: Most AV patients initiating IS did not receive prophylaxis for PJP or other infections and a majority discontinued prophylaxis within 6 months. This discordance with AV treatment guidelines highlights a need to investigate barriers and outcomes associated with prophylaxis in this population.

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P-050

Immunoglobulin replacement and risk of relapse in ANCA-associated vasculitis

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Background: ANCA-associated vasculitis (AAV) causes frequent relapses. Immunoglobulin (Ig) replacement therapy is indicated for secondary hypogammaglobulinaemia caused by rituximab with recurrent infections. A study of 5 AAV patients suggested an immunomodulatory effect of replacement dose Ig, with a reduction in the number of relapses and rituximab dose. Little is known about the changes in relapse rate of patients with AAV before and after Ig replacement therapy.

Methods: A single-centre retrospective study including patients with AAV who had received a first dose of rituximab between 2003 and 2018 and received Ig replacement therapy for secondary hypogammaglobulinemia. Follow-up began at the time of first rituximab infusion and ended on the date of death, loss to follow-up, or 1 March 2023. Relapse was defined by an increase in disease activity requiring augmented treatment (including prednisolone). The primary aim was to compare relapse rates during the 3 years before Ig replacement therapy with relapse rates after starting Ig replacement using Poisson regression analysis, censoring patients who stopped Ig replacement at time of discontinuation.

Results: Thirty-nine AAV patients with a total of 457 person-years were included. Mean age at first rituximab infusion was 45 years, 77% were female, 69% had GPA, 13% MPA and 18% EGPA. Median IgG levels at first rituximab infusion and at the time of starting Ig replacement were 6.7 g/L [IQR 5.6-9.3] and 2.6 g/L [IQR 2.1-3.6]. 31/39 patients (79%) received rituximab during the 3 years before Ig replacement and 30/39 patients (77%) discontinued maintenance rituximab at the start of Ig replacement. Twenty-two started intravenous (IV) Ig and 17 subcutaneous (SC) Ig, a median of 78 months [IQR 57.5-114] from first RTX infusion. 9/39 patients discontinued Ig replacement, 5 of whom then restarted SCIg due to increased infection rates. Relapses occurred in 29 patients (74%) in the 3 years before Ig replacement and in 17 patients (44%) during Ig replacement. Relapse rate during Ig replacement was 0.24/person-year, while those before Ig replacement was 0.52/person-year. Relapse rate decreased during Ig replacement (RR 0.49 (95%CI 0.28 to 0.85), p<0.01) despite reduced rituximab exposure (median 1 g/year [IQR 0.33-1.33] to 0 g/year [IQR 0-0.34], p<0.001). At last follow-up, 27/39 patients (69%) remained off rituximab with a median rituximab discontinuation period of 67 months [IQR 39.5-99.5], 4/39 patients (10%) had discontinued rituximab but continued other immunosuppressive agents, and 8/39 patients (21%) continued rituximab. Seven patients died during the follow-up.

Conclusions: Relapse rates decreased during Ig replacement therapy for rituximab associated secondary hypogammaglobulinaemia. In addition, 70 % of patients remained off rituximab potentially supporting an immunomodulatory role of Ig replacement in maintaining disease remission.

Disclosures: LU: None. RS: GlaxoSmithKline, Union Therapeutics. RJ: GlaxoSmithKline, Roche, CSL Vifor. AK: CSL Vifor, AstraZeneca, GlaxoSmithKline, Otsuka, Walden Biosciences, Delta4. DJ: GlaxoSmithKline, CSL Vifor, AstraZeneca, Novartis, Roche, Takeda, Chinook, Hansa, Aurinia.

P-051

Giant Cell Arteritis – Glucocorticoid treatment and disease phenotypes

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Background: Among the different giant cell arteritis (GCA) phenotypes, patients with involvement of non-cranial arteries have been shown to have an increased risk of relapse (1). Nonetheless, little is known about optimal treatment strategies for both cranial and non-cranial GCA. We conducted a retrospective observational cohort study including 257 patients diagnosed during 2013-2020 and defined four phenotypes (2).

Objectives: To examine the possible association between GCA-phenotype and use of glucocorticoids (GC) with regards to starting dose and subsequent tapering.

Methods: Dosage of GC treatment was recorded at the time of treatment initiation, and after 3, 6, 12, and 24 months of follow-up. Patients who did not experience a relapse were included in a linear mixed model to analyse tapering of GC for each phenotype. For the complete cohort a Least Absolute Shrinkage and Selection Operator (Lasso) regression was used to identify predictors for the initial GC-dose and the use of intravenous (IV) GC, with subsequent uncertainty quantification by linear and logistic regression, respectively**.**

We compared the proportions of patients experiencing relapse within each GCA-phenotype using Fisher's exact test. Analysis was performed with the statistical software R, using packages nlme and glmnet.

Results: We found no association between GCA-phenotype and the course of GC-tapering.

Visual symptoms was the only predictor for both a higher initial GC-dose and administration of IV GC.

However, the phenotypes differed regarding the proportion of patients experiencing a relapse ($p<0.001$). Merely 8 % of patients with cranial phenotype experienced a relapse, compared to 35% for non-cranial and 44% for mixed phenotypes, and 24% for those of unclassifiable phenotype.

Conclusions: In our study, treatment decisions for GCA seem unaffected by GCA-phenotype. However, more patients with documented involvement of non-cranial arteries experienced a relapse compared to those with cranial phenotype. This suggests that current treatment practices could be improved for these patients.

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Disclosures: None.

P-052

The Joint Vasculitis Registry in German-speaking countries (GeVas) - subgroup analysis of GCA patients

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Background: The most frequently diagnosed form of vasculitis in Germany is giant cell arteritis (GCA), with an incidence of 20 to 30 per 100,000 persons in patients over 50 years of age. Like most vasculitides, GCA is characterized by chronicity and relapses, leading to significant overall morbidity and mortality. A large number of studies are based on a retrospective and monocentric study design with small patient cohorts, which may be justified by the rarity of the disease.

Objectives: The aim of the Joint Vasculitis Registry in German-speaking countries (GeVas) is to record patients who have recently been diagnosed with vasculitis or who have undergone a change in therapy due to a relapse (inception cohort). The GeVas registry thus enables a unique and unprecedented long-term observation of a large cohort of vasculitis patients in a prospective and multicenter manner in German-speaking countries. This is the first analysis of primary data to uncover potential care problems, to evaluate new therapeutic approaches that have not yet been adequately studied in randomized trials, and to generate further research hypotheses.

Methods: GeVas is a prospective, web-based, multicenter, clinically driven registry to document organ manifestations, damage, long-term outcomes and treatment regimens for different types of vasculitis. Recruitment began in June 2019 and by April 2023, 15 centers in Germany had been initiated and started enrolling patients. More than 540 patients are now documented in the registry.

Results: Since April 2023, the participating centers have recruited 195 RZA patients in the registry. 21% of patients were included in the registry due to a relapse and 79% of patients were recruited due to first diagnosis. Regarding the epidemiology, 64% of patients were female and 36% were male. The average age was 76 years (max. 94 years, min. 53 years). Disease activity was documented according to organ group. Cranial symptoms (78%) and ocular involvement (31 %) were most frequently found in GCA patients. An Amaurosis fugax respectively a sudden visual loss were documented in 12%. Of the 195 patients, 100% received immunosuppressive therapy. 95% of patients were treated with G either in a stable oral long-term GC therapy or with i.v. pulses. The median dose on first assessment of the stable long-term oral therapy was 40mg [IQR=15;60] and the median i.v. pulse dose was 125mg [IQR=95;250]. After a year still 77% of patients received a GC therapy with a median oral dose of 5mg [IQR=4,75;5,25]. At time of inclusion in the study 48% of patients received tocilizumab, 20% methotrexate and 16% cyclophosphamide.

Conclusion: In June 2019, we successfully established the prospective multicenter vasculitis registry as the first of its kind in the German-speaking countries. After 4 years of follow-up, the first long-term results were systematically evaluated and interpreted. We see similar data regarding demographics, clinical manifestations, and diagnostics. In terms of therapy, our cohort shows a higher rate of cyclophosphamide, which is mainly used in complicated disease with extensive pan-aortitis and/or stenosing involvement of large arteries, including intracranial arteries. Further analysis must be performed.

P-053

Effectiveness and safety of TNF inhibitors and IL-6 antagonists for refractory Takayasu arteritis

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Background/ Objectives: Active Takayasu arteritis (TA) is primarily treated with corticosteroids (CS) and cytotoxic agents. The aim of this study is to assess the efficacy and safety of TNF-inhibitors (TNFi) and anti-IL-6 therapy in TA patients refractory to CS and cytotoxic agents.

Methods: In this single center retrospective cohort study we included adult patients with TA, diagnosed in accordance with the ACR classification criteria (1990 and/or 2022) and/or Chapel Hill Consensus Conference (2012) definition. All patients were on biologics due to resistance to therapy with corticosteroids and cytotoxic agents.

Results: We included 32 (100%) females with a median age of TA onset 26 (16; 32) years, who were followed for median of 6 (4; 10) years. All patients were initially treated with corticosteroids and conventional cytotoxic agents, including methotrexate, azathioprine, cyclophosphamide and mycophenolate mofetil. The median duration of TA before biological treatment was 2.5 (1.0; 4.8) years. TNFi were chosen in 23 (71.9%) patients and anti-IL-6 agents in 9 (28.1%) patients as the first-line biologic agent. Ten patients were later switched to another agent once (31.3%), two patients twice (6.3%), and one patient three times (3.1%). A total of 47 biologic treatment courses (18 certolizumab, 14 tocilizumab, 7 infliximab, 4 olokizumab, 1 levilimab, 1 adalimumab, 1 etanercept, 1 golimumab) were given (Table 1). There were 33 (70.2%) courses of biological therapy resulting in complete or partial remission, and there was no difference between the TNFi and anti-Il-6 groups. Eleven relapses were noted, which occurred more commonly in the TNFi group (Table 1). Adverse events (AE) were reported more commonly in the NFi-treated patients (27.6%) than in the anti-IL-6-treated patients (11.1%, p = 0,180). The most common AEs were infections with seven iTNF-treated patients reporting ≥1 event. Gastrointestinal disorders were reported in one anti-IL-6-treated patient, and skin and subcutaneous tissue disorders were reported in one iTNF-treated patient and one anti-IL-6-treated patient. During the follow-up period, among 47 lines of biologics, 24 lines were still being continued up until the last visit, three were stopped for inefficiency, six for adverse events or pregnancy, three for remission, six for unavailability of the drug, one patient stopped the drug on her own and four were lost to follow-up.

Table 1. Comparison of patients treated with TNFi and anti-IL-6 (N = 47 courses).

	Number of courses, n/N (%)	Remission, n/N (%)	Relapse, n/N (%)	AEs, n/N (%)
TNFi	29/47 (60.4)	20/29 (69.0)	8/20 (40.0)	8/29 (27.6)
anti-IL-6	18/47 (37.5)	13/18 (72.2)	3/13 (23.1)	2/18 (11.1)

Conclusion: Our results show the comparable efficacy of TNFi and anti-IL-6 in the treatment of refractory TA without serious side effects.

Disclosures: None.

P-054

Protocol for a randomised, phase II, double blind, experimental medicine study of obinutuzumab versus rituximab in ANCA-associated vasculitis: ObiVas

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Background: Relapses in ANCA-associated vasculitis (AAV) increase the incidence of end-organ damage and their prevention requires prolonged immunosuppressive therapy. Rituximab, a type I anti-CD20 B cell depleting monoclonal antibody, is the current standard of care for induction of disease remission. Rituximab induction is not always effective and is associated with a high subsequent relapse risk. Obinutuzumab is a type II anti-CD20 humanised monoclonal antibody with the potential to obtain greater tissue B cell depletion than rituximab and reduce relapse risk in AAV.

Methods: ObiVas is a randomised, phase II, double-blind controlled trial that will compare the mechanistic effects of rituximab and obinutuzumab in the induction treatment of AAV patients positive for proteinase 3 ANCA (PR3-ANCA). 26 patients, either newly diagnosed or relapsing, will be recruited from a single centre and randomised in a 1:1 ratio to receive 1000mg rituximab or obinutuzumab as induction therapy on Days 1 and 15, alongside a tapering glucocorticoid regimen. The primary endpoint is $CD19^{+}$ B cell depletion in nasal-associated lymphoid tissue (NALT), assessed as change from Baseline to Week 26. Secondary outcomes will compare the safety and clinical efficacy of rituximab and obinutuzumab and their impact on immune biomarkers. Exploratory outcomes will investigate the impact of both Investigational Medicinal Products (IMPs) on the tissue immune microenvironment, with next-generation sequencing technologies used on all NALT samples. Patients are followed through to week 78 (Figure 1).

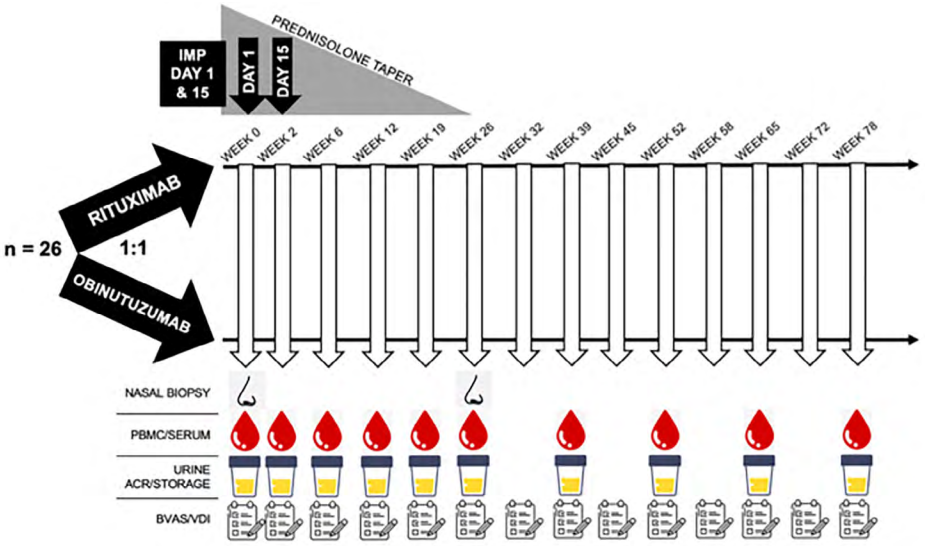

Figure 1. ObiVas trial schematic. IMP (investigational medicinal product); PBMC (peripheral blood mononuclear cells); ACR (albumin creatinine ratio); BVAS/WG (Birmingham Vasculitis Activity Score for Wegener's Granulomatosis); VDI (Vasculitis Damage Index)

Results: The trial opened for recruitment in January 2023 and is forecast to complete recruitment before the close of 2024. NALT data analyses will start before trial completion and are likely to be available at the close of 2025. Other analyses will be reported after trial completion.

Conclusion: ObiVas is a phase II clinical trial and experimental medicine study in AAV with a biomarker primary objective, in addition to multiple secondary and exploratory objectives of translational interest. ObiVas will compare obinutuzumab against rituximab as AAV induction therapy, whilst exploring the AAV tissue microenvironment and immune landscape – and how these change following treatment.

Funding: The trial has received funding from the UK Medical Research Council (MRC). Support has also been provided by Roche; including the supply of both Investigational Medicinal Products and grant funding for additional biomarker analyses. The trial is co-sponsored by Cambridge University Hospitals NHS Foundation Trust and the University of Cambridge.

Disclosures: RJ has investigator-initiated study collaboration with Roche and has received research grants from GSK, CSL Vifor, advisory board fees from CSL Vifor and GSK and Honoraria from Roche. DJ has received research grants from Roche/Genentech and CSL Vifor. RS has research research grants from GSK and Union Therapeutics.

P-055

Risk of GI perforation among patients with GCA who received tocilizumab

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Background/ Objectives: Exposure to the interleukin-6 inhibitor tocilizumab has been associated with an increased risk of gastrointestinal (GI) perforation in patients with rheumatoid arthritis. No studies to date have evaluated the risk of GI perforation in patients with giant cell arteritis (GCA) on treatment with tocilizumab. This study aimed to describe the incidence and risk factors associated with GI perforation among incident cases of GCA receiving treatment with tocilizumab.

Methods: We performed a retrospective cohort study of incident cases of GCA using the US- based TriNetX electronic health records database from 1/1/2010 to 4/23/2023. Patients were included if they had (1) 2 ICD-9CM/ICD10-CM codes for GCA separated by 30 days but within 1 year and (2) received any dose of prednisone within 30 days of the first GCA code. Gastrointestinal perforations were defined by ICD-9-CM/ICD-10-CM codes as described previously, and the incidence of gastrointestinal perforations as well as unadjusted incident rate ratios were calculated. Adjusted analysis using a Poisson regression was conducted. The clone- censor-weight approach was then used to account for immortal time bias. After cloning, censoring, and weighting using inverse probability of censoring, time-updated multivariable Cox proportional hazards models were used to calculate the hazard ratio (HR) and 95% confidence intervals for the risk of GI perforation.

Results: During the study period, 5,142 patients met the inclusion criteria (845 tocilizumab exposed and 4,297 tocilizumab unexposed), the majority of whom were female (3,624, 70.5%) and white (3,728, 72.5%). Incident GI perforations among tocilizumab exposed vs. unexposed were 2.0/1,000 person-years and 3.4/1,000 person-years, respectively, resulting in an incident rate ratio of 0.57 (95% CI 0.14-2.41). The adjusted rate ratio (RR) of GI perforation with tocilizumab use in a Poisson regression was RR 0.56 (95% CI 0.13-2.38). Factors associated with GI perforation included the history of diverticulitis (RR 3.51, 95% CI 1.55-7.96) and the use of intravenous methylprednisolone (RR 5.41, 95% CI 2.41-12.12). After implementing the clone- censor-weight approach, tocilizumab exposure was not associated with an increased risk of GI perforation (HR 1.05, 95% CI 0.30-1.65).

Conclusions: In this retrospective cohort study of patients with incident GCA, GI perforations were rare. When compared with steroid treatment, tocilizumab exposure was not associated with an increased risk of GI perforation. Risk factors for GI perforation included a history of diverticulitis and intravenous methylprednisolone use. These findings highlight the importance of judicious steroid use and will be useful for counseling patients considering initiation of IL-6 inhibitors.

Disclosures:

Author 1 has nothing to disclose.

Additional contributors:

Author 2: Reports research support from AstraZeneca, United States.

Author 3: Reports research support from Bristol-Myers Squibb, United States and Principia/Sanofi and consulting fees Zenas Biopharma, Horizon, Sanofi, Shionogi, Viela Bio, and MedPace.

Author 4 (Presenting author): reports research support from Astra Zeneca, Abbvie and receives consulting fees from Novartis.

P-056

Glucocorticoid-sparing effect of Mepolizumab: real life experience in a monocentric cohort of patients affected by Eosinophilic Granulomatosis with Polyangiitis

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Background/ Objectives: Oral glucocorticoids (GC) are the mainstay of treatment for eosinophilic granulomatosis with polyangiitis (EGPA) but chronic exposure to GC is associated with serious comorbidities. Mepolizumab (MEPO) demonstrated to be an efficacious treatment for EGPA in the randomized controlled MIRRA trial [1]. ACR guidelines suggest treating non-severe EGPA with MEPO associated with GC as first choice and adding MEPO in non-severe relapses occurred while receiving other immunosuppressants. There are insufficient data to support dosages and duration of GC treatment during MEPO treatment, although guidelines suggest prescribing the minimum effective dose to minimize GC toxicity [2].

The aim of the study was to evaluate the GC-sparing effect of MEPO in a monocentric cohort of patients affected by EGPA.

Methods: We enrolled 26 patients affected by EGPA according to MIRRA criteria and/or ACR criteria [1][3]. We compared cumulative GC dosage prescribed in the 6 months before beginning treatment with MEPO to the cumulative dosage prescribed in the 6 months after starting MEPO. We also analyse MEPO efficacy comparing median number of asthma attacks, BVAS and VDI.

Results: Twenty-six patients (M/F 16/10) affected by EGPA were diagnosed at a median age of 57 years (IQR 47-65) and started therapy with MEPO after a median disease duration of 6 (1.5-10) years. Overall clinical features of patients at diagnosis (Td), at MEPO starting (T0) and after 6 months of MEPO (T6) are described in table 1a. At MEPO starting (T0), 24/26 (92.3%) were treated with GC and 13/26 (50%) were on treatment with other immunosuppressants (1 cyclosporine, 2 methotrexate, 3 mycophenolate, 7 azathioprine). The cumulative GC dosage administered to patients in the six months after MEPO starting was significant lower if compared with dosage in the prior six months. After MEPO starting, there was also a significant reduction of asthmatic symptoms and BVAS score, with no increasing in VDI score (table 1b and 1c).

Conclusions: In our cohort MEPO had a significant GC-sparing effect and significantly reduced asthma manifestations and disease activity.

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Disclosures: None.

1a. Clinical features

	Td	T0	T6
Constitutionalsymptoms	12 (46%)	1 (4%)	1 (4%)
Cutaneous	9 (35%)	1 (4%)	0 (0%)
Ear, nose, throat	22 (85%)	9 (35%)	5 (19%)
Pulmonary	25 (96%)	18 (69%)	1 (4%)
Cardiovascular	6 (23%)	1 (4%)	0 (0%)
Gastrointestinal	4 (15%)	1 (4%)	0 (0%)
Neurological	14 (54%)	6 (23%)	2 (8%)
Renal	0 (0%)	0 (0%)	0 (0%)

1b. Disease activity before MEPO starting (T0) and after 6 months (T6)

	T0	T6	p
BVAS	2 (0-2)	0 (0-0)	0.0005*
VDI	2 (1.3-3)	2 (1.3-3)	0.5716

1c. Comparison of asthma activity and GC therapy between the 6 months before and the 6 months after MEPO starting (T0)

	In the 6 months before T0	In the 6 months after T0	p
GC cumulative dose (mg)	1376 (821-2045)	964 (521-1561)	0.0005*
GC daily dose (mg/day)	8 (5-11)	5 (3-9)	0.0007*
Patients with active asthma	18 (69%)	1 (4%)	0.0211*

Data express as median (IQR) or n (%). * p value < 0.05
BVAS: Birmingham vasculitis activity index, VDI: Vasculitis damage index.

P-057

Association between major adverse cardiac events and exposure to sodium glucose cotransporter-2 (SGLT2) inhibitors among patients with ANCA associated vasculitis

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Background/ Objectives: Treatment with sodium-glucose cotransporter 2 inhibitors (SGLT2i) has been associated with lower rates of major adverse cardiac events (MACE) as compared to dipeptidyl peptidase 4 inhibitors (DPP-4i) among patients with type 2 diabetes and lupus nephritis. Patients with ANCA-associated vasculitis (AAV) also experience high rates of MACE and ESRD, but no studies to date have described this risk.

Methods: We performed a new-user retrospective cohort study of patients with AAV using the US-based TriNetX electronic health records database from 2014 to 2023. Patients were included if they had 2 ICD-9CM/ICD10-CM codes for AAV separated by 30 days but within 1 year and received at least one prescription for an SGLT2i or DPP-4i after their first AAV code. The index date was defined by the first prescription for an SGLT2i or DPP-4i. Intention to treat (ITT) and per protocol (PP) analyses were performed for a composite outcome of MACE (myocardial infarction, cerebrovascular accident, heart failure, or death) and ESRD. Events were identified using a single ICD-9-CM/ICD-10-CM code and reported as incidence per 100 person years and unadjusted incidence rate ratios (IRR). Propensity score overlap weighting was used to adjust for confounding by relevant clinical and demographic characteristics and hazard ratios (HR) were calculated using weighted Cox proportional hazards models.

Results: We identified 357 patients with AAV who were followed for an average of 2.68 years (standard deviation (SD) 2.06). The average age at the index date was 61.7 years (SD 13.0); the majority received an SGLT2i (191, 53.5%) and were female (202, 56.6%). Patients who received an SGLT2 inhibitor had a numerically higher rate of the composite outcome of ESRD, MACE, or death, which was not statistically significant after adjustment for relevant confounders for both ITT analysis (28.3 events per 100 person-years SGLT2i vs. 24.2 events per 100 person-years DPP-4i, unadjusted IRR 1.17, adjusted HR 1.03, 95% confidence interval (CI) 0.61-1.72) and PP analysis (34.0 events per 100 person-years SGLT2i vs. 29.1 events per 100 person-years DPP-4i, unadjusted IRR 1.17, adjusted HR 1.07, 95% CI 0.60-1.92). Trends toward higher rates of ESRD and MACE with SGLT2i were observed for ESRD and MACE but these were not significantly different. Negative and positive control variables suggested the presence of residual confounding or bias.

Conclusions: This analysis of patients with AAV initiating therapy with SGLT2i or DPP-4i did not observe an association between treatment strategy and subsequent MACE, ESRD, or death. However, these results should be viewed in light of a limited sample size and substantive evidence of residual confounding.

References: None.

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Table 1: Unadjusted incidence rate ratios and adjusted hazard ratios for outcomes of interest, n = 357

	Events		Person-years Follow Up		Incidence		Unadjusted Incidence Rate Ratio	Adjusted Hazard Ratio**
	SGLT-2i	DPP-4i	SGLT2i	DPP-4i	SGLT2i	DPP-4i		
*Composite Outcome, ITT	68	69	240.4	284.6	28.3	24.2	1.17	1.03 (0.61-1.72)
Composite Outcome, PP	60	55	176.6	189	34.0	29.1	1.17	1.07 (0.60-1.92)
ESRD Outcome, ITT	57	58	257	305	22.2	19	1.17	1.31 (0.75-2.31)
ESRD Outcome, PP	50	46	191	199.6	26.2	23	1.14	1.33 (0.70-2.50)
MACE Outcome, ITT	35	34	284.9	341.3	12.3	10	1.23	0.66 (0.31-1.42)
MACE Outcome, PP	30	28	202	215.4	14.9	13	1.14	0.64 (0.27-1.51)
Negative Control (Trauma/Injury), ITT	54	54	261.3	302.2	20.7	17.9	1.16	1.56 (0.93-2.62)
Negative Control (Trauma/Injury), PP	43	41	194.2	199.9	22.1	20.5	1.08	1.59 (0.90-2.82)
Positive Control (Genital Infection), ITT	28	48	289.9	313	9.7	15.3	0.63	0.47 (0.23-0.92)
Positive Control (Genital infection), PP	22	38	213.3	197.9	10.3	19.2	0.54	0.55 (0.26-1.15)

Abbreviations: intention to treat (ITT), per protocol (PP), sodium-glucose cotransporter 2 inhibitors (SGLT2i), dipeptidyl peptidase 4 inhibitors (DPP-4i), end stage renal disease (ESRD), major adverse cardiac events (MACE).
*The composite outcome was defined by whichever came first of ESRD, MACE, or death.
** Adjusted hazard ratios calculated from weighted cox proportional hazards regressions that adjusted for age and gender. Models were weighted using overlap weighting to adjust for the following relevant confounders: age, gender, race/ethnicity, Charlson comorbidity index, baseline hemoglobin A1c, chronic kidney disease stage 3 at baseline, congestive heart failure, myocardial infarction, cerebrovascular accident, obesity, smoking, total visits, total encounters, angiotensin converting enzyme (ACE) inhibitor use, and the presence of diabetic complications.

P-058

Demographic and Clinical Profiling of ANCA-Associated Vasculitis in Turkey: A Comprehensive Analysis from Turkish Vasculitis Study Group (TRVaS) registry

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Background/ Objectives: ANCA-associated vasculitis (AAV) may show geographical differences in terms of involvement characteristics. We aimed to determine the demographic, disease-related, and treatment characteristics and outcome of a country-wide registry with a sample size that can reflect Turkey in general.

Methods: Data from the Turkish Vasculitis Study Group (TRVaS) registry, a multicentre, prospective, web-based registry, were used. Basic demographic characteristics of the patients, organ involvement, serological status, AAV type according to the European Medicines Agency algorithm [granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and unclassified AAV (uAAV)], basic comorbidities, treatments used until the time of enrolment in the database, and data on survival status were obtained from the database and included in the analysis. Factors associated with survival were analyzed by the Cox Proportional Hazard method.

Results: A total of 1023 patients were included in the analysis [670(65.5%) GPA, 140(13.7%) EGPA, 139(13.7%) MPA, 74(7.1%) uAAV)]. The female gender was slightly more prominent in EGPA patients and MPA and uAAV patients were diagnosed at an older age compared to others (Table). pANCA and MPO-ANCA positivity were prominent in MPA patients, while cANCA and PR3-ANCA positivity were prominent in GPA patients. The majority of EGPA and uAAV patients had pANCA and MPO-ANCA positivity. Constitutive, musculoskeletal, and ocular findings were prominent in GPA, mucocutaneous, cardiac, and neurological findings in EGPA, and renal and respiratory involvement in MPA. Chronic kidney disease was not detected in EGPA patients, and the frequency of CKD was significantly higher in other AAV groups. Cyclophosphamide was the most preferred immunosuppressive agent after oral and pulse steroids, and rituximab was used in 49.8% of EGPA patients and 39.5% of MPA patients at any stage of the disease. In EGPA patients, Mepolizumab was used in 27 (19.3%) of patients and omalizumab in 8 (5.7%) of patients. Ninety-one (13.6%) patients died during a median follow-up of 40 months in GPA patients, 7 (5%) patients died through a follow-up of 30.5 months in EGPA patients, 22 (15.8%) patients died after a median follow-up of 25 months in MPA patients, and 15 (20.3%) patients died after a median follow-up of 14.5 months in uAAV patients. Cardiac (2.6 [1.5-4.6, p=0.001]), gastrointestinal (2.7 [1.5-4.8, p=0.001]), and renal involvement (2.1 [1.3-3.5, p=0.002]), advanced age (1.04 [1-1.1, p<0.001]), and male gender (1.8 [1.2-2.6, p=0.001]) were independently associated with increased mortality.

Conclusions: Turkish patients with AAV have a sligtly younger age at diagnosis compared to general literature. During an over 3 years follow up, 13.2% of patients deceased. Male gender was found as a predictor of mortality in addition to Five Factor score. RTX was ever used approximately in half of GPA patients and 40% of MPA patients whereas MEPO was used in 20% of patients with EGPA.

Disclosures: None.

	GPA (n=670, 65.5%)	EGPA (n=140, 13.7%)	MPA (n=139, 13.7%)	uAAV (n=74,7.1%)	p
Sex, female (n, %)	295 (44.0)	79 (56.4)	68 (48.9)	34 (45.0)	0.06
Age at diagnosis, years mean (SD)	48.1 (15.5)	47.4 (16.8)	59.4 (13.2)	56.2 (15.8)	<0.001
Disease duration, months med(IQR)	40 (68)	30.5 (62)	25 (41)	14.5 (45)	<0.001
ANCA ELISA (n, %)					
- MPO	58/455 (12.7)	28/40 (70.0)	80/91 (87.9)	17/24 (70.8)	<0.001
- PR3	372/455 (81.8)	6/40 (15.0)	1/91 (1.1)	4/24 (16.7)	<0.001
ANCA IFA (n, %)					
- pANCA	88/580 (15.2)	37/128 (28.9)	95/108 (88.0)	24/42 (57.1)	<0.001
- cANCA	427/580 (73.6)	11/128 (8.6)	5/108 (4.6)	6/42 (14.3)	<0.001
Sites of involvement (ever) (n, %)					
- Constitutional	521 (78.5)	86 (61.9)	99 (71.2)	34 (45.9)	<0.001
- Musculoskeletal	428 (64.6)	75 (54.0)	63 (45.3)	18 (24.3)	<0.001
- Mucocutaneous	150 (22.6)	57 (41)	20 (14.4)	13 (17.6)	<0.001
- Eye	153 (23.1)	11 (7.9)	8 (5.8)	8 (10.8)	<0.001
- Ear-Nose-Throat	432 (65.1)	84 (60.4)	12 (8.6)	7 (9.5)	<0.001
- Respiratory	525 (79.1)	105 (75.5)	102 (73.4)	14 (18.9)	<0.001
- Renal	450 (67.9)	21 (15.1)	124 (89.2)	61 (82.4)	<0.001
- Cardiac	25 (3.8)	25 (18)	6 (4.3)	0	<0.001
- Gastrointestinal	35 (5.3)	9 (6.5)	6 (4.3)	3 (4.1)	<0.001
- Neurologic	117 (17.6)	59 (42.4)	18 (12.9)	7 (9.5)	<0.001
Comorbidities (n, %)					
- Type 2 Diabetes	87 (13)	12 (8.6)	19 (13.7)	3 (4.1)	0.071
- Hypertension	143 (21.3)	29 (20.7)	40 (28.8)	14 (18.9)	0.221
- Chronic kidney disease	71 (10.6)	0	17 (12.2)	7 (9.5)	0.001
- Coronary artery disease	47 (7)	8 (5.7)	11 (7.9)	3 (4.1)	0.691
Treatment details (n, %)					
- Pulse corticosteroid	486 (72.5)	52 (37.1)	113 (81.3)	52 (70.3)	<0.001
- Oral corticosteroid	613 (91.5)	135 (96.4)	130 (93.5)	62 (83.8)	0.012
- CYC	466 (69.6)	55 (39.3)	93 (66.9)	42 (56.8)	<0.001
- MMF	95 (14.2)	16 (11.4)	19 (13.7)	4 (5.4)	0.178
- AZA	326 (48.7)	61 (43.6)	64 (46)	31 (41.9)	0.528
- MTX	122 (18.2)	27 (19.3)	6 (4.3)	6 (8.1)	<0.001
- IVIG	53 (7.9)	21 (15)	5 (3.6)	3 (4.1)	0.002
- boRTX	293 (43.7)	19 (13.6)	43 (30.9)	11 (14.9)	<0.001
- bsRTX	41 (6.1)	4 (2.9)	12 (8.6)	1 (1.4)	0.066
- PLEX	119 (17.8)	3 (2.1)	35 (25.2)	24 (32.4)	<0.001
- Hemodialysis	66 (9.9)	0	18 (12.9)	6 (8.1)	0.001
- Omalizumab	-	8 (5.7)	-	-	
- Mepolizumab	-	27 (19.3)	-	-	
Exitus (n, %)	91 (13.6)	7 (5.0)	22 (15.8)	15 (20.3)	0.009

Table. Demographic, disease-specific and treatment characteristics of AAV patients (n=1023).

P-059

Treatment of ANCA-Associated Vasculitis with Diffuse Alveolar Hemorrhage with Avacopan

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Background/Objectives: Avacopan, a C5a receptor antagonist, is approved as an adjunct therapy for remission induction therapy for severe active antineutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV)[1]. Avacopan can reduce glucocorticoid exposure and improve renal outcomes [2, 3]. In the acute setting of diffuse alveolar hemorrhage (DAH) in AAV, questions and challenges remain related to the use of avacopan. To obtain data that can inform the design of trials addressing these unresolved issues, we conducted the present study.

Methods: We performed a retrospective analysis of all consecutive patients with DAH due to AAV treated with avacopan at all Mayo Clinic sites between 1/1/2021 and 3/1/2023. We identified patients who received avacopan prescriptions linked to a diagnosis of AAV. Inclusion criteria were age over 18 years, meeting Chapel Hill and ACR/EULAR consensus definitions for AAV, DAH, and avacopan use as part of remission induction treatment. Demographic data, clinical documentation, Birmingham Vasculitis Activity Scores (BVAS), imaging and laboratory results, and medication dosing were collected.

Results: Fifteen patients meeting eligibility criteria were identified. Patients were predominantly female (N=9) with a median age at presentation of 66 years (IQR 52-72). Nine patients (60%) were newly diagnosed with AAV and 53% (N=7) were PR3 positive. Median follow up time was 17 weeks (IQR 6-37) after avacopan initiation. Three patients (20%) developed respiratory failure requiring support ranging from high flow nasal cannula to mechanical ventilation. Eight patients (53%) started avacopan after their hospitalization, with a median overall time to initiation of 18 (IQR 2-24) days after traditional remission induction. Barriers to avacopan initiation were lack of inpatient availability and provider familiarity. No relapses or recurrences of DAH were observed. Of the 14 (93%) patients surviving at completion of follow up, all achieved remission, and 10 (66%) of whom achieved complete remission (BVAS/WG=0, off prednisone). Two serious adverse events related to infection were observed, including one opportunistic infection resulting in the patient's death.

Conclusions: Avacopan appears effective and safe in treatment of AAV with DAH. Adverse events including infection were observed during follow-up.

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P-060

Impact of induction immunosuppression for ANCA associated vasculitis on ANCA status at 6 months

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Background/ Objectives: Current international guidelines recommend the use of cyclophosphamide (CYC) or rituximab (RTX) with glucocorticoids as induction therapy for ANCA associated vasculitis (AAV). Studies examining the use of combination agents (CYC+RTX) remain limited. We aimed to evaluate the clinical characteristics and treatment outcomes of AAV patients who received CYC or RTX or CYC+RTX with glucocorticoids.

Methods: A retrospective single centre study using electronic medical records of AAV patients with biopsy confirmed kidney involvement was performed from 2014 to 2022. The CYC+RTX combination therapy consisted of a minimum 2 doses of intravenous CYC and 2 doses of RTX. The results were analysed using SPSS version 29.

Results: A total of 156 patients were included and followed for a median of 41 months (interquartile range, IQR 22-71). There was a male preponderance (n=98, 63%) with median age 69 years (IQR 59-75). Majority (n=91) presented with acute kidney injury, median eGFR at diagnosis 25 ml/min/1.73m^2 (IQR 12-48). Myeloperoxidase (MPO) ANCA was more common (n=88, 56.4%) than proteinase-3 (PR3) ANCA (n=68, 43.6%).

Seventy three (46.8%) received CYC, 43 (27.6%) received RTX while 40 (25.6%) received CYC+RTX. Patients who received CYC+RTX were younger, median age 62 years compared to 68 and 78 years for the CYC and RTX groups. The CYC+RTX group had a lower eGFR at presentation (16 ml/min/1.73m^2) compared to 26 ml/min/1.73m^2 and 30.5 ml/min/1.73m^2 for the CYC and RTX groups.

The median MPO ANCA level at 6 months post-induction was 2.6 iu/ml for the CYC+RTX group while the levels were 7.6 iu/ml and 11.5 iu/ml for the CYC and RTX groups respectively (p=0.6). The median PR3 ANCA level at 6 months was 6.3 iu/ml for the CYC+RTX group in comparison to 13 iu/ml for both CYC and RTX groups (p=0.44). Despite the reduction in ANCA levels, majority of patients still had persistent haemoproteinuria at 6 months. The relapse rate was comparable in all treatment groups.

Conclusions: The CYC+RTX combination therapy may reduce ANCA levels more rapidly than CYC or RTX alone for AAV patients with severe renal impairment. In this real life cohort, selection bias for treatment group interplays with clinical outcomes. Potential confounders to ANCA response at 6 months include disease severity, age, sex, starting ANCA level, and concomitant glucocorticoid dosing. Multivariate analyses will therefore be performed to adjust for the impact on confounders on ANCA response.

References: Nil.

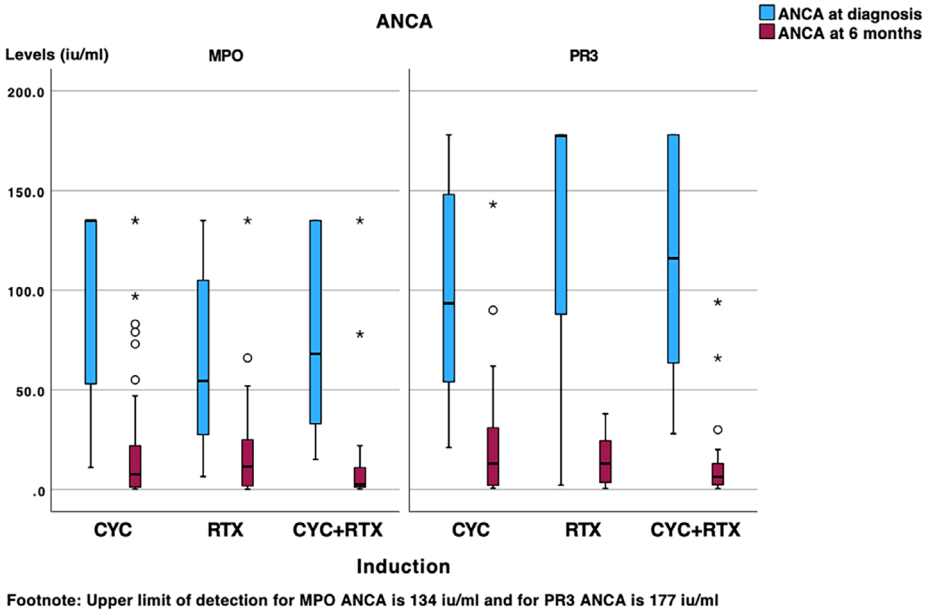

Figure: ANCA levels at diagnosis and at 6 months following induction.

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P-061

Short-chain fatty acids ameliorate experimental anti-glomerular basement membrane disease

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Background/ Objectives: Anti-glomerular basement membrane (GBM) disease is a rare but aggressive form of small vessel vasculitis. T-cell mediated injuries is pivotal in the disease initiation. Short-chain fatty acids (SCFAs), as the link between gut microbiota and the immune system, had been reported to be protective in many autoimmune diseases by the modulation of T cell differentiation. The present study investigated the therapeutic effects of SCFAs in a rat model of anti-GBM disease.

Methods: Experimental anti-GBM disease was constructed by immunizing Wistar Kyoto rats with a nephrogenic T cell epitope α3127-148, and intervened by sodium acetate, sodium propionate, or sodium butyrate, 150mM in the drinking water from day 0 to 42. Kidney injury was accessed by the biochemical analyzer, immunofluorescence, and immunohistochemistry. Antibody response was detected by ELISA. T cell clustering and proliferation were detected by flow cytometry. Human kidney 2 (HK2) cells were stimulated in vitro and cytokines were assessed by quantitative real-time PCR.

Results: Treatment with sodium acetate, sodium propionate, or sodium butyrate ameliorated the severity of kidney impairment in rats with anti-GBM glomerulonephritis. In the sodium butyrate-treated rats, the urinary protein, serum creatinine, and blood urea nitrogen levels were significantly lower; the percentage of crescent formation in glomeruli was significantly reduced; and the kidneys showed reduced IgG deposition, complement activation, T cell, and macrophage infiltration as well as the level of circulating antibodies against anti-α3(IV)NC1. The treatment of sodium butyrate reduced the α3127-148-specific T cell activation and increased the Treg cells differentiation and the intestinal beneficial bacteria flora. It also alleviated the damage of HK2 cells treated with inflammatory factors and complement.

Conclusions: Treatment with SCFAs, especially butyrate, alleviated anti-GBM nephritis in rat model, indicating its potential therapeutic effects in clinical usage.

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Disclosures: None.

P-062

Rituximab vs conventional therapy in a cohort of patients with ANCA associated vasculitis: potential risk factors for relapse after Rituximab treatment

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Background/Objectives: To describe the clinical characteristics and outcomes of a cohort of patients with ANCA-associated vasculitis (AAV) and to analyse potential risk factors for disease relapse after rituximab (RTX).

Methods: Retrospective, comparative subgroup analysis including all patients with granulomatosis with polyangiitis (GPA) and Microscopic polyangiitis (MPA) attended in our centre. Multivariate Cox regression analysis and long-rank test were performed.

Results: 151 patients (mean age at diagnosis 59.3, SD: 17.2) were included, 53.6% women. Eighty-nine patients (58.9%) had MPA and 62 (41.1%) GPA. The most frequent clinical manifestations were constitutional sd. (66.2%), renal failure (65.56%), and arthralgia (51.7%). The mean BVAS at diagnosis was 17.1.

Seventy-seven (51.0%) received cyclophosphamide (CYC) for remission induction (54.0% MPA, 46.1% GPA) and 52 (34.4%) RTX (73.1% MPA, 26.1% GPA). RTX was also given to 32 patients initially treated with CYC for a relapse. Clinical significant differences between patients initially treated with RTX and those treated with CYC are summarized in Table 1.

The mean follow-up was 9.83 (SD 7.43) years and was significantly longer for patients treated with CYC (13.7 years, SD 7.5 vs 4.2 years, SD: 3.0).

Seventy-three (48.3%) patients had a disease relapse, 8 (15.4%) of them initially treated with RTX and 65 (74.6%) treated with CYC (HR 5.5, 95%CI 2.4-12.4). The median number of relapses was 1 (0-3) for patients initially treated with CYC vs 0 (0-2) for those treated with RTX.

After RTX therapy, 26 patients had a relapse, 8 (30.8%) initially treated with RTX and 18 (69.2%) treated with CYC.

Possible predictive factors for relapse after RTX were age >65 years, ENT manifestations, cavitated lung nodules, renal failure, gastrointestinal manifestations, and anti-PR3+. COX multivariable regression model kept ENTz manifestations as the only independent predictor factor (HR 3.6, 95%CI 1.5- 8.9).

Patients treated with CYC significantly had more severe adverse events (Cushing's sd., Diabetes Mellitus, vertebral fractures, sterility, and infections) during follow-up. Thirteen (25.0%) patients initially treated with RTX died vs 39 (51.3%) treated with CYC (HR 1.6, 95%CI 0.7-3.7).

Conclusions: Relapses were less frequent in patients initially treated with RTX. Severe adverse events were more frequent in patients treated with CYC. ENT manifestations were the only independent predictive factor for relapse after RTX administration.

	RTX (52)	CYC (77)	p-value
Age (years)	66.1 (15.1)	55.2 (16.9)	<0,01
Fever	17 (32.7)	48 (62.3)	<0,01
Constitutional sd.	32 (61.5)	62 (80.5)	0,02
Althralgies	15 (28.9)	56 (72.7)	<0,01
Purpura	2 (3.9)	12 (15.6)	0,04
Nasal crusting	3 (5.8)	15 (19.4)	0,03
Septal perforation	0 (0.0)	6 (7.7)	0,04
Sinusitis	5 (9.6)	18 (23.4)	0,05
Otitis media	4 (7.7)	18 (23.4)	0,02
Hemoptisis	4 (7.7)	18 (23.4)	0,02
Cavitated lung nodules	3 (5.8)	15 (19.5)	0,03
Renal failure	42 (80.7)	48 (62.3)	0,03
Necrotizing glomerulonephritis	39 (79.6)	41 (53.2)	<0,01
Multineuritis	2 (3.9)	12 (15.5)	0,04
BVAS	16.4 (6.5)	19.3 (6.8)	0,02

Table 1: Clinical significant differences between RTX and CYC treated patients.
Continuous N(SD), Categorical N(%).

P-063

Mepolizumab efficacy in Eosinophilic gastroenteritis

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Background/ Objectives: Eosinophilic gastroenteritis (EGE) is defined as an immune-mediated inflammatory disorder characterized by an eosinophilic infiltrate in one or more organs of the gastrointestinal (GI) tract, as stomach, small intestine, and colon. EGE is usually idiopathic, but it can be also a manifestation of a systemic eosinophilic disease, such as Eosinophilic granulomatosis with polyangiitis (EGPA) and Hypereosinophilic syndrome (HES).

Mepolizumab (MEPO), a monoclonal antibody targeting interleukin-5 (IL-5), a key haematopoietin needed for eosinophil development and function, has been recently approved both for EGPA and HES [1]. To date there are no specific data on MEPO efficacy in EGE manifestation in patients with these diseases.

The aim of the study was to analyse MEPO efficacy in a cohort of HES and EGPA patients with GI involvement.

Methods: Five patients with EGE associated with EGPA (define according 2022 ACR/EULAR criteria [1]) or HES and treated with MEPO for active GI disease were enrolled in the study. Data were collected from clinical charts at diagnosis, at MEPO starting and after 12 months of treatment. MEPO efficacy, safety and steroid-sparing effect were analysed.

Results: Two patients had a diagnosis of EGPA, and three had a diagnosis of HES (table 1). Both patients with EGPA presented at diagnosis asthma, nasal polyps and eosinophilia; one had also pericarditis and purpura; the other one had multiple neuritis. In the group of patients with HES, two patients presented also pulmonary infiltrates. All three HES patients at diagnosis presented severe eosinophilia but myeloproliferative clonal variants of HES were excluded. All 5 patients presented GI involvement, confirmed by biopsy and histological examination. The most frequently involved organs were stomach, duodenum and colon and the most reported symptoms were abdominal pain, weight loss, nausea, bloody and/or mucous diarrhea.

All 5 patients presented active GI disease and were on treatment with systemic glucocorticoids when started treatment with MEPO 300 mg monthly. After MEPO starting all patients showed a clinical improvement, with reduction of symptoms until complete resolution. At the same time, in all patients glucocorticoids dose was reduced from a median dose of 12,5 (5-37,5) mg/day to 3 (0-3) mg/day (p: 0.015). No significant side effects were reported in the follow-up.

Conclusions: In this cohort MEPO demonstrated its efficacy in treating GI manifestations in patients with EGPA and HES, showing also a significant GC-sparing effect and a good safety profile.

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Disclosures: None.

Nr patient	Sex / Age at diagnosis	Diagnosis	EOS at diagnosis (cell/mmc)	GI involvement	Other organ involvements at diagnosis	Time between diagnosis and MEPO starting	Active disease manifestation at MEPO starting
1	M / 68	EGPA	1120	Colon	Asthma, nasal polyps, pericarditis, purpura	3	Asthma, nasal polyps, colon
2	M / 36	EGPA	4560	Stomach, duodenum, colon	Asthma, nasal polyps, multiple neuritis	10	Asthma, nasal polyps, colon
3	F / 64	HES	3200	Stomach, colon	Pulmonary infiltrates	2	Stomach, colon
4	F / 62	HES	8150	Stomach, duodenum	nd	1	Stomach, duodenum
5	M / 68	HES	8500	Stomach, duodenum	Pulmonary infiltrates	1	Stomach, duodenum

1. CLINICAL SCIENCE
1.03. Specialized management of specific situations: subglottic stenosis, vascular reconstruction and endovascular intervention, renal transplantation, cutaneous necrotic lesions, pregnancy...

P-064

Maternal and foetal outcomes in ANCA vasculitis: a review of the literature

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Background: The incidence of ANCA associated vasculitis (AAV) has increased over time.[1] Whilst typical age of onset remains between 65-74 years old, AAV can present in younger people.[2] With more advanced treatments and subsequent improved quality of life, increasing numbers of women with AAV are becoming pregnant.[3] Renal disease is a known risk factor for adverse pregnancy outcomes including pre-eclampsia, intrauterine growth restriction (IUGR) and deterioration of maternal renal function.[4] Despite this, there is limited research evaluating maternal and foetal outcomes in AAV. This study assesses whether AAV is associated with adverse maternal and foetal outcomes when compared to the general population.

Methods: A literature search using PubMed, Cochrane and WoS identified studies that included pregnant women with AAV and included at least one of the terms: pre-eclampsia; pre-term delivery; low birth weight; foetal loss; caesarean; deterioration of maternal renal function; disease relapse during pregnancy; disease relapse postpartum. Studies were screened and quality was assessed using the Newcastle-Ottawa scale.

Results: Five papers were included that detailed 60 women and 84 pregnancies (Table 1).

Study outcomes (n=patients)	AAV patients (n, (%))	Incidence in the general population (developed countries)
Pre-eclampsia (n= 83)	8 (9.6%)	0.4%
Pre-term births (n=84)	12 (14.3%)	4.3 - 8.7%
Foetal loss (n=45)	6 (13.3%)	10.0 - 25.0%
Premature rupture of membranes (n=32)	2 (6.3%)	8.0 - 10.0%
Low birth weight (n=80)	16 (20.0%)	7.0%
Caesareans (n=67) • Emergency • Elective	16 (23.9%) 9 (13.4%) 7 (10.4%)	6.0% 2.7% 2.3%
Deterioration of maternal renal function during pregnancy (n=35)	5 (14.3%)	-
Disease flare (n=84) • During pregnancy • Postpartum	21 (25.0%) 15 (17.9%)	-
Increase in serum creatinine (n=25)	10 (40%)	-

Table 1: Pregnancy outcomes comparing patients with AAV to the general population.

Conclusions: This study suggests a possible association between AAV and adverse pregnancy outcomes, with high rates of pre-eclampsia, pre-term birth, low birth weight and disease flare. Similarly, a recent review found increased rates of pre-term delivery, IUGR and disease flare during pregnancy (18%, 20% and 28% respectively).[5] When considering treatment, most women

received prednisolone and/or azathioprine and one-third received no treatment. While there were commonalities in treatment choice, this review highlights a limited evidence-base underpinning clinical decision making. Notably, there is increasing evidence of the safe use of rituximab in pregnancy and that active disease is a major risk factor for adverse outcomes.

There remains a lack of formal guidance regarding the management of fertile women with AAV. When considering the patient journey the literature emphasises the importance of pre-conception counselling including discussing individualized risk of adverse pregnancy outcomes. During pregnancy, regular access to an established multidisciplinary team is necessary and relapses should be treated promptly.

Our study suggests an association between AAV and adverse pregnancy outcomes. Our results must be interpreted with caution due to the small sample size and observational nature of identified studies. Further research should examine maternal health risks, the impact of disease relapse and the role of data registries for this cohort. The patient journey needs to be fully considered from pre-conception and followed well into the post-partum period.

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Disclosures: None.

P-065

Extra-vascular manifestations of Takayasu arteritis

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Background/ Objectives: There is currently a lack of organized research examining the non-vascular manifestations of Takayasu arteritis (TAK). The objective was to assess such manifestations in a large cohort of TAK patients.

Methods: Patients diagnosed with TAK from 4 independent cohorts in tertiary referral centres (2 from Italy and 2 from India) were included. Characteristics were retrospectively collected from an electronic dataset. Logistic regression analysis was performed to evaluate the association between vascular and extravascular manifestations. Variables determined statistically significant ($p<0.05$) at univariate analysis were included in a multivariate analysis.

Results: We included 407 patients (163 Italy; 244 India), 79.1% female, with a median follow-up of 80±123 months. Mean age at diagnosis was 32±13, with a diagnostic delay of 20±50 months. Mean baseline Disease Extent Index for TAK (DEI. Tak) and Indian TAK Clinical Activity (ITAS2010) scores were 8.8 ± 5.5 and 10.4 ± 6.6, respectively. Italian patients presented more frequently fatigue ($p<0.001$), arthralgia ($p<0.001$), carotidynia ($p<0.001$), acute coronary syndrome ($p=0.017$), but less vertigo ($p=0.020$), stroke ($p=0.005$), seizure ($p=0.032$), pulse loss ($p=0.002$), arterial hypertension ($p<0.001$), acute kidney injury ($p=0.003$) and heart failure ($p=0.002$). Only 0.7% were asymptomatic at diagnosis. At least one TAK extravascular manifestation was observed in 11.3% of patients (23.3% Italy vs 3.3% India, $p<0.001$), with the most common being erythema nodosum (4.2%), followed by inflammatory bowel diseases (4.1%), uveitis/scleritis (3.7%) arthritis/sacroiliitis (3.2%), oral ulcers (2.1%), peripheral neuropathy (1.4%). 7 (1.7%) patients had 2 concomitant extravascular manifestations, while 4 (1.0%) had 3, and only 1 (0.2%) had 4. Italian patients presented more frequently erythema nodosum ($p<0.001$) and uveitis/scleritis ($p=0.013$). Patients with extravascular manifestations were older ($p=0.005$), with a longer diagnostic delay ($p=0.030$). No differences were noted in acute phase reactants. On univariate analysis, syncope, retinopathy, and acute coronary syndrome were significantly associated with extravascular involvement ($p=0.039$, $p=0.021$, and $p=0.018$, respectively), while arterial hypertension and heart failure were inversely associated ($p<0.001$, $p=0.023$, respectively). On multivariate analysis, retinopathy ($p=0.033$) and acute coronary syndrome ($p=0.046$) remained significant. 348 (85.5%) cases received glucocorticoids, 331 (81.3%) conventional immunosuppressants, and 115 (28%) biologics. Those with extra-vascular involvement more frequently received biologics ($p<0.001$). Vascular procedures were performed in 101 patients (24.8%), with no differences between groups.

Conclusions: Extravascular manifestations of TAK are not rare, with a prevalence of 11.3% of patients, and erythema nodosum is the most common extravascular manifestation. Patients with extra-vascular manifestations are older and experience a longer diagnostic delay, significantly associated with the presence of retinopathy and acute coronary syndrome.

Disclosures: None.

P-066

Isolated subglottic stenosis: a localised presentation of AAV?

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Background: Subglottic stenosis (SGS), defined as airway narrowing below the vocal cords, is rare and potentially life-threatening. SGS may be acquired (e.g., following traumatic intubation), occur as part of a multi-system disorder (e.g., anti-neutrophil cytoplasm antibody-associated vasculitis (AAV)),[1] or be idiopathic. There is increasing speculation that idiopathic SGS may represent a localised form of AAV.[2] Here, we present a series of patients with idiopathic SGS managed with immunosuppression and report their outcomes.

Methods: Within a dedicated Vasculitis Service and using otolaryngology records, we identified patients with SGS and classified them into three groups: *1)* acquired; *2)* AAV; or *3)* idiopathic. We analysed demographic data, treatment, and outcome data. The primary outcome was time to recurrent surgical airway dilatation.

Results: We identified 44 patients with SGS, of whom 6 (14%) had acquired SGS (median age 57 years; 50% female), 5 (11%) had AAV-related SGS (48 years; 60% female), and 33 (75%) had idiopathic SGS (42 years; 97% female). Patients with AAV were all ANCA-positive (PR3, n=4; MPO, n=1). Patients with idiopathic SGS had variable ELISA/immunofluorescence ANCA positivity (MPO, n=3; PR3, n=2; p-ANCA, n=2; ANCA negative, n=17; not assessed, n=9). 31 airway biopsies were performed (acquired, n=6; AAV, n=0; idiopathic, n=25); of these, 29 (94%) showed non-specific inflammation and 2 (6%) showed fibrous tissue. 177 surgical dilatations were performed (acquired, n=0.4/patient-year; AAV, n=0.3/patient-year; idiopathic, n=0.7/patient-year). Of the 33 patients with idiopathic SGS, 9 (27%) received immunosuppression. These patients were ANCA positive (n=4), had aggressive disease requiring frequent dilatations (n=3), or had soft tissue inflammation around the SGS on magnetic resonance imaging (MRI) of the airway pre-treatment (n=7). Time to recurrent airway dilatation increased in these patients (365±178 days pre-treatment *vs.* 640±311 days post-treatment, p=0.02) (**Figure 1**). 3 patients had serial MRI scans, of whom 2 showed improving inflammation following immunosuppression.

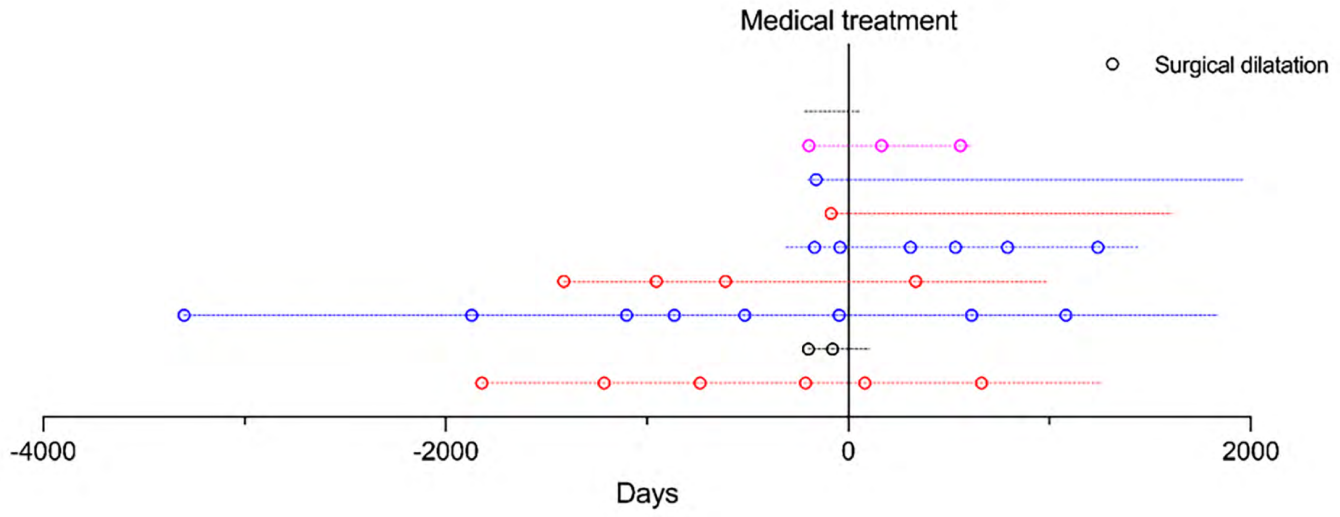

Figure 1: Surgical airway dilatations pre- and post-immunosuppression. Each line represents an individual patient. Immunosuppression regimens were oral glucocorticoid + MMF + rituximab (*red*); oral glucocorticoid + rituximab + cyclophosphamide (*black*); rituximab monotherapy (*blue*); or glucocorticoid monotherapy (*pink*).

Conclusions: Patients with idiopathic SGS are predominantly female and may be ANCA positive in the absence of multi-system disease. These patients may benefit from immunosuppression to reduce the frequency of surgical interventions. However, the optimal immunosuppressive regimen for this group remains uncertain.

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P-067

Ophthalmic manifestations in Takayasu arteritis patients: a cross-sectional monocentric study

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Background/Objectives: Takayasu arteritis (TA) is a chronic large-vessel vasculitis affecting the aorta and its branches[1]. TA can cause chronic ischemia in various territories, including the eyes. The most significant ocular manifestation is Takayasu retinopathy (TR)[2], characterized by small vessel dilation, microaneurysm formation and arteriovenous anastomosis. Ischemic ocular symptoms mainly result from carotid artery stenosis or occlusion, and hypertensive retinopathy can arise secondary to renal artery stenosis. A comprehensive evaluation of TA's ocular manifestations is though still lacking. Here, we aimed to thoroughly evaluate eye involvement in TA patients and investigate the relationship between disease characteristics and ocular manifestations.

Methods: Consecutive TA patients fulfilling the 2022 ACR/EULAR criteria and sex- and age-matched healthy controls (HCs) were included. TA patients and HCs underwent a comprehensive ophthalmic examination including visual acuity, indirect fundoscopy and multimodal imaging. Data on medical and ocular history, and disease features were collected. First, a comparison of central foveal avascular zone (FAZ) area, superficial (SCP) and deep capillary plexus (DCP) vessel density and choriocapillaris flow deficit density between TA and control eyes was performed[3]. Second, the association between retinal vascular metrics and clinical parameters in TA patients using linear mixed models was evaluated.

Results: 106 eyes from 53 TA patients (47 females, mean age ±15 years) and 53 HCs were included. No retinal vasculitis or TR was observed in TA patients. Notable findings included increased outer plexiform layer thickness and subfoveal choroidal thickness in TA patients compared to controls. In TA patients the FAZ area was significantly increased (0.38±0.19 vs .30±0.11 mm2, p=0.049), while the vessel density of the SCP was significantly lower (35.09±2.98% vs 36.75±2.43%, p=0.002) compared to HCs. Furthermore, higher FAZ area values were associated with arthritis, dizziness, and headache in TA patients (see Table 1). Lower SCP vessel densities correlated with carotid artery involvement and claudication of extremities, while lower DCP vessel densities were associated with fever at the time of diagnosis. Additionally, patients with a higher baseline ACR/EULAR 2022 cumulative score exhibited lower SCP vessel densities.

	FAZ (mm^2)		SCP-VD (%)		DCP-VD (%)	
	estimate	p-value	estimate	p-value	estimate	p-value
BP inequality (ref: no)	0.09	0.16	-0.9	0.25	0.86	0.56
Carotidynia (ref: no)	-0.02	0.76	-1.17	0.19	0.21	0.89
Arthritis (ref: no)	0.22	0.025**	1.74	0.19	-0.94	0.69
Fever (ref: no)	0.08	0.19	-0.24	0.78	-2.45	0.078*
Fatigue (ref: no)	0.06	0.34	-0.20	0.83	0.46	0.75
Headache (ref: no)	0.14	0.079*	-0.68	0.55	0.27	0.88
Dizziness (ref: no)	0.14	0.049**	-0.25	0.79	1.82	0.28
Pulse loss (ref: no)	0.003	0.97	-0.13	0.87	-1.86	0.18
Vascular bruits (ref: no)	-0.02	0.81	-1.26	0.19	-1.17	0.46
Claudication (ref: no)	-0.05	0.38	-1.48	0.081*	1.25	0.39
Hypertension (ref: no)	-0.06	0.34	1.39	0.10	0.86	0.54
Subclavian inv (ref: no)	0.03	0.43	0.82	0.22	-1.92	0.15
Carotid inv (ref: no)	0.03	0.57	-1.45	0.053*	-1.41	0.31
Sum of arteries affected (ref:0)	0.04	0.82	-0.13	0.57	-0.27	0.46
1990 score > 3 (ref: no)	-0.07	0.39	-1.41	0.22	-0.81	0.66
2022 score > 5 (ref: no)	0.09	0.93	-2.57	0.061*	-0.82	0.73

Table 1. Association between retinal vascular metrics and systemic parameters in TA patients.
FAZ: foveal avascular zone; SCP-VD: superficial capillary plexus vessel density; DCP-VD: deep capillary plexus vessel density.

Conclusions: Ocular vascular abnormalities with increased FAZ area and reduced vessel density of the SCP can be detected in TA patients even without TR. Chronic ischemia secondary to carotid involvement seems to be a major driver for eye involvement.

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Disclosures: None.

P-068

Histological aortitis increases risk of reoperation in patients undergoing aortic surgery

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Objectives: Aortitis is defined as inflammation of the aorta and can lead to aneurysms and dissections. Aortitis increases the risk of re-operations and intra-operative sampling is essential as many cases are idiopathic, presenting with no symptoms. Several patients get diagnosed only after surgical intervention for aortic aneurysms or dissections. Previous studies investigating aortitis in major aortic surgery have been limited by low intra-operative sampling. Hence, we performed this study to investigate the true prevalence of aortitis in thoracic aortic aneurysms and dissections.

Methods: This is a retrospective cohort study. All major aortic operations performed by the cardio thoracic team in a single centre (Oxford University Hospitals NHS Foundation Trust) from January 2012 to December 2022 were analysed. The medical history, histological reports, post-operative outcomes and follow-up were collected from electronic patient records. Data was analysed using Microsoft Excel and RStudio.

Results: 537 patients met the inclusion criteria for the study, representing an 88% histological sampling rate. The prevalence of aortitis was 10.6% (n=57), of which 75% were idiopathic. The re-operation rate in aortitis was twice that of the non-aortitis patients (17.5% v 9.4%, Pearson's Chi Squared, P=0.054). Multivariate logistic regression identified increased age, female sex, current smoking, and other inflammatory diseases as significantly associated with increased risk of aortitis, whilst bicuspid aortic valve was associated with a significantly decreased risk.

Conclusions: The prevalence of aortitis in our study is twice that reported in previous studies with lower sampling rates. The true prevalence is likely higher than reported. Due to the increased re-intervention rate, multidisciplinary follow-up with cardiothoracic, vascular and rheumatology is essential, and specialist referral centres should be formed to streamline the management of these conditions.

P-069

Dry eyes in ANCA associated vasculitis: due to impaired tear production?

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Background/ Objectives: Many patients with ANCA-associated vasculitis (AAV) have ocular symptoms. Ocular involvement includes (epi)scleritis, keratitis, uveitis, orbital inflammation, lacrimal duct stenosis, and/or retinal vasculitis. Furthermore, many AAV patients suffer from dry eyes and/or epiphora although these symptoms are only infrequently noted as a presenting symptom (1). It is not known whether dry eyes in AAV patients are caused by impaired tear production or increased tear evaporation.

Methods: Consecutive AAV patients in remission that visited our outpatient clinic were included in the study. Participants were tested with a 5-minute Schirmer test. In addition, all patients were tested for the presence of anti-SSA and anti-SSB antibodies, whereas patients filled out a 5-item questionnaire which distinguish Sjogren syndrome (SS) from non-SS patients (2). At the time of measurement, medications that might cause dry eyes (e.g., antidepressants, antipsychotics, beta blockers, diuretics, proton pomp inhibitors, GLP-1 receptor antagonists, NSAIDS, and/or MTX) were noted. SS (n = 11) and Healthy controls (n = 19) were also included in the study.

Results: 20 AAV patients (7 male; 13 females; median age: 55 years) were included in the study. Diagnoses were: 12 x GPA; 6 x EGPA; 2 x MPA. 3 patients tested positive for both PR3-ANCA and MPO-ANCA, 6 had PR3-ANCA only, 6 MPO-ANCA only, whereas 5 patients tested negative for both MPO-ANCA and PR3-ANCA. The interval between diagnosis and testing was 42 months (range, 3 – 165 months). Impaired tear production (defined as a Schirmer test <15 mm) was present in 15 of 20 patients, significantly more common than in HC (p=0.04). Severe impairment as found in SS (Schirmer test <5 mm) was found in 6 of 20 AAV patients. In none of these 6 patients SSA or SSB antibodies were detected, whereas in only one patient the SSSQ questionnaire was positive for possible SS. Impaired tear production did not correlate with CRP levels, disease phenotype, or ANCA subtype. All six patients with severe tear impairment, 5 of 9 patients with moderate impaired tear production and 4 of 5 patients with normal tear production used medications that potentially inhibit tear production.

Conclusion: Impaired tear production is a common finding in patients with ANCA associated vasculitis. Impaired tear production in these patients is often due to usage of medications that impair tear production. In addition, damage of lacrimal glands due to (previous) inflammation could be a contributing factor. Although the impairment of tear production may be severe, it is unlikely that AAV patients have a co-occurrent diagnosis of Sjogren's syndrome.

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Dr. Yacyshyn received advisory board honorarium from Otsuk.

1. CLINICAL SCIENCE
1.04. Disease Assessment: activity, damage, response and remission criteria, imaging...

P-070

Clinical characteristics of giant cell arteritis presenting visual loss: a single-center retrospective study

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Background/Objectives: Permanent visual loss is the most feared complication of giant cell arteritis (GCA). To examine characteristics of GCA presenting with visual loss. (reference 1, 2)

Methods: We retrospectively investigated the symptoms, clinical examination, imaging findings, and biopsy findings of GCA patients diagnosed at Juntendo University Hospital from 2013 to 2023.

Results: Visual loss was observed in 25 (35.2 %) of 71 GCA patients. It was more common in GCA with cranial involvement regardless of extracranial involvement (with and without visual loss group, 50.0% and 25.0%, respectively, p=0.037), and less common in GCA with extracranial involvement regardless of cranial involvement (8.70% and 31.8%, p=0.029). Following symptoms and signs are more frequent in GCA with visual loss in comparison with GCA without visual loss, jaw claudication (70.8% and 28.9%, respectively, p<0.001), temporal headache (76.0%, 50.0%, p=0.036) and abnormal examination of temporal artery (54.5%, 27.0%, p=0.035). The average number of the symptoms and signs (polymyalgia rheumatica, temporal headache, posterior neck pain, jaw claudication and temporal artery abnormality) seen before diagnosis was higher in patients with visual loss (2.48 and 1.50, p<0.001, Figure 1) The frequency of cerebrovascular disorders complicated with GCA (30.4, 2.6%, p=0.0018) and history of glaucoma were more frequent in visual loss group (70% and 27.8%, p=0.03). Imaging with ultrasound and PET-CT revealed that the vascular lesions located in the temporal artery area were more frequent in patients with visual loss. Of the 25 patients with visual loss, six patients resulted in permanent sight loss, and ischemic optic neuropathy was more frequent in patients with permanent sight loss than that in patients without permanent sight loss (80.0% and 25.0%, respectively, p=0.038). In the permanent sight loss group, five patients had cranial involvement alone and one had both cranial and extracranial involvement.

Conclusions: Visual loss was more common in patients with GCA who had cranial involvement and the number of clinical symptoms of GCA. Cerebrovascular complications were more frequent in GCA patients with visual loss. It is essential to quickly assess the presence of acute mural inflammation in area of temporal artery.

Disclosures: None.

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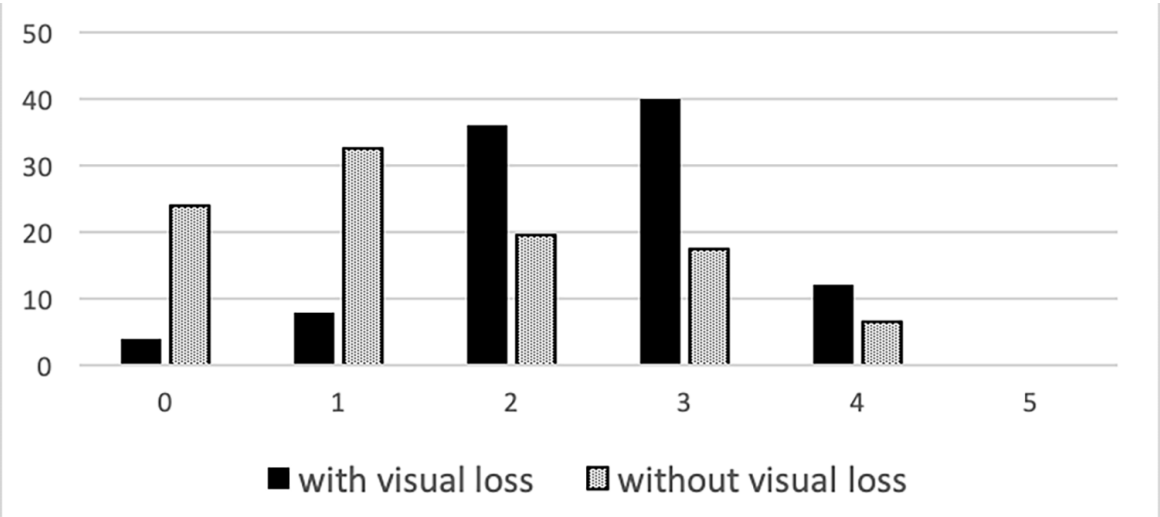

Figure 1: The average number of the symptoms and signs related to GCA (%).

P-071

Measurement of Sinonasal Disease Activity in Granulomatosis with Polyangiitis

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Background/Objective: In granulomatosis with polyangiitis (GPA), sinonasal inflammation can be severe and impact quality of life. Little is known about the most effective local and systemic therapies for sinonasal disease in GPA. The Sino-Nasal Outcome Test-22 (SNOT22) is a patient-reported outcome measure validated in chronic rhinosinusitis but it has not been well-studied in GPA. This study measured sinonasal disease activity using the SNOT22 and the Birmingham Vasculitis Activity Score for Wegener's Granulomatosis (BVAS/WG) in patients treated for active GPA.

Methods: This prospective, longitudinal cohort study included patients who met the 1990 ACR classification criteria for GPA, with active disease and at least one follow-up visit, 3 or more months later were included. Following therapy initiations were examined: I) saline nasal rinses; II) topical nasal glucocorticoids; III) topical nasal antibiotics; and IV) rituximab (within the prior 6 months); patients could be in more than one group. Outcome measures included: (a) percent of patients achieving the minimal clinically important difference (MCID) for SNOT22 of 8 as determined for chronic rhinosinusitis; (b) percent change in SNOT22; and (c) percent of patients achieving BVAS/WG=0 for sinonasal items. In secondary analyses models also adjusted for potential confounders, including prednisone, other concurrent treatments, and active sinus disease at relapse visit.

Results: It included 52 flares in 42 patients with GPA. 35 (83%) patients had a prior history of sinonasal involvement, 28 (67%) were PR3-ANCA positive, and mean disease duration was 2 (0-5) years. At the active visit, 37 (70%) visits had active sinonasal involvement, and mean SNOT-22 score was 27 (IQR 4,15). New medications prescribed included: 30 (58%) saline nasal rinse, 9 (18%) topical nasal glucocorticoids, 4 (8%) topical nasal antibiotics, and 8 (15%) rituximab. For topical nasal glucocorticoids, new initiation vs. no initiation was associated with a greater probability of achieving an MCID for SNOT22 (OR 8.5 [95% CI 1.3, 55.6], P-value 0.026) (**Figure 1**) and for saline nasal rinse it was associated with a greater percent change in SNOT22 (coefficient -0.60, [95% CI -1.17, -0.04], P= 0.037). No significant changes were seen between any treatment groups when using the sinonasal items on BVAS/WG.

Conclusion: In GPA use of SNOT22 enabled detection of response to topical nasal therapies. Specifically, use of saline nasal rinse and topical nasal glucocorticoids were associated with improvement in sinonasal symptoms. Treatment response was not detected when using the BVAS/WG, suggesting that SNOT22 may have more responsiveness and convergent validity when assessing sinonasal disease.

Figure 1: Proportion who Achieved Minimal Clinically Important Difference of SNOT22 Total Score.

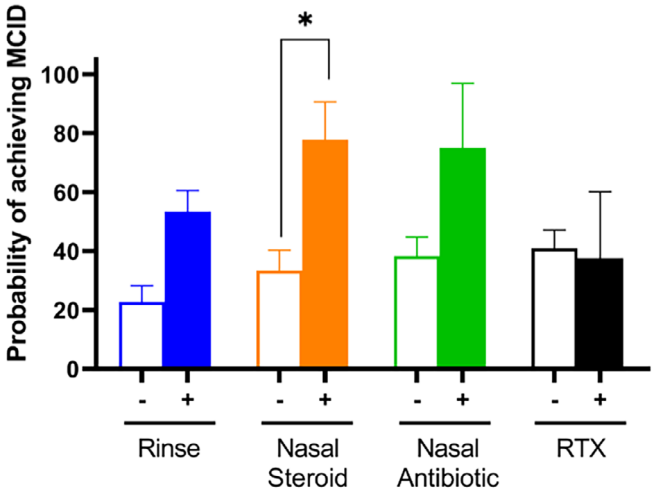

Figure 1: Bar graphs show mean (95% CI) MCID of the SNOT22 score. Four treatments were analyzed separately and were categorized based on no initiation of treatment (-) vs initiation of treatment (+). Logistic regression models at time of active disease. * P < 0.05.

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Consulting and stock options: Kyverna, Q32, Sparrow.

Royalties: UpToDate.

P-072

Angiographic findings of pulmonary arterial involvement in Behcet`s Disease: Do they correlate with symptoms and acute phase response?

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Objectives: Vascular involvement is observed in up to one third of patients with Behçet's disease (BD). Although venous involvement is more common, an increasing presence of pulmonary artery thrombosis (PAT) with or without aneurysms was also reported in recent studies. In this study, we aimed to describe computed tomography pulmonary angiography (CTPA) findings of pulmonary involvement and its correlation with symptoms and acute phase response (APR) in BD.

Method: In this retrospective study, 153 CTPA of BD patients were assessed by two radiologists. We described increased acute phase reactants (APRs) if C reactive protein (CRP) and/or erythrocyte sedimentation rate was more than twice the upper limit of normal within one week of angiography without a possible other explanation such as infection. Patients were grouped according to their symptoms and APRs levels. Pulmonary artery involvement (PAI) was defined as thrombus or aneurysm in CT angiography.

Results: Median age was 33.7±10 years during angiographic assessments, most of (85.6%) our patients were male and 71% of patients had major organ involvement. During angiography, immunosuppressive and anticoagulant usage was 51.4% and %13, respectively. CT angiographies were performed because of increased APR together with a symptom for 24 (16%) patients, increased APR without a symptom for 59 (39.3%) patients and a symptom without increased APR for 13 (8.7%) patients. (figure)

Sixty-two (40.5%) angiographies presented a thrombus: 14 subsegmental, 29 segmental, 13 lobar and 6 main branches. Among these, 82.3% (n=51) had bilateral involvement. Isolated PAT was present in 58 (93.5%) angiographies with only 4 (2.6%) angiographies displaying an aneurysm together with a thrombus. Pulmonary infarction was detected in 9 angiographies.

Conclusion: Isolated pulmonary thrombosis is the main form of PAI, and isolated pulmonary aneurysm formation is rare in our BD cases. In the presence of pulmonary symptoms with or without increased APRs, involvement of segmental or more proximal parts of pulmonary arteries is most commonly detected. We also observed that PAI may be seen in about one fourth of especially male BD patients without symptoms or increased APR. Our results suggest that BD patients with pulmonary symptoms should be screened by CTPA for PAI, however, further research is needed to clarify the role of routine CTPA screening in asymptomatic BD patients.

Disclosure: None.

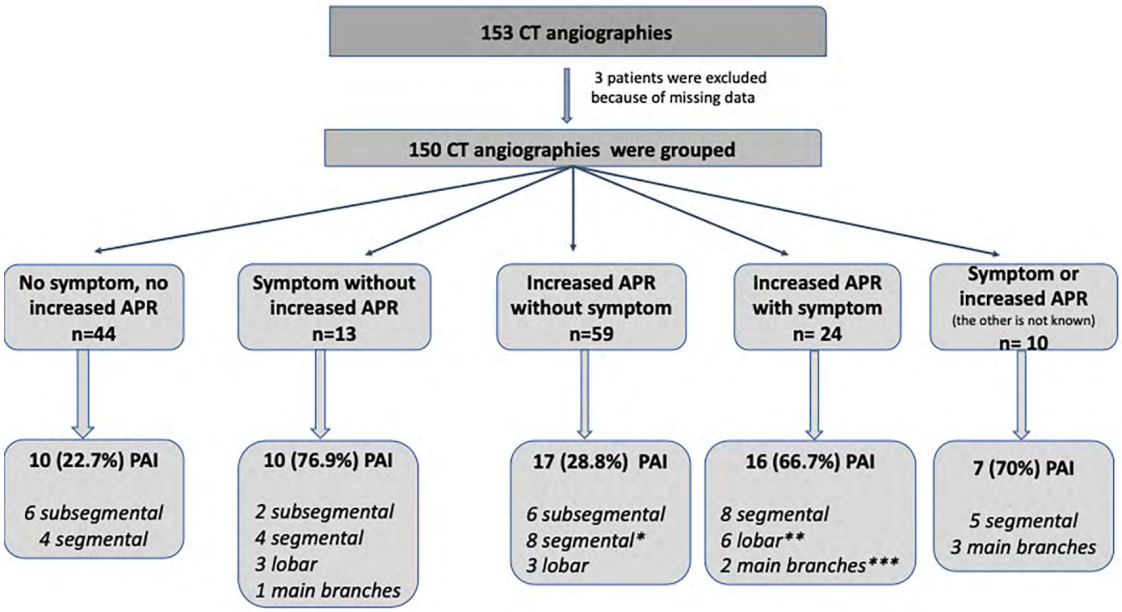

Figure: Pulmonary angiographic findings according to the presence of symptoms and/or increased acute phase response.

All PAI include pulmonary artery thrombus
: 1 angiography with aneurysm accompanied to thrombus, **: 2 angiographies with aneurysm accompanied to thrombus, *: 1 angiography with aneurysm accompanied to thrombus*

P-073

Free light chain expression and the impact of therapies in ANCA-associated vasculitis

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Background/ Objectives: The expression levels of free light chains, especially the κ-light chain, predict all-cause mortality of patients. This international study is the first to investigate the expression of free light chains in the blood and urine of patients with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis, the impact of B-cell depletion with rituximab on their expression levels, and differences between patients with ANCA-associated vasculitis patients and individuals with other kidney diseases.

Methods: Patients with ANCA-associated vasculitis were recruited from five centers, and free light chains were analyzed according to established test kits. Measurement of light chains based on a clinical indication, i.e. suspected underlying hematologic malignancy, was an exclusion criterion. As comparators, patients with other autoimmune disorders, chronic kidney disease (CKD) and kidney transplant recipients, were recruited. Statistical analyses were performed using Statistica version 13.3.

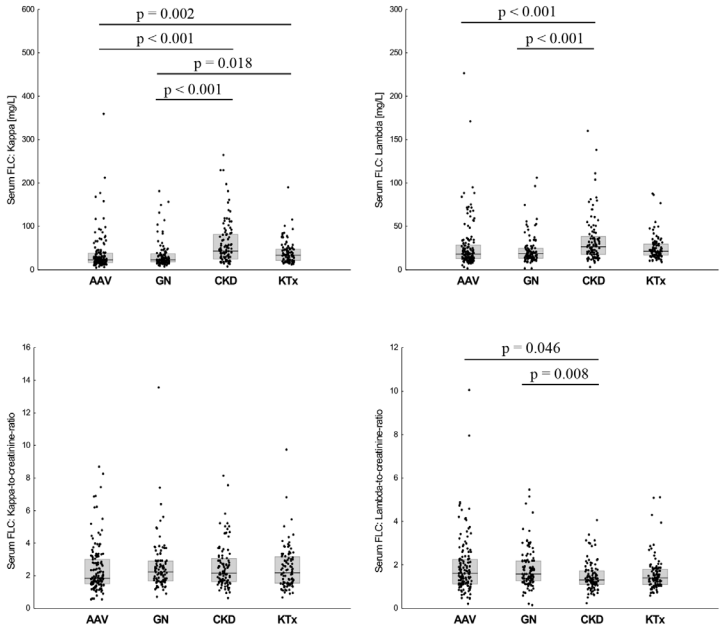
Results: A total of 137 patients with ANCA-associated vasculitis were recruited across the different sites, and compared to patients with other autoimmune disorders (n=100), CKD of different causes (n=101) and kidney transplant recipients (n=99). As kidney function was not well-balanced among different groups and patients with CKD and after transplantation had worse kidney function at the time of measurement, we focused on light chain-to-creatinine ratio. Patients with ANCA-associated vasculitis had a lower κ-to-creatinine ratio (1.9 (1.5-3.0)) in comparison to the comparators, while the λ-to-creatinine ratio was highest in those with ANCA-associated vasculitis and other autoimmune disorders (1.6 (1.1-2.3) for individuals with ANCA-associated vasculitis) (see Figure 1). Fifty-one patients with ANCA-associated vasculitis received rituximab within six months of blood sampling. These patients had a significantly lower κ-to-creatinine ratio (1.6 (1.4-2.5)) λ-to-creatinine ratio (1.2 (1.0-1.8)) in comparison to controls (2.2 (1.5-3.3) and 1.9 (1.3-2.8). Notably, patients receiving rituximab also had lower levels of IgG, IgM and IgA.

Conclusions: Patients with ANCA-associated vasculitis have similar adjusted expression levels of free light chains in comparison to diseased control groups. Rituximab-treated individuals with ANCA-associated vasculitis have lower expression levels of both light chains, and this might be impacted by lower immunoglobulin levels.

References: Nil.

Disclosures: The authors report no potential conflict of interests related to this work, but have received consultancy fees and/ or speaking fees from CSL Vifor, AstraZeneca and GSK.

Figure 1. Free light chain expression across different groups is given for A) serum free light chain κ, B) serum free light chain λ, and finally adjusted for serum creatinine at the time of blood sampling (C and D).



Abbreviations: AAV (ANCA-associated vasculitis), CKD (chronic kidney disease), GN (glomerulonephritis), KTx (kidney transplant recipients).

P-074

The Joint Vasculitis Registry in German-speaking countries (GeVas) – subgroup analysis of 266 AAV-patients

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Background/ Objectives: Until now, prospective long-term observational data on the disease course of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) were missing in Germany. Here we present baseline data of patients with newly diagnosed and relapsing AAV enrolled in the Joint Vasculitis Registry in German-speaking countries (GeVas) registry.

Methods: GeVas is a prospective, web-based, multicenter, clinician-driven registry for the documentation of organ manifestations, damage, long-term outcomes, and therapy regimens [1]. Recruitment started in June 2019 and is currently being conducted by 15 centers in Germany to date.

Results: Between June 2019 and October 2022, 266 patients with AAV were included in the GeVas registry, hereof 173 (65%) with new-onset and 93 (35%) with relapsing AAV. One hundred and sixty-two (61%) patients had a granulomatosis with polyangiitis (GPA), 68 (26%) microscopic polyangiitis (MPA), and 36 (14%) an eosinophilic granulomatosis with polyangiitis (EGPA). The median age was 59 years (51-70 years, IQR), 130 (51%) patients were female, 136 (49%) males. Most patients were ANCA positive (177; 67%) and affected by general symptoms, pulmonary, ear nose throat (ENT), renal and neurological involvement. Most patients received glucocorticoids (247, 93%) in combination with either rituximab (118, 45%) or cyclophosphamide (112, 42%) for the induction of remission (table 1).

Conclusions: Herein, we present baseline data from an inception cohort of AAV patients in the GeVas registry. Demographic characteristics are comparable to those in other European countries. Differences were found regarding ANCA-status, frequencies of organ manifestations, and therapeutic regimen [2-3].

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Disclosures: SA: None. PW: None. MJ: None. CIK: Chugai, GSK, Roche, Vifor, DGRh, John Grube Foundation. PL: BMS, FOFM, GSK, Janssen, UCB, Vifor Pharma, BMBF, DFG, DGRh, John Grube Foundation.

Table 1. Demographics and clinical characteristics of AAV patients enrolled in GeVas registry (06/2019 – 10/2022).

	AAV	GPA	MPA	EGPA
Number of patients, n (%)	266 (100)	162 (61)	68 (26)	36 (14)
Demographics				
Age (years); median [IQR]	59 [51-70]	59 [51-69]	64 [54-76]	56 [48-63]
Gender				
Male; n (%)	136 (49)	85 (52)	34 (50)	17 (47)
Female; n (%)	130 (51)	77 (48)	34 (50)	19 (53)
Reason for inclusion in the study				
Newly diagnosed vasculitis; n (%)	173 (65)	87 (54)	56 (82)	30 (83)
Relapse; n (%)	93 (35)	75 (46)	12 (18)	6 (17)
Relapse - major; n (%)	47 (18)	39 (24)	6 (9)	2 (6)
Relapse - minor; n (%)	46 (17)	36 (22)	6 (9)	4 (11)
Comorbidities				
Asthma	38 (14)	11 (7)	4 (6)	23 (66)
Diabetes; n (%)	16 (6)	10 (6)	5 (8)	1 (3)
Hypertension; n (%)	95 (36)	56 (35)	29 (44)	8 (23)

	AAV	GPA	MPA	EGPA
Hyperlipidemia; n (%)	29 (11)	16 (10)	10 (15)	2 (6)
Atherosclerosis; n (%)	32 (12)	18 (11)	11 (17)	3 (9)
Chronic kidney disease; n (%)	28 (11)	16 (10)	10 (15)	2 (6)
Malignancy; n (%)	16 (6)	13 (8)	1 (2)	2 (6)
Organ involvement				
General symptoms; n (%)	188 (71)	122 (75)	42 (64)	23 (66)
ENT; n (%)	139 (52)	105 (65)	11 (17)	23 (66)
Lung/chest; n (%)	151 (57)	95 (59)	32 (48)	24 (69)
Renal; n (%)	103 (39)	51 (31)	48 (71)	4 (11)
Heart; n (%)	17 (6)	7 (4)	1 (2)	9 (26)
GI; n (%)	15 (6)	7 (4)	2 (3)	6 (17)
CNS; n (%)	28 (11)	16 (10)	11 (17)	1 (3)
PNS; n (%)	62 (23)	27 (17)	19 (29)	16 (46)
Skin; n (%)	41 (15)	23 (14)	11 (17)	7 (20)
Eye; n (%)	27 (10)	22 (14)	2 (3)	3 (9)
Laboratory tests				
PR3-ANCA; n (%)	110 (42)	108 (67)	0 (0)	2 (6)
MPO-ANCA; n (%)	67 (25)	5 (3)	57 (84)	5 (14)
eGFR (ml/min/1.73 m²); median, [IQR]	73 [45-90]	75 [55-90]	50 [23-82]	90 [73-100]
Creatinine (µmol/l); median, [IQR]	82 [71-124]	80 [71-110]	100 [72-239]	77 [70-84]
Hematuria; n (%)	82 (31)	54 (33)	25 (38)	1 (3)
Proteinuria; n (%)	94 (35)	55 (34)	33 (50)	5 (14)
CRP (mg/l); median, [IQR]	19 [4-81]	25 [5-91]	16 [5-71]	6 [1-26]
Immunosuppressive treatment at baseline				
Prednisolone; n (%)	247 (93)	149 (92)	62 (94)	34 (97)
Avacopan; n (%)	6 (2)	2 (1)	4 (6)	0 (0)
Cyclophosphamide; n (%)	112 (42)	58 (36)	34 (52)	19 (54)
Rituximab; n (%)	118 (45)	83 (51)	34 (52)	0 (0)
Cyclophosphamide and rituximab; n (%)	26 (10)	16 (10)	10 (15)	0 (0)
Methotrexate; n (%)	46 (17)	34 (21)	4 (6)	8 (23)
Azathioprine; n (%)	20 (8)	13 (8)	5 (8)	2 (6)
Mycophenolate (mycophenolate mofetil or mycophenolic acid); n (%)	4 (2)	3 (2)	1 (2)	0 (0)
Leflunomide; n (%)	8 (3)	7 (4)	1 (2)	0 (0)
Mepolizumab; n (%)	7 (3)	0 (0)	0 (0)	7 (20)
Other immunosuppressive treatment; n (%)	7 (3)	4 (2)	2 (3)	1 (3)
Plasma exchange; n (%)	9 (3)	5 (3)	4 (6)	0 (0)
Comedication				
Pneumocystis prophylaxis; n (%)	192 (72)	116 (72)	52 (79)	22 (63)
Vitamin D; n (%)	237 (89)	148 (91)	59 (89)	28 (80)
BVAS; median, [IQR]	7 [4-13]	7 [4-12]	9 [5.5-14]	7 [4-12]
BVAS ³ 12; n (%)	78 (30)	40 (25)	26 (41)	10 (29)
VDI; median, [IQR]	1 [0-2]	1 [0-2]	0 [0-2]	0 [0-2]

AAV = Antineutrophil-cytoplasmic antibody-associated vasculitis, ANCA = Antineutrophil-cytoplasmic antibody, BVAS = Birmingham Vasculitis Activity Score, CNS = central nervous system, eGFR = estimated Glomerular Filtration Rate, EGPA = eosinophilic granulomatosis with polyangiitis, ENT = ear nose throat, GI = gastrointestinal, GPA = granulomatosis with polyangiitis, MPA = microscopic polyangiitis, MPO = myeloperoxidase, PNS = peripheral nervous system, PR3 = proteinase 3, VDI = Vasculitis Damage Index.

P-075

The utility of novel and emerging serological biomarkers for disease monitoring in large vessel vasculitis

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Background: Monitoring disease activity is a key challenge in large vessel vasculitis (LVV).[1] Current serological markers of disease activity may be falsely reassuring, particularly once treatment has started.[2] We examined the utility of five novel and emerging serological biomarkers of disease activity in a prospective, longitudinal cohort of patients with LVV.

Methods: Adults patients with active LVV were recruited from throughout Scotland. Subjects attended for study visits as baseline and again after ³6 months. At each visit disease activity was assessed clinically, and participants underwent hybrid 18F-fluorodeoxyglucose (FDG) positron emission tomography with magnetic resonance imaging (PET/MRI) alongside blood sampling. Blood samples were also obtained from age- and sex-matched healthy subjects and age- and sex-matched patients with active small vessel vasculitis (SVV). Plasma concentrations of leucine-rich α-2 glycoprotein 1 (LRG1), angiopoietin-2 (Ang-2), soluble fms-like tyrosine kinase-1 (sFlt-1), osteopontin, and calprotectin were assessed by ELISA and compared across groups. Exploratory multivariable regression analysis determined the ability of serological biomarkers to assess LVV disease activity alone or in combination with PET/MRI metrics.

Results*:* Twenty-two patients with LVV attended for 39 study visits. Twenty healthy subjects and 20 patients with SVV were also recruited. Plasma concentrations of all five candidate biomarkers were elevated in LVV *versus* health (P<0.05). LRG1, Ang-2 and osteopontin were able to distinguish active LVV from inactive LVV (P<0.05). None of the biomarkers distinguished LVV from SVV. We observed strong correlations between LRG1, Ang-2, osteopontin and calprotectin and established measures of disease activity including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and clinical assessment. The most consistent correlations were observed between the biomarkers described and a novel, PET/MRI-derived assessment of disease activity – the VAMP score (**Table 1**). Logistic regression analysis demonstrated that the combination of osteopontin and Ang-2 together with the VAMP score improved predictive power beyond any of these biomarkers in isolation.

Conclusions: This study demonstrates the utility of several novel and emerging serological biomarkers for disease monitoring in LVV. A biomarker panel may improve disease activity assessment compared with any one biomarker alone. Further studies will determine whether such a biomarker panel could be combined with imaging data, such as PET/MRI, to create a robust disease activity assessment for use in clinical practice.

Table 1. Correlations between candidate biomarkers and clinical metrics.

	CRP (mg/dL)	ESR (mm/h)	Platelets (x10⁹/L)	Graded clinical assessment	PET/MRI derived VAMP score
LRG1	0.79***	0.80***	0.60***	0.47**	0.69***
Ang-2	0.55***	0.52**	0.45**	0.51**	0.80***
sFlt-1	0.27	0.31	0.22	0.28	0.18
Osteopontin	0.35*	0.53**	0.43**	0.66***	0.64***
Calprotectin	0.79***	0.66***	0.64***	0.51**	0.67***

Values presented are r values denoting statistical correlation. Strength of correlation indicated by cell colour: red = r >0.75 or <-0.75, orange = r>0.5 or <-0.5, clear = r<0.5 or > -0.5. Asterisks indicate statistical significance: * = P<0.05, ** = P<0.01, *** = P< 0.001.

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Disclosures: None.

P-076

Is there a significance of C3 glomerular deposition in ANCA associated vasculitis patients?

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Background/ Objectives: Alternative complement pathway (ACP) activation has been known to play a role in ANCA associated vasculitis (AAV)[1]. We noticed that some of the AAV patients had positive C3 staining in the glomeruli. We explored differences between AAV patients based on C3 glomerular deposition.

Methods: Study included 106 AAV patients with biopsy proven renal involvement. We analyzed clinical, laboratory and pathohistological data. Patients were grouped based on: clinical phenotype (microscopic poliangiitis (MPA), granulomatosis with poliangitiis (GPA), eosinophilic granulomatosis with poliangitiis (EGPA) and renal limited vasculitis (RLV)), serologic phenotype (MPO or PR3 positive, MPO and PR3 positive and MPO and PR3 negative) and histological (Berden[2]) class (crescentic, focal, mixed and sclerotic). We analysed differences between the groups within individual phenotypes. Normaly distributed continouos variables were comapred using Student t-test and oneway variance analysis. Nonparametric continuous variables were compared using Mann-Whitney U test and Kruskal-Wallisovim H test. Categoric variables were comapred using χ^2-testom or Fisher exact test.

Results: Studied patients included 66 (61,1%) MPA, 20 (18,5%) GPA, 20 (18,5%) RLV. There were 14 (13%) PR3-ANCA positive patients, 57 (52,8%) MPO ANCA positive, 5 (4,6%) PR3-ANCA+MPO-ANCA and 32 (29,6%) ANCA negative patients. Average serum creatinine (SCr) was 316,5 µmol/l (IQR 207,0-548,5), 24-hour proteinuria median was 1,7g/24h (IQR 0,8-2,8). Histologicaly 43 (39,8%) patients had crescentic, 19 (17,6%) focal, 34 (31,5%) mixed and 12 (11,1%) sclerotic class. Though statistical significance in terms of p value was not reached, C3 deposits in glomeruli were more present in: MPA patients (48,5%) compared to GPA (25%) and RLV (35%); MPO (42,9%) and ANCA negative (46,9%) compared to PR3 (30,8%) and MPO and PR3 positive (20%); crescentic class with strong tendency towards significance (p=0,076) (51,2%) compared to focal (16,7%) and mixed (39,4%). While sclerotic class as well had more C3 deposits (50%) C3 is not uncommon in sclerotic lesion so it is hard to interpret its significance. Interestingly there was also tendency to statistical significance of C3 in glomeruli being more expressed in patients that required dialysis treatment (p=0,091).

Conclusions: ACP plays important role in renal disease in some AAV patients. Deposition of C3 in glomeruli of such patients might be important marker. Though no statistical significance was reached our data suggests that perhaps ACP activation plays prominent role in MPA and MPO-ANCA vasculitis as well suggesting it leads to more active and severe renal disease. Further multicentric research will be needed to prove this.

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Disclosures: None.

P-077

Clinical and laboratory features of Serbian patients with ANCA-associated vasculitis-a single center experience

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Background/ Objectives: Anti-neutrophil cytoplasmic antibody (ANCA) may target proteinase 3 (PR3) or myeloperoxidase (MPO). Clinical picture, organ involvement, and outcomes may differ between groups (*Nephrology Dialysis Transplantation,* Volume 38, Issue 7, July 2023, Pages 1655–1665) The objective of this study was to analyze the characteristics of patients with MPO- and PR3-ANCA-positive vasculitis in a cohort of patients from a single center in Serbia.

Methods: This was a cross-sectional descriptive study. We performed computer searches with terms related to patients with anti-neutrophil cytoplasmic antibody-associated vasculitis, between 2020 and 2023 who met the American College of Rheumatology classification criteria for vasculitis associated with anti-neutrophil cytoplasmic antibodies, and their clinical and laboratory characteristics. Clinical manifestations, treatment, and outcomes were evaluated. Differences between ANCA antibodies were analyzed.

Results: A total of 38 cases were included. The majority were female (n = 25, 66%), and the median age was 62 (53–68) years. Of 38 patients with ANCA and vasculitis included in this study, 20 (52.63%) had MPO-ANCA, 18 (47.37%) had PR3-ANCA. Patients with MPO−PR3+ANCA-associated vasculitis (AAV) were younger at diagnosis (median, 58 years; $p < 0.05$) than patients with MPO+PR3−AAV (67.0 years). The initial glomerular filtration rate in patients with MPO-PR3+AAV (14.0 ml/min) was lower than that in patients with MPO+PR3-AAV (31 ml/min), but no statistically significant difference was found. Twenty patients in total (54%) presented pulmonary symptoms. Anemia in patients with was more prominent in MPO−PR3+ANCA-associated vasculitis (AAV) (median hemoglobin 90; $p < 0.05$) than patients with MPO+PR3−AAV (median hemoglobin 102 g/l). The involvement of other organs did not differ according to ANCA type. Age at diagnosis, kidney involvement, and upper airway involvement were associated with ANCA type, but no statistical significance was found. In general, patients with MPO-PR3+AAV lower complement levels, higher ESR rate, worse kidney outcome and a higher rate of adverse outcomes.

Conclusions: We present clinical information on a group of patients with anti-neutrophil cytoplasmic antibody-associated vasculitis; renal involvement was the the most common type of affection, and patients with PR3 positivity had worse kindey function and outcomes in comparison with MPO-ANCA patients. Clinical and serological characteristics of our group was similar to those described in other cohorts.

Disclosures: None.

P-078

Dynamic behavior of the target molecule VAP2 of recombinant scFv of human IgG VasSF correlating with IL-16, MIF, and IL-1Ra in serum with ANCA-Associated vasculitis

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Background: We have proposed using a mouse model that vasculitis-associated apolipoprotein A2 (VAP2) would be a therapeutic target in vasculitis. Here, we estimated the target molecules of VasSF (recombinant single chain fragment of the variable region of human IgG) and the VAP2 association to cytokines in patients' sera.

Methods: Sera and clinical information were collected from consenting patients with MPA/GPA and with infectious diseases. Clinical information included C-reactive protein (CRP), creatinine, total cholesterol, HDL cholesterol, low-density lipoprotein cholesterol, triglyceride levels and estimated glomerular filtration rate (eGFR), cytokines, and other biomarkers were examined. Serum VAP2 signals were determined with western blotting by binding with VasSF and anti-APOA2 antibody.

Results: VasSF bound to a 24-kDa molecule in serum of active MPA/GPA patients, while VasSF bound to 17-kDa molecule in remission phase. Anti-AP2 antibody also bound with the 24-kDa molecule as VAP2, appearing different in size from normal APOA2. Signal of VAP2 was significantly higher in the active group and then significantly reduced in the remission. The VAP2 signal positively correlated with eGFR and did not correlate with Birmingham Vasculitis Activity Score (BVAS), CRP, MPO-ANCA nor PR3-ANCA levels. The VAP2 signal negatively correlated with MPO activity, IL-16, MIF and IL-1ra. Moreover, VasSF bound to a 17-kDa molecule in the remission phase.

Conclusion: The 24-kDa VAP2 may be associated with neutrophil functions because of its inverse correlation with MPO activity, IL-16, MIF, and IL-1ra, suggesting that the formation of VAP2-APOA1 in HDL triggers vascular injury. VasSF might cure the injury by removing APOA1-VAP2 heterodimers in peripheral blood vessels.

P-079

Retinal endothelial dysfunction in patients with acute COVID-19 and three months post-infection

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Background/ Objectives: Vascular involvement was postulated early in the COVID-19 pandemic. Endothelial activation and dysfunction by altering the integrity of vessel barrier, promoting pro-coagulative state, endothelial inflammation and mediation of leukocyte infiltration are crucial for disease progression. Retinal vessel analysis (RVA) provides insight into endothelial function. Static and dynamic parameters are reliable markers for systemic vascular alterations.

The aim of our study was to compare endothelial function of retinal vessels in patients with acute COVID-19 and healthy controls and to investigate endothelial function three months post-infection.

Methods: Patients with PCR proven SARS-CoV-2 infection and a NIAID-OS (National Institute of Allergy and Infectious Disease Ordinal Scale) score ³3 were included. Study visits were performed during hospitalisation and 3 months later for follow-up. Healthy controls were recruited from the ophthalmological department. Individuals with diseases that affect endothelial function were excluded. All patients and healthy controls underwent retinal vessel analysis (RVA, iMEDOS Health GmbH, Germany) to analyse static and dynamic retinal vessel parameters. Endothelial function was compared to age-, sex- and BMI-matched healthy individuals. At follow up, all parameters were analysed again and compared to baseline.

Results: 60 patients and 60 controls (mean age 60 years, 19 females) were included. 11 patients were lost to follow-up, 3 of whom died. Mean duration from first symptoms to hospitalisation were 7.9 (SD ± 4) and length of hospitalisation 13.1 (SD ± 10) days. 15 patients required intensive care with a mean ICU time of 10.9 (SD ± 8) days, 10 patients were on mechanical ventilation (mean 11.7, SD 7 days). Oxygen was required in 41 (68%) patients (mean 11.3 ± 8.7 days). Baseline static arteriolar diameters expressed as central retinal arteriolar equivalent (CRAE) were slightly but not significantly larger (mean CRAE 193 (SD ± 22) µm) compared to the controls (mean CRAE 187 (SD ± 21) µm, p=0.06). In follow up CRAE decreased, aligning with the controls (mean 188 (SD ± 22) µm). The venular diameters expressed as central retinal venular equivalent (CRVE) were significantly larger (mean CRVE 234 (SD ± 22) µm) compared to the controls (mean 217 (SD ± 19) µm, p<0.05). In follow up the CRVE decreased (mean 226 (SD ± 18) µm) but still significantly exceeded the controls (p<0.05). Dynamic vessel analysis indicated endothelial dysfunction. Flicker-induced maximal arteriolar (aFID) and venular (vFID) dilatation both were significantly reduced (aFID 1.68 ± 2.06%, and vFID 2.32 ± 2.44%) compared to the controls (3.20 ± 2.01% and 4.36 ± 2.05%, p<0.001). Endothelial function improved significantly after three months compared to baseline (aFID 3.14 ± 2.27, p<0.001; vFID 4.19 ± 1.69, p<0.001) and aligning with the controls (aFID p=0.44, vFID p=0.45).

Conclusions: This study indicates severe endothelial dysfunction at retinal vessels in patients with acute severe COVID-19. Three months post-infection flicker induced endothelial reaction recovered.

Disclosures: None.

P-080

Patient reported outcomes in ANCA-associated vasculitis cohort from single centre in Russia

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Background/ Objectives: ANCA-associated vasculitis (AAV) patient-reported outcome (AAV-PRO) questionnaire was developed to assess the impact of AAV and its treatment on the quality of life. We investigated the association between AAV-PRO and its specific domains score and Birmingham Vasculitis Activity Score (BVAS) and Vasculitis Damage Index (VDI).

Methods: We enrolled patients with AAV diagnosed according to the Chapel Hill 2012 definitions. AAV-PRO, BVAS, and VDI scores were calculated for all patients. Data on the patients' demographics, disease-related parameters, and comorbidities were also extracted. The data were analysed using IBM SPSS Statistics 23 software.

Results: We included 107 patients, among them 69 (64.5%) were diagnosed with granulomatosis with polyangiitis, 28 (26.2%) with microscopic polyangiitis, and 10 (9.3%) eosinophilic granulomatosis with polyangiitis. Mean age was 52.8 ±16.3, 72 (67.3%) patients were female. ANCA were positive in 75 (72.0%) patients, with positivity for proteinase-3 ANCA in 42 (39.3%), myeloperoxidase ANCA in 38 (35.5%), double positivity in 3 (2.8%). Comorbidities were observed in 96 (89.7%) patients, including arterial hypertension in 65 (60.7%), CKD in 41 (38.3%), obesity in 29 (27.1%), osteoporosis in 25 (23.4%), and Cushing syndrome 15 (14%) patients. Eleven patients had no comorbidities. In our cohort, at the time of inclusion median BVAS was 6.0 (4.0; 8.0), and median VDI – 2.5 (1.8; 4.0). Total AAV-PRO score median was 149.0 (94.0; 206.5). Among the domains of AVV-PRO, "Treatment Side Effects" has the smallest impact in total score (Table 1). Total AAV-PRO score did not depend on the AAV or ANCA types, as well as the number of co-morbidities, however it was higher in females (162.0 [100.5; 210.8]) than in males (109.0 [78.0; 183.00]) (p=0.03), however significant differences in mean scores was only found in the "Social and Emotional Impact" domain (p=0.04) (Table 1).

Table 1. Mean values and relative weights of AAV-PRO domains in the total score for the entire cohort, male, and female patients.

Domain	Mean (proportion in total score)	Females	Males	p-value
Organ-Specific Symptoms	29.1 (19.1%)	31.0	25.0	0.08
Systemic Symptoms	33.1 (21.7%)	35.0	29.0	0.11
Treatment Side Effects	14.2 (9.3%)	14.1	14.2	0.93
Social and Emotional Impact	26.5 (17%)	29.0	21.2	0.04
Concerns about the Future	31.7 (20.8%)	34.4	25.9	0.07
Physical Function	19.4 (12.7%)	20.7	16.7	0.42

Conclusions: Quality of life is an important outcome for patients with AAV that does not correlate with traditional disease activity and damage scores, but depends on gender. Therefore AAV-PRO should be incorporated in the spectrum of outcome measures both in clinical studies and real-life practice.

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Disclosures: None.

P-081

The Role of ^{18}F-FDG PET/CT scans in Takayasu Arteritis

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Background: Accurate disease activity assessment in Takayasu arteritis (TA) remains challenging. Inadequate treatment may result in irreversible damage. The Indian Takayasu Clinical Activity Scores (ITAS 2010, ITAS.A) are validated and reliable measures of disease activity. ^{18}F-FDG PET-CT imaging has been proposed as important tool to assess disease activity.

Methods: We retrospectively studied 26 TA patients between January 2008 - March 2023. The diagnosis was confirmed on clinical, laboratory and imaging criteria. Disease activity, as assessed by the ITAS 2010, clinical, laboratory and imaging techniques (including MRI, doppler ultrasound and/or digital subtraction angiography) was compared with the results of the PET-CT scans.

Results: Median age at TA diagnosis was 33 years (13-57). There were 22 females (84.6%) and 4 males. Majority were Caucasians (61.5%), Asians (30.8%) and Afro-Caribbean (7.7%). Median follow up was 156 months (20 - 444). Thirteen of 26 patients (50%) had positive antiphospholipid antibodies (aPL) and 3 were diagnosed with anti-phospholipid syndrome (APS).

Of 26 patients, there were 43 PET/CT scans performed in 22 patients. Ten patients had a single scan and 12 patients had multiple scans (maximum 4 scans). Nine scans were done for diagnosis and 34 during follow up. Of the 9 diagnostic scans, all 9 had clinically active disease (ITAS score≥ 2), 8 (88.9%) had raised inflammatory markers (median ESR 57, median CRP 46) and 7 (77.8%) had a positive PET scan (suggestive of active vasculitis). Of the 34 follow up scans, 27 scans (in 17 patients) had clinically active disease (ITAS score ≥ 2) and 7 scans (in 6 patients) were in remission (ITAS score 0). Of the 27 scans with clinically active disease, 12 scans were positive (44.4%). In the remaining 15 scans, 11 (73.3%) were done while on steroids and/or immunosuppression (median prednisolone dose 5mg (2.5 -10mg)). The 7 follow up scans in clinical remission and had no FDG uptake.

Conclusion: 18F-FDG PET-CT scanning is a helpful diagnostic and monitoring tool to assess disease activity in TA. PET scan imaging correlates with ITAS activity. Corticosteroid therapy may negatively impact the PET scan results and should be correlated carefully.

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Disclosures: None.

Table 1: Role of PET scan in Takayasu Arteritis (TA).

Groups	No. of scans (n)	Median ESR (range)	Median CRP (range)	ITAS ≥ 2 (n)	PET +ve (n)	%
1. Patients with active disease (symptomatic ± raised ESR/CRP)						
• For diagnosis	9	57 (20-115)	46 (1-126)	9	7	77.8%
• For flares	10	47 (11-118)	35 (8-48)	10	6	60%
2. Asymptomatic patients with raised ESR, CRP	2	65 (15-115)	18 (6-30)	0	0	-
3. Asymptomatic patients with radiological progression	7	15 (8-53)	9 (1-34)	7	2	28.6%
4. Symptomatic patients with normal ESR, CRP	10	5 (2-17)	1 (0-3)	10	4	40%
5. Patients in remission (normal ESR/CRP, asymptomatic)	5	6 (2-20)	2 (0-2)	0	0	-
Total	43					

P-082

Systemic treatments for ANCA-Associated Vasculitis can stabilise or improve lung function in patients with MPO-related Interstitial Lung Disease

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Background / Objectives: The relationship between Interstitial Lung Disease (ILD) and ANCA-associated vasculitis (AAV) is complex. Studies focused on therapeutic strategies to treat ILD progression in AAV are lacking and provide conflicting conclusions; clinicians often opt for systemic therapies evidenced for use in preventing kidney failure and mortality in AAV without the presence of ILD. We reviewed cases of Myeloperoxidase-related ILD (MPO-ILD) who developed and were treated for organ-threatening AAV with conventional vasculitis treatment regimens with a focus on respiratory outcome and death.

Methods: At a tertiary centre for vasculitis co-located with a tertiary ILD service, we identified patients with a dual diagnosis of ILD and organ-threatening AAV discussed at the Vasculitis MDT between 1/1/2019 and 1/1/2022. ILD (UIP or NSIP pattern) was confirmed at specialist ILD MDT. All patients were MPO-ANCA positive and had clinical features of multisystem vasculitis. Demographic, clinical and outcome data were collected using the electronic patient record in order to characterise key clinical, diagnostic and management features.

Results: See Table 1. Three male and six female patients were identified with an average age at ILD diagnosis of 68 years. One female had both MPO-ANCA and anti-glomerular basement membrane (anti-GBM) antibodies; all others were MPO positive alone. ILD symptoms and diagnosis preceded AAV diagnosis and MPO antibody detection in 6/9 and were diagnosed contemporaneously in 2/9. All patients had evidence of glomerular involvement in AAV. Four patients had significant improvement in lung function following systemic vasculitis treatment (≥10% change from baseline FVC in 3). Three patients died; two of these had end-stage renal failure (ESRF). Time from induction treatment to death was 26/102/60 months respectively.

Conclusions: Systemic treatments for AAV can stabilise or improve lung function in a proportion of patients with MPO-ILD. The presence of both MPO-ILD and ESKD confers poor prognosis. As new treatments for both AAV and progressive fibrotic ILD are becoming available, there is urgent need to develop safe and effective protocols for management of MPO-ILD, and to identify biomarkers that predict response to treatment which may identify treatment-responsiveness.

Table 1: Demographics, Management and Outcomes of Patients with MPO Interstitial Lung Disease Who Received Treatment for ANCA-Associated Vasculitis.

Gender	Age at ILD Diagnosis	ILD pattern	Time between ILD and AAV diagnosis (Months)	Initial indication for Treatment	Treatment	Pre Treatment FVC (L)	%Pred	Post Treatment FVC (L)	%Change in FVC Post Treatment
F	77	UIP	0	ILD progression; RPGN	MP, Pred, Cyclo, RTX	1.53	78.0	1.50	-2.0
M	67	UIP+GGO	30	RPGN	CYC, Pred, AZA	2.47	77.0	2.57	+4.0
M	69	UIP+GGO	32	RPGN	MP, Pred, Cyclo, RTX	3.36	98.0	2.02	+39.9
F	58	UIP+GGO	9	ILD progression	Pred, Cyclo, AZA	2.57	67.5	2.52	-2.0
F	77	Nodules+GGO	0	ILD progression; RPGN	Pred, AZA	2.20	105.0	2.42	+10.0
F	67	UIP+GGO	9	RPGN	Pred, Cyclo, AZA, RTX	2.48	113.0	2.04	-17.7
F	75	UIP+GGO	10	respiratory failure; RPGN	MP, Pred, Cyclo, RTX, PLEX	1.14	50.0	1.46	+28.0
M	86	UIP+GGO	48	respiratory failure; RPGN	MP, pred, RTX	2.50	114.0	Unable to do test; off oxygen, sats 95% on air	-
F	36	NSIP	132	respiratory failure;RPGN	Pred, MMF then Cyclo. RTX	1.10	36.0	Unable to do test; ambulatory oxygen 2L	-

Key for Table 1:

ANCA=Antineutrophil Cytoplasmic Antibodies; AKI=acute kidney injury; AZA=Azathioprine; CKD=chronic kidney disease; Cyclo=Cyclophosphamide; ESRF=End Stage Renal Failure; FVC= Forced Vital Capacity; GGO=ground glass opacity; ILD=Interstitial Lung Disease; MP=Methylprednisolone; MPO=Myeloperoxidase; MTX=Methotrexate; NSIP=non-specific interstitial pneumonia; PLEX=Plasma Exchange; Pred=Prednisolone; RTX=Rituximab; sats= oxygen saturations on pulse oximetry; UIP=Usual interstitial Pneumonia; %Pred=Percentage of Predicted FVC.

P-083

Peripheral Eosinophilia & Pulmonary Function in Granulomatosis with Polyangiitis and Microscopic Polyangiitis, a retroscpective study

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Background/ Objectives: Granulomatosis with polyangiitis (GPA) has been reported to have a rare eosinophilic variant [1]. The exact frequency of this association has not been established. Overlap with eosinophilic granulomatosis with polyangiitis (EGPA) has been entertained, but the associations are poorly understood. In this retrospective study, we investigated these associations.

Methods: Retrospective chart review of the Minnesota Multidisciplinary Vasculitis Program (MMVP) was conducted. Highest eosinophil count was recorded in all patients who had positive ANCA between 11/2018 & 9/2023, & pulmonary function tests results (PFT) data, excluding EGPA patients. Findings were compared with patients in the registry who had negative ANCA serologies as controls, majority of which had a diagnosis of systemic lupus erythematosus. Data was analysed using Excel ver. 16.79. Chi-square testing was used for categorical data, and two-sample t-test was used for continuous data comparison.

Results: We reviewed 307 patients in MMVP. Positive ANCA was found in 45 patients (table 1), & 2 were excluded for EGPA. Among those patients, MPO-ANCA was positive in 14 (32.6%), and PR3-ANCA in 21 (48.8%), & both antibodies in 8 (18.6%). ANCA-positive patients had a mean peripheral eosinophil count of 498 cell/mcL (+- 306) vs. 333 (+-305) in ANCA-negative patients, p=0.017.

Using eosinophilia definition as >300 cells per mcL, 29 ANCA-positive patients had eosinophilia (67%) vs 14 ANCA-negative patients (35%), p=0.002.

Obstruction was defined by forced expiratory volume 1 divided by forced vital capacity (FEV1/FVC) of < 70%. Among ANCA-positive patients, 20 had spirometry, with 5 having obstruction (25%). While in ANCA-negative patients, 8 had spirometry with 1 having obstruction, p=0.466.

	ANCA positive	ANCA negative	p value
N	43	40	
Age (SD)	59.97 (17.04)	45.19 (19.28)	< 0.001
Female sex (%)	23 (54.5)	28 (70)	0.122
Weight kg (SD)	95.95 (38.47)	81.56 (26.44)	0.051
Never smokers (%)	26 (60.4)	25 (62.25)	0.849
Max eosinophil count (SD)	498 (306)	333 (305)	0.017
Patients with Max eosinophils > 300	29 (69)	14 (35)	0.003
FEV1/FVC (SD) *	75.48 (12.73)	77.75 (11)	0.644
FEV1% (SD) *	82.67 (20.75)	78.25 (25)	0.666
Positive BD (%) †	2 (33.3)	1 (25)	0.778
DLCO % predicted (SD) ‡	83.65 (25.33)	86.57(23.24)	0.786
DLCOcor Hb % predicted (SD) §	98.2 (20.67)	80 (32.69)	0.442

Table 1. Demographics, maximum eosinophil count in record & PFT comparison in ANCA-positive vs ANCA-negative patients excluding EGPA. DLCO=diffusion capacity of carbon monoxide. * Only 20 vs 8 patients had spirometry. † Only 6 vs 4 patients had a bronchodilator test. ‡ Only 19 vs 7 patients had DLCO. § Only 9 vs 3 patients had DLCO corrected for Hb.

Conclusions: In this retrospective study, peripheral eosinophilia was significantly higher in ANCA-positive patients compared to ANCA-negative controls. Eosinophilic features in non-EGPA ANCA vasculitis are likely underreported or overlooked and warrant further research to better understand the potential pathologic role of eosinophils in small vessel vasculitis and overlap with asthma and atopy.

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P-084

Carotidynia is the main predictor of future relapses in a large early Inception Cohort in Takayasu's Arteritis

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Background/ Objectives: To present the preliminary results of a Takayasu Inception Cohort settled for long term, prospective follow-up of only newly-diagnosed patients with TAK.

Methods: TAK patients diagnosed in the last 12 months were included. Patients' data were recorded in an electronic database of an international "Takayasu's Arteritis Registry". Data is compared with an historical Turkish cohort previously published.

Results: The study included 215 patients with TAK from 15 tertiary centers in Turkey (age: 38.4±13.3 years, F/M: 181/34). The follow-up duration was median 46 (2-124) months. The most frequent symptom was limb claudication (58%). The most frequent angiographic type was type 1 (56%).

Compared to our retrospective cohort limb claudication was observed to be more frequent, whereas pulselessness was less in the inception cohort. Carotidynia was present only in the inception cohort. Mucocutaneous symptoms also seem to be a feature of newly-diagnosed disease (Table 1).

At diagnosis 87% patients received oral corticosteroid (CS) therapy (0.5-1 mg/kg), 13% also having CS pulses. In addition to CSs, 127 patients were given methotrexate, 38 azathioprine, 9 cyclophosphamide, 6 leflunamide, 4 patients mycophenolate mofetil and 20 patients biological agents (16 TNF inhibitors, 5 tocilizumab).

126 (59%) patients had follow-up data. At least one remission was observed in 79%, relapse was observed in 26% of the patients. Carotidynia was more frequent in patients with relapse (32% vs 10%, p=0.015). Also, carotidynia was associated with relapse in logistic regression (OR (95% CI): 4.13 (1.26-13.52), p=0.019).

CS was discontinued in 41 (33%) patients at the end of the follow-up. The treatment was cDMARDs in 66% and biological DMARDs in 34% patients (23 TNF inhibitors, 12 tocilizumab) at last visit.

Mortality rate was 1.6 % during the follow-up. In 9 (7.1%) patients a revascularization procedure was performed after diagnosis.

Conclusions: Our results suggest that, in an inception cohort, signs and symptoms of 'systemic inflammation' is more prominent in newly diagnosed TAK patients. Whereas vascular extent and damage accumulates during the disease course. During long-term follow-up 26% of patients relapse within 4 years after diagnosis. Carotidynia was found the main predictor factor for future relapses.

Disclosures: None.

Table 1. Comparison of the manifestations of the patients in the inception cohort and retrospective Turkish cohort.

	Inception cohort (n= 214)	Retrospective cohort Bıcakcigil et al (n=248)
Gender, F	181 (84)	228 (92)
Age, years	38.4±13.3	33.1±12
Systemic symptoms, n(%)	142 (66)	163 (66%)
Cardiovascular system, n(%)	154 (72)	141 (57)
Angina	39 (18)	
Carotidynia	36 (17)	-
Limb claudication	124 (58)	119 (48)
Pulselessness	72/201 (36)	218 (88)
Respiratory system, n(%)	50 (23)	22 (12)
Abdominal manifestations, n(%)	38 (18)	-
Nervous system, n(%)	82 (58)	156 (63)
Musculoskeletal system, n(%)	118 (55)	104 (42)
Mucocutaneous, n(%)	36 (17)	22 (8.8)
Ophthalmologic involvement, n(%)	27 (13)	57 (36)
Coroner artery involvement, n(%)	7/187 (4)	22 (8.9)
Pulmonary artery involvement, n(%)	7/190 (4)	17 (6.9)
Angiographic type, n(%)		
Type 1	120 (56)	79 (32%)
Type 5	43 (20)	126 (51%)

P-085

Biological treatment may be an option as first steroid-sparing agent in a subgroup of young Takayasu Arteritis patients with prominent acute-phase reactants and constitutional symptoms

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Background/ Objectives: There is no data regarding in which patients biologic disease-modifying anti-rheumatic drugs (bDMARDs) treatment should be chosen in Takayasu's arteritis (TAK). In this study we aimed to assess the characteristics of TAK patients needed biologic treatment during follow-up in daily practice.

Methods: Patients fullfilling the American College of Rheumatology 1990 criteria for TAK and who received conventional DMARDs (cDMARDs) or bDMARD were included in this retrospective multicentre study. Demographic and clinical data were collected from patient files.

Results: We included 329 patients (F/M: 284/45) in the study at last visit. The number of the patients who received bDMARD was 113 (34%)(89 TNF inhibitors, 24 tocilizumab) and who received only cDMARDs was 216 (66%) during follow-up. Mean age at the end of the follow-up was 43.0±13.5 years and mean follow-up duration was 78.7± 65.8 months. Patients who received bDMARDs were younger compared to patients who received cDMARDs (36.8±11.3 vs 46.2±13.2 years, $p<0.01$) at last visit assessment. The frequency of constitutional symptoms at baseline visit was higher in bDMARD group (85% vs 66%, $p<0.01$). Also baseline erythrocyte sedimentation rate (ESR) (bDMARD vs cDMARD: 66.7±33.5 vs 45.0±29.1 mm/h, $p<0.01$) and CRP levels (19 (0.3-280) vs 12.5 (0.2-286) mg/L, $p= 0.002$) were higher in patients who were given bDMARD treatments. Number of relapses were higher in patients who needed bDMARDs during follow-up.

Conclusions: In this study, TAK patients with biologic treatment need during follow-up had more frequent constitutional symptoms and higher acute phase reactants with a higher relapse rate compared to patients receiving cDMARD treatment. Our results may suggest that in young TAK patients with prominent acute phase reactants and constitutional symptoms at diagnosis, biologic treatment may be an option as first sparing agent.

Disclosures: None.

Table1. The comparison of the characteristics of TAK patients who received cDMARD and bDMARD treatments.

	cDMARD (n=216)	bDMARD (n=113)	p
Age, years, mean ±SD	46.2±13.2	36.8±11.3	**<0.01**
Gender, female, n(%)	186 (86)	98 (87)	0.80
Age at symptom onset, years, mean ±SD	34.9±12.9	25.4±8.3	**<0.01**
Age at diagnosis, years, mean ±SD	38.0±13.1	27.9±8.6	**<0.01**
Diagnostic delay, months, mean ±SD	38.7±54.9	31.9±41.6	0.57
Baseline clinical characteristics			
Constitutional symptoms, n(%)	143 (66)	96 (85)	**<0.01**
Claudication, n (%)	156 (72)	71 (63)	0.08
Carotydinia, n (%)	47 (22)	31 (27)	0.28
Cerebrovascular event, n (%)	17 (8)	3 (3)	0.07
Coronary artery disease, n (%)	19 (9)	3 (3)	0.08
Angiographic type 5, n(%)	84 (45)	49 (45)	0.99
Baseline disease activity			
PGA, active disease, n (%)	196 (96)	95 (93)	0.35
PGA (0-10), mean ±SD	7.3±1.6	7.3±1.9	0.50
Kerr, active disease, n(%)	187 (93)	91 (92)	0.72
ITAS 2010, mean ±SD	11.6±4.6	11.3±6.3	0.39
Laboratuvar			
ESR, baseline, mm/h, mean ±SD	45.0±29.1	66.7±33.5	**<0.01**
CRP, baseline, mg/L, median (min-max)	12.5 (0.2-286)	19 (0.3-280)	**0.002**
Follow-up duration, months, mean ±SD	73.0±58.3	73.2±53.2	0.97
Number of relapses, median (min-max)	0 (0-3)	1 (0-5)	**<0.01**
Mortality, n%	7 (3)	3 (3)	0.62

PGA: Physician global assessment, ITAS: Indian Takayasu Clinical Activity Score ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, bDMARD: biologic disease-modifying anti-rheumatic drug, cDMARDs: conventional DMARDs.

P-086

Impact of Clinical Predictors on Outcomes in ANCA Glomerulonephritis

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Background/ Objectives: Kidney involvement in anti-neutrophil cytoplasmic antibody (ANCA) vasculitis confers significant morbidity and mortality. Early response of kidney function to therapeutic intervention has not been incorporated in management guidelines yet. Here, we investigated three national registries for the impact of acute kidney disease (AKD) on long-term kidney outcomes.

Methods: We investigated patients with ANCA glomerulonephritis (GN) of German, Scottish and Irish registries (n=808) for clinical parameters predicting kidney and patient outcomes. Repeat measurement of kidney function after initiation of immunotherapy was used to define acute kidney disease (AKD). AKD stage 1 was present in the case of 25% improvement in serum creatinine. A stable kidney function meant AKD stage 2. A further 25% deterioration or the need for kidney replacement therapy was defined as AKD stage 3. Unadjusted and adjusted multivariable Cox regression analyses were performed to quantify the associations of patient characteristics, kidney disease and extra-renal manifestations with the development of end-stage kidney disease (ESKD) and mortality.

Results: Median follow-up was 42 months (interquartile range, IQR, 27-61). During follow-up, 147 patients (18.2%) died and 160 patients (19.8%) developed ESKD. The AKD stages predicted ESKD independently of age and the CKD stage at presentation ($p < 0.001$).

Conclusions: Adjusting management to individual patient risks is needed to personalise medicine in vasculitis. The newly defined AKD stages predicted kidney outcomes independently of other prognostic factors. AKD might therefore assist in timely adjustments of immunotherapy to improve kidney and patient survival. Incorporating AKD stages into risk stratifications will likely improve the prediction of ESKD and mortality.

References: None.

Disclosures: None.

P-087

Comparison of methotrexate and azathioprine as the first steroid-sparing immunosuppressive agent in patients with Takayasu's Arteritis

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Background/Objectives: There is limited data comparing conventional disease-modifying anti-rheumatic drugs (cDMARDs) as the first-line immunosuppressive (IS) treatment. We aimed to compare the outcomes of methotrexate (MTX) and azathioprine (AZA), which were used most frequently as the first-line cDMARDs, in TAK patients.

Methods: TAK patients who received cDMARDs as the initial therapy were included in this multicenter, retrospective cohort study. Clinical, laboratory and imaging data were assessed. A match analysis (cc match) was performed between patients who received MTX or AZA as the first-line cDMARD.

Results: We included 301 (F/M: 260/41, mean age: 42.2±13.3 years) patients from 10 centres. As the first-line cDMARD, 204 (67.8%) patients received MTX and 77 (25.6%) received AZA. First cDMARD was cyclophosphamide in 17 (5.6%), leflunomide in 2 (0.5%) and mycophenolate mofetil in one patient. The remission, relapse and radiographic progression rates were similar between patients who received MTX and AZA. Vascular surgery rate was higher in the AZA (23% vs. 9%, p=0.001), the frequency of patients receiving ≤5 mg/day GCs at last visit was higher in the MTX group (76% vs 62%, p=0.034) (Table 1). The rate of vascular surgery was higher in AZA group in match analysis. Drug survival was similar between MTX and AZA groups (median 48 months, MTX vs AZA: 32% vs 42%, p=0.34).

Conclusions: Remission, relapse, radiographic progression and drug survival rates of AZA and MTX were similar in TAK patients having the first-line of therapy. The rate of vascular surgery was higher and the rate of GC dose reduction was lower with AZA compared to MTX at the end of the follow-up.

Disclosures: None.

Table 1. Demographic and clinical characteristics of patients with Takayasu's arteritis.

	Total group (n=301)	First-line methotrexate (n=204)	First-line azathioprine (n=77)	p
Age, mean±SD	42,2±13,3	43,5±13,3	40,4±13,2	0,08
Gender, female, n(%)	260 (86)	184 (90)	63 (82)	0,055
Duration of first cDMARD, months, median (min-max)	35 (3-336)	35,5 (3-312)	35 (3-336)	0,64
Remission with first cDMARD, n(%)	193/296 (65)	138/199 (69)	50/77 (65)	0,48
Disease activity (baseline)				
PGA, active, n (%)	283/297 (95)	191/201 (95)	74/77 (96)	0,70
Kerr, active, n (%)	270/289 (93)	181/195 (93)	70/75 (93)	0,53
ITAS 2010, median (min-max)	9 (2-20)	9 (0-19)	10 (3-21)	0,61
Disease activity (12th month)				
PGA, active, n (%)	53/118 (45)	33/76 (43)	18/39 (46)	0,78
Kerr, active, n (%)	32/120 (27)	24/79 (30)	6/38 (16)	0,26
ITAS 2010, median (min-max)	1 (0-11)	1 (0-9)	1 (0-11)	0,48
Relapse rate, n(%)	95/192 (50)	68/138 (49)	24/49 (49)	0,97
Vascular surgery rate with first cDMARD, n(%)	40/291 (14)	17/196 (9)	18/77 (23)	**0,001**
GC dose reduction (≤5 mg) or discontinuation with first cDMARD, n(%)	153/220 (70)	110/145 (76)	100/65 (62)	**0,034**
Radiographic progression, n(%)	75/142 (53)	48/98 (49)	22/39 (56)	0,43
CRP, baseline, mg/L, median (min-max)	13 (0,4-235)	15,3 (0,5-280)	19,0 (0,4-145)	0,82
CRP, 12th month, mg/L, median (min-max)	3 (0,8-130)	4,4 (0,2-200)	3,7(0,4-83)	0,90

PGA: Physician global assessment, cDMARD: conventional disease-modifying anti-rheumatic drugs, ITAS 2010: Indian Takayasu's Activity Score, CRP: C-reactive protein.

P-088

Lower total skeletal score in patients with giant cell arteritis and polymyalgia rheumatica symptoms compared to patients with isolated polymyalgia rheumatica

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Background/Objectives: To evaluate the difference in articular FDG uptake between patients with isolated polymyalgia rheumatica (PMR) and patients with giant cell arteritis (GCA) and PMR symptoms.

Methods: Patients with PMR or GCA with PMR symptoms who underwent FDG PET imaging ≤3 days after initiation of glucocorticoids between 2003 and 2020 at the University Hospitals Leuven, were included retrospectively. FDG PET scans were visually scored in 12 articular regions (score 0-2), which were summed to a total skeletal score (TSS).

Results: We included 484 patients with PMR symptoms (age 70 years, 58% females), of which 121 (25%) GCA and 363 (75%) isolated PMR patients. GCA patients had a significantly lower TSS than PMR patients (13 [IQR 6-18] vs 19 [IQR 16-21], p<0.001) **(Table 1)**. However, there was no significant difference in the TSS in GCA patients with only PMR symptoms and isolated PMR patients without cranial symptoms (18 [IQR 13-21] vs 19 [IQR 16-22], p=0.08).

Conclusions: GCA patients with PMR symptoms had a lower TSS than isolated PMR patients. This should be confirmed in a prospective trial correcting for the severity of PMR symptoms.

References: None.

Disclosures: LM: Roche; DB: Roche, GSK, Eli Lily; LB, AB, SV: none.

Table 1: Comparison of the total skeletal score between isolated PMR patients and GCA patients with PMR symptoms.

Subgroup	N (%)	TSS, median (IQR)
Isolated PMR without vasculitis on TAB or PET	**363 (75%)**	**19 (16-21)**
• Without cranial symptoms	303 (63%)	19 (16-22)
• With cranial symptoms	60 (12%)	19 (17-20)
GCA with PMR symptoms	**121 (25%)**	**13 (6-18)**
• Only PMR symptoms	35 (7%)	18 (13-21)
• PMR and cranial symptoms	84 (17%)	11 (4-16)
• PMR symptoms and limb claudication	2 (0.4%)	5 (3-7)

Abbreviations: GCA, giant cell arteritis; PET, positron emission tomography; PMR, polymyalgia rheumatica; TAB, temporal artery biopsy.

P-089

Elicitation of physician opinions of the impact of dynamic changes in biomarkers on perceived relapse propensity in ANCA-associated vasculitis

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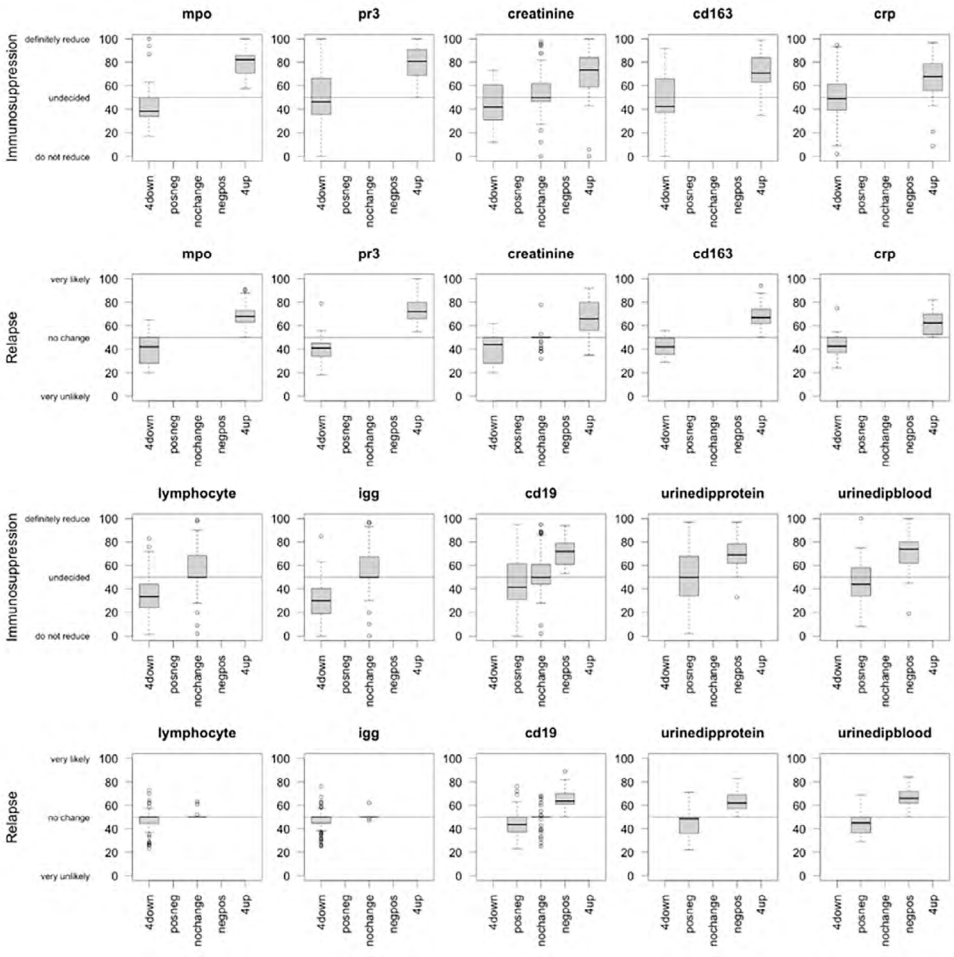
Introduction: ANCA-associated vasculitis (AAV) is characterised by a relapsing and remitting course. Accurate predictive algorithms do not exist. To address data sparsity, using prior knowledge can help to specify informative Bayesian prior distributions or generate synthetic observations from prior knowledge to augment available data. It has been demonstrated that prior expert knowledge on observable endpoints improves the performance of predictive models. To elicit prior knowledge on the association of changes in time-varying variables and clinical endpoints, we investigated the beliefs of AAV experts about how biomarker changes influence their assessment of relapse probability and intention to change treatment.

Methods: 10 synthetic clinical cases representing a range of clinical parameters and time points were devised. Clinical experts (immunology n=1, nephrology n=5, rheumatology n=4) with an average of 20.4 years' experience in treating patients with AAV were recruited from Ireland, UK, Spain, Netherlands, Germany and Australia. Following panel discussion 10 time-varying biomarkers were selected: creatinine, anti-MPO, anti-PR3, sCD163, lymphocyte count, urine protein, urine blood, IgG level and CD19 count. Considering pre-defined changes in these variables (e.g. 4-fold rise in creatinine over 3 months), we assessed the perception of change in relapse risk and intention to change immunosuppression (IS) over the 9-24 months after the time point in question. The questionnaire was iteratively refined in two test rounds using a Delphi approach. For each variable, where relevant, we assessed a rise and fall, positive to negative, or negative to positive switch. The 290-question survey was conducted using a dimensionless scale with a slider to capture responses, with extremes of responses labelled on oppositive ends. When considering IS response 100 represents a definite decision not to reduce IS, 50 an undecided viewpoint and 0 a definite decision to reduce IS. When considering relapse risk perception 100 represents that future relapse is very likely, 50 no change in relapse risk and 0 that relapse is very unlikely.

Results: Reduction in anti-PR3 and anti-MPO were associated with intention to reduce IS (median 46.5 and 38.5 respectively) and reduced relapse risk perception (41 and 42). Similarly, a rise in anti-PR3 and anti-MPO were strongly associated with a decision not to reduce IS (81 and 82.5) and increased relapse risk perception (72 and 68). Other variables are summarised in Fig 1. Clinicians intended to reduce IS if lymphocyte count (33.5) or IgG (30) levels fell, but these biomarkers did not influence perception of relapse risk (50- lymphocyte count, 50- IgG).



Conclusion: Clinical experts were more confident about reducing IS than about relapse probability. This reflects the challenge that clinicians face in accurately identifying long term remission in AAV. There was greater variability in responses regarding intention to reduce IS likely reflecting variation in clinical practice. Greater concordance was seen in responses on relapse prediction. This study provides valuable information on the opinions and practices of clinical experts in managing AAV.

No disclosures

P-090

In-depth analysis of disease manifestations in ANCA-associated vasculitides identifies distinct clinical phenotypes, emphasizing the impact of sex and age at diagnosis

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Background/ Objectives: Granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA), two different ANCA-associated vasculitides (AAV), are clinically heterogeneous. the aims of this study were to identify and characterize subgroups of AAV patients, stratified for sex, age at diagnosis and clinical manifestations.

Methods: In a multicenter study, adult patients diagnosed with GPA or MPA were included between 2008-2018. Clinical data including sex, age at diagnosis, ANCA-specificity, relapse and disease involvement ten different organs were collected from medical records. Organ involvements were analyzed for associations with sex, age at diagnosis and relapse, in GPA and MPA, separately, using logistic regression. Agglomerative hierarchical cluster analysis was performed using the Ward method, based on the n number of axes explaining ³90% of total variability in multiple correspondence analysis of the collected clinical data in GPA and MPA. The optimal number of clusters was estimated by determining the gain in within-cluster inertia achieved at each clustering step[1].

Results: 1156 patients (578 females, 578 males) were included; 922 were classified as GPA, 234 as MPA. In GPA, pulmonary and renal involvement and PR3-ANCA, were significantly associated with male sex, MPO-ANCA was associated with female sex. In MPA, the only difference between the sexes was an older age at diagnosis in males than females. In GPA, the age at diagnosis showed a bimodal pattern with two peaks of incidence with mean (range) at 22.4 (9-31) and 57.1 (32-91) years of age, respectively. Comparing GPA patients younger than 32 years old at diagnosis with those older than 32 identified a significantly higher prevalence of females, ear-nose and throat (ENT)- and gastrointestinal (GI) involvement and relapse rate in the younger group and peripheral nervous system (PNS) involvement in the older group. In all GPA patients, relapse was associated with pulmonary involvement.

Hierarchical cluster analysis of GPA and MPA identified five and seven distinct clusters. For both diseases, three of the clusters were defined by heart-, CNS- and GI involvement, respectively. In GPA, the largest cluster was defined by PR3-ANCA and ENT involvement and the fifth cluster by MPO-ANCA, female dominance and a low rate of ENT involvement. In addition, in several of the clusters in both GPA and MPA, there was a significant enrichment or depletion of additional clinical manifestations, in comparison with the largest cluster.

Conclusions: This study indicates distinct disease courses of GPA in females and males, and strongly suggest that sex and age at diagnosis should be considered in the clinical assessment of disease outcome in GPA patients. The associations between different clinical manifestations in the cluster analysis may facilitate the prediction of organ involvements in patients with AAV, and, subsequently, clinical decision-making.

References:

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Disclosures: None.

1. CLINICAL SCIENCE
1.05. Outcomes: remission, relapse, mortality, patient reported outcomes...

P-091

Pre-pulseless Takayasu arteritis: distinct clinical and angiographic features but similar outcomes – a cohort study

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Background/ Objectives: Nearly a third of Takayasu arteritis (TAK) present without pulse loss. However, differences in the presentation and prognosis of pre-pulseless TAK and TAK with pulse loss have not been systematically studied. This study compares the presentation, angiographic features, evolution, and prognosis of pre-pulseless Takayasu arteritis (TAK) with TAK with pulse loss.

Methods: Pre-pulseless TAK (defined as without pulse loss in the upper limbs, lower limbs, carotid, or subclavian arteries) were identified from a cohort of TAK. Demographic characteristics, clinical features, angiographic involvement, baseline and longitudinal patterns of disease activity, medication use, and mortality rates were compared between pre-pulseless TAK and TAK with pulse loss. Adjusted odds ratios (aOR, with 95%CI) for categorical variables between pre-pulseless TAK and TAK with pulse loss were computed using multivariable-adjusted logistic regression models. Time-to-event data was compared using hazard ratios (HR) with 95%CI.

Results: Compared with TAK with pulse loss, pre-pulseless TAK (91/238, 38.24%) more frequently were males (female: male ratio 57:34 vs 115:32), had deranged renal functions (aOR 4.43, 95%CI 1.58-12.37) and Hata's type IV disease (aOR 8.07, 95%CI 2.58-25.25), and less often had pulse or blood pressure asymmetry (aOR 0.34, 95%CI 0.18-0.63), limb claudication (aOR for upper limb 0.38, 95%CI 0.18-0.82, for lower limb 0.28, 95%CI 0.12-0.68), right subclavian (aOR 0.45, 95%CI 0.23-0.90) or left carotid artery involvement (aOR 0.42, 95%CI 0.21-0.84). Only two patients with pre-pulseless TAK developed pulse loss on follow-up (Figure 1A). Despite fewer pre-pulseless TAK having active disease at presentation (62.64% vs 80.27%), similar proportions of patients in both groups had active disease on follow-up. Mortality (HR 0.41, 95%CI 0.09-1.90, Figure 1B) and the duration of survival on first DMARD (HR 1.11, 95%CI 0.69 - 1.80) were similar in both groups.

Conclusions: Pulse loss on follow-up is uncommon in pre-pulseless TAK, reiterating the fact that triphasic disease in TAK is actually rare (1). Pre-pulseless TAK is associated with similar long-term outcomes to TAK with pulse loss.

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Disclosures: None.

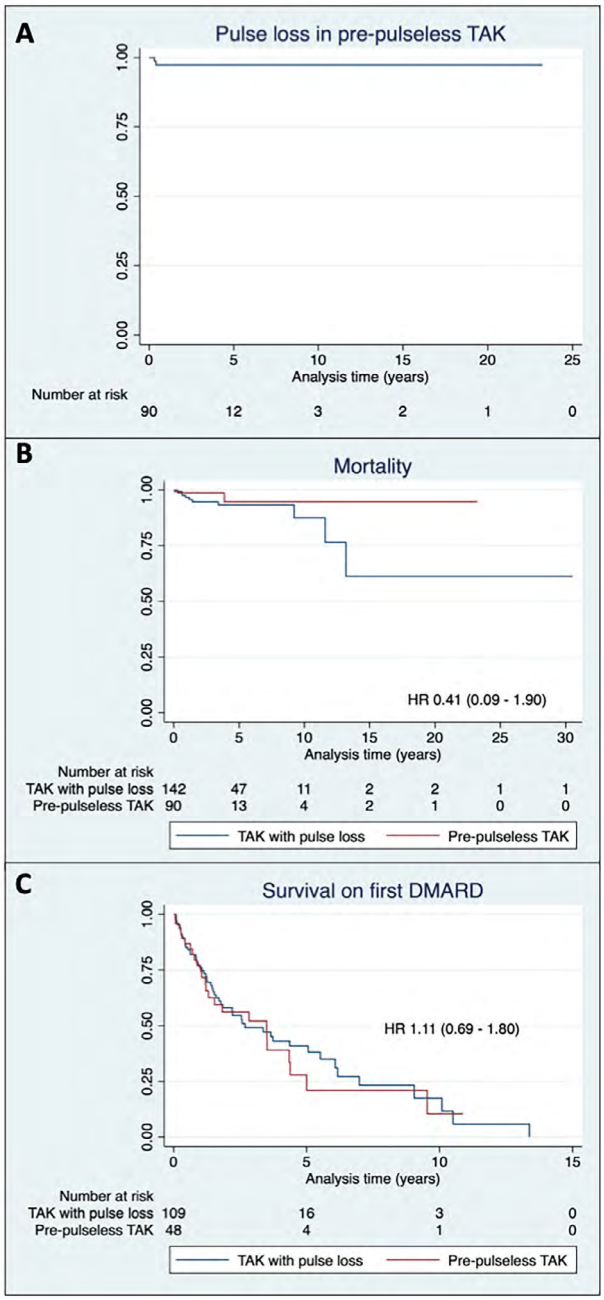

Figure 1: A: Kaplan-Meier curve for subsequent pulse loss in those with pre-pulseless TAK at presentation. B: Comparison of mortality between TAK with or without pulse loss. C: Comparison of duration of survival on the first disease-modifying antirheumatic drug between TAK with or without pulse loss.

P-092

Longitudinal exploration of changes in educational need among patients with newly diagnosed AAV using ENAT -a pilot-study

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Background/ Objectives: Previous studies have shown that disease duration associate with an increased need of educational support in ANCA associated vasculitis (AAV)[1]. Shorter disease duration showed to significantly increase educational needs although not yet investigated whether the disease duration or time itself is the deciding factor. Longitudinal studies using the Educational Needs Assessment Tools (ENAT) are in general scarce. The aim of this pilot study was to explore how educational needs changes over two years among newly diagnosed patients with AAV using ENAT.

Methods: This pilot study included longitudinal data from the Rheumatology and Nephrology clinics at the Karolinska University Hospital in Sweden during 2009-2022. Inclusion criteria were being diagnosed with AAV, minimum age of 18 years and literate in Swedish. Exclusion criterion was cognitive impairment interfering with literate capabilities. Disease activity was estimated using Birmingham Vasculitis Activity Score version 3 (BVAS). Educational needs were captured by patients' answers to the ENAT questionnaire at baseline and after 24 months. The ENAT consists of 39 questions, presented as total ENAT and seven domains each containing 4-7 items (item answers ranging from 'not at all important' = 0, to 'extremely important' = 3). Paired samples t-test was used to compare means between the two timepoints.

Results: 18 individuals (50% men) with GPA (n=16) and MPA (n=2) completed the questionnaire. At baseline mean age was 52 years, ranging from 20-66, and mean years of education 14.6. Mean disease duration at baseline was 0.2 years. All but three were newly diagnosed at baseline and 3 was diagnosed the year before inclusion. Mean BVAS was 14.8, range 1-25. The mean total ENAT decreased from 85.1 to 74.3 (p=0.03) (Table 1). Change in individual total ENAT scores ranged from +10 to -73. Educational needs decreased within 2/7 domains, 'Self-help measures' 15.4-13.1 (p=0.02) with individual score change ranging from +5 to -13 and 'Treatment' 16.9-12.4 (p=0.005) with individual score change ranging from +7 to -21. Domains indicating lower educational needs at baseline were still low after 2 years. Over time the domain with highest educational needs shifted from 'Self-help measures' at baseline to 'Disease process' at follow-up.

Conclusions: This pilot study demonstrates that patients newly diagnosed with AAV expressed high educational needs at baseline compared to previous studies on both patients with established and newly diagnosed AAV [1]. The educational need decreased over time in total and within two of the domains but was still high after 24 months**.** Our findings point to the fact that patients need continuous educational support during the first years of diagnosis. To further explore patterns and clusters of changes in educational needs more data is needed.

References:

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Disclosures: None.

	0 months n=18	24 months n=18	dif.	p
Managing pain (0–18)	10.6 (58,6%)	10.6 (59%)	+0,1	0,96
Movement (0–15)	8.9 (59.3%)	7.9 (53%)	-0,9	0,35
Feelings (0–12)	8.5 (70.8%)	7.3 (61.1%)	-1,2	0,26
Disease process (0–21)	17.9 (85.4%)	16.8 (79.9%)	-1,2	0,25
Treatments (0–21)	16.9 (80.7%)	12.4 (59.3%)	-4,5	**0,005**
Self-help measures (0–18)	15.4 (85.8%)	13.1 (72.8%)	-2,3	**0,02**
Support systems (0–12)	7.2 (59.8%)	6.5 (53.9%)	-0,7	0,30
Total ENAT (0–117)	85.1 (72.7%)	74.3 (63.5%)	-10,7	**0,03**

Table 1. ENAT raw scores, mean (percentage of domains maximum score).

P-093

Eosinophilic Granulomatosis with Polyangiitis in Southern Sweden – A population-based descriptive cohort study

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Objectives: To describe the clinical features, treatment, and outcome of patients with eosinophilic granulomatosis with polyangiitis (EGPA) in a population-based study from Sweden.

Methods: All patients diagnosed with EGPA between 1997-2019 using the European Medicine Agency (EMA) classification and living in a defined geographical area were analysed. All patients were followed from date of diagnosis to death or April 30th, 2023. Disease activity assessed at onset and 12 months using the Birmingham Vasculitis Activity Score (BVAS). Outcome was assessed by common comorbidities, vasculitis damage index (VDI) at 12 months and occurrence of end stage kidney disease (ESKD) or death. Descriptive statistics, discrete and continuous numerical variables were expressed as mean ± SD or median (IQR). Categorical variables were expressed as number of cases (%).

Results: Twenty-three patients (F/M: 14/9, median age at diagnosis: 60 [37-63]) were included into the study. Total average follow-up time was 100.5±39.3 months (Table 1). Mean BVAS at diagnosis was 13.3±6.3 and median five factor score was 0 (0-1). All but one (22/23), had active disease (BVAS≥1) at the time of diagnosis and received immunosuppressives. High (≥30 mg) and medium (>7.5-30) doses glucocorticosteroids (GC) were applied to 15 and 7 patients, respectively. Median initial GC dose was 45 (30-60) mg/day (Table 1). Cumulative GC dose at 26th week was 3.4±0.96 grams. Plasma exchange was applied to 2 patients presenting with severe cardiac involvement.

At the end of first year, 16 (69.5%) patients were in clinical remission (BVAS=0). Median BVAS was 0 (0-2.25). No stroke, myocardial infarction (MI), pulmonary embolism or ESKD were observed following the first year after diagnosis. One patient had deep vein thrombosis during the first month. At least one item of damage according to VDI (median VDI score= 1 (0-2)) was recorded in 16 patients (69.5%). Median GC dose at 24th month was 5 (5-10) mg/day. One MI at 45th month and one stroke at 68th month were recorded. Six patients (26%) suffered severe infection events, five of these events occurred during the first year. There were no deaths during the first five years of follow-up. Three deaths were recorded during the follow-up and mean time to death after diagnosis was 100±22.5 months. Causes of death were recorded as pancreas and colon malignancies in two patients, heart failure in one patient.

Conclusions: In our EGPA cohort, major organ involvement was relatively rare and high rate of remission was achieved at the end of first year. It is noteworthy that, severe infections were observed in one fourth of the patients within the first year despite relatively mild disease presentation. Absence of ESKD, low frequency of cardiovascular comorbidities, damage, and mortality during follow-up heralds an excellent prognosis.

Disclosures: None.

Table 1. Summary of clinical characteristics, treatment, and outcome of patients with eGPA. ANCA: Anti-neutrophil cytoplasmic antibody, BVAS: Birmingham Vasculitis Activity Score, MPO: Myeloperoxidase, PR3: Proteinase 3, VDI: Vasculitis Damage Index.

Patient characteristics	N	%	Initial manifestations according to BVAS	N	%
Age at diagnosis, years, median (IQR)	60 (37-63)		***General***	13	56.5
Sex, female	14	60.9	Myalgia	7	30.4
Ever- smoker	9	39.1	Arthralgia	4	17.4
MPO-ANCA (+)	8	35.0	Fever	5	21.7
PR3-ANCA (+)	1	4.3	Weight Loss	7	30.4
History of nasal polyposis	15	65.2	***Cutaneous***	4	17.4
History of asthma	23	100	Purpura	3	13.0
BVAS at diagnosis, mean±SD	13.3±6.3		Mouth ulcer	1	4.3
Eosinophil, mean±SD, 10^9	6.33±6.1		***Ear Nose Throat***	16	69.6
Hemoglobin, mean±SD, mg/dl	133.9±18.8		Nasal discharge	10	43.5
Platelet, mean±SD, 10^9	351.2±114.9		Sinusitis	10	43.5
Creatinine, median (IQR), µmol/L	62.5(51-74)		Sensorineural hearing loss	1	4.3
C-reactive protein, median (IQR), mg/dl	12 (2-55)		***Chest***	18	78.3

Patient characteristics	**N**	**%**	**Initial manifestations according to BVAS**	**N**	**%**
1-2 organs involved	6	26.1	Wheezing	14	60.9
3-6 organs involved	17	73.9	Pulmonary nodules	4	17.4
Induction treatment			Pleurisy	4	17.4
Glucocorticosteroids alone	4	17.4	Infiltrate	8	34.8
Cyclophosphamide	9	39.1	***Cardiovascular system***	3	13
Azathioprine	7	30.4	Pericarditis	2	8.7
Methotrexate	2	8.7	Cardiomyopathy	2	8.7
Maintenance treatment			Congestive heart failure	1	4.3
Azathioprine	16	69.6	***Abdominal***	1	4.3
Methotrexate	5	21.7	Bloody diarrhea	1	4.3
Rituximab	1	4.3	***Renal***	4	17.4
Mycophenolate mofetil	1	4.3	Proteinuria	3	13.0
Outcome			Hematuria	1	4.3
BVAS 12m, med (IQR)	0 (0-2.25)		Creatinine > 125 µmol/L	1	4.3
VDI score≥1	16	69.6	Creatinine rise > 30%	1	4.3
VDI 12m, med (IQR)	1 (0-2)		***Nervous system***	7	30.4
Severe infection, 12m	4	17.4	Polyneuropathy	3	13.0
Mortality (all time)	3	13	Mononeuritis multiplex	5	21.7

P-094

Patients with Takayasu arteritis experience worse quality of life, physical function, anxiety, depression, and fatigue than healthy individuals which persist over time

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Background/ Objectives: Since literature on patient-reported outcome measures (PROMs) in Takayasu arteritis (TAK) is scarce (1), we comprehensively assessed PROMs in a cohort of TAK longitudinally and compared them with healthy individuals.

Methods: Consecutive adult patients with TAK were prospectively evaluated for quality of life (QOL, using EQ-5D-3L questionnaire), physical function [using health assessment questionnaire (HAQ)], physical activity (using International Physical Activity Questionnaire – Short Form (IPAQ-SF)], work productivity [using Work Productivity and Activity Impairment- General Health v2(WPAI)], anxiety[using generalized anxiety disorder assessment 7 questionnaire (GAD-7)], depression [using patient health questionnaire 9 (PHQ-9)], fatigue [using 13-item Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT, lower FACIT scores indicate greater fatigue) and Multidimensional Fatigue Inventory (MFI)], and fibromyalgia[using 2010 diagnostic criteria from the American College of Rheumatology (ACR), including the polysymptomatic distress scale (PSD) score]. PROMs were compared between TAK and healthy controls, and between TAK with active or inactive disease as per physician global assessment. PROMs were reassessed in TAK after 6-18 months to assess the stability of observations. Medians with interquartile range (Q1-Q3) were used to represent the data (unpaired data compared using Mann-Whitney U test, paired data using Wilcoxon matched-pairs signed rank test). Categorical data were compared using Chi square test. $p<0.05$ were considered significant.

Results: Eighty-three patients with TAK [60 females, median age 34(26-44) years, disease duration 67 (37-126) months] were compared with 50 healthy controls [34 females, age 30(27-33.25) years]. TAK had worse QOL on EQ-5D visual analog scale and higher scores in domains of mobility, self-care, usual activities, pain/discomfort, and anxiety/depression of the EQ-5D-3L than control subjects. Patients with TAK had worse physical function (HAQ), greater impairment of activity (using the WPAI), higher anxiety (GAD-7) and depression (PHQ-9) scores, and worse fatigue scores (FACIT) than control subjects. Similar proportions of TAK (6/83) or controls (1/50) fulfilled fibromyalgia diagnostic criteria (**Figure 1A**). Active TAK (n=12) had worse scores on the mobility domain of EQ-5D-3L, higher activity impairment due to health (using WPAI) and worse fatigue and PSD scores than inactive TAK (n-71) (**Figure 1B**). Repeat measurements of PROMs in 75 patients with TAK after median 6.5 (6-9) months revealed no significant differences (**Figure 1C**).

Conclusions: Patients with TAK have worse patient-reported outcomes than healthy controls which remain similar on longitudinal assessment. Active TAK have worse fatigue and work impairment than inactive TAK.

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Disclosures: None.

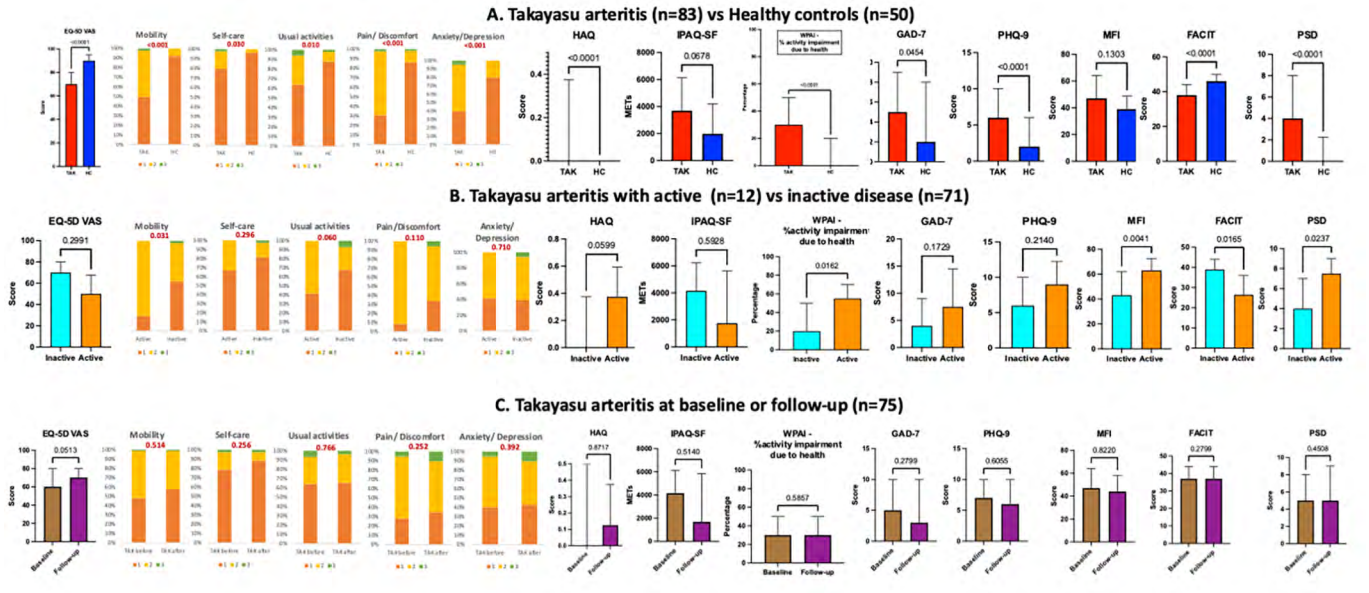

Figure 1: PROMs in TAK. 1A. Comparison between TAK and healthy controls 1B. Comparison between active and inactive TAK 1C. Comparison between TAK on longitudinal follow-up. p values for comparison presented in figures.

P-095

Immunoglobulin A vasculitis in Aotearoa New Zealand

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Background/ Objectives: Immunoglobulin A vasculitis (IgAV) is a small vessel vasculitis. Few studies describe the clinical features and outcomes in adults. Here we describe the clinical features and outcomes in patients, over the age of 16 years, with renal biopsy proven IgAV seen in two regions of Aotearoa New Zealand over an 18-year period.

Methods: Ethical approval was obtained (AHREC 25461). Potential cases were identified, in patients over the age of 16 years, who underwent renal biopsy between 2003-2020. A retrospective review of all potential cases was performed. Data was analysed using SPSS 29.

Results: Thirty-four patients were identified, 10 females and 24 males, of whom 15 were European, 5 Māori, 7 Pacific Peoples, and 7 Asians. There was 318.8 yrs of follow up, mean 9.38 +/- 4.97 yrs.

The incidence was 2.09 cases per 100,000 patient-yrs with no excess by ethnicity. Mean age at presentation was 42.8 yrs (range 16.4-70.5 yrs). Mean creatinine at presentation was 118µmol/L (range 51-410µmol/L). Twenty nine patients had albuminuria and 27 patients had haematuria.

Table 1 - Laboratory data from initial presentation and renal histology data.

Clinical parameter	All patients	No RRT	RRT	P value
Haemoglobin (g/dL)	133 +/- 22	134 +/- 21	128 +/- 26	.559
Platelets (x 10^9/L)	296 +/- 96	301 +/- 99	274 +/- 86	.547
White cell count (x10^9/L)	9.06 +/- 2.85	9.24 +/- 3.03	8.22 +/- 1.66	.433
Serum Albumin (g/l)	36 +/- 6	35 +/- 6	37 +/- 5	.456
Serum creatinine	118 +/- 76	112 +/- 61	146 +/- 130	.321
Urine red cells Absent Present	 7 27	 3 24	 4 3	.86
Albuminuria/Proteinuria Absent Present	 5 29	 4 24	 1 5	.647
Glomeruli (n) Fractional scarring of tubulointerstitium (%) Abnormal arterioles (n) Crescents (n)	17 +/- 11 11 +/- 16 12 10	17 +/- 11 9 +/- 12 1 8	15 +/- 8 21 +/- 25 4 2	 .068 .567 .584

Twenty-six patents received corticosteroids, with 2 patients also receiving cyclophosphamide and 5 patients also receiving azathioprine. Only 1 patient had an admission to hospital due to infection while on immunosuppression. One patient developed steroid-induced diabetes which resolved when steroids were halted and 2 patients developed diabetes during follow-up. Seven patients (20.6%) had cardiovascular events. Four patients (11.8%) developed cancer during follow-up.

Six patients (17.6%) needed chronic renal replacement therapy (RRT), all had dialysis initially with four patients going on to receive a renal transplant. At end of study 12 (35.3%) patients had chronic kidney disease (CKD). Four patients (11.8%) died two of whom were on dialysis.

Conclusions: We see an incidence of of IgAV of 2.09 cases per 100,000 patient-years. Morbidity was high with 17.6% needing RRT and 35.5% having CKD with 11.8% mortality.

References: Nil.

Disclosures: Nil.

P-096

Association between total vascular score and clinical presentation and outcome in giant cell arteritis: a retrospective cohort study

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Background/ Objectives: To evaluate if the extent and intensity of ^{18}F-fluorodeoxyglucose (FDG) uptake in large vessels is associated with the clinical presentation and outcome of patients with giant cell arteritis (GCA).

Methods: Patients with a diagnosis of GCA between 2003 and 2020 who have had FDG positron emission tomography (PET) imaging at diagnosis ≤3 days after initiation of glucocorticoids (GC) and who were followed for ≥12 months at the University Hospitals Leuven, were included retrospectively. PET scans were visually scored (0-3) in 7 vascular areas and a total vascular score (TVS) was calculated, ranging from 0 to 21.

Results: We included 239 GCA patients (mean age 71 year, 65% females). Median duration of follow-up was 46 months (IQR 25-87). Median TVS was 6 (IQR 1-14). TVS was negatively correlated with age (R=-0.24, p<0.001) and positively with symptom duration until diagnosis (R=0.33, p<0.001). Higher TVS was associated with female sex (OR 1.10 [95%CI 1.06-1.15], p<0.001), with a higher odds of having constitutional symptoms (OR 1.09 [95%CI 1.04-1.15], p<0.001) and a lower odds of having PMR symptoms (OR 0.96 [95%CI 0.92-0.99], p=0.02) and cranial symptoms (OR 0.95 [95%CI 0.91-0.98], p=0.005). In contrast, higher TVS was associated with a higher odds of a positive temporal artery biopsy (OR 1.07 [95%CI 1.03-1.12], p=0.002) and FDG uptake in cranial vessels (OR 1.08 [95%CI 1.04-1.13], p<0.001). Adjusted for age, sex, symptom duration and symptoms at diagnosis, logistic regression analysis showed a higher risk of relapse with higher TVS (OR 1.06 [95%CI 1.01-1.11], p=0.01). There was a trend towards a longer duration of GC treatment with higher TVS (R=0.12, p=0.06). The cumulative GC dose in the first 2 years after diagnosis was positively associated with higher TVS (R=0.18, p=0.007).

Conclusions: GCA patients with higher TVS more frequently reported constitutional symptoms and less frequently had PMR and cranial symptoms. Higher TVS was positively associated with the risk of relapse with a trend towards a longer duration of GC treatment with higher GC doses. Prospective studies are needed to determine if TVS can be used to stratify the treatment of GCA patients.

References: None.

Disclosures: LM: Roche; DB: Roche, GSK, Eli Lily; LB, GM, AB, SV: none.

P-097

Evaluation of group education for patients with large vessel vasculitis prescribed subcutaneous methotrexate

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Background: Patient education in Rheumatology has proved to be beneficial to patients for many years[1]. This has been delivered in a multitude of ways in person and more recently with the use of multi-media modalities. It has been recognised that patient education on long term conditions and its treatment improves health outcomes and has the potential to reduce demand on health care services[2]. There is little evidence to demonstrate the benefit of patient education for patients diagnosed with vasculitis. Education needs to be adapted to meet patient needs. As well as offering one-to-one appointments in person, on the telephone or via video, we decided to trial in-person group education for this patient group.

Methods: Patients prescribed subcutaneous methotrexate for large vessel vasculitis were given the opportunity to attend a group education session run by the specialist nurse. The sessions were held over a 4-month period, in groups of 3-5 individuals. Patients were provided with written information including the links to online resources prior to attending the group education session which consisted of a verbal presentation and a short video. Patients also had the opportunity to ask questions during the group session. If patients were happy to proceed with the planned treatment, a prescription for the subcutaneous methotrexate was provided and initial blood monitoring commenced. After attending the group session, patients were given an evaluation form to complete.

Results:

Q1 Did you feel the presentation of the session was clear and easy to follow?	Completely	25 (100%)	Mostly	0	Not at all	0		
Q2 Were any handouts clear and easy to read	Completely	25 (100%)	Mostly	0	Not at all	0		
Q3 How do you feel about the length of the session	Too long	0	About right	25 (100%)	Too short	0		
Q4 Did the session cover everything you felt you needed to know	Completely	23 (92%)	Mostly	2 (8%)	Not at all	0		
Q5 Did you feel you were given the opportunity to ask questions during or after the session	Completely	22 (88%)	Mostly	3 (12%)	Not at all			
Q6 Were all questions answered in a way you could understand	Completely	23 (92%)	Mostly	2 (8%)	Not at all	0		
Q7 Overall how useful did you find the educational session for understanding how to take methotrexate	Very useful	25 (100%)	Useful	0	Not useful	0	Not very useful	0

Conclusion: Group education has proved to be a successful way of providing education to patients with large vessel vasculitis needing to learn about the indications for use, along with the safe handling and administration of subcutaneous methotrexate.

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Disclosures: None.

P-098

The Impact of Neurologic Involvement in ANCA-Associated Vasculitis on Health-Related Quality of Life and Accumulated Disease-Related Damage

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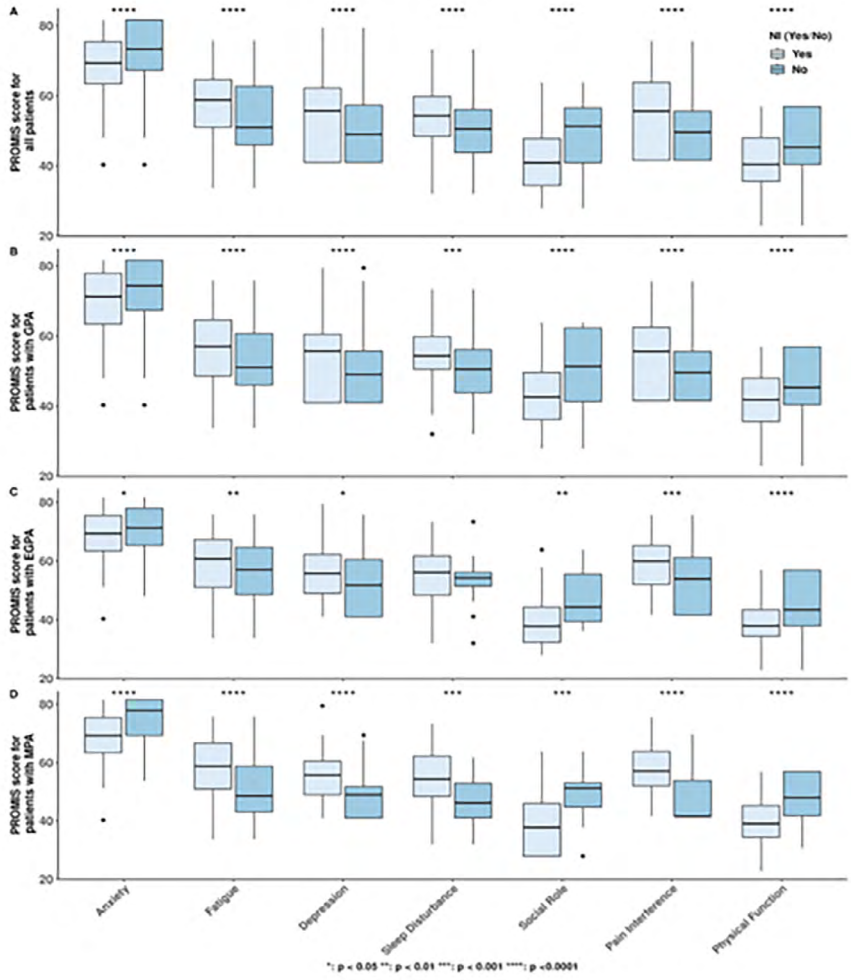
Background/Purpose: Neurologic involvement (NI) is common in patients with ANCA-associated vasculitis (AAV) and can lead to chronic pain and disability. This project assessed the impact of NI on health-related quality of life (HRQoL) in AAV.

Methods: Retrospective analysis of data from 2014-2022 by patients ≥18 years old with AAV [eosinophilic granulomatosis with polyangiitis (EGPA), granulomatosis with polyangiitis (GPA), or microscopic polyangiitis (MPA)] enrolled in Vasculitis Patient-Powered Research Network (VPPRN), an online registry. The VPPRN collects data regarding type of vasculitis, disease manifestations, diagnosis , HRQoL, including Patient-Reported Outcome Measurement Information System (PROMIS) domains. PROMIS measures generate T-scores with the mean T-score = 50 with a standard deviation of 10 in the U.S. general population. Data were analyzed according to NI involvement.

Results: 1465 patients with AAV were included in this analysis; 901 of 1465 (61.5%) patients reported NI. Compared to patients without NI, those with NI were older at the time of diagnosis of AAV, were more likely to be diagnosed with GPA (vs. EGPA or MPA), be positive for ANCA, and more likely to have constitutional, musculoskeletal, skin, mucous membranes, ear/nose/throat, cardiovascular, pulmonary, and thrombotic manifestations of disease. Renal involvement was the same among patients with or without NI. Patients with NI reported greater severity of vasculitis.

Overall, patients with AAV reported reduced HRQoL in almost all domains compared to a reference population. Compared to patients without NI, patients with NI report higher scores for fatigue, depression, sleep disturbance, and pain interference, and lower scores for anxiety, social role, and physical function (**Figure1**).

Figure 1: PROMIS measures in patients with ANCA-associated vasculitis with (light blue) and without (dark blue) neurologic involvement: Compared to patients without neurologic involvement, patients with neurologic involvement had higher scores for fatigue, depression, sleep disturbance, and pain interference, and lower scores for anxiety, social role, and physical function.



Conclusion: NI, as reported directly by patients, is common in AAV, occurring in approximately two-thirds of patients. This rate is higher than has been reported through clinician-documented data, implying that physicians may be under-appreciating the extent of NI in AAV. NI is more common in GPA, compared to EGPA or MPA. Patients with NI have involvement of more organ systems than patients without NI. NI in patients with AAV has a negative impact on multiple domains of illness and health-related quality of life. These patient-reported data are informative for clinicians and patients with AAV and should raise the awareness of the impairment in patients with NI in AAV.

Disclosure: **VPPRN**: VF GSK; **RHA**: Am, GSK, UTD. **PM**: Abb, Am, AZ, BI, BMS, GSK, InflaRx, Takeda.ArGenx, Cabaletta, CSL, Dynacure, HiBio, Janssen, Novartis, NS Pharma, Regeneron, Vistera.

Eicos, Electra, Forbius, Genentech, Genzyme, Neutrolis. Kyverna, Q32, Sparrow, UTD.

P-099

Prevalence, characteristics and outcome of subclinical vasculitis in polymyalgia rheumatica: a retrospective cohort study

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Background/ Objectives: The prevalence of subclinical vasculitis in patients with polymyalgia rheumatica (PMR) was 23% in a recent meta-analysis.[1] Our objective was to evaluate the prevalence, characteristics and outcome of PMR patients with subclinical vasculitis.

Methods: PMR patients without cranial symptoms and limb claudication who underwent FDG PET imaging ≤3 days after initiation of glucocorticoids (GC) between 2003-2020 and who were followed for ≥6 months, were included retrospectively. PET scans were visually scored (0-3). Vasculitis was defined as FDG uptake ≥ grade 2 in any vessel or a positive temporal artery biopsy. PMR patients with and without subclinical vasculitis were compared.

Results: We included 341 patients, of whom 35 (10%) with subclinical vasculitis. Among those with subclinical vasculitis, 20 (57%) had only large vessel vasculitis, 3 (9%) had only cranial vasculitis and 12 (34%) had both cranial and large vessel vasculitis. Patients with subclinical vasculitis had a longer time to diagnosis (23 vs 9 weeks, p=0.007), more frequently reported constitutional symptoms (71% vs 52%, p=0.03) and neck pain (38% vs 21%, p=0.02) and had a lower hemoglobin (11.5 vs 12.5 g/dL, p=0.01) and white blood cell count (8.0 vs 8.7 *109/L, p=0.008). The initial GC dose and GC doses during follow-up were higher in those with subclinical vasculitis until 15 months after diagnosis **(Figure 1)**. There was no difference in the duration of GC treatment (25 vs 20 months, p=0.11). Logistic regression analyses showed no difference in the proportion of patients able to stop GC (63% vs 68%, OR 0.80 [95% CI 0.39-1.69], p=0.54) and in the proportion of patients with relapse (54% vs 52%, OR 1.11 [95%CI 0.55-2.27], p=0.77). Those with subclinical vasculitis had a longer time to first relapse (15 vs 11 months, p=0.007).

Conclusions: Only 10% of our PMR patients had subclinical vasculitis with a predilection for large vessel vasculitis. Patients with and without subclinical vasculitis had a similar clinical presentation. There were no differences in relapse rate and duration of GC treatment, however those with subclinical vasculitis received higher GC doses until 15 months after diagnosis. Interventional trials are needed to evaluate the outcome of PMR patients with and without subclinical vasculitis treated with the same GC tapering protocol.

References:

1. Hemmig AK, Gozzoli D, Werlen L, Ewald H, Aschwanden M, Blockmans D, et al. Subclinical giant cell arteritis in new onset polymyalgia rheumatica. A systematic review and meta-analysis of individual patient data. Semin Arthritis Rheum. 2022;55(April):152017.

Disclosures: LM: Roche; DB: Roche, GSK, Eli Lily; LB, GM, SV, AB: none.

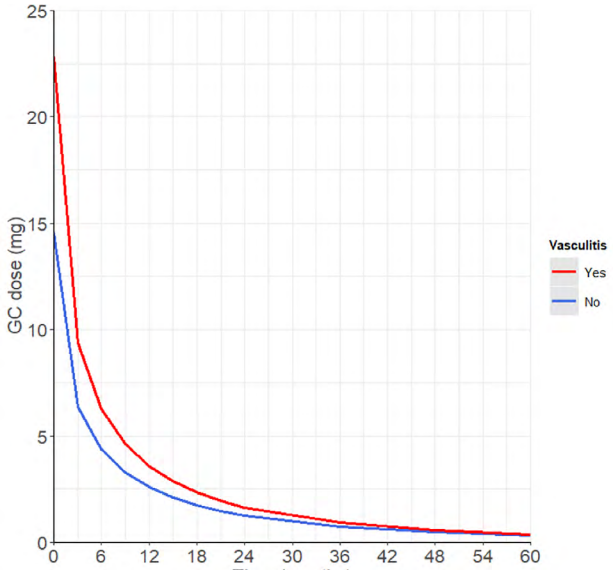

Figure 1: Change in GC dose (expressed in methylprednisolone equivalents) in PMR patients with and without subclinical vasculitis.

P-100

What are the impacts of appearance changes due to glucocorticoids in rheumatic diseases?

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Background/ Objectives: To explore patients' perspectives on the impact of appearance changes attributed to glucocorticoid treatment.

Methods: We conducted a secondary analysis of semi-structured interviews with patients with rheumatic conditions receiving glucocorticoids in the UK, USA, and Australia*. Interview data were analysed inductively to develop preliminary individual and overarching themes.

Results: Sixty patient interviews were analysed. Age 26-84 years; 39 (65%) females, patients with systemic vasculitis (n=19), inflammatory arthritis (n=14), crystal arthropathy (n=2), connective tissue disorders (n=16), other/multiple (n=9). Interviews contained rich data on how appearance changes impacted health-related quality of life. Three preliminary overarching themes were identified.

i) Societal norms: Participants reported pressure to conform to societal ideals which may vary depending on cultural background and gender: *"It didn't help because I grew up in a culture that - I was in fat club, where they take your weight every day."* [Asian female aged 30] and *"I think my main concern, particularly being female, was the weight gain that the steroids had."* [Female (Mixed/Multiple ethnicity) aged 27]

ii) Impact on mental health and sense of self: Glucocorticoids were often described as making participants 'not look like' themselves, associated with changes in mood and self-confidence: *"It makes you feel down. It makes you feel depressed. You don't want to socialise because you're not you."* [White male aged 65] and *"the moon face makes you become insecure because you have a face of a tomato"* [Black female aged 29]

iii) Burden of adjustments included impacts on diet, exercise, clothing (financial outlay), work, hobbies, activities of daily living, and key events: *"I mean I try, regarding weight, […] that's just become a way of life now."* [Male (Mixed/Multiple ethnicity) aged 53] and *"I have a wardrobe right now that goes four different sizes as my weight goes up and down and up and down."* [White female aged 55]

Conclusions: Patients attribute a variety of impacts on their health-related quality of life to glucocorticoid-related appearance changes and report a burden of adjustments above management of their chronic rheumatic condition. Further work is required to establish ways to mitigate these through improved information provision and support.

References:

*Bridgewater S et al. Measuring the impact of steroid therapy on health-related quality of life in patients with rheumatic diseases: international development of a glucocorticoid treatment-specific patient-reported outcome measure. Rheumatology (Oxford). 2023;62(11):3565-3575.

Disclosures: Above and Beyond Bristol Hospitals Charity, Arthritis Australia, and the UK National Institute for Health and Care Research.

P-101

Clinical impact of high medical costs on the management of ANCA-associated vasculitis

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Background/ Objectives: ANCA-associated vasculitis (AAV) is a rare, potentially life-threatening, systemic auto-immune disease. Patients require lifelong follow-up with vasculitis specialists due to a high risk for relapse, toxicity and infections. The most recent EULAR/ACR guideline recommends to consider medical costs during the care for AAV patients, but it does not indicate how[1]. In this study we determined the largest cost bearers and clinical characteristics related to high costs, to establish the clinical impact on management of AAV.

Methods: Direct medical costs per patient year were determined based on cost prices per registration code. We collected all registration codes registered between 2018-2019 in electronic health records of patients in a previously determined AAV cohort of an academic care centre with an AAV expertise centre[2]. Registration codes >3 months before AAV diagnosis and patients with a follow-up of <6 months were excluded. To increase generalizability we compared proportion of patients to proportions of costs instead of exact costs. Statistical significance was determined with the Pearson χ^2 test.

Results: We included 180 AAV patients (122 GPA, 43 MPA and 18 EGPA) with a median follow-up time of 1.8 years. Mean costs per patient year were of €9,887.45. As shown in **figure 1**, the largest cost bearers were in-patient clinics (32%), therapeutics (22%), out-patient clinics (14%) and the laboratory (13%). Striking, most clinical admission days were related to AAV (42%) or infections (28%). In laboratory costs, 2% was related to immunology, whereas 27% was related to microbiology.

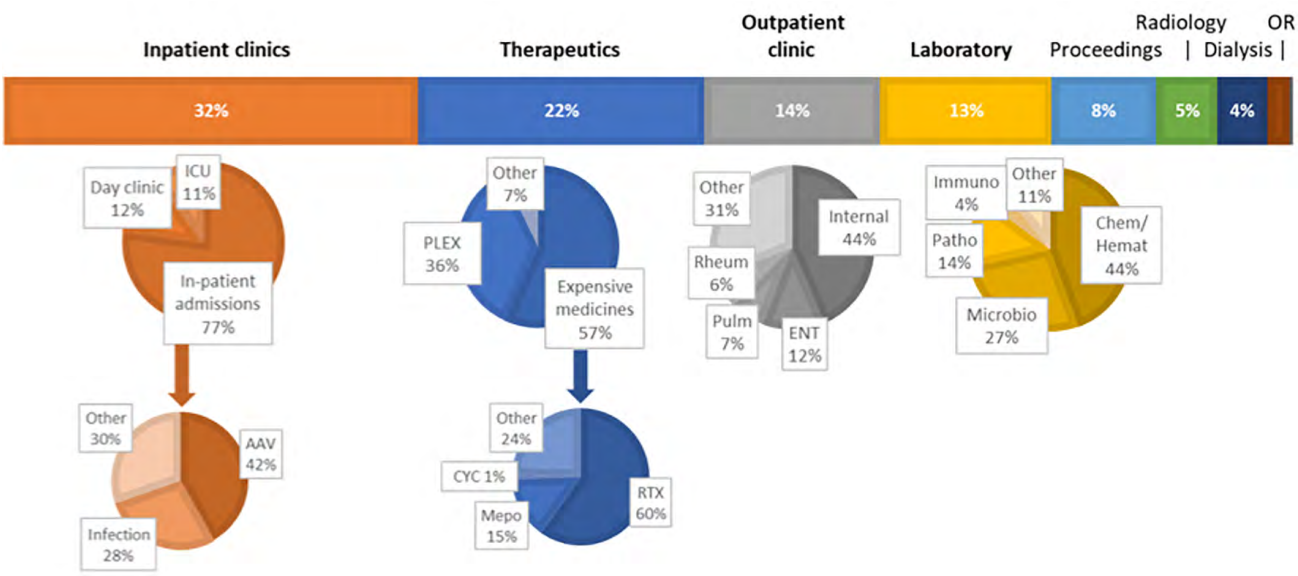

Figure 1.

A comprehensive analysis of baseline characteristics demonstrated patients with older age, relapsing disease or multiple comorbidities bore the highest medical costs. During follow-up, 23% of patients experienced active disease activity in one or more major organs and bore 50% of all health care costs ($p<0.01$). More interesting, in patients without major disease activity, 59% used steroids and bore 88% of costs and vice versa 41% did not use steroids and bore only 12% ($p<0.01$). Also, 42% of all patients experienced an infection and bore 71% of costs ($p<0.01$). Noteworthy, 93% of patients with an infection used steroids.

Conclusions: High medical costs bearers in AAV are not merely related to AAV activity and treatment, but predominantly determined by co-morbidity, infections and steroid use. These study results provide unique insights for clinicians when considering medical costs during the care for AAV patients. Future studies should be directed at evaluating whether reducing overall steroid use and aiming steroid-free remission as well as infection-prevention could reduce medical costs for the care of AAV patients.

References:

1. Hellmich, B., et al., *EULAR recommendations for the management of ANCA-associated vasculitis: 2022 update*. Annals of the Rheumatic Diseases, 2023.
2. van Leeuwen, J.R., et al., *Using an artificial intelligence tool incorporating natural language processing to identify patients with a diagnosis of ANCA-associated vasculitis in electronic health records.* Computers in Biology and Medicine, 2024. **168**: p. 107757.

Disclosures: None.

P-102

Clinical Outcomes With Dose Spacing Of Tocilizumab In Giant Cell Arteritis

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Background: Glucocorticoids are the mainstay of treatment for Giant Cell Arteritis (GCA) however side effects are often poorly tolerated. The only steroid sparing agent approved for treatment of GCA is the anti-interleukin-6 receptor antagonist tocilizumab. There remains uncertainty regarding treatment duration of tocilizumab and the optimal approach to medication withdrawal.

Methods: GCA patients who met the 2022 ACR/EULAR GCA classification criteria and had a clinical diagnosis of GCA were prospectively enrolled. As per ACR/ Vasculitis Foundation guidelines all GCA patients with a new diagnosis of GCA were started on tocilizumab if there were no contraindications. All patients had corticosteroid 26-week taper as per the GiACTA protocol. Tocilizumab was administered weekly for the first 12 months, and then every-other-week for an additional 12 months. Relapse of disease on tocilizumab was managed with temporary increases in systemic glucocorticoids.

Results: 55 patients with newly-diagnosed GCA were included. Of these, 27 patients did not receive tocilizumab treatment for a variety of reasons; active treatment for malignancy (7), history of diverticulitis (3), patient preference (5), co-existing inflammatory condition for which other biologic treatment was preferred (1), patient frailty and/or recurrent infections (9), death before start of tocilizumab (1). 1 further patient only had one month of treatment before discontinuation for a drug reaction. 27 patients (49%) had weekly treatment with tocilizumab for 1 year.

Of these, only 17 had every second week tocilizumab at one year. 5 remained on a weekly dose due to previous visual loss and concern about preserving the remaining eye. 2 had other coexisting inflammatory diseases for which weekly dosing was required. 1 died of natural causes before dose spacing, and 2 stopped tocilizumab before spacing due to side effects.

27 patients had tocilizumab weekly for a mean of 15.7 months and 17 of had tocilizumab every-other-week at one year for a mean of 8.1 months. 2 patients (11.7%) had a major relapse on every-other-week tocilizumab (one aortic dissection and one with monocular visual loss). There were two minor relapses, one in the weekly dosing group and one in the two-weekly dosing group.

While on weekly tocilizumab, 1 patient had a minor infection treated in the community and 1 had a major infection (diverticulitis) requiring hospital admission. In the every-other-week tocilizumab group, two patient had minor infections treated in the community and no patient had a major infection requiring hospitalisation.

Conclusions: In a real-world prospective study cohort, only 49% (27/55) of patients were eligible for tocilizumab therapy (with GIACTA protocol steroid). Overall, 96% of patients in the weekly dosing group had relapse-free remission compared to 82% in the every-other-week treatment group; p=0.157. Infection-free remission was comparable between the two groups at 92.5% and 88% respectively. A dose reduction in tocilizumab after 12 months appears to be safe and maintains most patients in remission. There was a trend towards more relapses in the every-other-week group, however this was not statistically significant.

Figure 1: Results.

	Tocilizumab weekly (27)	Tocilizumab two-weekly (17)
Mean duration tocilizumab (months)	15.7	8.1
Number of minor relapses	1	1
Number of major relapses	0	2
Overall relapse free remission	26 (96%)	14 (82%)
Number of minor infections not requiring hospital admission	1	2
Number of major infections requiring hospital admission	1	0
Infection free remission	25 (92.5%)	15 (88%)

P-103

Temporal change of prognosis in patients with ANCA-associated RPGN in Japan, from 1989 to 2019

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Background/ Objectives: Rapidly progressive glomerulonephritis can progress to end-stage kidney disease within a short period of time, and ANCA-associated vasculitis (AAV) is the most common cause of this disease. AAV in Japan is characterized a large number of elderly MPA patients with MPO-ANCA positive. While there was a trend to avoid concomitant use of immunosuppressive drugs to avoid infection death, rituximab emerged as an emerging option for concomitant use of immunosuppressive drugs during recent 10 years. The purpose of this study is to clarify these changes in treatment and the evolution of life and renal outcomes.

Methods: This was a retrospective observational study using a questionnaire-based approach involving major nephrology departments nationwide. We examined a total of 3019 ANCA-associated RPGN cases registered during five periods (1989-1998, 1999-2001, 2002-2008, 2009-2011, 2012-2015) plus 1221 cases in 2016-2019. As potential prognostic determinants, we investigated the onset period, the clinical severity (CS) grade [classified according to age, serum creatinine (sCr) and C-reactive protein levels, and presence/absence of lung lesions] and the treatment.

Results: Patients were older at onset (mean ± SD, 61.8 ± 14.8, 72.5 ± 11.1) and had lower sCr at onset (4.99 ± 3.09 mg/dL, 3.11 ± 2.62 mg/dL) during the period 2016-2019 compared to the period 1989-1998. The proportion of patients with the period 2016-2019 treatment including cyclophosphamide was lower than the period 1989-1998 (43.9%, 23.5%), and the proportion of patients with the most recent period use of rituximab was 17.0%. The cumulative survival at 24months for overall patients kept improving in the five periods, but cumulative survival was not significantly different period 2016-2019 compared to the period 2009-2011 and 2012-2015 (68.2%, 73.8%, 77.8%, 82.8%, 85.8%, 83.9%, $p < 0.001$ for trend). The cumulative renal survival at 24 months also did not differ significantly from the most recent period, although there was a trend toward improvement over time (69.3%, 81.7%, 79.0%, 74.9%, 82.4%, 82.9%, $p < 0.001$ for trend). Stratified by sCr value, sCr < 3 mg/dL(the 24-month cumulative renal survival: 97.6%) showed improvement compared to the first period.

Conclusions: Although there was a trend toward improvement over time in both life and renal prognosis in ANCA-associated RPGN, the number of mild cases increased, and renal deaths were thought to have increased in exchange for the improved patient survival.

References:

1. Epidemiology and temporal changes in the prognosis of rapidly progressive glomerulonephritis in Japan: a nationwide 1989–2015 survey. Clin Exp Nephrol. 2022;26:234–6

Disclosures: No COI.

P-104

Outcomes of Tracheobronchial Disease in ANCA Associated Vasculitis

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Background/Objectives: Anti-neutrophilic cytoplasmic antibody (ANCA) associated vasculitis (AAV) is a group of inflammatory small-medium vessel disorders which cause respiratory manifestations, renal failure, and neuropathies. It is estimated that tracheobronchial inflammation occurs in 20% leading to narrowing, stenosis, and obstruction (1).

Methods: A retrospective review was conducted on patients who had a diagnosis of AAV and had documented tracheobronchial disease throughout 01/2002 and 10/2022. Diagnosis of AAV was based on the 2012 International Chapel Hill Consensus Criteria. Patients were excluded if < 18 years of age or follow-up was < 6 months. Time to relapse of the airway disease, as defined by persistent inflammation with or without progressive narrowing, was estimated using the Kaplan-Meier method. Patients were censored at treatment end, start of new therapy (including switching from mono to combo therapy), or last follow-up.

Results: 111 patients with tracheobronchial involvement were included. Average age at diagnosis was 41.1 and 86 (77.5%) were female, majority were non-Hispanic white (88.3%). 105 (94.6%) had a diagnosis of granulomatosis with polyangiitis with the minority carrying a diagnosis of microscopic polyangiitis. 39 (35.1%) had MPO and 55 (49.5%) had PR3 positivity. Endoscopic procedures such as dilation and steroid injection were performed in 66 (59.5%), with 29 patients requiring 3 or more interventions. Tracheostomy occurred in 7. There were 63 patient-periods of rituximab monotherapy and 38 patient-periods of methotrexate monotherapy. The 12-month survival time estimate for rituximab was 88.4 (CI 80.7-96.9) and 92.1 (CI 83.9-100.0) for methotrexate (Figure 1). 60-month survival time estimates were 65.0 (CI 51.5-82.1) and 63.7 (CI 45.3-89.7), respectively. Of those on methotrexate, 11/37 (29.7%) discontinued the medication for an adverse reaction (5 for gastrointestinal symptoms, followed by 3 other and abnormal labs in 2). Rituximab was discontinued for adverse reaction in 4/62 (6.5%). 2 for severe infection, 1 for an abnormal lab, and 1 for non-severe infection. Two patients died during the follow-up period, one from vasculitis manifestations unrelated to tracheobronchial disease and one for unknown cause.

Conclusions: Despite the common use of immunosuppressive therapy, tracheobronchial disease tends to persist over time requiring additional intervention. Investigating the outcomes in patients with tracheobronchial disease during prospective studies should be prioritized.

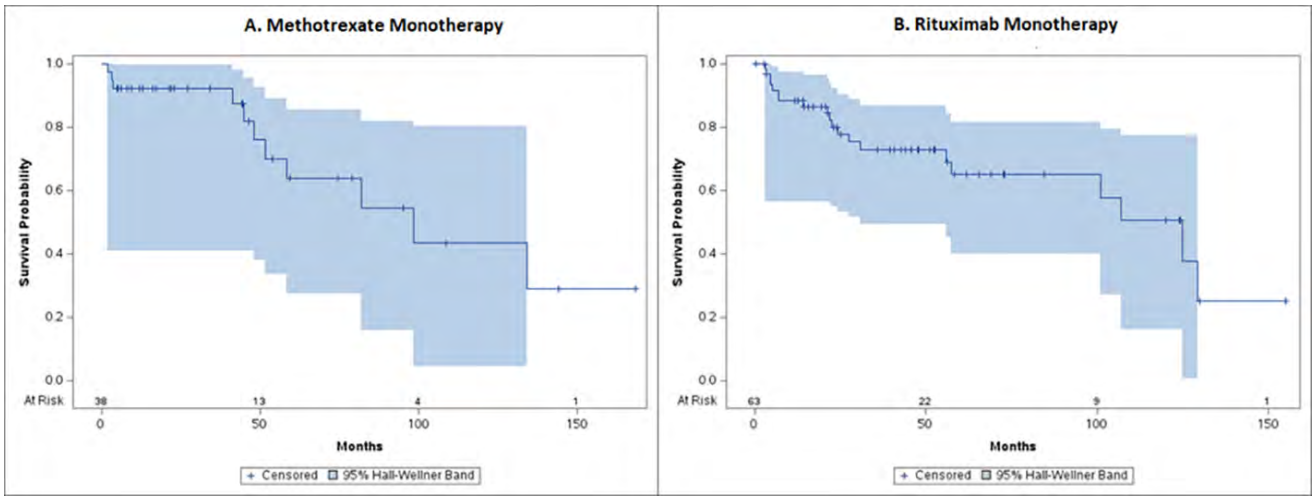

Figure 1: Progression Free Survival of Tracheobronchial Disease in Patients with ANCA Vasculitis.

References:

1. Marroquín-Fabián E, Ruiz N, Mena-Zúñiga J, Flores-Suárez LF. Frequency, treatment, evolution, and factors associated with the presence of tracheobronchial stenoses in granulomatosis with polyangiitis. Retrospective analysis of a case series from a single respiratory referral center. Semin Arthritis Rheum. 2019;48(4):714-9.

Disclosures: The authors declare no relevant disclosures.

P-105

Validation of a Brief Measure of Uncertainty in Vasculitis and Other Rheumatic Disease

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Background: Patients with vasculitis and other rheumatic disease are tasked with monitoring ambiguous and unpredictable physical symptoms. Higher uncertainty is associated with anxiety, depression, and sickness impact. Existing measures of uncertainty are adapted from longer instruments, limiting their use in research and clinical practice. We aimed to develop and validate a brief measure of uncertainty.

Methods: Patients with ANCA-associated vasculitis, IgG4-related disease, and systemic sclerosis seen at Mass General Hospital completed a survey assessing uncertainty (rheumatology version of the Mishel Uncertainty in Illness Scale, Survivor Version; MUIS-S), anxiety (GAD-7), depression (PHQ-8), and sickness impact (SIP). First, we performed an exploratory factor analysis (EFA) of the 22-item MUIS-S to identify the amount of variance loaded across each item following the established convention of 0.6 (stopping rule of 75% variance explained per factor) to select the final items. Second, we tested the 7-item brief uncertainty measure for internal consistency (Cronbach's alpha) and convergent validity. Third, we used hierarchal regression models to assess variance explained. Fourth, patients with vasculitis from the Vasculitis Patient-Powered Research Network (VPPRN) completed the brief 7-item measure and a confirmatory factor analysis was performed. VPPRN participants were asked about their interest in participating in a trial of a mind-body intervention for uncertainty and resiliency.

Results: For development, we included n=132: 31% with AAV, 46% with IgG4-RD, 23% with SSc. In the EFA of the 22-item MUIS-S, 7 items were retained and captured 2 factors: ambiguity and unpredictability. There was high internal consistency for the 7-item uncertainty measure (α=.85) and its subscales: ambiguity (α=.79) and unpredictability (α=.81). Convergent validity was found between the 7-item measure with anxiety (r=0.42, p<.001), depression (r=0.47, p<.001), and sickness impact (r=0.34, p<.001). Uncertainty, measured by the 7-item measure, explained a significant variance: 14.2% in anxiety (p<.001), 23.2% in depression (p<.001), and 14.8% in sickness impact (p<.001) after controlling for age and sex. For CFA, we included n=475, all with vasculitis (62% AAV) and confirmed that the 7-item measure with two subscales (ambiguity and unpredictability) had good model fit. Most patients expressed interest in participating in a trial evaluating a mind-body intervention in vasculitis (Yes: 56%, Maybe: 26%). Most patients reported use of at least one mind-body practice in the prior month (**Table**).

Conclusion: We developed a brief, 7-item measure of URD with high internal consistency and convergent validity with measures of anxiety, depression, and sickness impact in patients with vasculitis or other conditions. This measure may also be useful as part of research studies developing interventions aimed at improving resiliency in the face of uncertainty and in clinical practice to identify patients facing high levels of uncertainty. Additional validation is needed.

Disclosures: None.

Table: Interest in a Randomized Controlled Trial of a Mind-Body Intervention Among Patients with Vasculitis in the Vasculitis Patient-Powered Research Network

Interest in participating in a randomized controlled trial that evaluates a mind-body intervention	N (%)
Yes	268 (56.4)
Maybe	123 (25.9)
No	84 (17.7)
Interest in participating in this trial if the visits were held virtually over Zoom (n = 391)	
Yes	283 (72.4)
Maybe	92 (23.5)
No, does not want to participate virtually	11 (2.8)
No, prefers something other than Zoom or some other video meeting system	5 (1.3)
Access to a computer or tablet (e.g., iPad, Kindle) with internet access to access Zoom or another platform (n = 391)	
Yes	374 (95.7)
Maybe	8 (2.1)
No	9 (2.3)

Mind-Body Practices Used in the Month Prior to Survey	
Any mind-body practice	369 (77.7)
Specific mind-body practices	
Relaxation (e.g., breathing exercises, guided imagery, and progressive muscle relaxation)	145 (30.5)
Meditation (e.g., mindfulness meditation)	133 (28.0)
Modified diet	85 (17.9)
Massage	75 (15.8)
Yoga	69 (14.5)
Movement therapies	58 (12.2)
Chiropractor	31 (6.5)
Homeopathic remedies	30 (6.3)
Acupuncture	23 (4.8)
Tai Chi or Qigong	19 (4.0)
Spinal manipulation	12 (2.5)
Crystals and/or magnets	12 (2.5)
Healing touch	10 (2.1)
Eye movement desensitization and reprocessing	6 (1.3)
Hypnotherapy	5 (1.1)
Biofeedback	3 (0.6)
Somatic experiencing	2 (0.4)
None	106 (22.3)

P-106

Validation of the ANCA-associated vasculitis patient reported outcomes questionnaire in a Latin American vasculitis cohort

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Background/Objectives: The ANCA-associated vasculitis (AAV) patient reported outcomes (AAV-PRO) questionnaire is a new PRO developed to capture how AAV and its treatment impact on the health-related quality of life (HRQoL)[1] of the affected patients. The aim of this work is to validate the AAV-PRO questionnaire in a Latin America (Peru) AAV cohort.

Methods: We included patients from the Almenara Vasculitis cohort[2] who had at least one visit between December 2022 and November 2023. Sociodemographic features, disease activity measured with the Birmingham Vasculitis Activity Score version 3 (BVASv3) score, damage measured with the Vasculitis damage index (VDI) score, as well as the AAV-PRO (Spanish version) and the Short Form 36 (SF-36) were obtained. The AAV-PRO includes six domains [organ-specific symptoms (OSS), systemic symptoms (SS), treatment side effects (TSE), social and emotional impact (SEI), concerns about the future (CF), physical function (PF)] with twenty-nine items; the score ranges from 0 to 100: the higher the value, the worse the HRQoL. Active/relapsing disease was defined by BVASv3 ≥ 1. Correlations between domains of the AAV-PRO and the SF-36, BVASv3 and VDI were evaluated using Spearman's correlation.

Results: Forty-eight patients were enrolled; 36 (75.0%) of them were women. Their age and disease duration were 57.4 (13.5) and 5.1 (5.0) years, respectively. The BVASv3 and VDI scores were 4.7 (7.9) and 2.5 (1.7), respectively; patients with active/relapsing disease were 22 (45.8%). As to the SF-36, physical component summary (PCS) and mental component summary (MCS) were 44.5 (16.1) and 49.6 (16.1), respectively. As to the AAV-PRO domains, the scores for OSS, SS, TSE, SEI, CF, and PF were 35.4 (22.7), 48.4 (24.3), 39.4 (18.0), 49.2 (22.5), 53.1 (21.5), and 33.1 (22.6), respectively. Correlation analyses between the AAV-PRO and the SF-36 are depicted in Table 1. Overall, every domain of AAV-PRO correlated strongly with the global scores of the SF-36 (PCS and MCS) (all r ≥ 0.405 and p between 0.004 and <0.001). There was no correlation between the AAV-PRO domains and either the BVASv3 or the VDI.

Table 1. Correlation between AAV-PRO, SF-36, BVASv3 and VDI scores.

		AAV-PRO*					
		OSS	**SS**	**TSE**	**SEI**	**CF**	**PF**
SF-36	**PF**	**-0.298 (0.040)**	**-0.332 (0.021)**	-0.208 (0.156)	**-0.484 (<0.001)**	**-0.414 (0.003)**	**-0.703 (<0.001)**
	RF	-0.038 (0.795)	**-0.348 (0.015)**	**-0.386 (0.007)**	**-0.499 (<0.001)**	**-0.434 (0.002)**	**-0.354 (0.014)**
	BP	-0.268 (0.065)	**-0.493 (<0.001)**	**-0.377 (0.008)**	-0.280 (0.054)	**-0.313 (0.030)**	**-0.362 (0.011)**
	GH	**-0.518 (<0.001)**	**-0.440 (0.002)**	**-0.472 (<0.001)**	**-0.396 (0.005)**	**-0.368 (0.010)**	**-0.334 (0.020)**
	VT	**-0.482 (<0.001)**	**-0.493 (<0.001)**	**-0.496 (<0.001)**	**-0.576 (<0.001)**	**-0.495 (<0.001)**	**-0.437 (0.002)**
	SF	**-0.350 (0.015)**	**-0.321 (0.026)**	-0.268 (0.066)	**-0.458 (0.001)**	-0.244 (0.095)	-0.247 (0.090)
	RE	-0.176 (0.230)	**-0.409 (0.004)**	**-0.518 (<0.001)**	**-0.500 (<0.001)**	**-0.319 (0.027)**	**-0.465 (<0.001)**
	MH	**-0.454 (0.001)**	**-0.405 (0.004)**	**-0.369 (0.010)**	**-0.593 (<0.001)**	**-0.336 (0.020)**	**-0.356 (0.013)**
	PCS	**-0.405 (0.004)**	**-0.589 (<0.001)**	**-0.539 (<0.001)**	**-0.650 (<0.001)**	**-0.562 (<0.001)**	**-0.609 (<0.001)**
	MCS	**-0.470 (<0.001)**	**-0.554 (<0.001)**	**-0.587 (<0.001)**	**-0.670 (<0.001)**	**-0.419 (0.003)**	**-0.481 (<0.001)**
BVASv3		-0.134 (0.363)	-0.086 (0.563)	0.140 (0.341)	0.090 (0.541)	0.069 (0.643)	-0.054 (0.717)
VDI		0.204 (0.165)	0.056 (0.705)	-0.061 (0.678)	0.097 (0.514)	0.130 (0.380)	0.255 (0.080)

* Results are showed as Pearson correlation coefficient (r) and significance (p). The top numbers correspond to the correlations and the bottom ones to the p values.

AAV-PRO: ANCA-associated vasculitis patient reported outcomes. SF-36: Short form 36. OSS: Organ-specific symptoms. SS: Systemic symptoms. TSE: Treatment side effects. SEI: Social and emotional impact. CF: Concerns about the future. PF: Physical function. RF: Role physical. BP: Bodily pain. GH: General health. VT: Vitality. SF: Social functioning. RE: Role emotional. MH: Mental health. PCS: Physical component summary. MCS: Mental component summary. BVASv3: Birmingham Vasculitis Activity Score version 3. VDI: Vasculitis damage index.

Conclusions: The AAV-PRO questionnaire, Spanish version, correlated with the SF-36 in AAV patients from a Latin American cohort (Peru). However, in our population, AAV-PRO did not correlate with activity or damage. These findings might endorse the use of AAV-PRO in other Latin American populations.

References:

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2. Pimentel-Quiroz VR, Sanchez-Torres A, Acevedo-Vasquez E, et al. Demographic and Clinical Features of ANCA-Associated Vasculitides in a Peruvian Tertiary Center. *J Clin Rheumatol* 2021; **27**(6S): S246-S51.

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P-107

Does age at diagnosis of giant cell arteritis influence the clinical phenotype and outcomes?

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Background: Previous studies suggest that age at diagnosis influences the clinical features of giant cell arteritis (GCA). A better identification of patients at a higher risk of worse outcomes may prompt a more tailored treatment approach. Our work aims to assess how age at diagnosis of GCA influences its phenotype and prognosis.

Methods: Multicentre open cohort study, including all patients with GCA registered in the Rheumatic Diseases Portuguese Register (Reuma.pt) up to January 2023. Two groups were established using the median age at diagnosis as the cut-off. Patients who underwent baseline ultrasound evaluation were divided into three groups: exclusive large vessel GCA (LV-GCA) in cases of axillary or subclavian artery involvement, exclusive cranial-GCA in temporal artery involvement, and mixed pattern when both territories were involved. Eye involvement was defined as anterior ischemic optic neuropathy (AION), transient amaurosis or permanent vision loss. Independent predictors of different manifestations were identified through binomial logistic regression. Kaplan-Meier was performed to evaluate maintenance on glucocorticoid (GC) therapy and time to first relapse.

Results: A total of 294 patients were included, 65.6% females, with a median age at diagnosis of 75.2 years (IQR 11.0; range 51-91). Patients most commonly presented with new onset temporal headache (53.2%), weight loss (48.1%) and polymyalgia rheumatica (PMR; 45.5%). Cranial-GCA was identified in 78.4% of patients, LV-GCA in 11.5% and mixed pattern in 10.1%. Jaw claudication, transient amaurosis, permanent vision loss, AION, and cerebral ischaemic events (CIE) were more likely to be present in older patients (Table 1). In contrast, younger patients were more likely to have fever, night sweats, arm claudication and LV-GCA.

On multivariate analysis, older age at diagnosis (OR 1.07, 95%CI: 1.03-1.12) was an independent predictor of CIE, regardless of sex, disease duration, LV-GCA, PMR, and fatigue. The same model identified LV-GCA (OR 0.19, 95%CI: 0.06-0.63) and PMR (OR 0.40, 95%CI: 0.20-0.81) as protective factors. Age at diagnosis (OR 1.07, 95%CI: 1.02-1.11) was also an independent predictor of eye involvement, regardless of sex, disease duration, LV-GCA, fatigue and night sweats. LV-GCA (OR 0.15, 95%CI: 0.03-0.67) was a protective factor.

The mean disease duration of our cohort was 4.13±4.33 years. On survival analysis, no differences were found between patients ≤75 and >75 years old in time to first relapse (p=0.790) and time to first complete GC withdrawal (p=0.150).

Conclusions: Our study shows that older patients with GCA have more cranial symptoms and CIE, whereas younger patients present a more systemic disease phenotype. Older age at diagnosis is an independent predictor of eye involvement and CIE. These findings support the hypothesis that age at diagnosis in GCA influences disease manifestations and outcomes.

Disclosures: None.

Table 1 – Clinical and laboratorial characteristics in younger and older patients.

	Younger patients, ≤75 years old (n=145)	Older patients, >75 years old (n=149)	Univariate analysis
Age at diagnosis, mean ± SD years (N)	67.42 ± 5.85 (145)	80.86 ± 4.09 (149)	-
Female sex, n/N (%)	92/145 (63.4)	101/149 (67.8)	p=0.463
Diagnosis delay, mean ± SD years (N)	0.37 ± 0.87 (145)	0.38 ± 1.14 (149)	p=0.983
Patients who fulfil the classification criteria for GCA, n/N (%)			
ACR 1990	125/144 (86.8)	133/147 (90.5)	p=0.359
ACR / EULAR 2022	111/117 (94.9)	118/120 (98.3)	p=0.168
Clinical data			
Pattern of disease involvement according to ultrasound results, n/N (%)			
Exclusive cranial-GCA	75/99 (75.8)	88/109 (80.7)	p=0.404
Exclusive large vessel-GCA	**17/99 (17.2)**	**7/109 (6.4)**	**p=0.017**
Mixed pattern GCA	7/99 (7.1)	14/109 (12.8)	p=0.249

	Younger patients, ≤75 years old (n=145)	Older patients, >75 years old (n=149)	Univariate analysis
Symptoms/signs, n/N (%)			
Night sweats	**15/128 (11.7)**	**5/134 (3.7)**	**p=0.019**
Fever	**26/128 (20.3)**	**11/132 (8.3)**	**p=0.007**
Weight loss	61/127 (48.0)	64/133 (48.1)	p=1.000
Arthralgia	45/129 (34.9)	42/135 (31.1)	p=0.600
Polymyalgia rheumatica	63/130 (48.5)	58/136 (42.6)	p=0.389
Jaw claudication	**43/128 (33.6)**	**66/136 (48.5)**	**p=0.017**
Tong claudication	6/128 (4.7)	4/134 (3.0)	p=0.533
Arm claudication	**5/128 (3.9)**	**0/134 (0.0)**	**p=0.027**
Leg claudication	2/128 (1.6)	0/134 (0.0)	p=0.238
Scalp tenderness	24/128 (18.8)	22/135 (16.3)	p=0.629
New-onset frontal headache	36/129 (27.9)	49/135 (36.3)	p=0.150
New-onset temporal headache	62/128 (48.4)	79/137 (57.7)	p=0.141
Ischaemic cerebral event	**36/95 (37.9)**	**82/113 (72.6)**	**p<0.001**
Transient amaurosis	**9/126 (7.1)**	**26/134 (19.4)**	**p=0.006**
Permanent vision loss	**21/125 (16.8)**	**59/138 (42.8)**	**p<0.001**
Eye involvement*	**27/127 (21.3)**	**75/138 (54.3)**	**p<0.001**
Signs/physical examination changes, n/N (%)			
Loss of pulses	**7/125 (5.6)**	**1/132 (0.8)**	**p=0.032**
Abnormalities on temporal arteries	41/130 (31.5)	52/134 (38.8)	p=0.247
Abnormalities on other arteries	**14/128 (10.9)**	**5/134 (3.7)**	**p=0.031**
Anterior ischemic optic neuropathy (AION)	**15/127 (11.8)**	**48/135 (35.6)**	**p<0.001**
Laboratory examination at baseline, mean ± SD (N)			
C-reactive protein (mg/dL)	7.52 ± 6.61 (103)	6.40 ± 5.87 (108)	p=0.194
Erythrocyte sedimentation rate (mm/hr)	81.83 ± 29.24 (105)	85.33 ± 36.08 (113)	p=0.431
Haemoglobin (g/dL)	11.67 ± 1.62 (94)	11.53 ± 1.61 (103)	p=0.540
Platelets (/uL)	381000 ± 142048 (87)	368410 ± 148745 (94)	p=0.561
Treatment, n/N (%)			
IV methylPDN pulses	**27/88 (30.7)**	**60/102 (58.8)**	**p<0.001**
Methotrexate	**74/145 (51.0)**	**58/149 (38.9)**	**p=0.046**
Azathioprine	3/145 (2.1)	1/149 (0.7)	p=0.366
Tocilizumab	20/145 (13.8)	11/149 (7.4)	p=0.088
PDN cumulative dose/disease duration, mean ± SD grams per year (N)	8.82 ± 22.32 (77)	18.02 ± 58.30 (87)	p=0.195
Disease follow-up, n/N (%)			
Disease follow-up, mean ± SD years (N)	**5.05 ± 4.77 (145)**	**3.25 ± 3.65 (149)**	**p<0.001**
Patients who relapsed	46/90 (51.1)	43/93 (46.2)	p=0.555
Time to first relapse, mean ± SD years (N)	1.88 ± 3.02 (46)	1.15 ± 1.15 (43)	p=0.140
Number of disease relapses in the first two years	0.47 ± 0.69 (90)	0.49 ± 0.70 (92)	p=0.828
Number of relapses throughout follow-up	0.84 ± 1.09 (90)	0.77 ± 0.98 (93)	p=0.647

Abbreviations: n – number of patients positive for the variable of interest, N – number of patients without missing information regarding the variable of interest, PDN – prednisolone, SD – standard deviation;
* Eye involvement: presence of transient amaurosis, permanent vision loss or AION

P-108

Patient experiences of managing their rare rheumatic diseases

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Background/ Objectives: Systemic lupus erythematosus, systemic vasculitis, inflammatory myositis, Scleroderma and Sjogren's Syndrome are rare autoimmune rheumatic diseases (RAIRDs). A patient survey of people with RAIRDs found 61% were struggling, and 45% reported an impact on family life. A survey of NHS rheumatology departments found 80% do not offer access to self-management support to people with RAIRDs.[1] The objective is to understand the patients' experiences of their RAIRD and views on interventions to support self-management.

Methods: Online focus groups via Zoom using a topic guide developed with a multi-disciplinary team including patient partners with lived experience.

Focus groups were advertised via patient charities' social media platforms (Vasculitis UK, Scleroderma and Raynaud's UK, Lupus UK, Myositis UK and the British Sjogren's Society Syndrome Association) were audio-recorded, transcribed, organised using NVIVO, and analysed thematically.

Results: Twenty-six patients, 21 (80.76 %) female, median age 62 (range 34-82) participated in six focus groups. Diagnoses included systemic lupus erythematosus (4), inflammatory myositis (7), ANCA associated vasculitis (5), mixed connective tissue disease (2), scleroderma (1), undifferentiated vasculitis (2), and primary or secondary Sjogren's (16). Five patients (19%) were newly diagnosed (<2 years) and 21 patients (81%) reported active disease.

Two related main themes capture the data:

"I'm constantly doing medical admin along with surviving and fighting a disease"

A lack of joined-up healthcare ("I've got some great people but they're not working as a team"), difficulty accessing specialists' ("Everyone just passes you like the sort of parcel that no one wants to open") and disease complexity ("she said you're too complicated") makes managing RAIRDs hard, resource-intensive work ("I've had to push so hard for all of it and I think that only happens with very rare conditions").

"Because you have very rare conditions it's uniquely isolating"

The psychological impact of having complex autoimmune conditions can be exacerbated when they are poorly understood by family and friends ("I've encountered mental health problems having to manage family expectations of me") and health professionals ("they've never seen a patient like me in their life"). Patients described strategies that could be beneficial at an individual level ("acceptance, mindfulness, meditation and to not beat myself up about things") and the importance of addressing mental health ("you've got to build your self-esteem, so you don't feel rubbish all the time").

Conclusions: Patients with RAIRDs identified shared experiences to inform the development of a cross-condition self-management intervention. These include negotiating healthcare systems and managing the psychological impact of RAIRDs. Further work is needed with under-represented groups to identify whether their support needs are distinct.

References:

1. Robson, J. et al (2020). Psychological and self-management support for people with vasculitis or connective tissue diseases: UK health professionals' perspectives. Rheumatol Adv Pract, 27; 4(2).

Disclosures: None.

P-109

Anticoagulant treatment in addition to immunosuppressives decreases the relapse rate in Pulmonary Arterial Involvement of Behçet's Disease

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Objectives: Vascular inflammation in Behcet's Disease (BD) is one of the most important causes of mortality due to pulmonary artery involvement (PAI) or Budd-Chiari syndrome. In this study, we aimed to retrospectively evaluate the clinical features, course and factors affecting the recurrence risk of BD-associated PAI.

Methods: BD patients followed up between 1990-2022 were included. All data were acquired from the patient charts. Involvements were classified according to the vascular structures in which thrombotic or aneurysmal formation was detected. Factors affecting the risk of relapses were determined using multivariate Cox regression analysis.

Results: Among 1350 BD patients, 110 (8.1%) had PAI. The mean age (SD) of patients with PAI was 42.4 (11.6) years, and the male/female ratio was 2.2 (76/34). Thirty-two (29.1%) of 110 patients were asymptomatic. Symptomatic patients were significantly older (p=0.031), and female gender (p=0.001) and recurrence (p=0.019) rates were higher than asymptomatic patients. Thrombotic involvement was seen in 104 (94.5%) and aneurysms in 9 (6.6%) patients. (Figure 1) Relapses were observed at least once in 31 (28.2%) patients. In multivariate analysis, the Cox regression model was significant (p=0.015) and not starting anticoagulants (HR 5.11, 95% CI 1.21-21.6), p=0.026), independently increased the relapse risk. (Figure 2)

Conclusion: PAT is the main presentation type of PAI in BD while aneurysmatic formation is rare. In one-third of patients with PAI, relapses develop during follow-up despite immunosuppressive treatment. When added to immunosuppressive treatment, anticoagulant therapy significantly decreases the relapse rate in BD patients with PAI.

Disclosure: None.

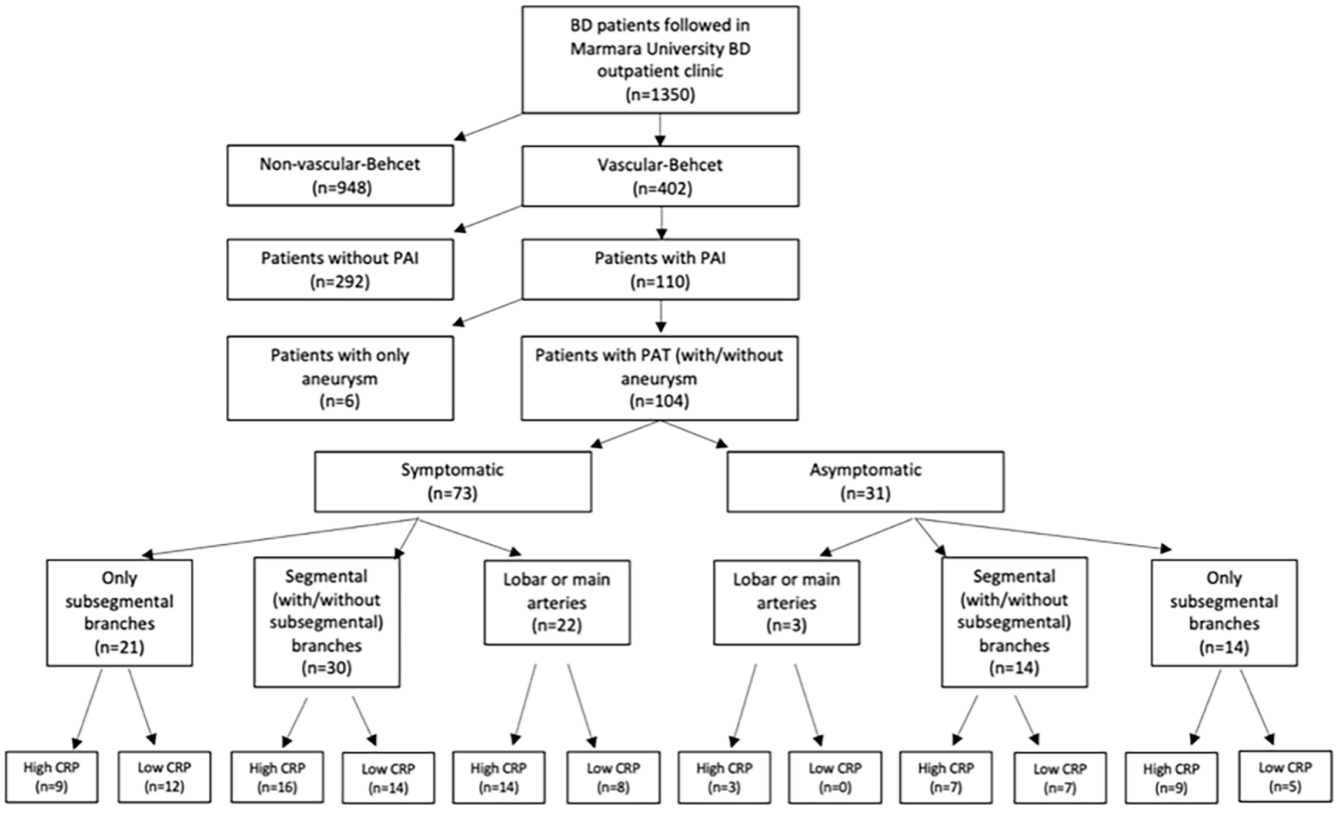

Figure 1. The distribution of patients is classified according to symptom status, size of involved vessels and acute phase reactant levels at the time of diagnosis of PAI.

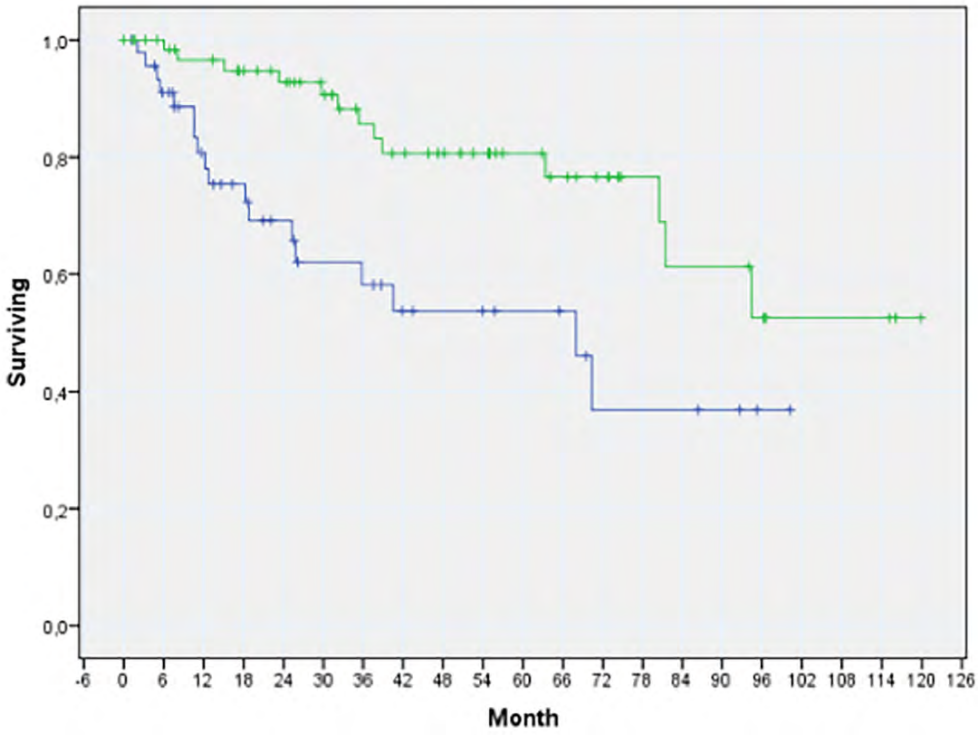

Figure 2. Kaplan-Meier survival analyses.

P-110

Phase Specific Health Care Costs Associated with Giant Cell Arteritis in Ontario, Canada

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Background/Objectives: Giant Cell Arteritis (GCA) is the most common vasculitis of older people and is becoming more prevalent. We estimated the additional health care system costs associated with GCA in the year pre-diagnosis, 1-year post diagnosis, and over long-term follow up in Ontario, Canada.

Methods: We performed a population-based study using health administrative data. Newly diagnosed cases of GCA (between 2002 and 2017 and ages 66 years and older) were identified using a validated algorithm and matched 1:6 to a comparator cohort using propensity scores. Follow up data was accrued until death, outmigration, or March 31, 2020. The costs associated with care for those with and without GCA were determined across three phases: the year before the diagnosis of GCA, the year after, and ongoing costs thereafter.

Results: The cohort consisted of 6,730 cases of GCA and 40,380 matched non-GCA comparators. The average age was 77 years (interquartile range 72-82) and 68.2% were female (Table 1). Individuals with GCA were more likely to have had a severe infection, vision loss, and/or rheumatoid arthritis in the years leading up to the pre-diagnostic year; there was a lower frequency of dementia and residency in long term care. In terms of the net attributable per patient costs, a diagnosis of GCA was associated with an additional cost of $6,619.4 (95% CI 5,964.9 – 7274.0) per patient during the 1-year pre-diagnostic period; $12,150.3 (95% CI 11,233.1 – 13,067.6) per patient in the 1-year post-diagnostic phase, and $20,886.2 (95% CI 17,195.2 – 24,577.2) per patient during ongoing care for year 3 onwards. Increased costs per 30-day service period were driven by inpatient, emergency, and outpatient hospital services, physician services, hospital outpatient clinic services, and emergency department visits.

Conclusions: A diagnosis of GCA was associated with increases in health care costs during all three phases of care. Given this substantial economic burden, strategies to reduce the healthcare utilization and costs associated with GCA are warranted.

Disclosures:

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AK – none.

TF – none.

JG – none.

JW – none.

Table 1: Demographics and costs of care in patients with GCA and matched comparators.

	GCA Subjects N=6,730	**Non-GCA Subjects** N=40,380
Median Age (median (IQR))	77 (72-82)	77 (72-82)
Female sex, n (%)	4,591 (68.2%)	27,546 (68.2%)
Long Term Care resident, n (%)	143 (2.1%)	2,231 (5.5%)
Comorbidities (at index date)		
Hypertension, n (%)	5,163 (76.7%)	29,806 (73.8%)
Severe infection, n (%)	1,970 (29.3%)	8,932 (22.1%)
Diabetes, n (%)	1,928 (28.6%)	10,530 (26.1%)
Hypertension, n (%)	5,163 (76.7%)	29,806 (73.8%)
Osteoporosis, n (%)	1,815 (27.0%)	10,102 (25.0%)
Asthma, n (%)	1,240 (18.4%)	5,882 (14.6%)
Cancer, n (%)	1,218 (18.1%)	7,575 (18.8%)
Congestive heart failure, n (%)	1,038 (15.4%)	4,877 (12.1%)
Cerebral Vascular Accident, n (%)	623 (9.3%)	2,761 (6.8%)
Vision Loss, n (%)	540 (8.0%)	1,113 (2.8%)
Rheumatoid Arthritis, n (%)	470 (7.0%)	1,065 (2.6%)
Dementia, n (%)	433 (6.4%)	3,914 (9.7%)

	GCA Subjects N=6,730	**Non-GCA Subjects** N=40,380
Myocardial Infarction, n (%)	424 (6.3%)	2,293 (5.7%)
Aortic aneurysm/dissection, n (%)	299 (4.4%)	1,025 (2.5%)
Venous Thromboembolism, n (%)	232 (3.4%)	890 (2.2%)
Costs of care per patient (2021 Canadian Dollars)		
1 year prior to diagnosis (mean (SD))	$17,011.0 (25,925.8)	$10,391.6 (21,664.3)
1 year after diagnosis (mean (SD))	$24,416.3 (37,214.5)	$12,265.9 (23,076.5)
Cumulative costs after year 2 (mean (SD))	$123,554.8 (137971.3)	$102,668.6 (125099.2)
Adjusted mean health care costs per patient per 30 days, by cost category and phase of care		
1 year prior to diagnosis	$ 1,402.00	$ 856.40
1 year after diagnosis	$ 2,131.50	$ 1,034.30
from year 2	$ 1,556.20	$ 1,258.90

P-111

Analysis of clinical features in eosinophilic granulomatosis with polyangiitis treated with Mepolizumab: a single center experience

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Background: Mepolizumab (MPZ) has been increasingly used in Eosinophilic granulomatosis with polyangiitis (EGPA) since 2018 in Japan. Therefore, we conducted a retrospective analysis of the clinical database of the 38 patients of EGPA treated with MPZ in our hospital.

Methods: 38 EGPA patients have been treated with MEP and followed for at least 6 months since 2018 (up to Aug 2023) were analysed for clinical course, including remission rates.

Remission was defined as BVAS 0 at 6 months. Disease flare defined as increased disease activity required intensification of immunosuppressive therapy.

Results: Of the 38 patients (18 ANCA positive and 20 negative), 11 patients (9 newly diagnosed or 2 relapsing diseases) received a remission induction with MEP and 27 patients received maintenance MEP therapy. The mean age onset was 56±12 years and BVAS 12.1±18.1. All patients used GC, and some required additional treatment [(GC pulse 79%, cyclophosphamide (CY) 39%, IVIG 39%)]. After 6 months of therapy, the achievement rates of GC dose below 5mg/day was 50% and improvement of sensory disorders was 44%. While no flare-up and no-death was observed.

Conclusion: These results showed that MEP is effective and has an acceptable safety profile in relatively EGPA patients in daily practice.

P-112

Interventions related to Takayasu arteritis, their clinical and angiographic associations, and prognostic relevance - a cohort study

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Background/ Objectives: Patients with Takayasu arteritis (TAK) might require endovascular or open surgical interventions for critical arterial ischemia compromising organ function or quality of life. We analysed interventions related to TAK, their clinical and angiographic associations and prognostic relevance from an ambispective, monocentric large cohort of TAK from India.

Methods: Information regarding endovascular or open surgical interventions (aortoplasty, nephrectomy for refractory hypertension) was retrieved from a cohort of patients with TAK. Demographic characteristics, clinical features, and angiographic involvement were compared between those patients with TAK who had undergone interventions with the rest of the cohort using univariable odds ratios (OR, with 95% CI). Hazard ratios (using Cox proportional hazards assumption) were used to compare the mortality rate among TAK who had undergone interventions with the rest of the cohort.

Results: Among 238 patients with TAK in the cohort, 41(17.23%) had undergone 69 interventions related to TAK (64 endovascular procedures, one open surgical aortoplasty, 4 nephrectomy) across 55 sittings (a single intervention sitting in 31, two in seven, three in two, and four in one). The most common arterial territories undergoing intervention were the renal arteries (n=21), subclavian artery (n=8), and descending thoracic aorta (n=6) **(Table 1).** Seven patients with TAK required repeated interventions in the same arterial territories. Three endovascular interventions had failed (two renal artery and one celiac artery interventions). Patients with TAK who underwent interventions had similar age at cohort entry (mean±SD 29.17±10.75 vs 29.65±11.26 years), sex (female:male 31:10 vs 141:56), ITAS2010 (9.71±7.54 vs 10.73±7.02), and DEI.TAK (8.24±6.75 vs 9.34±6.00), more frequent abdominal angina (OR 5.33, 95%CI 1.47-19.37), and less frequent constitutional features (OR 0.44, 0.21-0.92), right carotid artery (OR 0.44, 95%CI 0.21-0.95), or brachiocephalic artery involvement (OR 0.32, 95%CI 0.12-0.87) compared with those who had not undergone interventions. Survival was similar in TAK who had undergone interventions to those without (hazard ratio for mortality 0.91, 95%CI 0.23-3.55).

Conclusions: About a sixth of our cohort of TAK had undergone interventions, most often endovascular interventions. Repeated interventions were required in one-sixth of patients. Survival was similar in TAK with or without interventions.

References: None.

Disclosures: None.

Table 1: Interventions in patients with TAK.

Type of procedure (n=69)	**Number of procedures**
Stenting	49
Angioplasty without stenting	13
Embolization of bronchial artery	2
Open surgical repair	1
Nephrectomy	4
Arterial territory (n=65)	**Number of procedures**
Carotid artery	4
Subclavian artery	8
Vertebral artery	5
Aortic arch aneurysm repair	1
Descending thoracic aorta	6
Abdominal aorta	4
Renal artery	21
Celiac artery	2
Superior mesenteric artery	4
Iliac artery	4
Coronary arteries	4
Bronchial arteries	2
A patient could have undergone more than one intervention, or interventions in more than one arterial territory at a single sitting.	

P-113

Concordance of relapse symptoms with initial baseline presentation features among patients with giant cell arteritis

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Background/objectives: Relapse is common in giant cell arteritis (GCA). A clinically relevant question for both patients and providers is whether the initial symptoms at GCA diagnosis will be present at time of relapse or whether other clinical features may manifest. Given most cohorts describe both baseline and relapse symptoms in aggregate, evaluation of patient level concordance between initial symptoms and first relapse, the purpose of this study, has not been delineated.

Methods: Three previously described cohorts of patients with GCA were utilized (1-3). Cohort 1 (C1) – 286 patients with biopsy-proven GCA treated without tocilizumab (TCZ), Cohort 2 (C2) – 110 patients with biopsy-negative GCA treated without TCZ, and Cohort 3 (C3) – 114 patients with biopsy-proven or imaging-proven GCA treated with TCZ. An aggregate of all patients from C1-C3 was evaluated and termed cohort 4 (C4, n=510). Symptoms were grouped into categories: constitutional, musculoskeletal (MSK), cranial (non-visual), visual, and large vessel (LV). Patients could have more than one category present at each time point. Conditional probabilities were calculated.

Results: In C1, C2, C3, and C4, 183/286 (64%), 62/110 (56%), 58/114 (51%), and 303/510 (59%) patients had at least one relapse, respectively. In C1, 21%, C2, 18%, C3, 19%, and C4, 20% of patients presented with a symptom category on first relapse that was not present at baseline. Conditional probabilities of symptoms at first relapse according to presence or absence of baseline symptoms are shown in **Table 1**. No patient without cranial symptoms at baseline developed visual symptoms at first relapse. In C1 and C3, no patient without visual symptoms at baseline developed visual symptoms at first relapse. In C2 and C4, absence of baseline visual symptoms resulted in 6% and 1% probabilities of visual symptoms on first relapse, respectively. Among patients with baseline visual involvement, the conditional probabilities of visual involvement at relapse were 8% in C1, 22% in C2, 14% in C3, and 13% in C4.

Conclusions: In our study, approximately 1 in 5 patients reported a new symptom domain at relapse that was not present at baseline. Visual symptoms on first relapse were overall uncommon, but risk was higher if visual symptoms were present at baseline. The significance of this study lies in its potential to aid clinicians in providing patient-level data regarding relapsing GCA that will ultimately translate into better patient education and overall better disease monitoring.

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Table 1. Conditional probabilities of given symptom category at first relapse according to presence or absence of baseline symptom category.

Cohort 1 (C1, Biopsy proven, no Tocilizumab)										
Probability	*Pr(Relapse 1 symptom | baseline = No)*					*Pr(Relapse 1 symptom | baseline = Yes)*				
Baseline symptom	*Con.*	*Msk.*	*Cran.*	*Vis.*	*LV*	*Con.*	*Msk.*	*Cran.*	*Vis.*	*LV*
Constitutional	17%	52%	48%	1%	8%	27%	37%	53%	3%	7%
Musculoskeletal	24%	24%	68%	3%	3%	22%	55%	40%	2%	10%
Cranial	25%	42%	33%	0%	25%	23%	43%	53%	3%	4%
Visual	23%	46%	49%	0%	8%	23%	37%	56%	8%	6%
Large Vessel	23%	45%	53%	2%	2%	19%	29%	33%	5%	48%
Cohort 2 (C2, Biopsy negative, no Tocilizumab)										
Probability	*Pr(Relapse 1 symptom | baseline = No)*					*Pr(Relapse 1 symptom | baseline = Yes)*				
Baseline Symptom	*Con.*	*Msk.*	*Cran.*	*Vis.*	*LV*	*Con.*	*Msk.*	*Cran.*	*Vis.*	*LV*
Constitutional	13%	63%	50%	0%	0%	41%	43%	56%	15%	24%
Musculoskeletal	41%	27%	36%	9%	32%	35%	55%	65%	15%	15%
Cranial	60%	30%	20%	0%	60%	33%	48%	62%	15%	13%
Visual	31%	37%	57%	6%	31%	44%	56%	52%	22%	7%
Large Vessel	28%	54%	59%	15%	0%	52%	30%	48%	9%	57%
Cohort 3 (C3, Biopsy or imaging proven, treated with Tocilizumab)										
Probability	*Pr(Relapse 1 symptom | baseline = No)*					*Pr(Relapse 1 symptom | baseline = Yes)*				
Baseline symptom	*Con.*	*Msk.*	*Cran.*	*Vis.*	*LV*	*Con.*	*Msk.*	*Cran.*	*Vis.*	*LV*
Constitutional	4%	35%	54%	8%	19%	3%	47%	47%	3%	19%
Musculoskeletal	7%	17%	72%	7%	24%	0%	66%	28%	3%	14%
Cranial	0%	56%	11%	0%	33%	4%	39%	57%	6%	16%
Visual	5%	54%	46%	0%	22%	0%	19%	57%	14%	14%
Large Vessel	6%	38%	59%	6%	12%	0%	46%	38%	4%	29%
Cohort 4 (C4, combined cohort)										
Probability	*Pr(Relapse 1 symptom | baseline = No)*					*Pr(Relapse 1 symptom | baseline = Yes)*				
Baseline symptom	*Con.*	*Msk.*	*Cran.*	*Vis.*	*LV*	*Con.*	*Msk.*	*Cran.*	*Vis.*	*LV*
Constitutional	14%	49%	50%	3%	10%	27%	40%	53%	6%	14%
Musculoskeletal	23%	23%	63%	5%	13%	22%	57%	44%	5%	12%
Cranial	28%	42%	26%	0%	35%	21%	43%	56%	6%	8%
Visual	21%	46%	50%	1%	14%	24%	38%	55%	13%	8%
Large Vessel	22%	46%	55%	5%	3%	24%	35%	40%	6%	44%

Con. = Constitutional, Cran. = Cranial, LV = Large Vessel, Msk. = Musculoskeletal, Pr = Probability, Vis. = Visual.

Values are percentages and represent the observed risk for the given symptom in those without (baseline = no) and with (baseline = yes) each symptom category at baseline.

P-114

Associated factors with health-related quality of life in a Latin American vasculitis cohort

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Background/Objectives: Mortality in ANCA-associated vasculitis (AAV) has improved with the new therapy strategies[1] which might impact in the health-related quality of life (HRQoL). However, there are lack studies focusing on factors associated to HRQoL. The aim of this work is to describe associated factors of HRQoL in a Latin American (Peru) AAV cohort.

Methods: We included patients from the Almenara Vasculitis cohort[2] who had at least one visit between December 2022 and November 2023. Sociodemographic features, disease duration, type of diagnosis, treatment, disease activity measured by the Birmingham Vasculitis Activity Score version 3 (BVASv3) score, damage measured by the Vasculitis damage index (VDI) score, as well as HRQoL measured by the AAV-PRO (Spanish version) and the Short Form 36 (SF-36). The AAV-PRO questionnaire includes six domains [organ-specific symptoms (OSS), systemic symptoms (SS), treatment side effects (TSE), social and emotional impact (SEI), concerns about the future (CF), physical function (PF)] with twenty-nine items, with a score ranging from 0 to 100: the higher the value, the worse the HRQoL[3]. Active/relapsing disease was defined by BVASv3 ≥ 1. Association between HRQoL and numeric variables was evaluated using Spearman's correlation, and association between HRQoL and categoric variables was evaluated using Mann-Withney u or Kruskal-Wallis tests.

Results: Forty-eight patients were enrolled; 36 (75.0%) of them were female. Their age and disease duration were 57.4 (13.5) and 5.1 (5.0) years, respectively. Microscopic polyangiitis was the more frequent AAV [30 (62.5%)]. The BVASv3 and VDI scores were 4.7 (7.9) and 2.5 (1.7), respectively; patients with active/relapsing disease were 22 (45.8%). Associated factors with HRQoL in AAV Peruvian patients are depicted in Table 1. In brief, as to the AAV-PRO, have completed high school was associated to better OSS, TSE y PF, whereas non-use of immunosuppressive drugs was associated to better PF. As to SF-36, male gender was associated to better physical and mental component summaries whereas high socioeconomic level was associated to better general health. When we take prednisone as a continue variable, prednisone dose was not associated to HRQoL.

Conclusions: Have completed high school, non-use of immunosuppressive drugs, male gender and high socioeconomic level were associated to better HRQoL in a Latin American (Peru) AAV cohort.

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Table 1. Associated factors with HRQoL in AAV patients.

		AAV-PRO[a]						SF-36[a]									
		OSS	**SS**	**TSE**	**SEI**	**CF**	**PF**	**PF**	**RF**	**BP**	**GH**	**VT**	**SF**	**RE**	**MH**	**PCS**	**MCS**
Gender	Female	36.1 (21.1)	51.7 (23.2)	42.1 (16.8)	51.3 (23.3)	55.4 (21.9)	35.2 (22.8)	48.3 (23.2)	20.1 (31.0)	48.5 (18.5)	39.4 (14.4)	47.2 (17.5)	55.9 (20.2)	36.1 (36.9)	54.1 (18.7)	40.6 (14.5)	36.1 (15.7)
	Male	33.3 (27.9)	38.5 (25.7)	31.3 (19.8)	43.1 (19.4)	46.3 (19.6)	26.6 (21.3)	70.0 (24.4)	43.8 (44.1)	55.3 (22.3)	49.2 (17.6)	62.1 (16.2)	62.5 (11.9)	49.9 (41.5)	70.0 (8.8)	55.9 (15.7)	58.8 (14.4)
	p	0.676	0.104	0.144	0.288	0.272	0.293	**0.012**	0.097	0.341	0.097	**0.014**	0.268	0.290	**0.002**	**0.003**	**0.026**
SES	High	35.9 (24.7)	42.1 (25.4)	33.9 (17.3)	46.0 (24.5)	50.4 (22.7)	29.6 (23.2)	56.1 (25.8)	25.9 (34.3)	55.6 (22.7)	46.9 (17.0)	52.6 (20.4)	56.0 (18.5)	49.4 (40.8)	59.9 (19.9)	47.3 (18.1)	53.0 (18.3)
	Medium	37.5 (25.3)	50.0 (19.1)	41.5 (12.9)	52.9 (16.4)	58.0 (17.4)	35.0 (25.0)	56.0 (27.7)	37.5 (49.0)	46.3 (9.8)	32.9 (10.0)	49.5 (14.6)	63.8 (17.1)	29.9 (33.2)	54.8 (15.3)	44.3 (14.6)	46.2 (13.3)
	Low	35.6 (17.0)	62.5 (24.8)	50.0 (22.4)	60.4 (21.5)	61.3 (23.9)	42.2 (21.6)	41.3 (22.3)	9.4 (18.6)	39.1 (12.2)	38.9 (13.7)	48.8 (19.0)	57.8 (24.0)	24.9 (34.5)	58.0 (18.3)	35.5 (10.4)	45.8 (12.5)
	p	0.879	0.091	0.087	0.262	0.361	0.324	0.389	0.433	0.104	**0.033**	0.807	0.433	0.213	0.707	0.207	0.463

		AAV-PRO[a]						SF-36[a]									
		OSS	**SS**	**TSE**	**SEI**	**CF**	**PF**	**PF**	**RF**	**BP**	**GH**	**VT**	**SF**	**RE**	**MH**	**PCS**	**MCS**
Educational level	Higher education	30.0 (22.7)	42.0 (26.8)	34.3 (17.0)	44.5 (23.4)	47.9 (21.0)	25.5 (20.7)	57.5 (27.3)	27.7 (36.9)	55.2 (21.3)	45.2 (14.3)	53.8 (19.1)	57.6 (17.5)	46.4 (38.9)	60.7 (17.7)	47.8 (17.9)	52.7 (16.3)
	High school graduate or less	43.0 (20.9)	57.5 (16.9)	46.5 (17.2)	55.8 (19.9)	60.5 (20.4)	43.8 (21.1)	48.5 (21.3)	23.8 (34.9)	43.2 (14.3)	37.3 (16.6)	47.0 (16.7)	57.5 (20.4)	29.9 (35.7)	54.4 (18.5)	39.8 (12.1)	45.3 (15.2)
	p	**0.027**	0.060	**0.028**	0.083	0.080	**0.004**	0.232	0.685	0.074	0.085	0.338	0.787	0.137	0.228	0.164	0.184
Diagnosis	MPA	31.0 (21.5)	49.2 (24.6)	39.5 (18.9)	46.8 (24.9)	51.7 (21.4)	32.3 (21.7)	54.7 (22.7)	20.8 (30.9)	47.7 (18.2)	44.7 (15.0)	51.7 (18.9)	57.5 (17.9)	36.6 (39.5)	57.9 (19.6)	43.8 (13.9)	49.7 (16.0)
	GPA	46.0 (21.4)	49.6 (22.7)	39.3 (16.4)	55.3 (17.4)	57.3 (22.4)	37.5 (25.1)	50.3 (30.2)	28.3 (37.6)	54.1 (21.9)	37.4 (17.4)	47.0 (17.3)	55.8 (18.2)	40.0 (36.2)	57.9 (17.2)	43.3 (18.8)	47.6 (17.0)
	EGPA	26.7 (30.6)	35.4 (34.4)	38.3 (23.6)	43.1 (19.3)	46.7 (22.6)	18.8 (16.5)	61.7 (27.5)	66.7 (57.7)	55.7 (22.2)	36.3 (6.0)	63.3 (14.4)	66.7 (31.5)	66.7 (33.5)	61.3 (6.1)	56.7 (24.0)	58.7 (14.0)
	p	0.077	0.779	0.966	0.603	0.678	0.438	0.793	0.283	0.549	0.215	0.278	0.915	0.368	0.970	0.621	0.513
Disease status	Remission	36.5 (24.5)	49.0 (23.3)	36.9 (19.2)	44.4 (20.2)	49.2 (19.6)	35.1 (22.7)	57.1 (23.6)	28.9 (36.5)	54.4 (20.6)	44.1 (12.3)	53.5 (16.3)	57.2 (18.8)	44.9 (41.1)	61.9 (15.8)	47.5 (15.3)	52.3 (16.5)
	Active/ relapse[b]	34.1 (20.8)	47.7 (25.9)	42.3 (16.4)	54.9 (24.2)	57.7 (23.1)	30.7 (22.7)	49.8 (26.8)	22.7 (35.3)	45.3 (17.2)	39.2 (18.8)	48.0 (20.3)	58.0 (18.7)	33.2 (34.2)	53.6 (20.0)	40.9 (16.6)	46.5 (15.4)
	p	0.959	0.917	0.240	0.130	0.191	0.519	0.213	0.436	0.141	0.177	0.399	0.615	0.381	0.221	0.065	0.230
Prednisone doses	None	41.0 (26.3)	23.8 (16.8)	35.0 (10.0)	40.0 (28.2)	38.0 (32.3)	18.8 (29.0)	64.0 (26.3)	55.0 (32.6)	62.6 (17.1)	45.8 (20.8)	63.0 (20.8)	55.0 (27.4)	73.4 (28.0)	64.8 (19.3)	57.8 (17.8)	60.6 (17.8)
	≤7.5mg/d	40.4 (24.3)	51.6 (21.8)	37.4 (18.0)	52.7 (18.0)	59.1 (16.9)	33.7 (21.9)	54.6 (24.9)	19.6 (35.3)	52.0 (21.0)	41.3 (15.0)	47.8 (16.1)	57.6 (18.0)	43.4 (40.8)	56.5 (15.0)	42.9 (14.6)	49.3 (16.3)
	>7.5mg/dl, ≤30mg/dl	29.7 (20.7)	53.1 (24.5)	42.5 (20.2)	51.3 (25.3)	51.6 (23.1)	39.1 (21.6)	51.6 (28.1)	25.0 (37.6)	44.0 (14.9)	43.0 (17.0)	51.6 (21.0)	55.5 (18.2)	22.8 (29.1)	59.8 (22.5)	43.0 (18.0)	46.6 (15.7)
	>30mg/dl, ≤60mg/dl	22.5 (6.5)	42.2 (33.2)	43.8 (19.7)	32.3 (26.2)	43.8 (17.0)	23.4 (18.7)	45.0 (13.5)	31.3 (23.9)	49.3 (26.6)	36.3 (9.5)	51.3 (14.9)	68.8 (12.5)	41.5 (42.0)	52.0 (17.3)	42.5 (10.5)	50.0 (14.5)
	p	0.344	0.117	0.534	0.350	0.204	0.219	0.711	0.075	0.224	0.807	0.418	0.375	0.067	0.610	0.352	0.506
IS drugs	None	30.0 (10.0)	33.3 (41.6)	33.3 (16.1)	47.2 (43.4)	35.0 (21.8)	8.3 (14.4)	63.3 (27.5)	41.7 (38.2)	60.0 (33.3)	60.7 (18.5)	50.0 (27.8)	66.7 (26.0)	66.7 (33.5)	53.3 (38.4)	55.0 (27.5)	59.7 (25.5)
	CYC	27.2 (21.7)	45.1 (20.7)	45.6 (20.4)	52.8 (23.9)	60.0 (20.5)	43.8 (19.3)	49.4 (25.4)	16.7 (35.4)	42.1 (13.2)	39.0 (20.8)	49.4 (24.0)	54.2 (14.0)	22.2 (37.3)	56.4 (21.8)	39.3 (18.2)	44.2 (18.0)
	RTX	39.4 (26.3)	61.1 (19.2)	40.0 (17.7)	46.8 (22.1)	43.9 (20.6)	35.4 (19.8)	53.3 (28.2)	27.8 (34.1)	53.2 (19.7)	42.7 (10.3)	54.4 (12.1)	61.1 (9.8)	40.6 (36.5)	62.7 (17.3)	46.2 (13.2)	52.3 (10.9)
	AZA	37.6 (23.1)	49.0 (25.1)	39.7 (19.7)	49.3 (21.5)	55.3 (22.0)	37.2 (24.6)	52.6 (26.7)	15.8 (27.9)	49.3 (17.8)	40.4 (14.2)	48.7 (19.1)	54.6 (17.3)	36.8 (39.9)	53.9 (15.4)	41.2 (14.3)	46.9 (16.1)
	Others[c]	36.9 (24.3)	42.2 (23.8)	33.1 (12.5)	48.4 (20.9)	57.5 (20.2)	18.0 (14.4)	58.1 (21.4)	53.1 (45.2)	54.4 (24.7)	40.8 (15.3)	54.4 (14.3)	60.9 (30.2)	54.1 (35.5)	66.5 (10.7)	52.0 (15.5)	55.4 (15.5)
	p	0.847	0.371	0.572	0.962	0.284	**0.025**	0.898	0.115	0.616	0.455	0.881	0.764	0.211	0.550	0.346	0.546

[a] Results are showed as mean and standard deviation (SD). $p<0.05$.

[b] BVASv3 ≥ 1

[c] Mycophenolate, leflunomide or methotrexate.

HRQoL: Health-related quality of life. AAV: ANCA-associated vasculitis. AAV-PRO: ANCA-associated vasculitis patient reported outcomes. SF-36: Short form 36. OSS: Organ-specific symptoms. SS: Systemic symptoms. TSE: Treatment side effects. SEI: Social and emotional impact. CF: Concerns about the future. PF: Physical function. RF: Role physical. BP: Bodily pain. GH: General health. VT: Vitality. SF: Social functioning. RE: Role emotional. MH: Mental health. PCS: Physical component summary. MCS: Mental component summary. SES: Socioeconomic status. MPA: Microscopic polyangiitis. GPA: Granulomatosis with polyangiitis. EGPA: Eosinophilic granulomatosis with polyangiitis. IS: Immunosuppressive. CYC: Cyclophosphamide. RTX: Rituximab. AZA: Azathioprine.

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Prognostic factors for end-stage renal disease in ANCA associated vasculitis patients – data from Croatian referal center

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Background/ Objectives: End -stage renal disease (ESRD) is serious complication in ANCA associated vasculitis (AAV) patients with renal involvement[1]. We aimed to explore independent predictors for ESRD in AAV patients in our center.

Methods: Study included 106 consecutive AAV patients with biopsy proven renal involvement in the period from 2007-2017. We analyzed clinical, laboratory and pathohistological data. Patients were grouped based on: clinical phenotype (microscopic poliangiitis (MPA), granulomatosis with poliangitiis (GPA), eosinophilic granulomatosis with poliangitiis (EGPA) and renal limited vasculitis (RLV)), serologic phenotype (MPO or PR3 positive, MPO and PR3 positive and MPO and PR3 negative) and histological class (crescentic, focal, mixed and sclerotic). Survival analysis was done using Kaplan-Meier analysis and log-rank (Mantel-Cox) test. Multivariate Coxovim regression proportional hazard model (Backward Stepwise method) determined independent predictors for ESRD by including variables with p<0,1 in univariate analysis, alongside sex and age.

Results: Cohort consisted of: 66 (61,1%) MPA, 20 (18,5%) GPA, 20 (18,5%) RLV patients. There were 14 (13%) PR3-ANCA positive, 57 (52,8%) MPO ANCA positive, 5 (4,6%) PR3-ANCA+MPO-ANCA and 32 (29,6%) ANCA negative patients. Average SCr was 316,5 µmol/l (IQR 207,0-548,5), 24-hour proteinuria median 1,7g/24h (IQR 0,8-2,8). Histologicaly (Berden classification[2]) 43 (39,8%) patients had crescentic, 19 (17,6%) focal, 34 (31,5%) mixed and 12 (11,1%) sclerotic class. Follow up time was 1 to 127 months (median 21 months; IQR = 7 - 44) and medium follow up time of 28,6 months (SD = 26,6). All the patients recieved the same induction treatment (cyclophosphamide and glucocorticoids +/- acute haemodialysis and plasma exchange treatment) and remission maintenance treatment (azathioprine). During follow-up 26 (24,5%) patients reached ESRD. In multivariate analysis acute dialysis (HR = 4,674, 95% CI =1,996-10,946; p = < 0,001) and IFTA more than 50% (HR = 2,652, 95% CI =1,157-6,081; p = 0,021) were independent predictors for ESRD. Event free survival for ESRD after 12, 24, 36 and 60 months was 80,6, 77,9, 76,1 and 71%.

Conclusions: ESRD in our cohort is mainly determined by the need for acute dialysis, which indicates serious renal involvement, and IFTA >50% which suggests disease was present for certain time undiagnosed on time or there was subclinical presentation which allowed for development of more renal fibrosis. Though clinical presentation may vary emphasis should be put on both timely diagnosis and treatment of AAV.

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Disclosures: None.

P-116

Development of a Renal Prognostic Score for ANCA-Associated Vasculitis Based on a Comprehensive Analysis of Renal Pathology

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Background/Objective: Glomerulonephritis is frequent in ANCA-associated vasculitis (AAV) and crucial to disease outcomes. We conducted a detailed assessment of renal pathology in Japanese patients with AAV, and developed a new score that would predict renal outcome.

Methods: Two-hundred-twenty-one patients who were diagnosed with AAV and underwent a kidney biopsy were enrolled. Patient characteristics and information on disease course for up to 60 months from the time of biopsy were collected. Data on glomerular, tubular, interstitial, and vascular lesions from kidney biopsies were analyzed; the three established classification and prognostic scoring systems (Berden Classification, Mayo Clinic/RPS Chronicity Score (MCCS) and ANCA Renal Risk Score (ARRS)) were validated. Further, we developed a new prognostic score by including variables relevant for Japanese patients with ANCA-glomerulonephritis.

Results: End-stage kidney disease (ESKD) risk prediction for the MCCS and the ARRS was confirmed. Moreover, our analysis identified four items with significant ESKD risk prediction capacity: percentage of cellular, fibrocellular, and fibrous crescents, and sclerotic glomeruli. Based on our findings, we created a score evaluating the percentage of these lesions to total glomeruli, the Percentage of ANCA Crescentic Score (PACS). The area under the curve evaluating PACS was 0.783. The optimal PACS cut-off for ESKD risk over 60 months was 43%. In addition, the percentage of cellular crescents and presence of interstitial inflammation were independent predictors of kidney function recovery.

Conclusion: We developed a new score predicting renal prognosis using histopathological data of Japanese ANCA-glomerulonephritis patients. Studies are needed to validate our results in international cohots.

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Disclosures: None.

P-117

Clinical characteristics of biopsy-proven Giant Cell Arteritis (GCA) in Australia: Results from the South Australian Giant Cell Arteritis (GCA) Registry

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Background/ Objectives: To determine clinical characteristics of biopsy-proven GCA in Australia.

Methods: GCA patients were enrolled in the South Australian GCA Registry. Data was collected using patient surveys and structured case note review, a subset (n=68) also had HLA DR4 typing completed. Results expressed as either percentages (N/D) or medians and interquartile range (IQR).

Results: 287 GCA patients with a positive temporal artery biopsy (1991-2023) were included in the study: 69% female, age 75 (70,81), 99% Northern European / Caucasian, BMI 26 kg/m^2(23,28), 11% current smokers and 32% former smokers, HLA-DR4 positive (60%). 26% (50/189) reported polymyalgia rheumatica prior to diagnosis. The most frequent baseline comorbidities were hypertension (44% 108/243), osteoporosis (42%, 99/235), hypercholesterolemia (28%, 64/231), ischaemic heart disease (13%, 30/233) and diabetes (10%, 24/237). The most frequent GCA clinical manifestations at presentation were temporal or other headache (176/222, 78%; 159/217, 73%), visual disturbance (158/223, 71%), malaise (115/170, 68%), jaw claudication (144/220, 65%) and fatigue (115/186, 62%). Laboratory findings, within 7 days of steroid initiation, indicated ESR (64mm/hr (39,94)), CRP (41mg/L (14,123)) above normal range, with elevated platelets (356 10^9/L (259,460)). The median prednisone initiation dose was 60mg/day (50,75). Patients reported multiple glucocorticoid (GC) adverse effects (median 4 (2,7)) with 94% experiencing at least one. The most frequently reported GC side effects were thin skin/bruising (59%), sleep disturbance (44%) and change in face shape (41%).

Conclusions: This study highlights the key clinical manifestations of GCA at presentation, as well as the high burden of steroid treatment in these elderly patients.

Disclosures: No Disclosures.

P-118

Clinical phenotypes in adult IgA Vasculitis using unsupervised cluster analysis

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Introduction: IgA vasculitis (IgAV), formerly called Henoch-Schönlein purpura, is an immune complex vasculitis affecting small vessels with dominant IgA deposits. Based on previously published data, we hypothesized that there were very specific initial phenotypes of adult patients who differ in terms of outcomes.

Objective: Find clinically relevant phenotypes to predict patient's outcome and to enable more personalized patient management.

Methods: We used a French nationwide retrospective registry of adult patients presenting with IgAV (IGAVAS). A total of 7 relevant clinically variables with no missing data were used for clustering (gender, age, general signs, skin necrosis, initial joint, digestive or renal involvement). We measure the (dis)similarity of observations using euclidean distance and Ward's method. Unsupervised hierarchical clustering was used for grouping phenotypic variables and patients: a heat map was generated, and participants were separated into clusters statistically and phenotypically relevant.

Results: The IGAVAS database comprises 260 patients, 37% of whom were women and the mean ± SD age of the patients with IgAV at diagnosis was 50.1 ± 18 years. Baseline manifestations included purpura (100%), arthralgias/arthritis/myalgia (61%), kidney disease (70%), and/or gastrointestinal involvement (53%).

For clusters have emerged. Cluster 1 (n=79, 30%) comprised middle-aged patients (median 52 years) with predominantly renal involvement initially and a middle kidney-prognosis. Cluster 2 (n=63, 24%) included young patients with almost exclusively digestive and/or joint involvement, whose renal prognosis was good but who were at high risk of clinical relapse. Cluster 3 (n=88, 34%) comprised patients with multi-system involvement, biologically highly inflammatory, with the most important immunosuppressive treatment. Cluster 4 (n=30, 12%) included elderly patients (median 72 years) with poor kidney prognosis. After a median follow-up of 17.2 [9.1–38.3] months, both clinical relapse (n=24, p=0.044) and distant chronic renal failure rate (n=79, p<0.001), were different for the 4 clusters.

Discussion and Conclusion: These baseline phenotypes could be used by clinicians. Age and type of organ initially involved appear to be critical factors in clustering to refine the future medical management and prognosis of these IgAV patients. These clusters could help guide clinicians as we move toward personalized medicine.

P-119

Prognostic assessment of the 2022 ACR/EULAR classification criteria for Takayasu arteritis: a multi-centre international study

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Background/ Objectives: The 2022 ACR/EULAR classification criteria for Takayasu arteritis (TAK) rely on a point-based clinical and imaging scoring system (from 0 to 22)[1]. The aim of this study is to investigate whether the baseline cumulative score and the fulfillment of each item included in the score correlate with the long-term prognosis of TAK patients.

Methods: Data of TAK patients from 4 centres (2 from Italy; 2 from India) were retrospectively reviewed. For each patient, the score provided by the 2022 classification criteria was calculated and the following outcomes were evaluated: glucocorticoid (GC) suspension, need of conventional and biologic DMARDs (cs- and bDMARDs) introduction, need of vascular procedures. Data on bDMARDs were retrieved only from the Italian cohorts. Correlation of these outcomes with the cumulative baseline score and with single item fulfillment was assessed. Additionally, the correlation between baseline ACR/EULAR 2022 score and disease activity indexes (i.e., DEI.Tak, ITAS2010) was evaluated. Univariate and multivariate logistic analyses and Spearman correlation analyses were performed as appropriate.

Results: We included 407 patients (163 from Italy; 244 from India) with a median follow-up of 80 (IQR, 37-143) months. Mean baseline score was 10.1 ± 3.5 and 378 (92.9%) patients were classified as TAK according to the 2022 ACR/EULAR criteria. GCs were started in 348 patients (85.5%) and suspended in 110 (31.6%) after a median of 43 (IQR, 23-87) months. csDMARDs were started in 331 patients (81.3%) after a median of 1 (IQR, 0-5) month. bDMARDs were started in 108 patients (66.3%) after a median of 16 (IQR 8.8-39) months. Vascular procedures were performed in 101 patients (24.8%). Mean baseline DEI.Tak and ITAS2010 scores were 8.8 ± 5.5 and 10.4 ± 6.6, respectively. A higher baseline cumulative score was negatively associated with GC suspension (OR 0.901 [95%CI 0.844- 0.962], p=0.002) and positively associated with csDMARD introduction (OR 1.102 [95%CI 1.027-1.184] p=0.007). No correlation with bDMARD start and vascular procedures was found. **Table 1** shows the association of each item with different outcomes. At multivariate analysis, difference in blood pressure ≥20 mmHg and abdominal aorta + renal/mesenteric involvement were negative predictors of GC suspension; limb claudication and carotid abnormalities were predictors of csDMARD introduction. Angina/ischemic cardiac pain was predictor of need for vascular procedure, conversely to carotid abnormalities. Finally, a higher score strongly correlated with both baseline DEI.Tak (rho=0.549, p<0.001) and ITAS2010 (rho=0.575, p<0.001).

Table 1 legend.

Univariate and multivariate logistic analyses evaluating the association of each item with different outcomes.

	GC SUSPENSION						INTRODUCTION OF ≥ 1 csDMARD						INTRODUCTION OF ≥ 1 bDMARD						NEED OF ≥ 1 VASCULAR PROCEDURE					
	Univariable			Multivariable			Univariable			Multivariable			Univariable			Multivariable			Univariable			Multivariable		
	OR	CI	p-value	OR	CI	p-value	OR	CI	p-value	OR	CI	p-value	OR	CI	p-value	OR	CI	p-value	OR	CI	p-value	OR	CI	p-value
Female sex	1.365	0.763-2.440	0.294				0.997	0.541-1.838	0.992				1.314	0.530-3.259	0.556				1.342	0.755-2.388	0.316			
Angina/ischemic cardiac pain	0.517	0.205-1.303	0.162				0.930	0.391-2.211	0.869				1.020	0.293-3.548	0.975				2.692	1.336-5.424	0.006	2.682	1.313-5.479	0.007
Limb claudication	1.022	0.648-1.612	0.925				2.106	1.208-3.673	0.009	2.035	1.155-3.585	0.014	1.071	0.550-2.086	0.840				1.406	0.893-2.214	0.141			
Vascular bruits	0.593	0.362-0.971	0.038	0.810	0.471-1.393	0.446	1.652	0.975-2.800	0.062				1.869	0.945-3.694	0.072				0.925	0.564-1.517	0.758			
Reduced pulse	0.932	0.590-1.472	0.762				1.282	0.775-2.119	0.333				1.445	0.748-2.792	0.273				0.970	0.616-1.527	0.894			
Carotids abnormalities	0.933	0.591-1.474	0.766				2.285	1.301-4.016	0.004	2.121	1.184-3.798	0.012	1.074	0.520-2.217	0.848				0.422	0.256-0.696	0.0007	0.423	0.255-0.700	<0.001
Blood pressure difference ≥20	0.474	0.294-0.765	0.002	0.537	0.327-0.880	0.014	1.318	0.787-2.207	0.295				1.980	0.891-4.399	0.094				0.713	0.449-1.133	0.153			
1 artery involved	2.290	0.924-5.674	0.074				0.480	0.200-1.150	0.099				0.407	0.139-1.189	0.100				1.125	0.459-2.759	0.797			
2 arteries involved	1.573	0.836-2.961	0.160				0.802	0.401-1.606	0.533				1.254	0.511-3.080	0.621				1.530	0.829-2.822	0.174			
≥ 3 arteries involved	0.536	0.312-0.920	0.023	0.745	0.407-1.365	0.341	1.597	0.901-2.831	0.109				1.342	0.654-2.754	0.422				0.704	0.415-1.193	0.192			
Symmetric involvement	0.711	0.442-1.145	0.160				1.840	1.106-3.060	0.019	1.450	0.851-2.472	0.172	1.053	0.535-2.071	0.882				1.075	0.669-1.728	0.766			
Abd. aorta + renal/mesenteric involvement	0.479	0.293-0.782	0.003	0.577	0.341-0.976	0.040	0.788	0.475-1.309	0.358				1.233	0.592-2.569	0.576				1.074	0.679-1.699	0.761			

Conclusions: A higher baseline score obtained from the ACR/EULAR 2022 TAK classification criteria was associated with a more aggressive disease course. No specific item was associated with disease prognosis. At baseline, the ACR/EULAR 2022 score might be a surrogate of disease activity scores.

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Disclosures: None.

P-120

Prevalence and causes of hospitalization in Giant Cell Arteritis: analysis of a large cohort of patients in the first 5 years following diagnosis

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Background/ Objectives: Giant Cell Arteritis is a chronic autoimmune disease, associated with severe complications, multiple comorbidities, and treatment side effects, which can lead to hospital admission.

The aim of this study was to explore rates and causes of hospitalization in GCA patients, focusing in the first 5 years following diagnosis.

Methods: A cohort of 150 patients with GCA diagnosed between 2005 and 2020 in our Center and fulfilling the 2022 ACR/EULAR criteria for GCA [1] was analyzed. Records of hospital admissions in the first 5 years following diagnosis were collected. Hospitalizations at diagnosis were excluded.

Results: We enrolled 150 patients (F 69%, M 31%, median age at diagnosis 74 (IQR 67-78) years) with GCA: 96 (64%) had cranial arteritis (C-GCA), 22 (15%) extracranial large vessel vasculitis (LV-GCA) and 32 (21%) both cranial and large vessel involvement (LV-C-GCA).

Forty-nine patients (33% of the cohort) had at least one hospital admission, with 25 patients having only 1 hospitalization, 11 having 2, and 13 having 3 or more hospitalizations.

A total of 101 hospital admissions were recorded: 5 for disease relapse and 96 for other causes. The 5 hospitalizations for disease relapse (4 for temporal headache and 1 for temporal headache and visual impairment) occurred after a median time to first diagnosis of 24 (12-24) months and 4 patients out of 5 were out of treatment.

In the remaining 96 cases, the main causes of hospitalization were infectious diseases (26%), followed by cardiovascular diseases (23%) and surgery (17%, of which 88% elective surgery and 12% emergency surgery).

Among infections, the main site was the respiratory system (28%), followed by sepsis (24%), urinary tract (20%), gastrointestinal (16%) and skin (12%). The median time to first hospitalization was 12 months (IQR 6-18), and the median hospitalization length was 9 (5-13) days.

Conclusions: Patients with GCA have a high risk of hospitalization with approximately one third of the patients hospitalized during follow-up. Infections and cardiovascular diseases were the main causes of hospitalizations.

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Disclosures: None.

P-121

Development of a relapse risk score in patients with ANCA-associated vasculitis treated with cyclophosphamide induction

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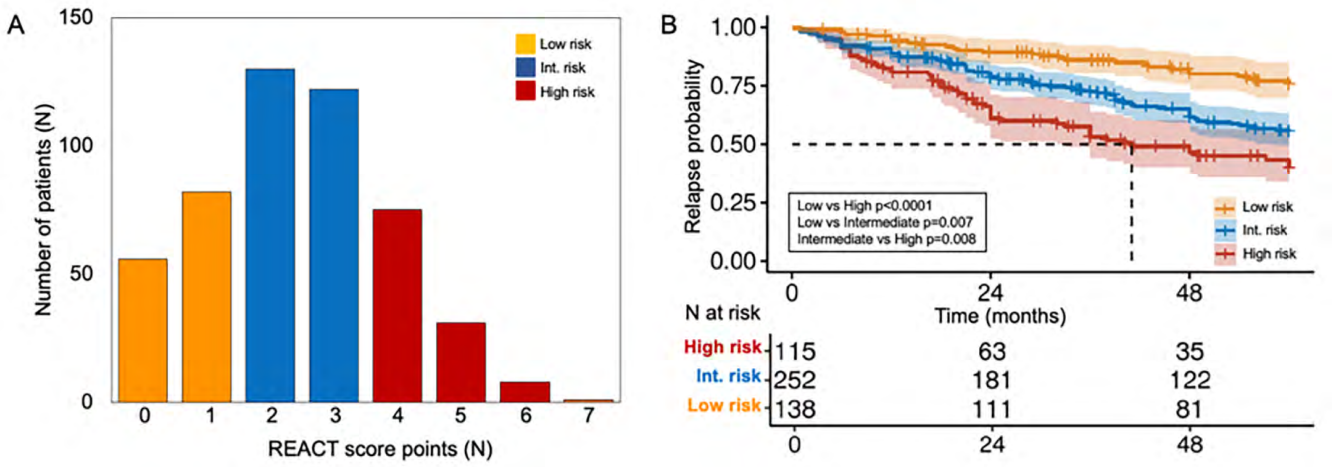
Background/Objectives: Cyclophosphamide (CYC), together with rituximab, is a mainstay for induction therapy in ANCA-associated vasculitis (AAV) [1]. The risk factors influencing the likelihood of relapse in individuals undergoing CYC induction are still unclear. This study aims to score the more robust predictors of relapse in these patients, thereby building a clinically useful tool.

Methods: Patients' characteristics were pooled from three cohorts from Italy, Ireland, and Spain. Eligibility criteria were a diagnosis of GPA, MPA, or EGPA, age >18 years, induction treatment with CYC [either as intravenous therapy (IV) and/or oral], and at least 12 months of follow-up. Baseline assessment included clinical data, laboratory testing, and assessment of manifestations of GPA, MPA, and EGPA in each organ system according to the Birmingham Vasculitis Activity Score (BVAS). Relapse was defined as the presence of ≥1 new vasculitis manifestation after a remission lasting at least 3 months; remission was defined as no disease activity (BVAS=0) irrespective of the glucocorticoid use. Time-to-remission and relapse-free survival probabilities were estimated using the Kaplan-Meier method. A multivariate Cox analysis, including the statistically significant factors at a previous univariate analysis, was employed to develop a practical prognostic score, defined as "Relapse Evaluation And Cyclophosphamide Treatment (REACT) score", in which each independent predictor was assigned a number of weighted points proportional to its β regression coefficient.

Results: The score development cohort comprised 505 patients. 223 patients (44.2%) had MPA, 217 (43.0%) GPA, and 65 (12.9%) EGPA. 183 patients (36.2%) experienced a relapse, with a median time to relapse of 33 months (IQR: 13-61). A multivariate Cox regression analysis proved that PR3-ANCA (HR: 1,30, 95% CI 1,01-1,87), IV CYC (HR: 1.78, 95% CI 1.31-2.41), cardiovascular involvement (HR: 1.82, 95% CI 1.01-3.25), arthralgias/arthritis (HR: 1.46 95% CI 1.08-1.98) and the absence of rapidly progressive glomerulonephritis (HR: 1.37, 95% CI 1.02-1.85) were all independent risk factors of relapse. These variables were used to build the REACT score, with each item receiving 1 point except for CV involvement and IV CYC, each receiving 2 points. We then identified three risk categories according to the score of each patient (**Fig 1A**). We identified 138 (27%) patients with low risk of relapse (score 0-1), 252(49%) with an intermediate risk (score 2-3), and 115 patients (22%) with a high risk (score 4-7). These three groups showed different relapse probabilities on Kaplan-Meier analysis (pairwise comparisons between the groups were all statistically significant) (**Fig. 1B**).

Conclusions: The REACT score can be employed at diagnosis to predict the risk of relapse in patients with AAV treated with cyclophosphamide induction. Its value needs to be confirmed in external cohorts.



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Disclosures: None.

P-122

Rates of relapses and serious adverse events in patients with GPA or MPA receiving rituximab for maintenance therapy: a multicentre, retrospective study

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Background/Objectives: There are limited real-life data regarding relapses and serious adverse events (SAEs) in patients with microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA) receiving rituximab (RTX) for remission-maintenance (1). We aimed to estimate the incidence of relapses and SAEs, as well the factors associated with the time-to-relapse in MPA/GPA patients under RTX-maintenance.

Methods: Retrospective study of newly diagnosed/relapsing GPA/MPA patients who received RTX-maintenance (≥1 RTX-cycle and ≥6 months follow-up) after complete-remission (Birmingham-Vasculitis-Activity-Score-version-3 [BVASv3] =0 plus prednisolone ≤7.5mg/day) with induction regimens. Relapses (BVASv3>0) were defined as major/minor, while SAEs included serious infections (SI), COVID-19-associated hospitalizations, deaths, cardiovascular events (CVE), malignancies and hypogammaglobulinemia. Incidence rates (IR) and relapse-free survival through Kaplan-Meier were estimated. Cox-regression analysis was conducted to investigate for factors associated with the time to first relapse.

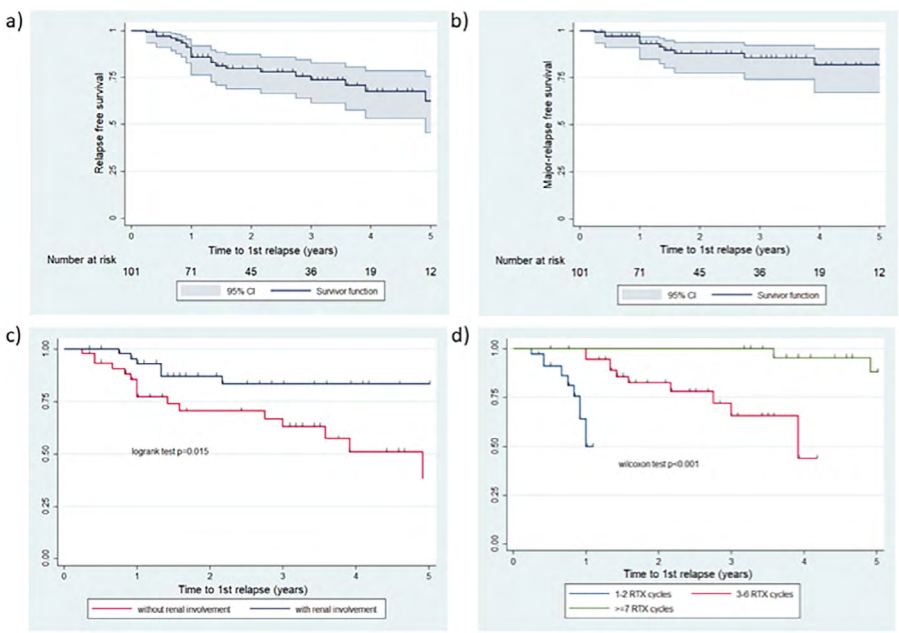

Figure-1 a) Relapse-free and b) major-relapse free survival in the total cohort during the first RTX-maintenance course. Relapse-free survival according to c) renal involvement and d) number of RTX-cycles received.

Results: 101 patients were included; GPA: 69%, 48% females, 53% newly diagnosed, median age: 63 years. During follow-up (294.5 patient-years, median [IQR] 3 [2-6] RTX-cycles), we identified 30 relapses in 24 patients (24%, IR 10.2/100 patient-years, 57% major). By Cox-regression, renal involvement (adjusted Hazard-Ratio [95% Confidence-Interval]: 0.23 [0.06-0.78], p=0.019) and number of RTX-cycles (adjusted Hazard-Ratio [95% CI]: 0.20 [0.09-0.44], p<0.001) were associated with a longer time to first relapse (Figure-1). We also recorded 17 SIs in 14 patients (14%, IR 5.8/100 patient-years), 11 COVID-19-associated hospitalizations (IR 3.7/100 patient-years), 4 malignancies (IR 1.4/100 patient-years), 6 CVE (IR 2/100 patient-years) and 10 deaths (10%, IR 3.4/100 patient-years). Among patients with normal IgG levels at baseline (n=42 among 53 with available IgG), 8 developed hypogammaglobulinemia (20%) but only 2 a SI.

Conclusion: Relapses occur in approximately one quarter of GPA/MPA patients under RTX-maintenance. The time to first relapse was longer in those with renal involvement and those who received ≥3 RTX-cycles. An increased rate of COVID19-associated hospitalizations was observed. Longer RTX therapy and close monitoring is required in these patients.

References:

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Disclosures: Supported by the Special Account for Research Grants, NKUA, Athens, Greece (DV #12085, 12086). Master thesis in Epidemiology – Research Methodology in biomedical sciences, clinical practice and public health (CG), Department of Hygiene, Epidemiology and Medical Statistics, Medical School, NKUA.

P-123

Mapping the ANCA Associated Vasculitis (AAV) care pathway. Qualitative insights from Physicians and Patients

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Objectives: To understand the ANCA-Associated Vasculitis (AAV) patient journey, associated burden of disease, and unmet needs.

Methods: Qualitive in-depth interviews with AAV-treating specialists – rheumatologists (n=9), nephrologists (n=5), pulmonologists (n=2), and immunologists (n=2) – and with AAV patients (n=13) in the US and Germany to foster learning about individual experiences and perspectives on the real-world journey for AAV patients from presentation of symptoms through diagnosis and treatment. Research conducted in September 2023.

Results: AAV patient journey varied by symptom severity and by country, with a more complex and longer journey for severe AAV patients (as defined by pulmonary involvement and acute kidney failure) in both the US and Germany. Patients consulted their general practitioner (GP) multiple times before being referred to a rheumatologist, nephrologist or pulmonologist who confirmed AAV diagnosis. Most patients were misdiagnosed by their GP (estimated time from initial symptoms to AAV diagnosis was 3 weeks to 12 years). After diagnosis, patients are treated with high-dose steroids as an induction therapy and severe patients receive maintenance treatment with rituximab or cyclophosphamide. 80% of the patients experienced periods of remission, with symptoms improving. AAV was also associated with significant physical and emotional burden. Once treated, patients experienced long-term physical and emotional side effects of the treatments and lived with the constant threat of an AAV relapse/flare. Patients and physicians identified two main unmet needs in the patient pathway – improving HCP awareness of AAV symptoms to reduce time to referral and diagnosis, and availability of new therapeutic options with fewer side effects to support chronic treatment.

Conclusions: This research provides a more detailed understanding of the AAV patient journey, highlighting the challenges with obtaining rapid treatment and the significant level of disease burden, and showing that improved awareness of AAV and new therapeutic options are needed.

Disclosures: None.

P-124

Assessment of Factors Affecting Pregnancy Outcomes in Takayasu Arteritis

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Background: Takayasu's arteritis (TA) is chronic granulomatous large vessel vasculitis commonly seen in reproductive women. Despite the lack of data about the effect of delivery type on feto-maternal outcomes and disease course in patients with TA, cesarean section is generally preferred in TA with aortic involvement to prevent increase in intraabdominal pressure during vaginal birth. In this study, we aimed to assess the feto-maternal outcomes and the choice of delivery type on TA patients.

Methods: TA patients diagnosed according to the 1990 American College of Rheumotology (ACR) classification criteria having at least one pregnancy history were included. Pregnancy complications;spontaneous abortion (SA), gestational hypertension (GHT), pre-eclampsia(PRE), gestational diabetes mellitus (GDM), fetal complications;prematurity(PRM), intrauterine growth retardation (IUGR), intensive care unit stay(ICU), intrauterine death (IUD) and neonatal death(ND) were evaluated. SA was defined as spontaneous pregnancy loss before 20 weeks of gestation, PRM was defined as delivery before 37 weeks of gestation, IUGR was defined as birth weight below the 10th percentile for gestational age(1). Outcomes of TA patients were compared with the aged matched healthy Turkish population.

Results: 94 patients(median age: 43 years (36-53) were included, 6 patients had infertility. Median disease duration was 9 years (5-16). Hata angiographic classes were classified as type 1 in 44 patients (45.8%), type 2 in 10 patients (10.4%), type 3 in 2 patients (2.1%), type 4 in 3 patients (3.1%), and type 5 in 37 patients (37.5%).A total of 254 pregnancies were detected, of which 199 (78.3%) occurred before TA diagnosis and 55 (21.7%) occurred after diagnosis. Mean gestational age was 30.1 ± 5.21 years in pregnancies after TA, 26 (47.3%) pregnancies received corticosteroids, 26 (47.3%) pregnancies received conventional synthetic disease-modifying antirheumatic drugs (DMARD), 7(9.1%) pregnancies received biologic-DMARD treatment. Cesarean section and normal vaginal delivery rates in pregnancies before and after Takayasu's disease are 41 (20.6%) - 120 (60.3%) and 25 (45.5%) - 7 (12.7%) respectively. Cesarean section was preferred 14 (%77,8) pregnancies with aortic involvement, normal vaginal delivery in 4 (%22,2) pregnancies. The fetal and maternal pregnancy outcomes of our study are shown in Figure 1.

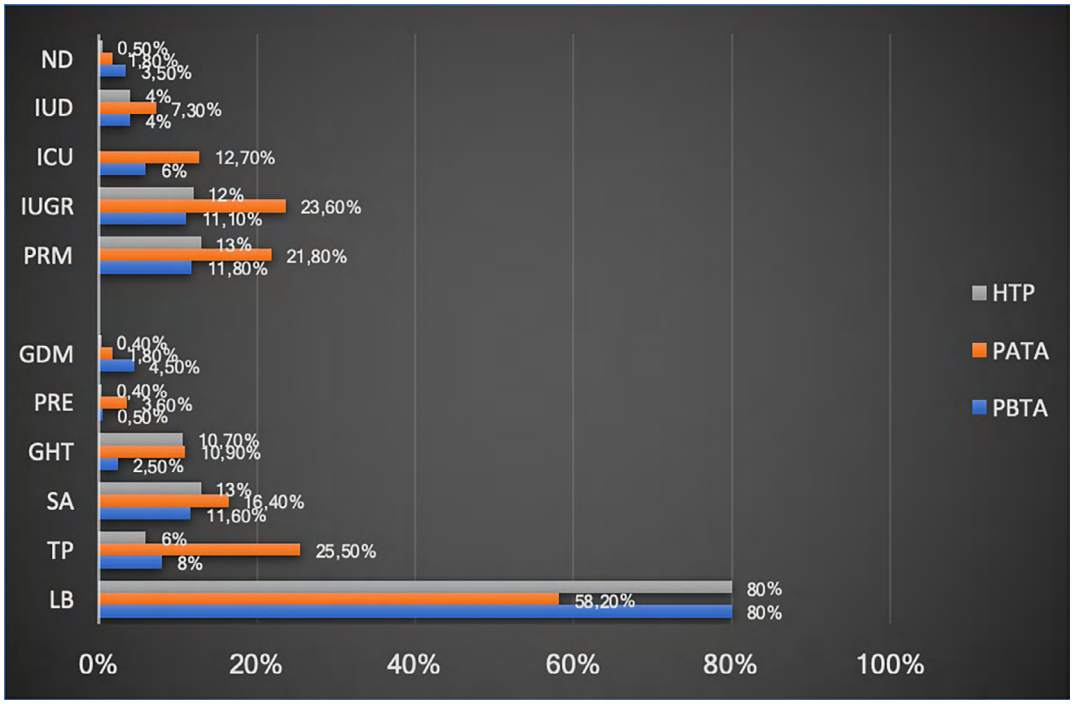

Figure **1: Maternal and fetal outcomes.**
LB: Live birth**, TP:** Termination of pregnancy**, PBTA:** Pregnancy before Takayasu arteritis
PATA: Pregnancy after Takayasu arteritis, HTP: Healthy Turkish population

Conclusions: Our results were compared with smilar age healthy turkish population, it was found that the incidence of fetal and maternal complication rates of PATA was higher than the HTP(2-3). We also found that cesarean section rate was increased while vaginal birth rate was decreased in TA patients after diagnosis.

References:

Keywords: Takayasu, pregnancy outcomes.

Disclosures: None.

P-125

Cluster analysis of plasmapheresis-treated subgroup of ANCA-associated vasculitis from the POLVAS registry

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Objectives: To assess the characteristics of plasmapheresis-treated granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) patients and to identify their phenotypes differing in mortality rates.

Methods: A retrospective analysis of the POLVAS database[1], including cluster analysis through both hierarchical and non-hierarchical methods.

Results: 125 patients (17.6%) were treated with plasmaphereses in the remission induction phase, whereas 586 (82.4%) were not. The former subgroup had a higher prevalence of constitutional symptoms (80.0 vs. 61.2%, p<0.001) and renal manifestations (91.2 vs. 72.9%, p<0.001), and was more likely to require chronic (38.4 vs. 16.6%, p<0.001) or temporary (25.6 vs. 5.3%, p<0.001) dialyzes. Among those who underwent plasmaphereses, three clusters were identified. Cluster one consisted of 39 patients (31.2%), mainly GPA (n=34, 87.2%), characterized by the lowest median age at diagnosis (49 years), the lowest prevalence of constitutional symptoms (n=30, 76.9%), and central nervous system involvement (n=1, 2.6%), but the highest frequency of ocular signs (n=18, 46.2%). Cluster three comprised 29 patients (23.3%), had the highest percentage of MPA (n=13, 44.8%), the highest median age at diagnosis (62 years), and the highest prevalence of constitutional symptoms (n=28, 96.6%) and central nervous system involvement (n=13, 46.4%). The hazard ratio of mortality in comparison to the whole subgroup not treated with plasmaphereses was lowest for cluster one (HR=0.999, 95%CI 0.73-1.36) and highest for cluster three (HR=5.96, 95%CI 2.55-13.93). The phenotype of the second cluster comprising 56 patients (44.8%), who in most cases had GPA (n=42, 75.0%), was intermediate between the first and third clusters, with HR 2.28, 95%CI 1.55-3.35.

Conclusions: Renal involvement and insufficiency were characteristic of patients qualified for plasmaphereses. Specific clinical phenotypes of vasculitis treated with plasmaphereses are associated with a higher risk of death compared to individuals not treated with plasmaphereses.

References:

1. Polish Vasculitis Registry: POLVAS - Polish Archives of Internal Medicine. Accessed February 26, 2023. https://www.mp.pl/paim/issue/article/3920/

Disclosures: None.

P-126

Occupational exposure to silica and clinical presentation in ANCA-associated vasculitis: a monocentric retrospective study

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Background/ Objectives: Exposure to silica is associated with an increased risk of autoimmune diseases, including ANCA-associated vasculitis (AAV)[1–3]. It remains unclear whether silica exposure modifies clinical presentation of AAV, and it is not known whether it affects prognosis. The aim of this work is to address these questions.

Methods: This is a retrospective, monocentric observational study comparing clinical and prognostic features between two groups of patients with ANCA-positive AAV: cases with a well-documented history of occupational exposure to silica (confirmed by industrial hygienists) and controls with no exposure. Each case was matched to 2 controls based on time of diagnosis (± 1 year relative to the case).

Results: We identified 25 patients with AAV and a clear-cut history of occupational exposure to silica and 50 controls with no exposure, diagnosed between 2000 and 2023. Compared to controls, patients exposed to silica were more frequently males and smokers (Table). Average age at presentation was 66±14 years and most patients had microscopic polyangiitis and MPO-ANCAs, with no significant differences according to silica exposure (Table). Patterns of organ involvement were also comparable across the two groups (Table). Renal vasculitis was present in almost all patients, probably reflecting a referral bias, with no significant differences in terms of severity of renal impairment and evolution to end stage renal disease between exposed and unexposed individuals. There was a trend for lower survival in patients with exposure to silica (median survival from AAV diagnosis: 172 months in cases and 111 months in controls, log-rank test p=0.065). In multivariate Cox regression, the risk of death was independently associated with age at diagnosis (HR 1.09 per year, 95% CI 1.04-1.14, p<0.001) and not with silica exposure (HR 0.96, 95% CI 0.39-2.41, p=0.936) or smoking history (HR 2.06, 95% CI 0.80-5.33, p=0.135).

Conclusions: Patients with AAV and exposure to silica were more frequently males and smokers, likely reflecting socio-economic factors. We did not identify otherwise distinct clinical features in exposed patients, similarly to other Authors such as Hogan et al..[2] Exposure to silica did not seem to significantly affect renal prognosis or survival either. The limited sample size and lack of quantification of silica exposure must be acknowledged and may have reduced statistical power.

References:

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3. Pollard, K. M. Silica, Silicosis, and Autoimmunity. *Front. Immunol.* **7**, (2016).

Disclosures: None.

	Silica exposure (cases) n=25	No silica exposure (controls) n=50	p-value
Age at diagnosis (years)	68 ± 10	65±15	0.337
Male sex	24 (96%)	18 (36%)	<0.001
Cigarette smoking	19 (83%)	20 (43%)	0.004
Microscopic polyangiitis.	20 (80%)	37 (74%)	0.774
MPO-ANCA positive	19 (76%)	37 (74%)	1
Other autoimmune diseases	3 (12%)	11 (22%)	0.463
Creatinine at diagnosis (mg/dl)	3.48 ± 2.76	3.73 ± 2.38	0.690
Proteinuria at diagnosis (g/24h)	2.20 ± 1.49	1.61 ± 1.46	0.173
DEI score at diagnosis	5.00 ± 1.38	5.16 ± 2.35	0.755
Organ involvement			
Renal±	25 (100%)	47 (94%)	0.532
ENT	4 (16%)	10 (20%)	0.917
Eye	0	6 (12%)	0.176
Lung nodules	7 (28%)	6 (12%)	0.161
Lung infiltrates	4 (16%)	11 (22%)	0.759
Peripheral neuropathy	2 (8%)	8 (16%)	0.548
Skin	0 (0%)	4 (8%)	0.364
Muskoloskeletal	8 (32%)	18 (36%)	0.932
Constitutional symptoms	19 (76%)	40 (80%)	0.921

Table: Comparison between patients with AAV with or without exposure to silica. Data are reported as mean ± standard deviation, with p values of Student's t tests, or numerosity (percentage), with p values of chi-squared tests.
DEI=Disease Extent Index.

P-127

Conditional survival in anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis

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[1]Department of Rheumatology, Health Sciences University, Gulhane Training and Research Hospital, Ankara, Turkey; [2]Department of Rheumatology, Gazi University Faculty of Medicine, Ankara, Turkey.

Background/ Objectives: Despite the introduction of new immunosuppressive agents, there is still a significant risk of mortality among patients with antineutrophil cytoplasmic antibody (ANCA)–associated vasculitis (AAV). However, conventional survival analysis plays a limited role in patients who survive for some time after initial treatment. Conditional survival (CS), defined as the probability that a person will survive an additional number of years if they have already survived "x" years, provides a dynamic and updated prediction of survival over the disease course (1). We aimed to estimate CS in AAV patients 5 years after diagnosis and the impact of baseline prognostic factors on CS.

Methods: Medical records of patients diagnosed with AAV between July 2016 and November 2023 were retrospectively reviewed. Adult patients who fulfilled the 2022 ACR/EULAR Classification Criteria for AAV and had complete medical records to collect clinical and laboratory data were included. Kaplan-Meier analysis was used to estimate overall survival (OS) and AAV-specific survival. The five-year CS was calculated to show the dynamic changes in mortality.

Results: A total of 191 patients with a median diagnosis age of 48.4 years and consisting of 105 (55%) males were included. At AAV diagnosis, PR-3ANCA (or c-ANCA) and MPO-ANCA (or p-ANCA) were detected in 134 (70.2%) and 28 (14.7%) patients, respectively. Renal involvement was the most (55.5%), followed by lungs (49.2%), ear, nose, and throat (44.0%), and gastrointestinal system (GIS) (3.7%). Baseline median birmingham vasculitis activity score (BVAS) and five factor score (FFS) were 15 and 1, respectively. Thirty-four (17.8%) patients had hypertension, 9 (4.7%) type 2 diabetes mellitus and 16 (8.4%) coronary artery disease. During a median follow-up of 6.7 years, 25 (13.1%) patients died. In the Kaplan-Meier analysis for OS, the survival rate did not fall below 80% during the follow-up period. Among the parameters that may affect survival in AAV patients, male gender (p=0.004), renal involvement (p=0.042), GIS involvement (p<0.001), plasmapheresis (p<0.001) and presence of hypertension (p=0.14) decreased survival time. The 5-year CS for patients with AAV was 89.5% at baseline and increased to 95.0% after 2 years. Detailed 5-year CS of patients according to conditions found to be associated with decreased survival in Kaplan-Meier analysis were presented in Table 1.

Conclusion: The probability of achieving 5-year overall survival after AAV diagnosis was increased with each 1, 3, 6 and 12 months of survival. Hazards of mortality are not fixed and need to be dynamically evaluated as a function of time. CS calculations can provide more accurate prognostic predictions than unconditional survival estimates.

References:

1. Zabor EC, Gonen M, Chapman PB, Panageas KS. Dynamic prognostication using conditional survival estimates. Cancer. 2013 Oct 15;119(20):3589-92. doi: 10.1002/cncr.28273.

Disclosures: None.

Table 1. Five-year conditional survival rate among patients with AAV.

		Conditional 5-year relative survival (%)				
Variables	**5-year relative survival at baseline (%)**	**At 1 month**	**At 3 months**	**At 6 months**	**At 1 year**	**At 2 years**
Total	89.5	91.7	92.4	93.9	95.5	95.0
Sex						
Male	84.9	85.8	88.3	91.0	92.9	91.3
Female	95.2	96.4	96.4	97.4	99.7	98.7
Gastrointestinal system involvement at diagnosis						
Yes	35.7	35.7	41.7	41.7	50,0	50,0
No	91.5	92.5	93.6	95.6	96.8	97.3
Renal involvement at diagnosis						
Yes	85.4	87.1	88.8	92.3	95.4	96.5
No	94.7	94.7	95.9	95.9	95.9	93.5
Hypertension at diagnosis						
Yes	78.4	78.4	78.4	86.0	88.9	88.9
No	91.9	93.1	94.9	95.5	96.8	96.3
Plasmapheresis						
Yes	72.7	75.7	82.2	89.8	96.1	90.0
No	93.6	94.3	94.3	94.8	95.5	95.5

P-128

ANCA associated vasculitis in the elderly. How different is it? Data from a Spanish University Hospital

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[1]Bellvitge University Hospital, Barcelona, Spain; [2]Axentiva Solutions, Barcelona, Spain.

Background/ Objectives: ANCA-associated vasculitis (AAV) has a peak incidence between 65-74 years old. Older patients present more comorbidities, immunosenescence and are more prone to develop serious infectious diseases and cancer. Besides, symptoms of vasculitis such as asthenia are usually masked by age-related normal involution (1-3). Therefore, we wanted to study the different presentation, clinical and analytical data and evolution between AAV in elderly and young patients.

Methods: Retrospective data from AAV incident patients from 2013 to 2022 from a University Hospital was used. We performed a Redcap database based on EUVAS registry. Data included demographic, clinical and analytical information, as well as details on treatments and outcomes (including Birmingham Vasculitis Activity Score -BVAS-, complications and deaths). The study compares the 'Young' group (<75 years old) with the 'Elder' group (≥ 75 years old).

Results: We analyzed 60 patients in the young group and 26 patients in the elder group. At diagnosis, the mean age in the young group was 63.72 (+/- 12.32) vs 84.31 (+/- 84.31) in the elder group ($p < 0.001$). There were no differences in demographics characteristics. Elder patients were more comorbid ($p < 0.05$ in hypertension, hyperlipidemia, coronary heart disease and COPD) and had lower EGFR than young patients at diagnosis 19.32 +/- 10.4 vs 37.22 +/- 32.19, $p = 0.005$), lower lymphocyte count, ($p = 0.003$), lower C3 levels ($p = 0.005$). There were no differences in kidney biopsy characteristics or BVAS at diagnosis. More patients debuted as End Stage Kidney Disease in the elder group (30.77%) than in the young group (10%), $p = 0.038$.

At one year follow up, infections were more frequent in older patients (61.9%) than in the young group (40.74%), $p = 0.5$, also malignancies $p = 0.018$. Elderly more frequently needed hospitalization (95.24% vs 72.22%, $p = 0.009$) and their hospitalization time was longer (37.7 +/- 32.04 vs 16.62 +/- 14.77 days, $p = 0.001$). They also yielded lower EGFR (28.9 +/- 13.88 ml/min vs 53.17 +/- 24.82 ml/min) and higher inflammation parameters (C-Reactive protein and Neutrophil Count). There were no differences in the number of relapses. 5 patients in the older patients and none in the young group died in the first year ($p < 0.001$).

At follow-up, survival curves were different between the groups (Figure 1).

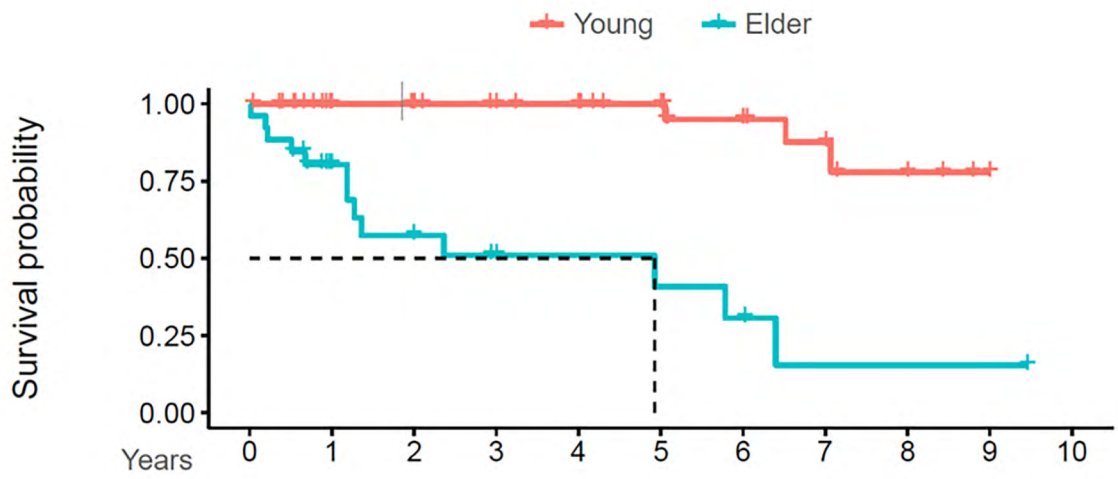

Figure 1. Kaplan-Meier curves of death in patients <75 yo and ≥ 75 yo.

Conclusions: Older patients show greater incidence of infection, malignancies and death after vasculitis diagnosis than younger patients. Different approach to treatment and care should be considered.

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Disclosures: Statistical analysis was performed with funds provided by CSL Vifor, without influence in the elaboration of the abstract.

P-129

Causes of mortality in patients diagnosed with Giant Cell Arteritis: infections as the main cause

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Background/ Objectives: Giant Cells Arteritis (GCA) is considered the most common of systemic vasculitis. It is more frequent in Northern European women over 50 years old[1]. The diagnosis must focus on the established classification criteria[2], supported by epidemiology and biopsy results. Immunosuppressive treatment is required in these patients, making them more susceptible to side effects[3]. The aim of this study is to review the death causes of the patients diagnosed of GCA.

Methods: Retrospective descriptive study complied from the registry of 90 patients diagnosed of GCA who were admitted in the Internal Medicine Department of the University Hospital of Navarra (UHN), from March 2007 to October 2023. Age, sex and causes of death were analyzed. We performed a statistic analysis of the data collected, comparing living patients with dead ones.

Results: In this study, women were 50 out of the 90 collected patients. Regarding mortality, 28 out of 90 patients analyzed died (31,1%), the majority were women (71.4%). The average of months between the diagnose and death was 32.28 months. Regarding death causes, 12 out of 28 died due to an infection of any kind (42,85% of deaths), 2 patients died of stroke (7,14% of deaths), 1 died because of an acute myocardial infarction (3,57% of deaths), 1 died from another kind of thrombosis (3,57% of deaths) and the rest died because of other types of illnesses, such as trauma, respiratory problems and general deterioration.

Conclusions: In the serie of patients studied, the most frequent cause of mortality was infections. It would be interesting to analyze, in subsequent studies, whether GCA contributes to a state of immunosuppression that leads to more infections than in the general population or if it is a side effect of the treatment administered.

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Disclosures: None.

P-130

Long-term clinical and immunological efficacy of different modes of therapy of ANCA-associated vasculitis

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Background/ Objectives: Treatment strategies for the antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) such as granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) depend on the course of the disease. In case of organ/life-threatening disease cyclophosphamide or rituximab (RTX) with concomitant glucocorticoids (GCS) are recommended as an induction therapy. As a maintenance therapy RTX, azathioprine (AZA) or methotrexate are recommended [1].

Methods: Patients with organ-threatening form of AAV (GPA or MPA) and BVAS/WG score minimum 3 points treated with rituximab as an induction therapy between 2016 and 2023 were included. RTX was administrated 4 times in the dose of 375 mg/m^2 at weekly intervals. After the induction oral (AZA or mycophenolate mofetil) or intravenous (RTX) maintenance therapies were used. They formed respectively RTX+oral group and RTX +RTX group. The second group received 500mg of RTX according to schedule: 0-14 days-6months-12months-18 months [2]. In all patients GCS were used. Statistical analysis was performed using Statistica 13.

Results:

	RTX+ oral	**RTX + RTX**	**p**
Number of patients	20	12	
Mean age	49.7 ± 4.9	44 ± 7.7	
Mean **BVAS/WG** median (max-min)	6 (10-3)	4 (10-3)	0.182
Mean BVAS/WG after 6 months	0 (3-0)	1 (2-0)	0.182
Mean BVAS/WG after 12 months	0 (2-0)	0 (1-0)	0.983
Mean BVAS/WG after 24 months	0 (1-0)	0 (1-0)	0.428
p (for comparison between 0-6-12-24 months)	**<0.001**	**<0.001**	
PR-3 ANCA number of patients (%)	15 (75%)	12 (100 %)	
Mean PR-3 ANCA level median (min-max) IU/ml	30 (146-4)	48.5 (198-4.4)	0.981
Mean PR-3 ANCA level after 6 months	7.2 (76-0)	6.45 (51-0)	0.905
Mean PR-3 ANCA level after 12 months	8.1 (61-0)	2.9 (36-0)	0.145
Mean PR-3 ANCA level after 24 months	6.5 (70-0)	0 (11-0)	**0.016**
p (for comparison between 0-6-12-24 months)	**<0.001**	**0.029**	
MPO ANCA number of patients (%)	5 (25%)	0 (0%)	
Mean MPO ANCA level median (min-max) IU/ml	10 (52-4.5)	-	
Mean MPO ANCA level after 6 months	4.2 (12-0)	-	
Mean MPO ANCA level after 12 months	7 (9.9-0)	-	
Mean MPO ANCA level after 24 months	7 (7.7-0)	-	
Recurrence rate after 12 months	1 (5%)	0 %	
Recurrence rate after 24 months	4(20%)	0 %	
ANCA seroconversion from positive to negative after 12 months	5 (25%)	5 (41.6%)	
ANCA seroconversion from positive to negative after 24 month	5 (25%)	10 (83 %)	
Number of patients being ANCA negative after 24 months of treatment	5 (25%)	10 (83%)	

Recurrence rate was significantly higher in RTX+oral group than in RTX+RTX group after 12 months (4 vs 0 %) and after 24 months of therapy (20% vs 0 %).

ANCA seroconversion rate after 12 months (25 vs 41%) and after 24months (25 vs 83%) were lower in RTX+oral group than in RTX+RTX.

Conclusions: Clinical symptoms rather than ANCA level changes are recommended for the diagnosis of the vasculitis recurrence. However in our retrospective analysis a combination of treatment with RTX followed by oral maintenance therapy was associated with lower ANCA seroconversion rate and higher recurrence rate in comparison to the treatment with RTX followed by RTX maintenance therapy.

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Disclosures: None.

P-131

Effect of Body Mass Index at presentation on mortality and development of kidney failure in ANCA-associated vasculitis. Results from the RITA-Ireland Vasculitis (RIV) Registry

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Background: The prognosis of ANCA-associated vasculitis (AAV) has been improved in recent years. However, patients still experience premature mortality, chronic ill health and lower quality of life. We sought to define the Body Mass Index (BMI) characteristics of patients presenting with AAV, identify changes in BMI over time and further elucidate the association between BMI at presentation and clinical outcomes including kidney failure and death.

Methods: The RITA-Ireland Vasculitis Registry is a nationwide registry encompassing the majority of university-affiliated public hospitals in Ireland. It captures the majority of cases of AAV in Ireland and prospectively follows their clinical course. Subjects were categorised into BMI ranges <20kg/m^2, 20-25 kg/m^2, 25-30 kg/m^2, 30-35 kg/m^2, 35-40 kg/m^2 and > 40 kg/m^2. Clinical outcomes assessed included BMI at presentation, BMI trends over time, death and the development of kidney failure (GFR <15mls/min or need for RRT).

Results: We identified BMI at presentation in 655 subjects. A further 141 subjects had serial measurements of BMI over their clinical course. The median age at presentation was 59 years (IQR 48-70). The male female ratio was 1:0.84. The percentage of PR3-AAV vs MPO-AAV was 48% vs 52%. The mean BMI at presentation was 27.6kg/m^2 (SD: 5.9kg/m^2). In those patients for whom serial BMI measurements were available the median change in BMI over the observed period was -0.23kg/m^2 (IQR -1.8 – +1.34kg/m^2).

There was a trend toward higher mortality for those subjects presenting with a BMI <20kg/m^2 (n=25) as compared to those with a normal BMI of 20-25kg/m^2 (n=199), however this did not reach statistical significance (OR = 2.73, 95% CI: 0.9- 8.1, p = 0.07). Patients at the other extreme of BMI, >40kg/m^2 did not manifest an enhanced risk of death (OR 1.27, 95% CI: 0.27 - 6.0, p = 0.7). No effect of BMI on the development of kidney failure was observed across all BMI groups.

13% of those patients with serial BMI measurements demonstrated a >5kg/m^2 change in BMI during their period of follow up. No effect on mortality was observed in this group as compared to those whose BMI remained within a range of +/-2kg/m^2 during follow up (OR = 2.15, 95% CI 0.36-12.7, p = 0.39).

Conclusions: In many illnesses extremes of BMI associate with adverse clinical outcomes. In this large observational cohort study BMI was not a significant predictor of death or kidney failure in subjects with AAV. A trend toward higher mortality in those with a low BMI was suggested but given the small numbers of underweight patients statistical significance was not observed. A relatively stable BMI was observed in those for whom serial data were available and no effect of dramatic weight gain or loss on overall mortality was observed. These data suggest that current weight-based treatment strategies in AAV may mitigate against enhanced mortality at extremes of BMI.

Disclosures: None.

P-132

Interstitial Lung Disease and ANCA Vasculitis: a review of the literature

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Background/ Objectives: Interstitial lung disease (ILD) is now recognised as a common feature of ANCA-associated vasculitis (AAV). There is emerging evidence that AAV-associated-ILD (AAV-ILD) is associated with higher mortality risk and poorer outcomes [1], and there is predominance for anti-myeloperoxidase (MPO) antibodies and a strong associated with Microscopic Polyangiitis (MPA) phenotype. The exact pathophysiology of AAV-ILD remains unclear, although some hypotheses suggested that anti-MPO antibodies may potentially trigger autoimmune, inflammatory response resulting in pulmonary fibrosis [2]. This review examines the outcomes in AAV-ILD patients according to their characteristics, ILD pattern and treatment received.

Methods: A literature search using PubMed, Embase, and Cochrane Library was conducted in May 2023, to identify all published studies including more than ten patients with diagnosis of AAV and ILD and reports of disease outcomes. Included manuscripts were screened and assessed for quality.

Results: Sixteen papers were included with a total of 1126 AAV-ILD patients from 2011 to 2023. The diagnosis of ILD typically preceded or occurred simultaneously with the onset of AAV (n=465, >90%). AAV-ILD most commonly displays a usual interstitial pneumonia (UIP) pattern of fibrosis (n=390, 58%), which was associated with higher risk of mortality and poorer prognosis compared to non-UIP pattern. MPA was dominant subtype of AAV (n=665, 90.6%). Anti-MPO antibodies were strongly associated with ILD (n=1002, 89%), while only a small proportion of patients were anti-Proteinase-3 (PR3) positive (n=52, 4.6%). The majority of patient received corticosteroids and/or cyclophosphamide as remission induction therapy, while azathioprine was used most frequently as maintenance treatment. A small proportion of patients received anti-fibrotic therapy (Pirfenidone or Nintedanib) alongside immunosuppression. AAV-ILD was found to be associated with high relapse rate (n=112, 25.9%) and mortality rate (n=403, 35.8%), with infections being the most common cause of death (n=143, 35.5%).

Conclusions: Despite the growing evidence demonstrating adverse outcomes in AAV-ILD patients, there is a lack of standardised guidance in risk stratification, treatment and follow up for this cohort of patients. This review emphasises the need for further research to confirm the existing evidence and propose a standardised international guidance in diagnosis, classification to allow earlier identification of high risk group and improved treatment strategies. Management of AAV-ILD should comprise a multidisciplinary approach with input from pulmonologists, radiologists and vasculitis experts.

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2. Kadura S et al, Eur Respir Rev. 2021 Nov 8;30(162):210123.

Disclosures: None.

P-133

Renal recovery for patients with ANCA-Associated Vasculitis and Low eGFR in a Spanish cohort

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Background and objective: Renal failure secondary to ANCA-associated vasculitis represent a clinical and therapeutic challenge (1). Fifteen percent to 38% of the patients develop end-stage kidney disease within 5 years, and once patients need dialysis, 29% to 82% die or still on dialysis 3 to 6 months after initiation of dialysis (2). Therefore, effectively managing renal vasculitis and preventing patients from reaching dialysis have important consequences (2).

In the post hoc analysis of ADVOCATE trial examines the result in the patient subgroup with severe renal insufficiency at enrollment into the trial, i.e., estimated glomerular filtration rate (eGFR) ≤20 ml/min per 1.73 m^2) and observed an eGFR increased on average 16.1 and 7.7 ml/min per 1.73 m2 in the avacopan and prednisone groups, respectively (P=0,003) (2).

This study aimed to compare the eGFR increased on average in our cohort of ANCA-associated vasculitis treated with different induction treatment scheme.

Methods: A retrospective study with two different subgroups: 19 patients with AAV diagnosis and severe renal insufficiency at enrollment with eGFR between 15 to 20 ml/min per 1.73 m^2 and 43 patients with AAV diagnosis and severe renal insufficiency at enrollment with eGFR between 15 to 30 ml/min per 1.73 m^2.

We compared the eGFR increased, after 12 months of follow-up, according to the induction treatment scheme: cyclophosphamide, rituximab, a combination of cyclophosphamide and rituximab and other (prednisone alone, prednisone with plasma rechange or prednisone with mycophenolic acid).

Results: In the subgroup of eGFR between 15 to 30 ml/min per 1.73 m^2, patients had at enrollment eGFR on average of 21±5 ml/min per 1.73 m^2 and after 12 months on follow-up eGFR on average was 41±23ml/min per 1.73 m^2 with an increase of 20±23 ml/min per 1.73 m^2.

In the in the subgroup of eGFR between 15 to 20 ml/min per 1.73 m^2, patients had at enrollment eGFR on average of 17±2 ml/min per 1.73 m^2 and after 12 months on follow-up, eGFR on average was 35±20 ml/min per 1.73 m^2 with an increase of 18±21 ml/min per 1.73 m^2. After 12 months of follow-up, eGFR increased on average 18, 17, 10 and 23 ml/min per 1.73 m^2 in the cyclophosphamide, rituximab, a combination of cyclophosphamide and rituximab and other groups, respectively. We compared our results with the post hoc analysis of ADVOCATE trial in Table 1.

	eGFR between 15 to 20 ml/min						ADVOCATE trial	
	Total (19)	**CFM (11)**	**RTX (4)**	**Combination (1)**	**Others (3)**	***p***	**Avacopan**	**Prednisone**
Age (yr.), mean ± SD	61.6±19.7	64.5±14.5	56±18.8	10	75.7±13	*0.29*	67.1±11.13	64.7±17.22
Sex, Male/Female (n)	10/9	7/4	1/3	0/1	2/1	*0.65*	15/12	11/12
BVAS, mean ± SD	19 ± 8.1 (n=12)	18.8±12.5 (n=5)	21.3±2.5 (n=3)	21	16.3±4.5 (n=3)	*0.41*	17.8±5.77	15.7±3.8
ANCA type • **MPO, n (%)** • **PR3, n (%)**	 12 (63) 6 (32)	 7 (70) 3 (30)	 3 (75) 1 (25)	 1 (100) 0	 1 (33) 2 (67)	*0.49*	 22(81.5) 5(18.5)	 20(87) 3(13)
eGFR at enrollment mean ± SD	17±1.7	16.2±1.7	17.5±1.9	15	18.2±1.6	*0.22*	17.6±1.86	17.5±2.04
UACR, g/g mean ± SD	1.71±1.9	1.34±1.3	2.1±3	4	1.4±0.6	*0.64*	0.593	0.739
Δ eGFR after 12 months of follow-up	18.3±21	18.1±21.6	17.5±31.8	10	22.7±7.6	*0.49*	16.1 ± 1.88	7.7 ± 2.01

Table 1. Comparation our cohort with ADVOCATE trial. BVAS: Birmingham vasculitis activity score at enrolment; CFM: cyclophosphamide; eGFR: estimated glomerular filtration rate (ml/min per 1.73 m^2); RTX: rituximab. UACR: urinary albumin-to-creatinine ratio.

Conclusions: In our cohort of eGFR between 15 to 20 ml/min per 1.73 m2 at enrollment, eGFR increased after 12 months of follow-up was similar to avacopan group and major than prednisone group.

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2. Cortazar FB, Niles JL, Jayne DRW, Merkel PA, Bruchfeld A, Yue H, et al. Renal Recovery for Patients with ANCA-Associated Vasculitis and Low eGFR in the ADVOCATE Trial of Avacopan. Kidney Int Rep. abril de 2023;8(4):860-70.

Disclosures: None.

P-134

Differences in clinical presentation and outcome between Mexican Mestizo and European Spanish patients with ANCA-associated vasculitis: a comparative study of two cohorts

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Background/ Objectives: Most studies detailing the clinical course, epidemiology, and outcome of ANCA-associated vasculitis (AAV) have been done in European and Asian populations[1].We compared the initial presentation and outcome of two well-defined cohorts of patients with AAV, one from Mexican Mestizos (MMM-AAV), and the other from Spanish Europeans (SC-AAV).

Methods: Baseline clinical manifestations, relapses, chronic kidney disease (CKD), and mortality were compared between both groups. Disease extent and chronic damage accrued from vasculitis were calculated using the Disease Extent Index (DEI) and the Vasculitis Damage Index (VDI), respectively. Analyses were performed by separating into both, the clinical phenotype and the ANCA specificity.

Results: The distribution of groups is shown in Figure 1. According to the clinical entity, MM-AAV patients with granulomatosis with polyangiitis (GPA) were younger, with higher PR3-ANCA prevalence (86.8% vs 64%, p=0.021), but a lower prevalence of fever (34% vs 88%, p<0.0001), arthralgia and myalgia (5.7% vs 76%, p<0.0001), ENT disease (47.2% vs 84%, p=0.002), lung (39.6% vs 84%, p<0.0001), and peripheral nervous (13.2% vs 60%, p<0.001) involvement. For microscopic polyangiitis, MM-AAV patients were younger and had less severe kidney involvement (median creatinine level 0.86 vs 1.2 mg/dL, p=0.012). When analyzed according to serotype, PR3-ANCA MMM-AAV patients were younger, had a higher median initial DEI but lower VDI, and showed less frequent fever (35.4% vs 83.3%, p=0.001), arthralgia, myalgia, ENT manifestations, and peripheral nervous system involvement. For MPO-ANCA vasculitis, MMM-AAV were younger and had a higher initial DEI, but a lower prevalence of myalgias, ENT symptoms (38.5% vs 69.4%, p=0.040), and lung involvement (38.5% vs 69.4%, p=0.040). They relapsed more frequently than SC-AAV subjects. Overall survival at 5 years was decreased for MMM-AAV patients.

Conclusions: In this study from two tertiary referral centers, there were different frequencies of clinical manifestations between both geographical areas, and M-AAV patients relapsed more frequently than SC-AAV both in patients with PR3-ANCA or MPO-ANCA. There were no differences between populations when they were stratified according with clinicopathologic syndrome suggesting that stratification according with ANCA specificity might bring better accuracy to the estimation of outcomes in patients with AAV when comparing groups from different geographical areas.

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Disclosures: None.

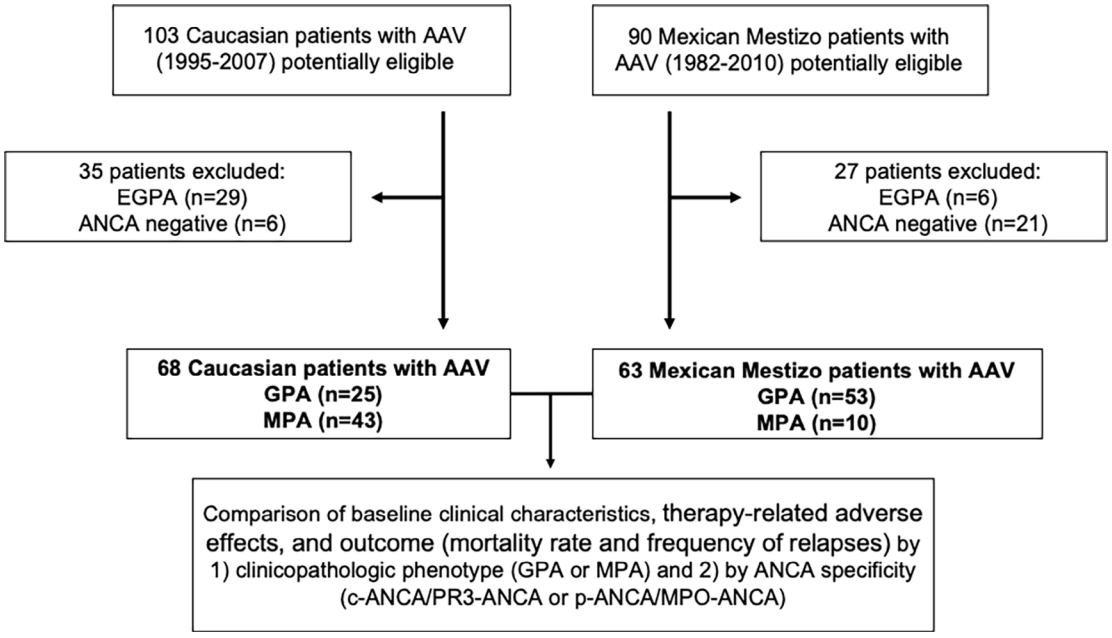

Fig. 1: STROBE flowchart for patient selection for inclusion in the retrospective cohort study of comparison between Spanish Caucasian and Mexican Mestizo patients with ANCA-associated vasculitis.

P-135

Patient Perspectives on the Burden of Eosinophilic Granulomatosis With Polyangiitis

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare vasculitis that can cause multi-organ damage and disability, despite current treatments. More effective therapies, and insight into patient experiences and treatment of EGPA, are needed.

Methods: A longitudinal, qualitative interview sub-study of patients with relapsing/refractory EGPA on systemic glucocorticoids ± stable immunosuppressants, enrolled in the randomised, double-blind, Phase 3 MANDARA study (NCT04157348) comparing benralizumab with mepolizumab. A sub-group of patients were invited for two, 1-hour, one-to-one interviews conducted by trained interviewers, to characterise their perceptions of the burden of EGPA and their treatment experience. Interview 1 focused on EGPA symptoms/impacts before entering the study and expectations of treatment, and occurred soon after treatment initiation between 7 and ≤21 days post-baseline. An exit interview (Interview 2) occurred between 7 and ≤21 days after the last dose of blinded treatment (Week 48). We present data from Interview 1.

Results: 35 (mean age 51.9 [standard deviation 12.0] years; 71.4% female) participants from MANDARA participated in the sub-study and completed Interview 1. The 35 participants reported experiencing a total of 42 symptoms. The most common symptoms were difficulty breathing/shortness of breath (n=31, 88.6%), nasal congestion/discharge (n=29, 82.9%), and fatigue (n=28, 80.0%). The most commonly reported impacts were ability to exercise or engage in more strenuous activities (n=26, 74.3%), quality and quantity of sleep (n=25, 71.4%), ability to work (n=22, 62.9%), ability to engage in social activities (n=21, 60%), and difficulty walking (n=19, 54.3%).

Conclusions: These results provide insight into patients' perspectives on the burden and impact of EGPA, highlighting the need for effective treatments to improve patients' symptoms and quality of life.

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Disclosures of interest: PAM reports receiving consulting fees and research support from AbbVie, Amgen, AstraZeneca, Boehringer-Ingelheim, Bristol-Myers Squibb, GlaxoSmithKline, InflaRx, and Takeda; consulting fees only from ArGenx, Cabaletta, CSL Behring, Dynacure, HiBio, Janssen, Novartis, NS Pharma, Regeneron Pharmaceuticals, and Vistera; research support only from Eicos, Electra, Forbius, Genentech/Roche, Genzyme/Sanofi, and Neutrolis; has consulting and stock options in Kyverna, Q32, and Sparrow; and receives royalties from UpToDate. **BH** reports receiving speaker fees and/or consultancies from AbbVie, Amgen, AstraZeneca, Boehringer, Bristol-Myers Squibb, Chugai, GlaxoSmithKline, InflaRx, Janssen, MSD, Pfizer, Novartis, Phadia, and Roche. **CP** reports receiving consulting and speaker fees from GlaxoSmithKline, Otsuka, Pfizer, and Roche, grants and personal speakers or advisory board fees from Roche, has served on advisory boards for AstraZeneca, GlaxoSmithKline, and Otsuka, and received educational grants from GlaxoSmithKline, Otsuka, and Pfizer. **US** reports receiving consulting fees from Amgen, Argenix, AstraZeneca, Boehringer Ingelheim, and CSL Vifor, and research grants from AstraZeneca, Bristol-Myers Squibb, Genentech, GSK, NorthStar Radioisotopes, and Syneos. **MEW** reports receiving consulting fees from Amgen, AstraZeneca, Boehringer Ingelheim, Cohero Health, Equillium, Genentech, GlaxoSmithKline, Novartis, Regeneron, Sanofi–Genzyme, Sentien Biotechnologies, and Teva. **CNH** and **LBS** are employees of AstraZeneca and may own stock/stock options. **CR** and **JH** are employees of IQVIA. **VHS** is a current employee of Insmed and a former employee of AstraZeneca.

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Does serial ANCA testing help predict the risk of relapse in granulomatosis with polyangiitis?

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Background: ANCA-associated vasculitis (AAV) is a frequently relapsing disease for which a meta-analysis concluded that serial ANCA measurements in remission are of limited use in guiding treatment decisions for individual patients. However, this analysis used heterogeneous ANCA assays and combined different subgroups of AAV patients or PR3 and MPO-AAV patients, whereas granulomatosis with polyangiitis (GPA) and PR3-AAV have a higher risk of relapse. We investigated whether serial ANCA testing with a uniform ELISA assay could be of interest in predicting the relapse risk in a cohort of GPA patients.

Methods: To be included, patients had to have GPA follow-up at a referral centre, at least two measurements of ANCA titer by ELISA, one less than 12 months apart during inactive disease, and a follow-up visit and assessment of disease activity within 12 months. The primary objective was to assess the association of an increase in ANCA titer at the time of inactive disease with any relapse within the following 12 months. The primary endpoint was the cumulative incidence of relapse over the following 12 months and the secondary endpoint was the incidence of major relapse. We estimated 12-month adjusted restricted mean survival times (RMST) for patients with an increase in ANCA levels compared with those without. To obtain confounder-adjusted relapse-free survival curves, we used direct standardisation (G-computation) using a Cox regression model with potential confounders. The results were analysed in patients with elevated ANCA titer compared to those without and in a subgroup of PR3-AAV patients. In a sensitivity analysis, we compared patients with ANCA doubling versus no doubling.

Results: A total of 357 countable periods were analysed in 121 GPA patients. We observed 52 relapses: 5 in patients with an increased ANCA titer vs. 47 in those without (unadjusted relapse rate: 18.8% vs.13.0%). The adjusted relapse rate was 13.3% (3.2-32.0) in 23 patient-periods vs. 13.0% (8.9-17.5) in 334 patient-periods. In PR3-AAV patients (101 patients, 297 periods), the corresponding relapse rate was 15.6% (3.8-36.7) vs. 14.5% (9.7-19.8) (Fig.). When restricted to patients with a doubling of the ANCA titer, the relapse rate was 18.0% (4.4-41.2) in 18 patient-periods vs. 12.7 (8.7-17.1) in 339 patient-periods. Similarly, RMST in the adjusted analysis was 342.4 (307.8-359.9) vs. 343.0 (334.3-350.8) days in the two groups. The difference in RMST was -1.8 (-39.0-19.8) and -9.6 (-53.8-13.9) days in patients with PR3-AAV and a doubling of the ANCA titer, respectively, compared to those without. In the secondary analysis, the adjusted risk of major relapse was 10.6% (1.2-29.4) vs. 8.1% (5.2-11.7), with a difference in RMST of -4.3 days (-36.3-13.5) in patients with an elevated ANCA titer vs. those without.

Conclusions: Despite using the same ELISA test consistently over time in a homogeneous population of GPA patients followed at a reference centre, the predictive value of an increase in ANCA, a doubling of ANCA or an increase in PR3-ANCA alone is not sufficient to predict relapse at one year to consider escalating treatment.

Disclosures: None.

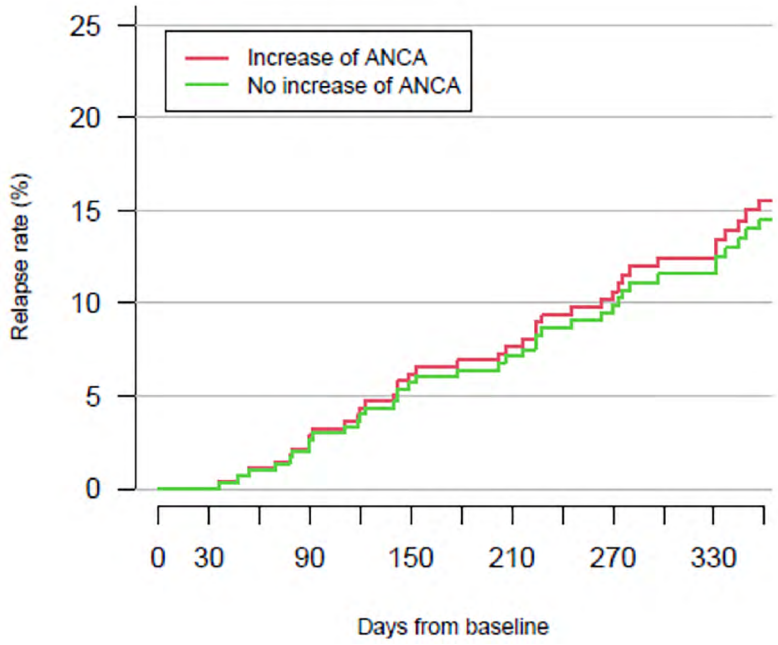

Figure. Adjusted relapse rate for the subset of GPA patients restricted to PR3-AAV patients.

P-137

Management and outcomes in patients with concurrent ANCA associated vasculitis related diffuse alveolar hemorrage and venous tromboembolism

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Background/Objectives: Diffuse alveolar hemorrhage (DAH) is one of the common presentations of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) and may lead to hypoxemic respiratory failure requiring intensive care (1). An increased risk of venous thromboembolic events (VTE) is also recognized in patients with AAV (2,3). In this study we aimed to identify the clinic characteristics, management, and outcomes of patients of patients with AAV who had DAH complicated by VTE, or vice versa.

Methods: This was an observational retrospective study of patients who were diagnosed with DAH and VTE during the same episode of care. Demographics, clinical features, and outcomes were collected.

Results: Nineteen patients (4.3%) of 440 patients with DAH caused by AAV between 1996 to 2022 were diagnosed with VTE during the same hospitalization. Patients were predominantly male (n=13) and median age (range) at diagnosis was 61 (54, 72). Thirteen patients had c-ANCA/PR3-ANCA and 6 patients had p-ANCA/MPO-ANCA. Seven patients were diagnosed with DAH before the VTE, and median time (min, max) between the diagnoses was 5 (4,19) days. Four of them had deep vein thrombosis (DVT), one of them had only pulmonary embolism (PE) and 2 of them had PE and DVT. Five patients were iagnosed with VTE prior to developing DAH with the median time (min, max) between the two diagnoses being 2 (1,4) days. Three of them had DVT, one of them had PE and DVT and one of them had only PE. Six patients were diagnosed as DAH and VTE on the same day. One patient developed DAH 10 days after being diagnoses with DVT and initiation of anticoagulant therapy and inferior vena cava filter placement; anticoagulation was stopped, and he suffered a second DVT and PE.

During the hospitalization, 11 (61%) patients needed mechanical ventilation support and 12 (67%) intensive care unit admission, and one patient with usual interstitial pneumonia in addition to DAH and VTE died. Fifteen patients had 6 or more months of follow-up, 14 of them had achieved remission by month 6.

Conclusions: Respiratory symptoms of patients with DAH caused by AAV should be monitored carefully, and the threshold to look for VTE should be low. The management of patients with DAH and VTE is challenging and needs to be decided individually according to the severity of hemorrhage, and the localisation and severity of VTE and other clinical factors.

Table 1. Disease related features of patients with AAV and related DAH and VTE.

	Patients with DAH before VTE (n=7)	Patients with VTE before DAH (n=5)	Patients with DAH and DVT (n=6)
Gender, male, n (%)	5 (71)	4 (80)	3 (50)
Age at diagnosis, median (range)	61 (57,72)	73 (73,79)	58 (56, 62)
ANCA IIF/ELISA, n (%) p-ANCA/ MPO-ANCA c-ANCA/ Pr3-ANCA	 1 (14) 6 (86)	 3 (60) 2 (40)	 2 (33) 4 (67)
VTE, n (%) DVT PTE DVT+PTE	 4 (57) 1 (14) 2 (29)	 3 (60) 1 (20) 1 (20)	 2 (33) 1 (17) 3 (50)
Time between DAH and VTE, median day (min, max)	5 (4, 19)	2 (1, 4)	0
Induction Therapy, n (%) IV methylprednisolone Rituximab Cyclophosphamide Plasmaspheres Hemodialyses	 8 (100) 4 (57) 2 (29) 5 (71) 3 (43)	 5 (100) 2 (40) 2 (40) 1 (20) 0	 6 (100) 4 (67) 1 (17) 3 (50) 1 (17)
Inferior vena cava filter, n (%)	4 (57)	3 (60)	4 (67)
Duration of follow-up, *median months (IQR25-75)*	67 (25-191)	51 (5-197)	41 (3-60)
ICU admission, *n (%)*	4 (57)	3 (60)	4 (80) /5
Mechanical ventilation (yes), *n (%)*	3 (43)	3 (60)	4 (80) /5
Hospital mortality (yes), *n (%)*	0	0	1 (17)
Complete remission at 6th month (yes), *n (%)*	7(100)	3 (75) /4	4 (100) /4
All cause mortality (yes), *n (%)*	1 (14)	3 (60)	2 (33)

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Association of dynamic changes in ANCA with subsequent vasculitis relapse- an encounter-centric analysis

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Background: Prior studies of ANCA as a relapse predictor have not adequately considered the effect of time and the recurrent nature of relapse. We aimed to examine the impact of dynamic switches of autoantibody level over time on relapse propensity.

Methods: We studied patients with granulomatosis polyangiitis or microscopic polyangiitis recruited to the Irish National Rare Kidney Disease Registry. The Standard Cox Regression model was used to analyse the effectiveness of ANCA Status in predicting the first relapse. Considering the recurrent nature of relapses per individual, we employed a recurrent event survival model called the Prentice-Williams-Peterson (PWP) GAP time model to assess the role of ANCA Switch in predicting the first and subsequent relapse (Sagara, I., Giorgi, R., Doumbo, O.K. *et al.*). Additionally, we adopted a multilevel logistic regression approach, treating each patient as a distinct cluster, to examine the impact of changes in continuous ANCA levels on predicting relapse occurrences.

Results: Of 565 recruits during a median follow-up time of 6.2 months, 146 (25.8%) encountered a single relapse, while 69 (12.2%) patients had multiple relapses. We observed no clear relationship between static ANCA positivity and first relapse (Hazard Ratio (HR): 1.094, Confidence Interval (CI): 0.584 – 2.05, p-value=0.779). However, the occurrence of a Negative to Positive (Neg-Pos) ANCA switch was associated with relapse (all relapses: HR:8.759, CI: 3.052-25.137, p<0.001, first relapse: HR: 6.873, p = 0.061) with a positive likelihood ratio of 4.25. Of patients with a 'Vasculitic phenotype' (renal, nerve, or lung hemorrhage) 12.7% experiencing a Neg-Pos switch suffered a relapse. After controlling for multiple clinical variables, the rate of change of anti-MPO/PR3 (Odds Ratio (OR) =6.78, CI=1.60 – 28.84, P=0.009) was more significantly associated with subsequent relapse than the ratio or delta anti-MPO/PR3 levels.

Conclusions: A dynamic change in ANCA Status, especially the transition from negative to positive ANCA, demonstrates a significant predictive capacity for the first and subsequent relapses.

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	PWP-GAP Univariate Analysis HR (95%CI, P-Value)	PWP-GAP Multivariate Analysis HR (95%CI, P-Value)
Male (ref: female)	0.928 (0.713 –1.211, p=0.586)	
Age at Diagnosis	0.994 (0.987 – 1.003, p=0.199)	
GPA (ref: MPA)	1.824 (1.38 – 2.41, p<0.001)	
Anti-PR3 (ref: Anti MPO)	2.070 (1.5688– 2.871, p<0.001)	2.044 (1.499-2.786, p<0.001)
Other (ref: Anti-MPO)	1.025 (0.335-3.140, p<0.965)	1.533 (0.526-4.466, p=0.433)
Vasculitic phenotype (ref: non-vasculitic)	3.928 (2.657 – 5.809, p<0.001)	3.908 (2.652 - 5.761, p<0.001)
Neg-Pos ANCA switch (ref: Pos-Neg)	8.141 (2.972 – 22.30, p<0.001)	8.759 (3.052-25.137, p<0.001)
Pos-Pos ANCA switch (ref: Pos-Neg)	2.099 (0.844 – 5.223, p=0.111)	2.017 (0.7914-5.141, p=0.141)
Neg-Neg ANCA switch (ref: Pos-Neg)	2.127 (0.812 – 5.575, p=0.124)	2.718 (1.009-7.319, p=0.047)
Switch Status Unknown (Ref: Pos-Neg)	1.631 (0.674 – 3.944, p=0.278)	1.722 (0.684-4.339, p=0.248)
On Treatment at the time of encounter (ref: Not on treatment)	0.965 (0.757 – 1.232, p=0.777)	0.917 (0.696-1.208, p=0.537)

Table 1: The Hazard Ratios (HR, 95% CI, and P- value) are reported for the PWP -Gap model used for the prediction of the first as well as subsequent relapses. The final multivariate models include only the variables statistically significant in univariate analysis or highly associated with the risk of relapse (Treatment status).

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Diffuse Alveolar Hemorrhage in patients with ANCA associated vasculitis and Interstitial Lung Disease

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Background/Objectives: Microscopic polyangiitis (MPA) is a small vessel vasculitis that affects mainly kidneys and lungs. Diffuse alveolar hemorrhage (DAH) and interstitial lung disease (ILD) are detected often in patients with MPA. An association of ILD and MPA is well-recognized, and ILD with usual interstitial pneumonia (UIP) pattern was found to increase mortality in patients with MPA. DAH is one of the severe manifestations of MPA and may lead to hypoxemic respiratory failure requiring support in intensive care units (ICU). In patients with MPA who also have ILD, DAH may become life-threatening more quickly and be more difficult to treat. In this study, we aimed to investigate the clinical features and prognosis of patients with MPA and DAH with or without concurrent ILD.

Methods: Observational retrospective study of patients diagnosed with MPA and DAH with concurrent ILD, and comparison to patients with MPA and DAH without ILD, matched for gender, age, and ANCA-type. Demographics, clinical features, and outcomes were collected.

Results: Sixteen patients of 440 patients with DAH (3.6%) caused by AAV between 1996 to 2022 had pre-existing ILD. Patients were predominantly male (n=10) and median age was 76 (range 66, 81). Six patients had never smoked. All patients had p-ANCA/MPO and 15 patients had renal, and one patient had peripheral nervous system involvement. Eleven patients had a radiographic usual interstitial pneumonia (UIP) pattern. For remission induction, glucocorticoids were used in all patients (12 patients received iv methylprednisolone, 4 patients received high dose oral prednisolone) combination with rituximab (n=9) or cyclophosphamide (n=6). Three patients also received plasmaspheres. Ten patients were hospitalized, and 5 required ICU management with mechanical ventilation support. Two patients died during the hospitalization for DAH treatment, both had UIP. We compared the 16 patients with MPA- DAH with ILD to 15 matched patients with MPA-DAH without ILD. There were no significant differences in overall mortality between the two groups (p=0.05).

Conclusions: Pre-existing UIP pattern and its severity rather than non-UIP may be a risk factor for hospital mortality in patients with MPA-DAH.

Table 1. Demographic and disease related features of patients with MPA -ILD and DAH and MPA-DAH- non ILD.

	MPA with ILD and DAH (n=16)	MPA with DAH without ILD (n=15)	p
Demographic characteristics			
Male sex, n (%)	10 (63)	9 (60)	1.0
Current age, median (IQR25-75) years	76 (66, 81)	75 (65, 81)	1.0
Age at DAH diagnosis, median (IQR25-75) years	69 (61, 74)	68 (61, 75)	0.8
Smoking history, never, n (%)	6 (38)	5 (33)	1.0
p-ANCA positivity, n (%)	16	15	1.0
MPO ANCA positivity, n (%)	16	15	1.0
***Remission Induction therapy,* n (%)**			
Cyclophosphamide	6 (38)	5 (33)	1.0
Rituximab	9 (56)	8 (53)	1.0
High dose steroid	16	14 (93)	1.0
Plasma exchange therapy	3/15 (20)	7 (47)	0.3
***Outcomes,* n (%)**			
Hospital admission	10/14 (71)	9/14 (64)	1.0
ICU admission	5/13 (39)	5/14 (36)	1.0
Mechanical ventilation	5/13 (39)	5/14 (36)	1.0
Hospital mortality	2 (13)	0	0.5
All-cause mortality	9 (56)	6 (40)	0.05

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ANCA-associated vasculityis in patients aged 75 years or more at diagnosis: clinical features and outcome of a multicentric Spanish cohort

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Background/ Objectives: There are few data related to ANCA-associated vasculitis (AAV) outcomes in very elderly patients. We aim to describe the clinical characteristics and outcomes of a group of patients diagnosed after 75 years old and compare them with those younger.

Methods: Data from patients aged ≥ 75 years at AAV diagnosis were extracted from the Spanish Registry of Systemic Vasculitis (REVAS), a multicentric retrospective and prospective cohort study that includes patients diagnosed with systemic vasculitis over the last 20 years.

Patients were included if they had a diagnosis of AAV according to the 2012 revised Chapel Hill Consensus Conference and were followed up for at least at least 1 year or deceased.

Variables are described as mean (standard deviation), median (quartile 1 – quartile 3) or proportions, as appropriate. Statistical analysis was performed using SPSS v21.

Results: From a cohort of 664 patients diagnosed with AAV, a total of 105 patients aged ≥ 75 years at diagnosis were identified: 22 with granulomatosis with polyangiitis (GPA), 71 with microscopic polyangiitis (MPA), and 12 with eosinophilic granulomatosis with polyangiitis (EGPA). The median age at diagnosis was 79 years, (IQR 76-82), 50.5% men. The median diagnosis delay was 6 (3-11.5) weeks. ANCAs were positive in 91.4% of cases. The median BVAS was 16 (13-20), the median FFS 1996: 1 (1-2), and the median FFS 2009: 3 (2-3). Renal biopsy was performed in 35.2% of patients. 55% of patients received IV pulses of glucocorticoids; 36.2% IV pulses of cyclophosphamide (CYC); 23.8% oral CYC, and 18.1% rituximab as remission induction therapy. 19% of patients required dialysis, and 5.7% plasma exchange.

Patients aged ≥ 75 years had more frequent cardiovascular risk factors (p=0.002); MPA (p<0.001); renal involvement (p<0.001), severe renal failure (creatinine >5.66 mg/dl, p=0.024 and lower EGFR (median 30 vs p<0.001), compared to younger patients. They also had more lymphopenia (p=0.005); positive ANCA (p=0.029); MPO-ANCA (p<0.001), and less frequent ear, nose, and throat (ENT) involvement (p<0.001) than younger. BVAS was similar in both groups but a high proportion of elder patients had FFS 1996 >1, and FFS 2009 >2. Nineteen (18.1%) patients had a disease relapse in the elder group compared to 239 (36%) in the younger (p<0.001), and 66 (62.9%) died compared to 25.7% (p<0.001). Moreover, elder patients died more frequently during the first year of follow-up (p=0.005).

Elder patients who died had a more severe renal failure (creatinine ≥ 5.66, p=0.003, 95%CI 2.62-4.93) and lung infiltrates (p=0.048), required more frequent dialysis (p= 0.037), had received less frequent rituximab (p=0.002), and suffered more frequent bacterial pneumonia p=0.049, OR 3.67 (1.01-10.9).

Age ≥ 75 years at diagnosis (p= 0.005), FFS2009 ≥ 2 (p=0.006), EGFR< 30 ml/min (p= 0.004), and creatinine ≥ 1.4 mg/dl (p= 0.024) were related to death in the first year of follow-up.

Conclusions: Patients aged ≥ 75 years had more frequent MPA and severe renal failure, and fewer ENT manifestations compared with younger patients. Elder patients had fewer relapses than younger patients and died more frequently during the first year of follow-up due to severe disease and infections. Rituximab therapy was associated with less mortality.

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Disclosures: None.

Table 1. Factors related to death during the first year of follow-up.

	Death 1-year	death >1 year	p	OR (95%CI)
Age ≥ 75 years	17 (56.7%)	13 (43.3%)	0.005	3.23 (1.45-7.17)
Creatinine>1.4 mg/dl	24 (80.0%)	6 (20.0%)	0.024	2.97 (1.15-7.65)
Mean EGFR<30 ml/min	19 (63.3%)	11 (36.7%)	0.004	3.24 (1.44-7.28)
FFS2009≥2	28 (93.3%)	2 (6.7%)	0.006	6.04 (1.38-26.38)

1. CLINICAL SCIENCE
1.06. End-organ damage: kidney failure, pulmonary and cardiac fibrosis...

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Characteristics of ANCA Patients with Tracheobronchial Disease

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Background/Objectives: ANCA associated vasculitis is a systemic disorder that leads to vascular inflammation, respiratory symptoms, and early morbidity and mortality. Tracheobronchial disease may also develop, and has been associated with younger age and female gender (1,2). Symptoms of large airway involvement can include cough, hoarseness, stridor, and dyspnea.

Methods: A retrospective review was conducted on patients with a diagnosis of AAV who had underwent evaluation for tracheobronchial disease throughout 01/2002 and 10/2022. Diagnosis of AAV was based on the 2012 International Chapel Hill Consensus Criteria. Patient were excluded if age < 18 or follow-up period was < 6 months. Differences between groups were tested using equal variance two sample t-tests or Fisher's exact tests. Sensitivity and specificity with exact binominal confidence intervals were calculated for unique baseline symptoms for prediction of large airway involvement.

Results: 136 patients with ANCA associated vasculitis who had been assessed for tracheobronchial involvement were included. 111 (81.6%) patients had tracheobronchial involvement and 25 (18.4%) did not **(Table 1)**. Younger age (Mean 41.1 vs 50.9, p=0.015) and female gender (77.5% vs 56.0%, p=0.043) were associated with large airway involvement. MPO positivity is represented more frequently in the large airway group (12% vs 35.1%, p=0.030). Renal disease was inversely associated (40% vs 19.8%, p=0.039). Nasal disease was present in similar distribution between the groups, though saddle nose deformity occurred more often in those with tracheobronchial disease that had nasal manifestations (0/16 [0%] vs 19/77 [24.7%], p=0.036). Upper airway symptoms, including cough, stridor, hoarseness, and dyspnea were more common among those with large airway manifestations. Stridor and hoarseness were common among patients with large airway disease (0% vs 54.1% and 0% vs 52.3%, p<0.001). Pooled sensitivity for the combined variable of hoarseness and stridor was 74.77 (95% CI 65.65-82.54) with a specificity of 100 (95% CI 86.28-100.00).

Conclusions: Younger age, female gender, and saddle nose deformity were positively associated with development of tracheobronchial disease in our ANCA vasculitis cohort. Renal involvement had an inverse association. Evaluating patients for hoarseness or stridor in the clinic may help to detect tracheobronchial involvement.

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Table 1: Demographics and clinical characteristics by large airway involvement				
	True diagnosis of airway involvement?			
	No (N=25)	Yes (N=111)	Total (N=136)	P-value
Age at vasculitis diagnosis				0.015[1]
Mean (SD)	50.9 (19.35)	41.1 (17.62)	42.9 (18.28)	
Range	20.3, 87.0	11.4, 78.8	11.4, 87.0	
Sex, n (%)				0.043[2]
Female	14 (56.0%)	86 (77.5%)	100 (73.5%)	
Race, n (%)				>0.999[2]
White	24 (96.0%)	106 (95.5%)	130 (95.6%)	
Other	1 (4.0%)	5 (4.5%)	6 (4.4%)	
Diagnosis, n (%)				>0.999[2]
GPA	25 (100.0%)	105 (94.6%)	130 (95.6%)	
MPA	0 (0.0%)	4 (3.6%)	4 (2.9%)	
Unspecified ANCA-associated vasculitis	0 (0.0%)	2 (1.8%)	2 (1.5%)	
ANCA Positive, n (%)				0.738[2]
Yes	23 (92.0%)	96 (86.5%)	119 (87.5%)	
ANCA Type				
C-ANCA, n (%)	21 (84.0%)	51 (45.9%)	72 (52.9%)	<.001[2]
P-ANCA, n (%)	4 (16.0%)	41 (36.9%)	45 (33.1%)	0.059[2]
PR3, n (%)	21 (84.0%)	55 (49.5%)	76 (55.9%)	0.002[2]
MPO, n (%)	3 (12.0%)	39 (35.1%)	42 (30.9%)	0.030[2]
Symptoms				
Constitutional, n (%)	8 (32.0%)	37 (33.3%)	45 (33.1%)	>0.999[2]
Musculoskeletal, n (%)	13 (52.0%)	36 (32.4%)	49 (36.0%)	0.105[2]
Cutaneous, n (%)	6 (24.0%)	14 (12.6%)	20 (14.7%)	0.207[2]
Ear, n (%)	4 (16.0%)	29 (26.1%)	33 (24.3%)	0.438[2]
Eye, n (%)	4 (16.0%)	11 (9.9%)	15 (11.0%)	0.477[2]
Nasal, n (%)	16 (64.0%)	77 (69.4%)	93 (68.4%)	0.638[2]
	n=16	**n=77**	**n=93**	
Nasal perforation, n (%)	5 (31.3%)	8 (10.4%)	13 (14.0%)	0.044[1]
Saddle nose deformity, n (%)	0 (0.0%)	19 (24.7%)	19 (20.4%)	0.036[1]
Unspecified inflammation, n (%)	7 (43.8%)	18 (23.4%)	25 (26.9%)	0.122[1]
Crusting, n (%)	9 (56.3%)	28 (36.4%)	37 (39.8%)	0.167[1]
Cardiovascular, n (%)	0 (0.0%)	3 (2.7%)	3 (2.2%)	>0.999[2]
Gastrointestinal, n (%)	0 (0.0%)	5 (4.5%)	5 (3.7%)	0.584[2]
Renal, n (%)	10 (40.0%)	22 (19.8%)	32 (23.5%)	0.039[2]
Nervous, n (%)	2 (8.0%)	11 (9.9%)	13 (9.6%)	>0.999[2]
Upper airway symptoms:				
Stridor, n (%)	0 (0.0%)	60 (54.1%)	60 (44.1%)	<.001[2]
Hoarseness, n (%)	0 (0.0%)	58 (52.3%)	58 (42.6%)	<.001[2]
Dyspnea, n (%)	1 (4.0%)	94 (84.7%)	95 (69.9%)	<.001[2]
Cough, n (%)	2 (8.0%)	83 (74.8%)	85 (62.5%)	<.001[2]
Hemoptysis, n (%)	0 (0.0%)	10 (9.0%)	10 (7.4%)	0.207[2]

[1]Equal variance two sample t-test p-value; [2]Fisher's exact p-value

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Kidney Phenotype in Interstitial Lung Disease Associated with ANCA-Vasculitis: European Multicentre Study

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Background/Objectives: Interstitial Lung Disease (ILD) in ANCA-associated Vasculitis (AAV) has the appearance of a progressive fibrotic disease on imaging and primarily affects the interstitial lung compartment and is usually associated with MPO-ANCA. Whether patients with AAV-ILD display a similar fibrotic pattern in their kidneys is unclear.

Methods: A European multicentre retrospective study included patients with AAV-ILD. The diagnosis of ILD was confirmed by a CT chest pattern of usual interstitial pneumonia (UIP), non-specific interstitial pneumonia (NSIP), organising pneumonia or chronic hypersensitivity pneumonia. We aimed to determine if kidney involvement in AAV-ILD exhibited a more fibrotic pattern compared to AAV-related nephritis without ILD, using data from the Cambridge AAV cohort.

Results: 135 patients with AAV-ILD were included; 94 (70%) had also kidney involvement, in whom the mean age was 71±11 years and 87% MPO-ANCA positive. The ILD diagnosis preceded AAV in 17%, 64% presented concurrently with kidney involvement, 20% with pulmonary haemorrhage. The most common lung radiological pattern was UIP (67%).

At presentation, the median glomerular filtration rate (GFR) was 27 ml/min per 1.73m^2 (interquartile range 12-50), with a median albumin-to creatinine ratio 23 mg/mmol (IQR 10-97). Among 72 patients with available kidney biopsy, the most prevalent Berden class was focal in 45%, followed by mixed in 33%, crescentic in 18% and sclerotic in 4%. Although, the prevalence of Berden classes did not significantly differ between ILD-nephritis and no ILD-nephritis groups, the former group had a higher baseline GFR (p=0.05), lower albuminuria level (p=0.002), higher percentage of normal glomeruli (p=0.027), lower glomerular necrosis percentage (p=0.002) and higher interstitial fibrosis score (p=0.049). Within five years, the ILD-nephritis group demonstrated renal recovery, as indicated by an adjusted mean delta GFR of 13.4 ml/min per 1.73m^2, without a significant difference compared to the no ILD-nephritis group. Over a median follow-up of 4.9 years (IQR 2-9), the progression to end-stage kidney disease (ESKD) was comparable between the groups. However, notably, the ILD-nephritis group experienced significantly poorer survival rates (mean 10.9 years vs 17.9 years, log-rank p<0.001).

Conclusions: In AAV-ILD, kidney involvement is often characterized by fewer inflammatory and a higher prevalence of fibrotic lesions than on non-ILD-AAV. Despite initial differences in renal pathology and kidney function between these groups, both demonstrated similar risks of progressing to ESKD. Nevertheless, it's crucial to underscore the significant influence of ILD on the overall outcomes of AAV patients with kidney involvement.

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Interstitial Lung Disease in Antineutrophil Cytoplasmic Antibody-Associated Vasculitis

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Background/ Objectives: Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is characterized by inflammation of small to medium-sized blood vessels, and usually associated with the presence of serum antigens (either myeloperoxidase, MPO or proteinase 3, PR3)[1-4]. In this retrospective study we aimed to (i) analyze the radiologic ILD patterns in subjects with AAV and (ii) correlate differing CT patterns of ILD with of clinical presentation, temporal relationship with the onset of vasculitis, and clinical outcomes.

Methods: We conducted a retrospective cohort study of all patients with AAV (microscopic polyangiitis [MPA] and granulomatosis with polyangiitis [GPA]) and ILD as seen on chest CT scans evaluated at our institution between 1997 and 2021. ILD patterns were classified according with the 2018 Fleischner Society criteria. Demographics and clinical features were abstracted via electronic chart review.

Results: We analyzed 143 patients with AAV-associated ILD; median age at the time of AAV diagnosis and ILD were 68 years (IQR 60–75) and 69 years (IQR 61–75), respectively (Table 1). In 44 patients (30.8%) a typical UIP pattern on chest CT was documented, whereas 13 (9.1%) manifested probable UIP pattern, 37 (25.9%) indeterminate for UIP, and 49 (34.3%) consistent with non-UIP pattern (Table 1). Most patients were male (86, 60.1%) but there was a predominance of females in the group of patients with non-UIP pattern which differed in comparison with the other CT pattern groups (p=0.019) (Table 1). Patients with typical UIP pattern were more commonly male and were more likely to be MPO-ANCA positive when compared to those with non-UIP ILD and was more often diagnosed before the onset of AAV, more likely to have reduced diffusion capacity on pulmonary function test (Table 1). Moreover, ILD pattern most consistent with non-UIP was more likely to be associated with an obstructive pattern on PFT. Survival at 1 and 5 years was significantly different between groups; lower survival was observed in patients with non-UIP compared to UIP pattern.

Conclusions: In AAV-ILD, patients with UIP pattern of fibrosis manifest differences in terms of sex distribution, onset related to vasculitis diagnosis, type of ANCA, PFT, and survival, when compared to non-UIP pattern.

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Disclosures: None.

P-144

Combined Activity, Recovery, and Chronicity Kidney Biopsy Grading for Prognostic Assessment in ANCA-associated Vasculitis with Glomerulonephritis

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Background/ Objectives: Glomerulonephritis (GN) is a frequent presentation of antineutrophil cytoplasmic antibodies (ANCA) associated vasculitis (AAV) , and an important factor of morbidity and mortality.[1] The present study on kidney histology from patients with AAV-GN was conducted to (i) grade kidney biopsies of AAV-GN based on AAV-GN combined score (CS), (ii) and evaluate clinical characteristics and outcomes in response to remission-induction treatments based on the AAV-GN-CS.

Methods: A retrospective cohort study of MPO- or PR3-ANCA positive patients with AAV and active renal disease. Inflammatory activity was assessed by the Activity Index (AI): a ratio between the number of crescents and/or necrosis and the total number of glomeruli (in percent). Recovery potential was assessed by the Normal Index (NI): a ratio between the number of normal glomeruli and the total number of glomeruli (in percent). For calculating the combined AAV-GN Combined Score (AAV-GN-CS) we assessed: a) activity: <10%=0;10% – 25%=1; 26%–50%=2; and >50%=3; b) normal (or recovery potential): <10%=3;10%–25%=2;26%–50%=1; and >50% =0. Chronicity was evaluated with the Mayo Clinic Chronicity Score (MCCS). For the combined score, we summed all the components. Our findings were further validated in 132 biopsies.

Results: We analyzed 329 patients with kidney biopsies available to score. The population was classified according with the risk of progression to end-stage kidney disease (ESKD) in 4 classes: minimal (0-5)–107 (32.5%); low (6-11)–140 (42.6%), intermediate (12-14)–52 (15.8%), and high (≥15)–30 (9.1%). Median eGFR at baseline correlated with the overall risk categories: 42.3 vs. 22.0 vs. 15.9 vs. 10.7 mL/min/1.73 m^2, p<0.0001. ESKD at 12 months was more frequent in patients at higher risk (50.0% vs. 21.2% vs. 12.9% vs. 4.7%, p<0.0001) (Figure 1). The AAV-GN-CS independently predicted the risk of ESDK at 12 months (IRR 1.615, 95%CI 1.189–2.194, p=0.002), particularly increased in patients classified as high risk (IRR 4.406, 95%CI 1.538–12.623, p=0.006) independently of ANCA specificity, IV methylprednisolone, and adjusted for severity of renal involvement and age.

Conclusions: The combined assessment of acute inflammatory activity, recovery potential and chronic changes on kidney histology predicted renal outcomes in patients with AAV-GN.

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Disclosures: None.

P-145

Impact of Sex in Clinical Presentation and Outcomes of Patients with ANCA-Associated Vasculitis with Severe Kidney Disease

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Background/ Objectives: Biological sex has been associated to a more rapid rate of chronic kidney disease progression (ie, speed of kidney function loss) in male than female[1]. The impact of sex in the clinical presentation and outcomes of patients with anti-neutrophil cytoplasmic antibodies (ANCA) associated vasculitis (AAV) with glomerulonephritis (AAV-GN) has not been studied, particularly in patients with severe kidney involvement at presentation (eGFR<15mL/min/1.73m2).

Methods: A retrospective cohort study on MPO- or PR3-ANCA positive patients with AAV (MPA or GPA) and eGFR<15 ml/min/1.73 m2 or ESKD at presentation. Clinical presentation and outcomes (renal recovery, dialysis at presentation, and ESKD) were analyzed according with sex.

Results: We analyzed 166 patients with biopsy proven active AAV-GN and eGFR <15mL/min/1.73m2 at the time of diagnosis: 78 (47%) were females and 88 (53%) were males. Arterial hypertension was more frequently present in males (85.2% vs. 70.5%, p=0.022). Median serum creatinine (SCr) was higher in males when compared with females (5.2 [IQR 4.2-7.4] vs. 3.6 [IQR 2.8-5.1] mg/dL, p<0.001) but there were no differences in eGFR at presentation. When analyzing only the 71 (24 females and 47 males) patients that started dialysis within 4 weeks, infections at 12 months were more common in females (75.0% vs. 36.2%, p=0.017). The rate of dialysis initiation or progression to ESKD was not different between males (15, 62.5%) versus females (29, 61.7%) being on dialysis at 12 months. By multivariable logistic regression, factors related with dialysis initiation within 4 weeks in our cohort were SCr (OR1.478, [95%CI1.231-1.776], p<0.001), alveolar hemorrhage (OR2.726, [95%CI 1.099-6.763], p=0.031) and PR3-ANCA (OR3.155, [95%CI 1.485-6.702], p=0.003) adjusted to sex. In addition, we found that the progression to ESKD at 12 months in patients who started dialysis within 4 weeks was predicted by the chronicity score (moderate [OR4.172, (95%CI 1.188-14.650), p=0.036] and severe chronicity [OR6.686, (95%CI 1.755-25.473), p=0.009]) and higher SCr levels (OR1.085, [95%CI 1.007-1.170], p=0.033) and this was independent of male sex (Table 1). Finally, we found that in this group, female patients developed higher rates of infections at 12 months.

Conclusion: In our cohort, male patients presented with higher SCr, and dialysis was started within 4 weeks more frequently. However, this did not result in different outcomes in terms of kidney recovery, overall dialysis rates, and progression to ESKD in patients with AAV-GN and eGFR<15mL/min/1.73m2 between groups.

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Disclosures: None.

P-146

Elderly Versus Younger Patients with Microscopic Polyangiitis vasculitis (MPA): A Single-Centre Retrospective Study

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Objective: Our objective was to analyze the clinical presentation and response to treatment at 6 months based on the age of disease onset amongst younger patients (age <65) and elderly patients (age>=65) with microscopic polyangiitis (MPA).

Methods: All patients seen at a tertiary vasculitis clinic between 2015 and 2023 with a diagnosis of MPA were included. Patients were divided into an elderly group (age>=65 years) and a younger group (age <65). Organ involvement, Birmingham Vasculitis Activity Score (BVAS) scores, Vasculitis damage index (VDI) scores and response to treatment were analyzed at disease onset and at a 6-month follow-up visit.

Results: Thirty-one patients were included. Younger MPA patients (n=18) with mean age atof diagnosis of 53.17 years were compared with older MPA patients (n=13) with mean age atof diagnosis of 76.08 years. The younger patients had statistically significant higher BVAS scores, along with higher incidence of renal, pulmonary, and cutaneous manifestations at disease onset. Furthermore, there was noted statistically significant clinical improvement in MPA's clinical presentation at 6 months, particularly in the domains of general symptoms, MSK, cutaneous, ENT, and pulmonary symptoms. In contrast, the elderly population presented with higher incidence of non-specific constitutional symptoms, with statistically significant improvement in the domain of general symptoms at 6 months.

Conclusion: MPA clinical presentation differed by age group. Younger patients had more aggressive vasculitis with higher incidence of renal, pulmonary, and cutaneous manifestations, whereas, elderly patients had more constitutional and non-specific symptoms.

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Clinical evolution of ANCA-associated vasculitis in a population with confirmed renal involvement through biopsy. Myeloperoxidase and proteinase 3 antibodies, which is worse?

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Backgrounds/Objectives: Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a group of rare but potentially serious diseases with high mortality. Renal involvement is frequent in AAV with patients developing end-stage renal disease (ESRD) or becoming dependent on dialysis in up to 23% of patients (1)(2)(3). Several studies suggest the presence of clinical factors as predictors of survival in these diseases (1)(4).

The objective of this study was to analyze clinical evolution of AAV and to identify potential risk factors for developing renal events (ESRD or dialysis) and death in patients with AAV, with special attention to the implications that the presence of myeloperoxidase (MPO) or proteinase 3 (PR3) antibodies at diagnosis may have on the disease progression.

Methods: We conducted a retrospective observational study of patients under follow-up for AAV. We considered only those with a confirmed diagnosis of AAV through renal biopsy for the present study. We collected clinical and laboratory variables at the time of disease presentation. We divided the patients based on the presence of MPO or PR3. Subsequently, we analyzed the patients' progression towards the occurrence of renal events (ESRD or dialysis) and mortality.

Results: Out of the 42 studied patients, 29 were MPO-positive and 13 were PR3-positive. We observed statistically significant differences in age and the frequency of hypertension, with the MPO group being older and more hypertensive than the PR3 group. On the contrary, PR3-positive patients exhibited a higher percentage of diabetes and increased severity of vasculitis at diagnosis as measured by the Birmingham Vasculitis Activity Score (BVAS). While most MPO-positive patients met criteria for microscopic polyangiitis (MPA), all PR3-positive patients met criteria for granulomatosis with polyangiitis (GPA) according to the ACR/EULAR 2022 guidelines. There were no statistically significant differences regarding clinical or laboratory variables analyzed, neither with induction nor maintenance treatment. We did not observe differences in the progression towards renal events or mortality between groups. However, we did observe a higher percentage of disease recurrence among PR3-positive patients (Table 1).

Conclusion: There were no statistically significant differences observed in the progression towards renal events (ESRD and dialysis) or mortality regardless of MPO or PR3 antibodies

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Disclosures: None.

Table 1: Baseline characteristics for the cohort comparing patients with MPO and PR3 groups and study outcomes.

CHARACTERISTICS	MPO (n= 29)	PR3 (n= 13)	p-value
Age (mean ± SD) Age older than 65 years (n, %)	70±14 25 (86)	53±12 5 (38)	0'002
Male sex (n, %)	12 (41)	9 (69)	0'095
CVRF (n, %) • HBP • DM	 19 (66) 5 (17)	 4 (31) 6 (46)	 0'036 0'049
Main clinical symptoms (n, %) • General • Proteinuria / Hematuria	 25 (86) 26 (90) / 27 (93)	 11 (85) 13 (100) / 12 (92)	 0'89 0'23 / 0'93
BVAS (mean ± SD)	18±5	21±3	0'027
Vasculitis criteria (n, %) • EGPA • GPA • MPA	 3 (10) 3 (10) 23 (80)	 0 (0) 13 (100) 0 (0)	< 0'001
Serum creatinine (mg/dl, median (IQR)	3'21 (1'7-5'08)	3'4 (1'1-4'5)	0'41
eGFR (ml/min/1'73m^2; median (IQR)	18'2 (9 -33)	27'5 (15-75)	0'09
Proteinuria g/24h (median (IQR)	1 (0'45-1'82)	1'3 (1-2'1)	0'16
Hematuria > 5 RBC/field (n, %)	27 (93)	12 (92)	0'93
% of response (n, %)	26 (90)	11 (85)	0'641
Time to response (months, median (IQR))	3 (2-5)	1'7 (1-10'5)	0'566
% of remission (n, %)	22 (76)	8 (62)	0'342
Time to remission (months, median (IQR))	10'5 (6'2 – 6'7)	11 (4'7 – 33)	0'926
% of AAV-recurrence (n, %)	8 (28)	9 (69)	0'01
VDI-lv (median (IQR))	3 (2-5)	3 (1'5-4'5)	0'914
Induction treatment (n, %) • Corticosteroids • Cyclophosphamide • Rituximab	 28 (97) 20 (69) 7 (24)	 13 (100) 10 (77) 3 (23)	 0'5 0'29 0'941
Maintenance treatment (n, %) • Corticosteroids • Rituximab • Mycophenolic acid	 9 (31) 15 (52) 8 (28)	 6 (46) 5 (38) 4 (31)	 0'344 0'426 0'833
Endpoints (n, %) • ACKD • Dialysis • Death	 15 (52) 7 (24) 9 (31)	 5 (38) 3 (23) 2 (15)	 0'43 0'94 0'29

SD: standard deviation; IQR: interquartile Range; CVRF: Cardiovascular Risk Factors; HBP: High Blood Pressure; DM: Diabetes Mellitus; BVAS: Birmingham Vasculitis Activity Score; EGPA: eosinophilic granulomatosis with polyangiitis; GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis; eGFR: estimated glomerular filtration rate; RBC: red blood cells; VDI-lv: Vasculitis Damage Index on last visit; ESRD: end-stage renal disease; OR: Odds Ratio; CRP: C-Reactive Protein; Cr: Creatinine.

P-148

Prognostic value of urine retinol binding protein in ANCA-associated vasculitis

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Background/Objectives: Renal involvement in ANCA-associated vasculitis is indicative of disease severity, characterized by pauci-immune extracapillary glomerular involvement. However, glomerular involvement is typically accompanied by secondary tubulointerstitial histological lesions, which strongly correlate with renal prognosis[1]. Neither the urine protein-to-creatinine ratio nor albuminuria specifically indicates tubular involvement. Retinol binding protein (RBP), a small-sized protein excreted in urine but normally reabsorbed by the proximal tubule, becomes detectable in urine in cases of tubular injury[2]. Our aim is to investigate the correlation between urinary RBP concentration at diagnosis as a marker of tubular involvement and analyze its predictive prognostic value in ANCA-associated vasculitis.

Methods: We included adult patients with a kidney biopsy proven ANCA-associated vasculitis (granulomatosis with polyangiitis or microscopic polyangiitis) between January 2014 and June 2023 at the Nephrology Department of Tenon Hospital, AP-HP, Sorbonne University, Paris, France. Clinical characteristics were prospectively collected through a REDCAP survey at the time of kidney biopsy.

Results: Forty-one patients with a new diagnosis of ANCA-associated vasculitis were included, with a median age of 67 years and a female predominance (55%). MPO was the predominant ANCA serotype (61%). At the time of kidney biopsy, the median urinary RBP/creatinine ratio was six times the normal range (normal values < 0.25 mg/mmol), with a median eGFR at 19 mL/min/1.73m² (CKD-EPI formula). The median follow-up period was 33 months, during which six patients (14.6%) developed end-stage renal disease (renal replacement therapy (RRT) or renal transplantation), four of whom required RRT at the time of diagnosis. The urinary RBP/creatinine ratio at baseline was associated with acute tubular necrosis (ATN) lesions (median ratio at 0.015 mg/mmol in the absence of ATN versus 2.2 mg/mmol in cases of ATN, p=0.0013). A negative correlation was observed between levels of urinary RBP/creatinine ratio and eGFR at the last follow-up.

Conclusions: The urinary RBP/creatinine ratio at the time of diagnosis in ANCA vasculitis is associated with the presence of ATN and renal prognosis. Thus, this tubulointerstitial biomarker could represent a novel prognostic marker for kidney prognosis in ANCA vasculitis. We plan to conduct a multivariate analysis, including a larger number of patients, to refine our statistical analysis.

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Disclosures: None.

1. CLINICAL SCIENCE
1.07. Comorbidities: cardiovascular risk, frailty, osteoporosis, infection and its prevention, vaccines...

P-149

Carotid Intima-Media Thickness Correlated with Age and Pulse Wave Velocity in ANCA-Associated Vasculitis Patients

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Background/ Objectives: Cardiovascular diseases are the main causes of mortality in ANCA-associated vasculitis (AAV) patients. Carotid intima-media thickness measurement (CIMT) and pulse wave velocity (PWV) were performed to determine atherosclerosis and arterial stiffness as cardiovascular risk markers.

Methods: The data of 31 patients with AAV were compared with 21 healthy controls. Demographic and laboratory findings were recorded.

Results: Seventeen patients (54.8%) were male. Mean age was 52.6±11.5 years. CIMT was higher in the patient group [0.74 (0.65- 0.84) vs 0.63 (0.57-0.74) mm; p=0.048]. PWV [7.9 (6.7-9.3) vs 7.8 (6.8-8.5) m/s; p=0.295] and augmentation index [22.5 (11.0-30.0) vs. 23 (9.5-30.5) mm/Hg, p=0.801] were similar in both groups. CIMT was correlated with age (r: 0.538, p<0.001) and PWV (r: 0.554 p< 0.001) (Figure 1) while there was no correlation with AI (r: 0.047, p= 0.764).

Conclusions: The main finding of the present study is that CIMT is significantly increased and correlated with age and PWV in patients with AAV compared to controls. Despite the fact that cardiovascular disease is one of the most common causes of mortality in AAV patients, overt cardiac disease is rare. [On the other hand, AAV is characterized by vascular inflammation which can cause endothelial dysfunction, leading to subclinical atherosclerosis.[1] CIMT can be used as a screening tool as part of patient follow-up to identify patients at cardiac risk.

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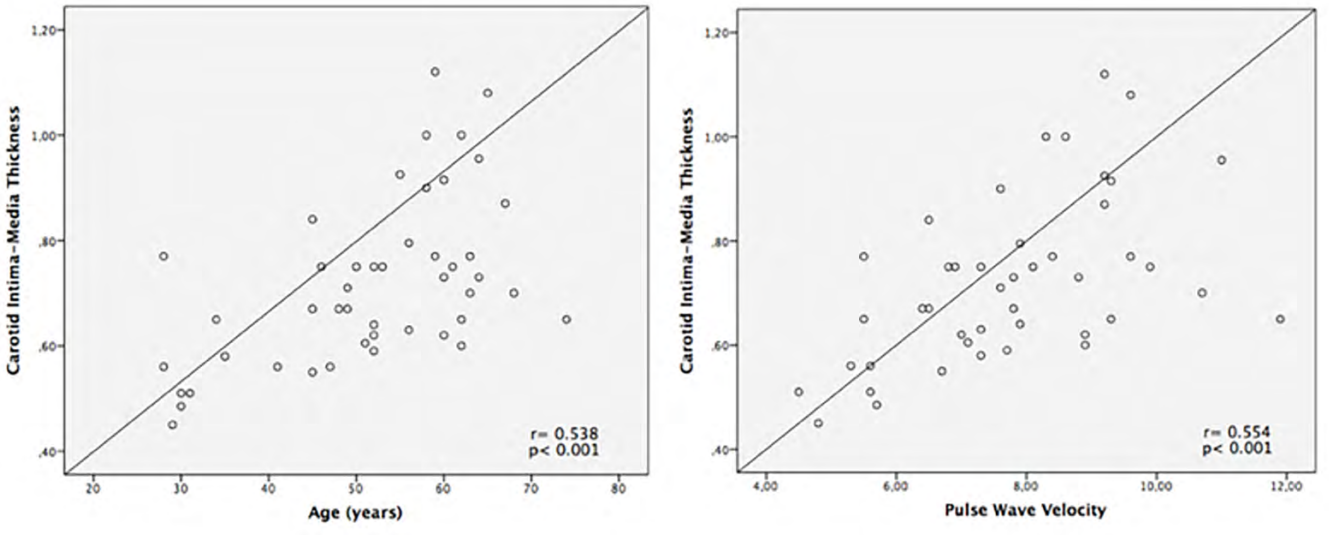
Disclosures: None.

Figure 1. Carotid intima media thickness is correlated with age and pulse wave velocity.



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The Different Characteristics of Infections Observed in Systemic Lupus Erythematosus and ANCA-Associated Vasculitis Patients Treated with Rituximab or Cyclophosphamide

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Objectives: Systemic lupus erythematosus (SLE) and ANCA-associated vasculitides (AAV) are systemic autoimmune diseases that are characterized by pathogenic autoantibody production and treated by immunosuppressive agents. Infectious complications secondary to treatment are significant causes of morbidity and mortality. In our study, we examined infections associated with the use of rituximab (RTX) and cyclophosphamide (CYC) in SLE and AAV patients.

Methods: Twenty-two SLE and 41 AAV patients with renal involvement were included. Data was retrospectively collected from hospital records as well as the national health registry system. The demographic, laboratory data, site and type of infections, hospitalizations and mortality were recorded. Severe infection was defined as infection requiring intravenous antibiotics, hospitalization or resulting in death.

Results: There were 39 infection episodes in 22 SLE patients and 70 infection episodes in 41 AAV patients. Demographic data of the study groups are shown in Table 1. Overall, more patients with SLE had genitourinary infections (45.5% vs 22.0%, p=0.009). SLE and AAV patients were further compared depending on whether they received RTX (SLE:12, AAV:25) or only CYC (SLE:10, AAV:16). Regarding RTX treatment, more patients with SLE had genitourinary infections (66.7% vs 28.0%, p=0.025), sepsis (33.3% vs 8.0%, p=0.05) and intensive care admission (33.3% vs 8.0%, p=0.05) than AAV patients. On the contrary, when SLE and AAV patients who had only received CYC were compared, more patients with AAV developed lower respiratoy tract infections (50.0% vs 10.0%, p=0.037) and were admitted to the hospital (31.3% vs 0.0%, p=0.04). Out of 63 patients, 17 (27.0%) had severe infections. Patients who developed severe infections had lower IgG levels (6.2 ± 2.1 vs 8.5 ± 2.5, p=0.026).

Conclusions: We showed that genitourinary infections are more frequent in SLE patients whereas lower respiratory tract infections are more common in AAV patients treated with CYC. Furthermore, immunoglobulin levels may have an impact on severe infection development. We also demonstrated that SLE and AAV can manifest with different sites and severity of infections depending on the immunosuppressant agents used. We believe careful examination of SLE patients for genitourinary infections and AAV patients for lower respiratory tract infections may benefit patients regarding morbidity and mortality. Larger studies are needed to confirm our results.

Disclosures: None.

Table 1. Demographic and infection data of SLE and AAV patients.

	SLE (n=22)	AAV (n=41)	p
Female, n (%)	19 (86.4)	17 (41.5)	**<0.01**
Age (years)	33.5 ± 11.7	55.8 ± 11.8	**<0.01**
Follow-up time (months)	32.7 ± 25.1	23.1 ± 18.4	0.089
Diabetes mellitus, n (%)	0 (0.0)	6 (14.6)	0.059
Hypertension, n (%)	15 (68.2)	30 (73.2)	0.676
Cardiovascular disease, n (%)	3 (13.6)	7 (17.1)	0.722
Cumulative steroid use (g)	14.3 ± 6.7	11.1 ± 5.8	**0.05**
TMP-SMX prophylaxis, n (%)	0 (0.0)	14 (34.1)	**<0.01**
eGFR (ml/min/)	73.8 ± 51.7	45.6 ±35.7	**0.01**
Infection, n (%)	22 (100.0)	37 (90.2)	0.13
Serious infection, n (%)	6 (27.3)	11 (26.8)	0.97
Upper respiratory tract infection, n (%)	12 (54.6)	23 (56.1)	0.91
Lower respiratory tract infection, n (%)	5 (22.7)	16 (39.0)	0.19
Genito-urinary infection, n (%)	10 (45.5)	9 (22.0)	**<0.01**
Gastrointestinal infection, n (%)	2 (9.1)	6 (14.6)	0.53
Skin infection, n (%)	10 (45.5)	16 (39.0)	0.62
Mortality, n (%)	2 (9.1)	5 (12.2)	0.71
Micro-organisms, n (%)			
Bacterial	17 (77.3)	33 (80.5)	0.76
Viral	9 (40.9)	15 (36.6)	0.74
Fungal	6 (27.3)	6 (14.6)	0.22
Infection Treatment, n (%)			
Antibiotics	17 (77.3)	31 (75.6)	0.88
Antivirals	4 (18.2)	10 (24.4)	0.57
Antifungal	6 (27.3)	15 (12.2)	0.13
IVIG	3 (13.6)	2 (4.9)	0.22

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Risk factors of major adverse cardiovascular events in patients with ANCA-associated vasculitis: a single center experience from Austria

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Background: Alongside infections, cardiovascular events are among the main causes of death in anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) during the first year after diagnosis. Despite improved control of traditional and disease-related risk factors, the cardiovascular outcome of patients with AAV is still unsatisfactory. This study aimed to investigate possible risk factors for major cardiovascular events (MACE) in AAV using long-term follow-up data.

Material and Methods: A single-center retrospective data analysis was performed among 73 AAV patients, who were followed up for at least three years between 2005 and 2020 at the Department of Internal Medicine of the Medical University of Graz, Austria. MACE were defined based on the International Classification of Diseases criteria (ICD-10; I11, I20-I25, I42-I45, I50, I51, I61-I69). Differences in baseline characteristics between AAV patients with and without MACE were analyzed. Risk factors for MACE were investigated using Cox regression analyses.

Results: Thirteen (17.8%) patients experienced at least one MACE over a median follow-up period of 86 months. One (7.7%) MACE occurred within the first year after starting induction therapy, while the median time to first MACE was 49 months (IQR: 22.3 -83.0). Patients who experienced MACE were of higher age (med: 62, IQR: 58-72 vs. med: 55, IQR: 45-65 years, p=0.001) and presented with arterial hypertension at the time of diagnosis (10/13 (76.9%) vs. 27/60 (45.0%, p=0.037), while the proportion of patients with male sex (9/13 (69.2%) vs. 27/60 (45.0%), p=0.113) and the clinical diagnosis of granulomatosis with polyangiitis (12/13 (92.3%) vs. 37/60 (61.7%), p=0.131) tended to be higher. MACE occurred earlier in patients receiving rituximab in induction therapy (med: 21, IQR: 15-26 vs. med: 61, IQR: 7-162 months, p=0.042). In univariate Cox regression analysis age (HR: 1.066, 95% CI: 1.013 to 1.121, p=0.014), male sex (HR: 3.080, 95% CI: 0.828 to 11.460, p=0.093), arterial hypertension (HR: 3.302, 95% CI: 0.893 to 12.207, p=0.073), low-dose oral cyclophosphamide in maintenance therapy (HR: 5.187, 95% CI: 1.067 to 25.212, p=0.041) and rituximab in induction therapy (HR: 3.643, 95% CI: 0.957 to 13.867, p=0.058) were associated with an increased risk of MACE. A multivariate analysis was not performed due to the low number of events.

Conclusion: In this cohort of patients with AAV, MACE occurred predominantly after the first year of induction therapy. Besides arterial hypertension as a traditional cardiovascular risk factor, immunosuppressive agents other than glucocorticoids may have an influence on major cardiovascular events in patients with AAV. Further analyses using larger patient cohorts are needed to validate these observations.

Disclosures: None.

P-152

Incidence of adrenal insufficiency in patients with giant cell arteritis tapering glucocorticoids with the Norwich Prednisolone Regimen

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Background: Glucocorticoids continue to be the main treatment for GCA. It is widely recognised that treatment with oral glucocorticoids is associated with adverse events including adrenal insufficiency [1]. Reports suggest the risk of adrenal insufficiency is dependent on the dose and the duration of therapy. The Norwich Regimen has been devised to deliver prednisolone at a rate 1mg/kg of lean body mass tapering over 100 weeks [2]. We report the incidence of adrenal insufficiency related to the Norwich regimen.

Method: The Norwich Regimen has been used in all patients diagnosed with GCA from 01/01/2012. A notes review of all patients diagnosed after that date was undertaken to look for evidence of adrenal insufficiency. We routinely check 9am cortisol when symptoms of adrenal insufficiency were reported. The 9am cortisol was recorded as normal, indeterminate, or low. Patients with a low 9am cortisol remained on long term prednisolone; no further test was required. Patients with an indeterminate result were referred for a short synacthen test. If the results of the SST were normal patients were weaned off prednisolone, patients with an inadequate SST result remained on long term prednisolone.

Results: From 01/01/2012-31/05/2022 353 patients diagnosed with GCA were treated with the Norwich regimen.

9am cortisol was checked in 76 patients (21.5%).

Of these, 34 patients (9.6%) had a normal result, 35 patients (9.9%) had an indeterminate result requiring SST.

7 patients (2.0%) had a low 9am cortisol.

Of the 35 patients referred for SST:

27 patients (7.6%) had an adequate result, 8 patients (2.3%) had an inadequate result resulting in long term prednisolone.

Conclusion: We report the incidence of adrenal insufficiency in patients diagnosed with GCA, tapering prednisolone using the Norwich Regimen. In total 15/353 (4.3%) patients developed adrenal insufficiency because of long-term glucocorticoid use.

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Disclosures: None.

P-153

The Burden of Multimorbidity in ANCA-Associated Vasculitis: A 2002-2021 Cohort Study

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Background: With improvements in the risks of relapse and mortality in ANCA-associated vasculitis (AAV), a better understanding of disease- and treatment-related complications is necessary to optimize outcomes and personalize care. Multimorbidity (MM) is a patient-centered approach to measuring complications and is associated with risk of death and quality of life in other conditions. It is defined as having multiple chronic conditions but remains poorly understood in AAV. We sought to determine the burden of multimorbidity in AAV.

Methods: We used the 2002-2021 Mass General Brigham (MGB) AAV cohort: an inception cohort of consecutive MPO- or PR3-ANCA+ incident AAV cases at a multi-center healthcare system. Up to 10 comparators without systemic rheumatic disease were identified from MGB and matched to each case by encounter date, age, sex, and race. We adapted a definition of MM as the presence of ≥ 2 of 37 chronic conditions, identified by use of ICD-9/10 codes. Manifestations of AAV (e.g., kidney disease) were excluded from this definition. Pre-existing comorbidities were excluded. We determined the proportion of cases and comparators with MM using the Aalen-Johansen method, accounting for the competing risks of death and loss to follow up. We used Cox proportional hazard models to estimate the risk of MM in cases vs comparators. Among patients with AAV, we used latent class analysis to characterize clusters of morbidity among people with MM and time-varying multivariable-adjusted Cox proportional hazards models to assess the association of MM with mortality risk.

Results: There were 882 cases matched to 6,908 comparators. At 1 year, 19% of cases and 10% of comparators had MM (Table). By 5 years, 51% of cases and 39% of comparators had MM. AAV cases had nearly a 2-fold higher risk of MM vs comparators (age, sex, and race-adjusted HR 1.96, 95% CI 1.76-2.19). At 1 year, two clusters of MM in AAV were identified: Clusters 1A (76%) and 1B (24%). Hypertension and hyperlipidemia were common in Cluster 1A; Cluster 1B was characterized by painful conditions (e.g., headache, back pain, GERD). At 2 years, two clusters were identified: Clusters 2A (82%) and 2B (18%). Cluster 2B was distinguished from 2A by a high burden of cardiovascular (CV) and pulmonary disease. At 5 years, three clusters were identified: Cluster 5A (81%), 5B (11%), and 5C (8%). Morbidities most common in Cluster 5A were hypertension and hyperlipidemia. Cluster 5B was distinguished by a high burden of CV and pulmonary disease; 5C had a high burden of glucocorticoid toxicities (e.g., osteoporosis, obesity, hypertension). Among AAV patients, developing MM is associated with a 67% higher risk of death than not having MM (age, sex, and race-adjusted HR 1.67, 95% CI 1.24-2.25).

Conclusions: AAV is associated with a high burden of MM and greater risk of MM than the general population. MM in AAV is characterized by clusters defined by morbidity burdens that vary over disease course and reflect a high impact of disease and its treatment. MM in AAV is associated with mortality risk. The development of interventions to prevent MM and minimize its impacts are needed.

Disclosures: None.

Table: Rate of Multimorbidity in Patients with ANCA-Associated Vasculitis vs Comparators.

Follow-Up (months)	Cumulative incidence in AAV (n = 882)	Cumulative incidence in comparators (n =6908)
6	0.11 (0.09, 0.14)	0.05 (0.04, 0.06)
12	0.19 (0.17, 0.22)	0.10 (0.09, 0.10)
18	0.28 (0.25, 0.31)	0.14 (0.14, 0.15)
24	0.32 (0.29, 0.35)	0.18 (0.17, 0.19)
30	0.37 (0.33, 0.40)	0.23 (0.22, 0.24)
36	0.39 (0.36, 0.43)	0.27 (0.25, 0.28)
42	0.43 (0.40, 0.47)	0.31 (0.29, 0.32)
48	0.47 (0.43, 0.50)	0.34 (0.32, 0.35)
54	0.49 (0.45, 0.52)	0.36 (0.35, 0.38)
60	0.51 (0.47, 0.54)	0.39 (0.38, 0.41)

P-154

Investigating the concomitance of anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitides and inflammatory bowel disease (IBD)

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Background/ Objectives: Anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis is the most prevalent small vessel vasculitis with systemic involvement (1). ANCA positivity has been studied in patients with inflammatory bowel disease (IBD), with higher incidence in ulcerative colitis (2). A pathogenic significance of ANCA positivity in IBD was not found and ANCA testing has not been shown to have utility in classifying IBD. Concern has been raised that IBD may possibly initiate a pathogenic mechanism paving the way for vasculitis development (2). We aim to study and identify a possible connectivity between the two disease processes.

Methods: This is a retrospective study design. Approval from Mayo Clinic Institutional Review Board was sought. The pre-existing data was assessed by generating a list of patients who have the diagnosis of ANCA associated vasculitis including a diagnosis of granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) or eosinophilic granulomatosis with polyangiitis (EGPA) with overlapping inflammatory bowel disease (Crohn's disease or ulcerative colitis) in the time period from 01/01/2020 to 08/03/2023. 129 patients were identified and individually reviewed.

Results: We identified 43 patients that met criteria. 24 patients had GPA, 6 had MPA and 4 patients with EGPA. There were 8 cases of unspecified ANCA vasculitis. In 68.8% of cases IBD diagnosis preceded the diagnosis of ANCA vasculitis. The median diagnosis time lapse between development of both diseases was 9 years. In the patients with GPA, 43.5% had pulmonary involvement, 21.7% had renal involvement and 30.4% had upper airway symptoms. 52.2% GPA patients were female and 52.2% were Caucasian. 14 GPA patients had ulcerative colitis while 8 had Crohn's disease. 75% EGPA patients had pulmonary symptoms, 75% had renal involvement. 2 EGPA patients had ulcerative colitis and 2 had Crohn's disease. Out of the 6 MPA cases, 4 had ulcerative colitis and 2 with Crohn's disease. 44% of the ANCA vasculitis patients were proteinase 3 antibody positive, while 27.9% were anti-myeloperoxidase antibody positive. 72.5% of the patients had remission of their vasculitis and 73.7% achieved IBD remission.

Conclusions: There is limited literature that describes concomitance of IBD with ANCA vasculitis and studies dual disease activity and remission. We confirm that IBD precedes the diagnosis of vasculitis and that highlights a concern for predisposition to ANCA vasculitis development which calls for further investigation. We note similar remission rates, suggesting a control of either disease may be beneficial for remission of the other.

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P-155

Clinical Presentation and Outcomes of SARS-CoV-2 Infection in Patients with Pauci-immune Glomerulonephritis: A Multicenter Study

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Parameter N(%) or mean (SD)	**N=29**
Age at diagnosis of GN (years)	61,0 (16,4)
Gender (males)	13/29
Time since diagnostic biopsy (months)	61,2(56,2)
Induction treatment Corticosteroids Cyclophosphamide Mycophenolate mofetil Rituximab	 29(100) 20 (95,2) 1(3,4) 7 (26,9)
First outcome of GN Remission Relapse	 27 (96,4) 1 (3,5)
Immunosuppressive treatment at SARS-CoV-2 infection Mycophenolate mofetil Glucocorticoids Rituximab AZA	N=12 2 3 4 3
Symptoms Arthralgias Myalgias Fever Fatigue Cough Shortness of breath	 2(6,9) 1(3,4) 22 (75,8) 3 (10,3) 9 (31,0) 1 (3,4)
Hospitalization requirement	7 (24,1)
Mechanical ventilation requirement	1(14,3)
SARS-CoV-2 outcome Complete recovery Death Long COVID	26 23 (88,4) 3 (11,5) 0
Relapse of GN after SARS-CoV-2 infection	1 (3,8)

Table 1. Demographics, baseline patients' characteristics, symptoms and outcomes of SARS-CoV-2 infection and GN.

Background-Objectives: SARS-CoV-2 infection is characterized by multi-system involvement, affecting not only the respiratory system[1,2]. This study aimed to outline the clinical presentation and outcomes of SARS-CoV-2 infection in patients with pauci-immune GN (PIGN).

Methods: A retrospective analysis was conducted on 29 individuals with PIGN and positive SARS-CoV-2 PCR test, excluding those in end-stage kidney disease (ESKD) prior to infection. Data encompassed immunosuppressive regimens at PIGN diagnosis, treatment outcomes, SARS-CoV-2 infection's clinical course and outcome of PIGN post infection.

Results: The mean age of patients was 61.0(±16.4) years, with 16(55.1%) being female. Upon SARS-CoV-2 infection, 12(41.3%) were on immunosuppressive therapy, of whom 4 (13.7%) were on rituximab maintenance therapy. Almost all patients were symptomatic in terms of the infection and 7(24.1%) required hospitalization. 23(88.4%) experienced complete recovery from Covid-19, 3(3.1%) had prolonged symptoms and 3(11.5%) died due to Covid-19. Among patients in remission, 1(3.8%) experienced a relapse of PIGN following SARS-CoV-2 infection.

Conclusions: In this cohort of patients with PIGN, SARS-CoV-2 infection impacted morbidity and mortality of this vulnerable population.

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Disclosures: None.

P-156

Adverse Events Following SARS-CoV-2 Vaccination in Patients with Pauci-immune Glomerulonephritis: A Multicenter Study

Dimitra Petrou[1], Evangelia Ntounousi[2], Dimitra Galitsiou[3], Konstantina Kantartzi[4], Pelagia Kriki[4], Vasileios Liakopoulos[5], Smaragdi Marinaki[6], Vasileios Vaios[5], Louiza Gkika-Zervou[2], Petros Kalogeropoulos[1], Ioannis Boletis[7], Georgios Moustakas[3], Stylianos Panagoutsos[4], Sofia Lionaki[1].

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Parameter N (%) or mean (SD)	N**=69**
Age at PIGN diagnosis (years)	61,75(15,55)5)
Sex (male)	32 (43,4)
Time since kidney biopsy (months)	76,1 (60,9)
Induction treatment Glycocorticoids Cyclophosphamide Mycophenolate mofetil Rituximab	 65 (97,0) 55 (83,3) 2 (3,0) 11 (18,0)
Maintenance treatment Rituximab AZA	 20 (39,2) 23 (45,0)
First outcome of PIGN Remission Resistant disease	N=63 58 (92,0) 5 (7,9)
Number of doses	3,2 (1)
Adverse Events **Systematic** Arthralgias Myalgias Headache Fever Diarrhea **Local** Pain	 10 (20,4) 2 (4,25) 5 (10,6) 7 (14,9) 5 (10,9) 2 (4,25) 27 (55,1) 12 (24,5)

Table 1. Demographic, baseline patients' characteristics and adverse events following vaccination against SARS-CoV-2.

Background-Objectives: After almost four years of the COVID-19 pandemic, SARS-CoV-2 vaccination has been shown crucial in stemming the pandemic[1,2] . This study aimed to describe adverse events associated with SARS-CoV-2 vaccination in patients with a history of pauci-immune glomerulonephritis (PIGN).

Methods: A retrospective analysis was conducted on individuals with PIGN who received the SARS-CoV-2 vaccine, excluding those in end-stage kidney disease prior to vaccination. Recorded data included the histopathological diagnosis, immunosuppressive regimens, clinical outcomes, vaccination type and related adverse events and assessment of the potential impact of vaccination on the clinical course of PIGN.

Results: A cohort of 67 individuals diagnosed with PIGN, with a mean age of 59.6 (±17.5) years, was studied. Among them 34(50.7%) had a medical history of hypertension, and 16(23.9%) had type 2 diabetes. Induction therapy had been administered in 66(98.5%) cases, with 87.7% of them achieving remission. 50(74.6%) patients had received maintenance therapy and 50 (94.3%) were vaccinated against SARS-CoV-2, with a mean time of 79.5(±70.8) months from the diagnostic biopsy with 3.2(±1.0) vaccine doses. At the time of vaccination, 90% of the patients were in remission, and 44% were on immunosuppressive therapy. Systemic adverse events related to vaccination were reported in 26% of patients. 62% experienced local reactions at the administration site. 2 (4.3%) patients experienced a relapse of PIGN, with a mean time to relapse of 5.7 (±3.4) months from the first vaccine dose.

Conclusions: SARS-CoV-2 vaccination was well-tolerated, with non-significant impact on PIGN relapse probability. Local side effects were common, seen in the majority of patients, while systemic ones occurred in 20.4% of them.

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Disclosures: None.

P-157

Age-Stratified Analysis of ANCA-Associated Vasculitis: Insights from a Swedish Population-Based Cohort

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Objective: ANCA-associated vasculitides (AAV) are more often observed in older people but can occur at any age. Little is known about differences in clinical characteristics and outcome when comparing younger to older adults, and earlier studies often employ an age cut-off around 60-65 years. In this study we compare cases diagnosed with AAV with an age cut-off of 40 years.

Methods: Incident cases diagnosed with granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic GPA (EGPA) between 1997 and 2019 from a defined geographical area in southern Sweden were included in this analysis. Case ascertainment was verified by case record review and patients were classified into the three disease phenotypes of AAV using the EMA-algorithm. Clinical and serological characteristics, vasculitis disease activity at diagnosis as well as outcome in terms of organ damage, comorbidities during follow-up, renal and overall survival were analysed. Vasculitis disease activity at diagnosis assessed by the Birmingham vasculitis activity score (BVAS). Irreversible organ damage was assessed by the vasculitis damage index (VD). The cohort was divided into two groups based on age at AAV diagnosis, ≤ 40 vs. >40 years.

Results: The AAV cohort comprised 374 cases, 36 (mean age 32) were ≤ 40 years at diagnosis and 338 (mean age 68) >40 years at diagnosis. There was no difference in sex distribution (47% female). Patients diagnosed at age ≤ 40 years were more likely to be diagnosed with GPA and EGPA and were more likely to be PR3-ANCA positive whereas MPA and MPO-ANCA positivity were more common in older ages. Median BVAS did not differ between the groups; 14.5 (IQR 9-17.5) vs. 15 (IQR 12-19) in age group >40 years. Organ involvement at diagnosis showed more ENT in the ≤ 40 years group with significant differences for BVAS items nasal discharge and subglottic stenosis, whereas renal disease was more common in the >40 years group. Forty patients (12%) had severe renal disease at diagnosis with creatinine >500 µmol/L at diagnosis in the >40 group vs. none in the age group ≤ 40-year age-group. ESKD during follow-up was observed in 8% in the ≤ 40-year group vs. 15% in >40 years group (p=0.3). There was no difference in total VDI score or in critical organ damage assessed by VDI at 1 year, however treatment related damage was only observed in the >40 age group (7%). During follow-up, myocardial infarction and severe infections were more common in the >40 age group. Type of treatment regimens received were comparable between the groups, but patients diagnosed at age ≤ 40 years received higher cumulative doses of CYC (Table 1).

Conclusion: When comparing patients with AAV based on age at diagnosis, substantial differences were evident between those younger vs. older than 40 years at diagnosis. These findings may have impact on care of patients with AAV.

Table 1.

	All	Age ≤40 years	Age >40 year	P
	374	36 (9.7)	338 (90.3)	
Age, years mean ±SD	64.4±16.2	32 ± 6.7	68 ± 11.9	
Sex, female (%)	174 (47)	17 (47)	157 (47)	0.9
GPA, n (%)	192 (51.3)	22(61)	170(50)	0.20
MPA, n (%)	159 (42.5)	8(22)	151 (45)	0.01
EGPA, n (%)	23 (6.1)	6(17)	17(5)	0.006
PR3-ANCA n (%)	188 (50.3)	21 (58)	167 (49)	0.30
MPO-ANCA n (%)	161 (43.0)	10 (28)	151 (44.7)	0.05
ANCA negative n (%)	25 (6.7)	5 (14)	20 (6)	0.07
Creatinine, µmol/L	132 (73–299)	80 (62–125)	140 (74–326)	<0.001
eGFR, ml/min x1,73m^2	55.3 ±41.3	96.3 (52.4–114.1)	40.6 (15.6–83.8)	<0.001
Hemoglobin g/L	109.8 ±19	120 ±22.8	108 ±19.1	0.001
Platelets, x10^9/L, SD	374.7 ±148.4	362.8 ± 102.0	376.1 ±152.5	0.90
CRP mmol/L, SD	93.3 ±83.9	45.0 (9.7–101.0)	78 (23–136.8)	0.06
BVAS at diagnosis, median (IQR)	15 (12-19)	14.5 (9–17.5)	15 (12–19)	0.10
BVAS Renal, any item n (%)	258 (69)	16 (44)	242 (72)	<0.001
BVAS ENT, median score (IQR)*	0 (0—4)	3.5 (0—6)	0 (0—4)	0.03

	All	Age ≤40 years	Age >40 year	P
	374	36 (9.7)	338 (90.3)	
BVAS_ENT Nasal discharge, item present, n (%)	122 (37)	17 (47)	105 (31)	0.05
BVAS ENT Subglottic stenosis, item present, n (%)	2 (0.5)	2 (6)	0	0.001
BVAS, Renal, median score (IQR)*	10 (0—12)	0 (0—10)	12 (0—12)	<0.001
VDI at 1 year, median (IQR)**	1 (0–2)	1 (0–2)	1 (0-2)	0.07
Severe damage, 1 year (VDI≥5), n (%)	11 (3)	1(3)	10 (3)	0.60
Critical damage, 1 year, n (%)	42 (11.2)	3 (8.3)	39 (11.5)	0.60
Treatment related damage, 1 year, n (%),	24 (7.1)	0	24 (7.9)	0.06
CYC dose g, median (IQR)	8.5 (4.5–12)	12 (9.7–20)	8 (4.5–12)	<0,001
EKSD, n (%)	55 (14.7)	3 (8)	52 (15)	0.30
Mortality n, (%)	178/374 (48)	2 (5.6)	176 (52)	<0.001
Comorbidities during follow-up				
Severe infection, n (%)	142 (38)	6 (17)	136 (40)	0.006
MI, n (%)	39 (10)	0 (0)	39 (13)	0.03
Stroke, n (%)	27 (7)	1 (2.8)	26 (7.7)	0.29
VTE, n (%)	56 (15)	4 (11)	52 (15)	0.50

GPA: granulomatosis with polyangiitis, MPA: microscopic polyangiitis, EGPA: eosinophilic GPA, eGRF estimated glomerular filtration rate (MDRD), BVAS: Birmingham vasculitis activity score, ENT: Ear-nose and throat, VDI: vasculitis damage index, EKSD: End-stage kidney disease IQR: interquartile range, SD: standarddeviation, MI: Myocardial infarction,VTE: Venous thromboembolism. *Maximum score in BVAS category: ENT 6, Renal 12, **VDI at 1 year available for 275 cases.

Disclosures: None.

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Tixagevimab-cilgavimab as pre-exposure prophylaxis for COVID-19 in 63 rituximab-treated patients with ANCA-associated systemic vasculitis: twenty-month follow-up

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Background/ Objectives: COVID-19 pandemic has created new problems in the management of ANCA- associated vasculitis (AAV). In particular, antibody response to COVID-19 vaccination is impaired in immunosuppressive patients (pts), and absent in most pts with a recent dose of rituximab (RTX). A new strategy for the prevention of COVID-19 are virus-neutralizing monoclonal antibodies (MAB). Combined long-acting MAB tixagevimab-cilgavimab (TC) may be effective within 6 mos. The aim: in AAV pts treated with RTX, to evaluate the efficacy and safety of TC and assess patient's satisfaction with the medication.

Methods: The prospective observational study included 63 pts with AAV treated with RTX: 36 had granulomatosis with polyangiitis (GPA), 23 - microscopic polyangiitis (MPA), 2 - eosinophilic granulomatosis with polyangiitis, 2- undifferentiated AAV. 57 pts was ANCA positive: 77% with aPR3, 19% - aMPO and 7% with uncertain specificity. Median age 59 [19–79] yrs.; M:F=1:1,1. 34 pts received once intramuscular TC, other repeat TC in 6 mos. interval (8 pts– 3 times). From Mar to Aug 2022, total dose of TC was 300 mg, from Oct 2022 to June 2023 – 600 mg, as prescribed. The duration of observation was 20 mos. A telephone survey has been conducted to detect cases of COVID-19 and adverse events of TC. The survey also included four questions from TSQM-9: Q1 (from effectiveness domain) and Q7-9 (global satisfaction domain).

Results: Confirmed COVID-19 have been detected in 22% (8 pts– GPA, 5– MPA, 1– undifferentiated), 4 [2-8] mos. after TC. 85% had mild COVID-19. Two pts required hospitalization (1 death, 8 mos. after TC). Also, one hospitalized due to non-COVID-19 pneumonia (6 mos. after TC). One death was occurred in case active MPA, hemodialysis, developing neutropenia and sepsis (3 mos. after starting RTX). Post- injection reactions and other adverse events related to TC were not observed. 58 pts responded to the survey. Analysed TSQM-9 questions, median global satisfaction domain was 71,4 [14,3-100]. 72,4% pts answered "satisfied"–"extremely satisfied" to Q1.

Conclusions: The data evidence the effectiveness of TC for COVID-19 pre-exposure prophylaxis. AAV pts treated with RTX have favorable safety profile of TC. There is positive patient global satisfaction. TC regimens requires further clarification. The introduction of virus-neutralizing MAB, a new drug class for the infection diseases prevention, opens significant prospects for improving prognosis of pts with vasculitis.

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Disclosures: None.

P-159

Incidence of Stroke in Giant Cell Arteritis – A population-based study from Sweden

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Purpose: Stroke is relatively common in the elderly, with an estimated incidence of 5-10/1000 among those aged 65-84 in Sweden[1], and it has been particularly associated with active vasculitis in the setting of giant cell arteritis (GCA). The purpose of this study was to determine the incidence rate (IR) of stroke in GCA, and to study the impact of incident stroke on mortality in patients with biopsy-confirmed giant cell arteritis (GCA).

Methods: Patients diagnosed with biopsy-confirmed GCA from 1997 through 2019 within Skåne, a defined geographical area in south Sweden, were included. Stroke events which occurred after the diagnosis of GCA were identified through linkage of the cohort to the regional healthcare register of Skåne by use of ICD-10 codes. Subsequent case records review was performed to ascertain stroke diagnosis according to the World Health Organization (WHO) 1970 definition of stroke. Sex-specific and age-specific (50–59 years, 60–69 years, 70–79 years and ≥80 years) IR were estimated. In addition, IR within different specific time periods relative to the time of diagnosis of GCA were calculated (Table 1). A time dependent Cox regression analysis was performed to investigate the relationship between incident stroke and mortality.

Results: The cohort comprised 1360 patients with GCA. Of them, 253 had been assigned a diagnosis code of stroke during the study time. So far, 208 cases have been reviewed. The mean follow-up was 7.3 years (SD 5.4). One hundred twenty-four patients suffered a stroke during 9401 person-years (py) of follow-up, yielding an IR of 13.1 per 1000 py (95% CI 11.0–15.7). The IR was 15.2 (95% CI 11.0–20.9) among males compared to 12.4 (95% CI 10.0–15.3) among females. The median age at GCA diagnosis was 77.7 years (IQR 72.2–82.1) among those who suffered a stroke compared to 75.5 years (IQR 70.2–81.1) among those with no stroke diagnosis. The IR increased with age with the highest incidence estimated in the age group ≥80 years, 22.3 (95% CI 17.2–29.0) compared to 11.3 (95% CI 8.5–15.0) among patients in the age group 70–79. The highest IR of stroke was estimated within the first 3 months fter the diagnosis of GCA (Table 1). Mortality was higher in GCA patients diagnosed with incident stroke vs. those without stroke with an age-adjusted HR of 2.36 (95% CI 1.87–2.98).

Conclusions: The incidence rate of stroke among patients with GCA is considerably higher than what has been reported in the background population. The incidence of stroke in GCA was greatest within 3 months following GCA diagnosis and increased with age. Incident stroke has a major impact on mortality in GCA patients.

Table 1. Incidence rate* of stroke in GCA.

Time period	Events	PY	IR	95% CI
0-3 months	22	308	71.2	46.9-108.2
4-6 months	5	298	16.7	6.9-40.2
7-12 months	2	589	3.3	0.84-13.5
Year 2	13	1085	11.9	6.9-20.6
Years 3-5	25	2723	9.1	6.2-13.5
Years 6-10	40	2777	14.4	10.5-19.6
Year 10 to end of follow-up	17	1606	10.5	6.5-17.0
Entire follow-up	124	9401	13.1	11.0-15.7
Age groups at GCA diagnosis				
50-59 yrs	2	453	4.4	1.1-17.6
60-69 yrs	17	2124	8.0	4.9-12.8
70-79 yrs	49	4319	11.3	8.5-15.0
≥80 yrs	56	2504	22.3	17.2-29.0

*Per 1000 person year (PR); IR: incidence rate: CI: confidence interval.

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Disclosures: None for all authors.

P-160

A Close Look to the Osteoporosis in Patients with ANCA-Associated Vasculitis (AAV) From Eastern Mediterranean: TRVaS Cohort

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Background/Objectives: Osteoporosis is estimated to be a common comorbidity occurring in 20-30% of AAV patients. However, this issue has been studied less in the Eastern Mediterranean Region. This study aimed to investigate osteoporosis awareness among rheumatologists treating AAV patients in a prospective nationwide cohort in Turkey.

Methods: Data from the Turkish Vasculitis Study Group (TRVaS) registry were screened and analyzed for AAV patients who had any prior DXA examination. Demographic and clinical characteristics were recorded in a case report form in which osteoporosis and its treatment were evaluated in detail.

Results: A total of 453 AAV patients (GPA= 310, MPA= 57, EGPA= 45, and unclassified AAV= 41) were included in the study; 259 (57.2%) were male, and the mean age was 56 years (interquartile range, IQR, 44-66). Median disease duration was found to be 33 months (IQR, 9-75).

Dual x-ray absorptiometry (DXA) was performed in a total of 161 (35.5%) patients during their follow-up, and in 46 (10.1%) at the time of AAV diagnosis. Patients scanned with DXA had similar demographic and clinical characteristics compared with unscreened patients (n=292), except for disease duration (median, 22 vs. 45 months, p<0.001).

Osteoporosis was diagnosed in 41% of the patients and osteopenia in 40.4%. Only 18.6% of patients had normal bone mineral density (BMD). Secondary causes of osteoporosis in patients and their immunosuppressive treatments were shown in Table 1. Patients with osteoporosis were older (median, 64 vs 55 years, p<0.001) and had lower body weight (median, 62 vs 74 kg, p=0.04) compared to patients without osteoporosis. The frequency of osteoporotic bone fractures in patients with osteoporosis was found to be higher than in patients without osteoporosis (13.6% vs. 7.4%, p=0.041). The median 25-OH vitamin D level was lower in patients with osteoporosis than in patients without osteoporosis, but the difference was not statistically significant (25 vs. 30 ng/ml, p=0.236). Oral or IV bisphosphonate was administered to 71.2% of patients with osteoporosis, and denosumab was administered to 7.7%. Oral bisphosphonate was given to 12.7% of patients with osteopenia.

Conclusion: This study showed that osteoporosis was investigated in only one third of patients with AAV, and most DXA evaluations were performed during the first three years of follow-up of the disease rather than at the beginning of treatment. It also suggested that the frequency of osteopenia or osteoporosis (80%) was much higher compared to the general population. Physicians should consider the evaluation and treatment of secondary osteoporosis in the management of AAV to decrease the risk of osteoporotic fracture which is a severe comorbidity.

Table 1, Characteristics of AAV patients screened for osteoporosis

	Normal BMD (n=30)	Osteopenia (n=66)	Osteoporosis (n=65)
Gender, male, n (%)	21 (70)	39 (60)	33 (50)
Age, median, years, (IQR)	53 (40-61)	56 (44-66)	64 (55-72)
AAV disease duration, median, months, (IQR)	41 (21-86)	39 (21-86)	48 (17-87)
BMI, median, kg/m², (IQR)	27 (25.0-29,4)	25 (23.0-28,8)	23,5 (21,7-27,7)
Rituximab, n (%)	10 (33,3)	20 (30,8)	22 (33,3)
Cyclophosphamide, n (%)	22 (73,3)	39 (60)	49 (74,2)
Mycophenolate mofetil, n (%)	3 (10)	12 (18,5)	15 (22,7)
Azathioprine, n (%)	15 (50)	33 (50,8)	38 (57,6)
Methotrexate, n (%)	6 (20)	11 (16,9)	15 (22,7)
Cumulative glucocorticoid dose >10g, n (%)	13 (43,3)	31 (53,4)	31 (48,4)
Pathological bone fracture, n (%)	2 (6,7)	5 (7,7)	9 (13,6)
Family history of fractures, n (%)	1 (3,3)	3 (4,6)	3 (4,5)
Menopause, n (%)	5 (16,7)	18 (27,7)	27 (40,9)
Alcohol, n (%)	2 (6,7)	6 (9,2)	4 (6,1)
Malignancy, n (%)	0	6 (9,2)	3 (4,5)
Hyperthyroidism, n (%)	0	0	2 (3)
Hypothyroidism, n (%)	1 (3,3)	6 (9,2)	3 (4,5)
Hypogonadism, n (%)	1 (3,3)	1 (1,5)	1 (1,6)
Anorexia nervosa, n (%)	0	1 (1,5)	0
Chronic renal failure, n (%)	8 (26,7)	21 (32,3)	23 (34,8)
Immobilization, n (%)	0	1 (1,5)	4 (6,1)
Primary biliary cirrhosis, n (%)	0	1 (1,5)	0
Hemochromatosis, n (%)	0	0	1 (1,6)
Gastrectomy, n (%)	0	0	1 (1,6)
Malnutrition, n (%)	0	0	1 (1,6)
Proton pump inhibitors, n (%)	21 (70)	53 (81,5)	47 (72,3)
Low molecular weight heparin, n (%)	1 (3,3)	7 (10,6)	7 (10,8)
Ca+ vitamin D supplementation, n (%)	24 (80)	55(84,6)	62(93,9)
Oral bisphosphonate, n (%)	2 (6,7)	8(12,3)	33(50)
Iv bisphosphonate, n (%)	0	0	14(21,2
Denosumab, n (%)	0	0	5(7,6)

AAV, ANCA-Associated Vasculitis; BMD, Bone Mineral Density; BMI, Body Mass Index; IQR, Interquartile Range

P-161

First breakthrough COVID-19 infection following two SARS-CoV-2 vaccinations among Primary Systemic Vasculitis Patients

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Background/ Objectives: Primary systemic vasculitis (PSV) patients on immunosuppression are at higher risk of adverse outcomes following COVID-19 infection and often mount suboptimal vaccine responses to SARS-CoV-2 vaccination. The aim of this study was to investigate risk factors for first breakthrough COVID-19 infection after two vaccine doses in this patient group.

Methods: PSV patients enrolled in a prospective, UK-based multicentre observational cohort study investigating serological responses to SARS-CoV-2 vaccination (ethics reference: 20/EM/0180) were included if they had two SARS-CoV-2 vaccine doses. Patients were excluded if they had a previous documented history of COVID-19 or if their SARS-CoV-2 anti-nucleocapsid antibody titre (anti-N IgG) was >6104 median fluorescence intensity (MFI) indicating previous infection[1]. The outcome of interest was first symptomatic breakthrough SARS-CoV-2 infection (PCR or lateral flow positive) >14 days after two SARS-CoV-2 vaccinations. SARS-CoV-2 IgG spike antibody (anti-S IgG) and anti-N IgG titres were measured using a Luminex assay, and seroconversion was defined as an anti-S IgG titre >1896 MFI[1]. Clinical details were obtained via electronic health records.

Results: 252 PSV patients were identified from 02 January 2021 to 01 April 2023, with 13 being excluded (n = 9 had COVID-19 prior to or within 14 days of their second vaccination, n = 4 withdrew consent), leaving 239 eligible patients (49% male, median age 59 years). 59% had ANCA-associated vasculitis (AAV) and a 42% of patients had a history of rituximab within 6 months of vaccination. Median follow-up was 400 (range 78–756) days. During follow-up, 117 patients (49%) had a first breakthrough COVID-19 infection, representing a crude incidence rate of 12 per 10,000 person-days. 14 required hospital admission, with two being admitted to intensive care. Median time from second vaccination to first breakthrough infection was 350 (interquartile range 285–442) days. Univariable and multivariable analyses of first breakthrough infection were conducted using the Fine and Gray method to adjust for competing events of death and study withdrawal. In the fully adjusted model, seroconversion and third and subsequent vaccinations were associated with a lower hazard of breakthrough infection, with hazard ratios of 0.48 (95% confidence interval [CI] 0.27–0.87; p=0.015) and 0.43 (95% CI 0.31–0.58; p<0.001) respectively. Patients with a history of malignancy (p=0.031) and chronic kidney disease (p=0.01) also had a reduced risk, while IgA (p=0.003) and large vessel vasculitis (p=0.012) patients relative to AAV were at higher risk of breakthrough infection (Table 1).

Conclusions: In this cohort of PSV patients on immunosuppression who had two SARS-CoV-2 vaccinations, a third and subsequent vaccine doses were independently associated with reduced risk of breakthrough COVID-19 infection. Our study highlights the importance of booster vaccinations and support anti-S IgG titres as a correlate of protection against COVID-19 in this PSV patients.

References: Smith RM et al. *BMC Nephrol*. 2022 May 31;23(1):199.

Disclosures: Research funding from GSK.

Table 1. Univariable and multivariable predictors of first breakthrough COVID-19 infection.

	Univariable model		Fully adjusted model*	
	Hazard ratio (95% CI)	**p-value**	**Hazard ratio (95% CI)**	**p-value**
Age (years)	**0.98 (0.97, 0.99)**	**0.003**	1.00 (0.98, 1.02)	0.879
Sex				
Female	1.00 (Reference)		1.00 (Reference)	
Male	0.80 (0.56, 1.15)	0.234	0.94 (0.61, 1.43)	0.758
Diagnosis				
ANCA-associated vasculitis (AAV)	1.00 (Reference)		1.00 (Reference)	
Systemic lupus erythematosus (SLE)	1.39 (0.88, 2.18)	0.157	0.79 (0.30, 2.08)	0.635
Medium vessel vasculitis	0.77 (0.19, 3.15)	0.715	0.91 (0.16, 5.18)	0.911
Large vessel vasculitis	1.98 (0.85, 4.59)	0.111	**3.51 (1.31, 9.41)**	**0.012**
Behcet's disease	**2.6 (1.51, 4.47)**	**0.001**	1.88 (0.87, 4.04)	0.106
IgA vasculitis	1.4 (0.73, 2.66)	0.313	**4.21 (1.655, 10.72)**	**0.003**
Other	2.91 (1.22, 6.91)	0.016	0.99 (0.45, 2.16)	0.972
Comorbidities				
Hypertension	**0.61 (0.42, 0.88)**	**0.008**	0.63 (0.38, 1.03)	0.065
Chronic lung disease	1.11 (0.75, 1.64)	0.603	1.43 (0.87, 2.35)	0.153

	Univariable model		Fully adjusted model*	
	Hazard ratio (95% CI)	**p-value**	**Hazard ratio (95% CI)**	**p-value**
Chronic kidney disease ≥ stage 3	**0.78 (0.66, 0.91)**	**0.002**	**0.80 (0.67, 0.95)**	**0.01**
Diabetes	0.92 (0.48, 1.78)	0.813	1.34 (0.68, 2.65)	0.395
History of malignancy	1.23 (0.6, 2.5)	0.576	**2.38 (1.08, 5.22)**	**0.031**
Cardiac disease	0.91 (0.56, 1.47)	0.694	0.91 (0.48, 1.74)	0.780
Medications				
Prednisolone	1.15 (0.8, 1.64)	0.445	0.91 (0.61, 1.37)	0.67
Antiproliferatives	1.14 (0.78, 1.65)	0.499	1.32 (0.73, 2.39)	0.354
Methotrexate	1.3 (0.59, 2.87)	0.521	0.54 (0.15, 1.93)	0.344
Calcineurin inhibitors	1.31 (0.56, 3.04)	0.528	1.06 (0.33, 3.50)	0.914
Rituximab within 6 months of vaccination	0.78 (0.53, 1.14)	0.199	0.88 (0.52, 1.48)	0.622
Cyclophosphamide within 6 months of vaccination	0.59 (0.32, 1.06)	0.078	0.63 (0.31, 1.29)	0.211
Anti-TNF agents	**2.05 (1.18, 3.54)**	**0.01**	1.52 (0.72, 3.20)	0.271
Seroconversion (anti-S IgG > 1896 MFI)	0.74 (0.49, 1.11)	0.141	**0.48 (0.27, 0.87)**	**0.015**
Booster vaccination doses	**0.48 (0.36, 0.64)**	**<0.001**	**0.43 (0.31, 0.58)**	**<0.001**

*n=237, competing risks regression using Fine and Gray model to adjust for competing events of death or withdrawal during study; adjusted for age (years), sex, diagnosis, comorbidities, medications, seroconversion and subsequent vaccination doses.

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Severe acute respiratory syndrome coronavirus 2 seroprevalence in antineutrophil cytoplasm autoaantibodies-associated vasculitides patients

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Background/Objectives: Regarding coronavirus disease 19 (COVID-19), the effect of immunosuppression on the severity of this infection, and the predisposition to it according to antineutrophil cytoplasm autoantibodies vasculitides (AAV) status are unknown. We evaluated the presence of specific antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in AAV patients, identified the role of the AAV status and its treatment on the presence or the course of COVID-19, and of those same factors on the seroprevalence against SARS-CoV-2.

Methods: In one hundred AAV patients, anti-spike antibodies against SARS-CoV-2 were sought. Their presence and relationship with the status of the disease and its treatment were evaluated. Analyses were done with descriptive statistics. Data are presented as means ± SD; for categorical data, the X^2 test was used.

Results: Table 1 shows the clinical characteristics. There were 29 males and 71 females. Anti-spike antibodies developed in 92% of the sample, and 91% were positive in those with COVID-19 (n-47). Two patients had severe disease (4.3%). COVID-19 diagnosis was done with RT-PCR in 48.9%, antigen testing in 34%, and 17% according to the clinical presentation. Main symptoms: fatigue (63.8%), fever (61.7%), headache (61.7%), myalgias (53.3%) and cough (52.2%). Symptomatic treatment was prescribed in 93.6%, 25.5% received antibiotics, and 21.3% glucocorticoids (GC). Ninety-one per cent of patients continued DMARDs, while 10.5% of those under GC therapy stopped it. Mean time elapsed between vaccination and infection: 7.4 months. Of the patients treated with rituximab, 71.4% caught COVID-19 in the following 6 months after its prescription.

Table 1. Clinical characteristics

	Total n=100	COVID-19 n=47	Without COVID-19 n=53
	% (n)	% (n)	% (n)
AAV phenotype			
Granulomatosis with polyangiitis	86% (86)	87.2% (41)	84.9% (45)
Microscopic polyangiitis	9% (9)	6.4% (3)	11.3% (6)
Eosinophilic granulomatosis with polyangiitis	5% (5)	6.4% (3)	3.8% (2)
Disease status at the time of COVID-19			
Remission	84% (84)	74.5% (35)	92.4% (49)
Active disease	10% (10)	12.8% (6)	7.6% (4)
Undetermined*	6% (6)	-	-
Glucocorticoid treatment	36% (36)	40.4% (19) (at time of infection)	32.1% (17)
Rituximab treatment	23% (23)	23.4% (11) (at time of infection)	22.6% (12)
Non-treated	16% (16)	29.7% (14)	3,7% (2)
SARS-CoV-2 vaccination	94% (94)	93,6% (44) (pre or post COVID-19)	94.3% (50)
Vaccination prior to COVID-19	NA	72,7% (32)	NA

*At the time of COVID-19, the AAV diagnosis was not confirmed, but symptoms/signs attributable to AAV had been present. NA-not applicable.

Conclusions: Almost half the AAV patients in this sample had COVID-19, being mild in the majority. Their treatment was much like that in the general population. In our sample, neither the treatment for the disease nor its status (active or in remission) influenced the severity of COVID-19. However, in those who had been RTX-treated, COVID-19 was present within the following 6 months, which is similar to what has been reported regarding RTX treatment in other rheumatologic diseases. The presence of anti-spike antibodies was not modified by the AAV phenotype, the state of the disease, its treatment, or the SARS-CoV-2 vaccination status. Patients achieved an adequate seroconversion.

Disclosures: None.

P-163

Venous thromboembolism in ANCA-associated vasculitis might be associated with disease activity: results of TR-VaS cohort

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Background: An incereased frequency of venous thromboembolism (VTE) in ANCA- associated vasculitis (AAV) has been reported previously. However it is not clear yet which AAV patient would benefit prophylactic anticoagulant treatment. Therefore the aim of the present study is to evaluate the occurence and the associated factors with VTE in a multicenter large national AAV cohort of TR-VAS.

Method: In this nationwide study, we included patients with granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and unclassified AAV (uAAV) according to the European Medicines Agency algorithm from TRVaS, multicenter, and e-database of Turkey. Data recorded in the TRVaS database (baseline demographic, disease related characteristics [including organ/system involvements, data regarding disease activity and severity], comorbidities, serologic and other laboratory data as well as the treatment initiated for AAV, the development of end-stage renal disease and the survival status during follow up were withdrawn. Additionally, data about VTE were collected from participating centers by using a structured questionnaire. A VTE that occurred within the three months prior the diagnosis of AAV and during the follow up was included in the current analysis. Presence of classical risk factors for VTE and disease activity at the time of VTE (BVAS score), antiaggregant/anticoagulant usage were also recorded. The analysis was performed by using the statistical package program [Statistical Package for the Social Science; SPSS 16.0]. A p value of <0.05 was considered statistically significant.

Results: In total, 521 (239 female [45.8], mean age 54.4±1.08 years) patients with AAV were included in the analysis. The majority of the patients was diagnosed as GPA (357/521 [68.5%]) and as expected 60.4% (265/443) of them were PR3-ANCA positive. The demographic and main clinical characteristics of the patients with AAV was summarized in table. In total 43 (8.3%) patients suffered from VTE. When we compared AAV patients with and without VTE (table) we showed that cutaneous and eye involvement was statistically significantly higher (P<0.05) in patients with VTE. Baseline BVAS score was significantly higher in patients with VTE (15.7 ± 1.5 vs 13.3 ± 0.6 and P=0.002). Although we saw that renal involvement was tended to be higher in patients with VTE this was not reached statistically significance. AAV patients with VTE had higher baseline risk factors for the development of VTE. In multivariate analysis we revealed that baseline BVAS score was the only independent risk factor (OR=1.059, 95% CI 1.008-1.113) for the development of VTE in our AAV patients.

Conclusion: The results of the present study showed that beside well-known risk factors AAV patients with high baseline disease activity, patients in particular with the cutaneous, eye and renal involvement could have higher risk for the devlopment of VTE. The determination of AAV patients with increased risk of VTE would be important to timely start anticoagulant treatment.

References:

Keywords: AAV VTE, cohort study.

Disclosures: None of the authors have any financial relationships.

Table 1. The comparison of AAV patients with VTE and without VTE.

	All AAv patients (521)	AAV patients with VTE (43)	AAV patients without VTE (478)	P
Age, mean (SD) years	54.4(1.08)	55.1(3.1)	54.3(1.16)	0.97
Sex, female, n (%)	239 (45.8)	20(46.5)	219 (45.8)	0.93
Duration of follow up, mean (SD) days	1511 (103)	1434(298)	1521(110)	0.61
Diagnosis, n (%) GPA, MPA, EGPA, RLV and Others	 357(68.5) 72(13.8) 53(10.2) 39(7.5)	 27(62.8) 8(18.6) 6(14) 2(4.7)	 330(69) 64(13.4) 47(9.8) 37(7.7)	 0.54
PR3-ANCA n (%)	265/443(60.4)	20(55.6)	245(60.8)	0.54
MPO-ANCA n (%)	135/447(30.5)	11(30.6)	124 (30.5)	0.99
Baseline clinical manifestations (involvement)				
General symptom n (%)	369/462 (79.9)	37(88.1)	332(79)	0.22
Cutanous n (%)	**101/462(21.9)**	**14(33.3)**	**87(20.7)**	**0.06**
Eye n (%)	**89/462(19.3)**	**13(31)**	**76(18.1)**	**0.04**
ENT n (%)	249/462 (53.9)	21(50)	228 (54.3)	0.59
Pulmonary n (%)	341/462(73.8)	35(83.3)	306(72.9)	0.14
Cardiac n (%)	21/462 (4.5)	2(4.8)	19(4.5)	0.94
Gastrointestinal n (%)	18/462 (3.9)	2(4.8)	16(3.8)	0.76
Renal n (%)	280/462 (60.6)	31(73.8)	249 (59.3)	**0.06**
Neurologic n (%)	66/462 (14.3)	7(16.7)	59(14)	0.64
Proteinuria (spot urine) (mean SD mg)	1182 (241)	1067(300)	1196(269)	0.75
Serum creatinine, mean (SD) mg/dl	2.5(0.2)	2.4(0.5)	2.5(0.2)	0.23
CRP, mean (SD) mg/L	93.8(6.4)	74.8 (19.1)	96.18 (6.8)	0.53
ESR, mean (SD) mm/h	68.4(2.6)	67.4(9.1)	68.11(2.7)	0.29
BVAS core, mean (SD)	**13.5(0.5)**	**15.7(1.5)**	**13.3(0.6)**	**0.002**
Revised five factor,mean (SD)	1.07(0.07)	1.22(0.2)	1.06(0.07)	0.20
Presence of risk factors				
Any risk factor,n(%)	**266 (51.1)**	**30 (69.8)**	**236 (49.4)**	**0.01**
Immobolization,n(%)	**30(5.8)**	**12 (27.9)**	**18(3.8)**	**<0.001**
Surgery,n(%)	**12(2.3)**	**3 (7)**	**9 (1.9)**	**0.03**
Cardiac failure,n(%)	30(5.8)	3 (7)	27 (5,6)	0.72
Ever smokers,,n(%)	137(26.2)	15 (34.9)	122 (25.5)	0.18
Atrial fibrilation n(%)	10(1.9)	0 (0)	10 (2.1)	0.34
Diabetes mellitus,n(%)	82(15.7)	9 (20.9)	73 (15.3)	0.33
Family history,n(%)	4(0.8)	1 (2.3)	3 (0.6)	0.22

AAV: ANCA-Associated Vasculitis, ENT: ear nose throat, PR3-ANCA: proteinase-3, MPO-ANCA:myeloperoxidase.

P-164

Blood stream infections in patients with ANCA-associated vasculitis

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Background: Infection due to the immunosuppressive treatment, is among the most frequent causes of hospitalization and death in patients with ANCA-associated vasculitis (AAV). Information on prevailing causal microbial aetiologies is crucial for improving treatment and prevention of such events. Here we examined causal bacteriology, incidence, and risk of blood stream infections (BSIs) in incident and prevalent AAV patients, as compared to the general population.

Methods: All data were retrieved from the Danish nationwide registries and the Danish Microbiology Database. Prevalent patients between 1998-2010 were all included at the same index date 1.1.2010; Incident patients diagnosed after 2010 were included with index being the day of diagnosis. Both groups were followed until first time BSI, death, or a maximum of 12 months. Background controls were matched 1:4 on age and sex. Cumulative incidence was assessed by the Aalen-Johansen estimator, and cox analyses adjusted for age, sex, kidney involvement, hypertension, diabetes, dialysis, and plasma exchange (PLEX), were used to model survival time.

Results: A total 19 (2.3%) BSIs were identified in 818 prevalent patients, and 55 (5.9%) BSIs in 939 incident patients (P<0.001). As in the background control group, primary causal microbial agents among prevalent patients were *E. coli* (26.3%) and *S. aureus* (21.1%), with an overall Gram-negative predominance (58.8%). *E. coli* (17.5%) remained the most frequent microbial cause of BSIs in incident patients, however with a relatively higher frequency of gram-positive bacteria (50.9%) dominated by Coagulase-negative Staphylococci (12.3%), Enterococci (14%), and Streptococci (14%). Difference in bacteriology between prevalent and incident patients disappeared when patients on dialysis were excluded, whereas the difference in BSI frequency remained significant (p<0.001).

One-year HR of first-time BSI was significantly higher in patients with AAV as compared to controls (prevalent AAV: HR 3.17 [95% CI 1.63-6.18], p<0.0001; Incident AAV; HR 8.64 [95% CI 4.88-15.31], p<0.0001), with significant difference between incident and prevalent patients (HR 2.73 [95% CI 1.39-5.35], p=0.003). Dialysis (HR 3.15 [95% CI 1.86-5.31], p<0.0001) and PLEX (HR 1.87 [95% CI 1.05-3.33], p<0.033) were solitary risk factors of BSI as well as higher age, hypertension, diabetes, and kidney disease (figure). Risk of BSI remained significantly increased for both prevalent and incident patients as compared to matched background controls when patients on dialysis were excluded.

Conclusion: *E. coli* and *S. aureus* were predominant causal isolates in prevalent AAV patients and controls, and the gram-positive predominance seen with incident AAV was primarily caused by patients on dialysis. Risk of BSI was higher in incident AAV as compared to prevalent AAV, and the AAV diagnosis was associated with increased risk of BSI at all times, with highest risk initially after first diagnosis. Interventions requiring a central venous catheter were solitary risk factors of BSI.

Disclosures: None.

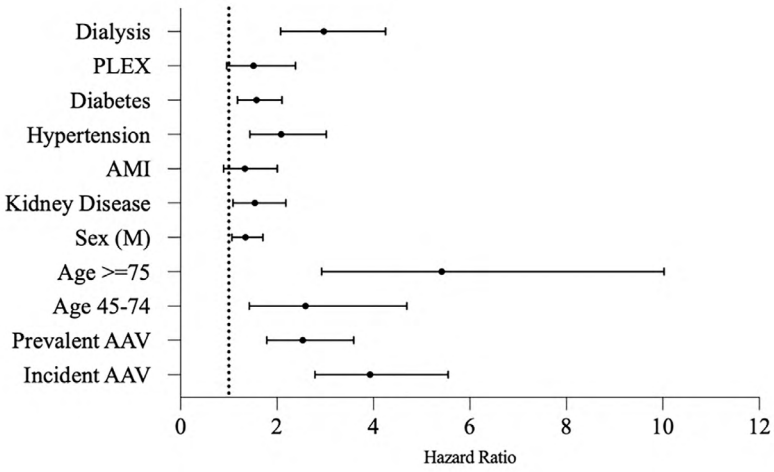

Figure: One-year hazard ratio of BSI as compared to controls.

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Cognitive Function and its associated factors in Polymyalgia Rheumatica

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Background: Over the past decade our understanding of the prevalence, and indeed impact of cognitive impairment in rheumatic diseases has increased. An aging population, coupled with systemic inflammation have been postulated as key drivers of increased cognitive decline in these conditions.

Intact cognitive function is imperative not only for quality of life and maintenance of one's functional capacity, but also for the successful therapeutic management of disease, namely the adherence to treatment regimens. The prevalence of cognitive impairment in community dwelling adults above the age of 65 in Ireland has been estimated at 13%.[1] To date the prevalence of cognitive impairment in PMR has not been studied.

Methods: Patients with a diagnosis of PMR (fulfilling the 2012 EULAR/ACR Provisional Classification Criteria), who were in clinical remission and on active treatment with glucocorticoids were recruited from two centres. Cognitive function was evaluated using the Montreal Cognitive Assessment (MoCA) test which was conducted by trained interviewers. Cognitive impairment was defined by the previously validated MoCA cut-off score of <26. Demographics, clinical and laboratory data, in addition to patient reported outcomes (PRO's) were collected. Patient reported outcomes included anxiety, using the Generalised Anxiety Disorder Assessment (GAD-7), mood using the Patient Health Questionnaire (PHQ-9), fatigue using the Functional Assessment of Chronic Illness Therapy – Fatigue Scale (FACIT-F), pain using the visual analogue scale (VAS) and overall health related quality of life using the Health Assessment Questionnaire- Disability Index (HAQ-DI).

The associations between categorical variables were compared using the χ^2-test or Fishers exact test. The association between continuous variables and categorical variables were assessed using the Kruskal-Wallis test. Correlations were calculated using Pearson's r. All analyses were conducted using R (R Core Team, 2022). A p-value of <0.05 was considered as statistically significant.

Results: 51 consecutive patients with PMR were recruited, of which 56.9% (n=29) were female.

70.6% (n=36) of patients were cognitively impaired, with visuo-spatial, delayed recall and abstraction the most commonly affected cognitive domains. Interestingly, those with cognitive impairment had a younger age, versus those without (p=0.514). Although not statistically significant, median BMI, anxiety, depression and pain scores were all higher in those who were cognitively impaired. Moreover, median fatigue scores were also worse in the cognitively impaired group. No statistically significant difference in serum markers was observed.

Conclusion: This study demonstrates that the burden of cognitive impairment in PMR is significant, and is markedly higher than that observed usually at population level. Future studies exploring specific etiologic contributors are needed.

Characteristic	Impaired cognitive function (n=33)	Normal Cognitive function (n=14)	p-value
Sex, female, n(%)	23 (63.9)	6 (40)	0.135
Age, median (IQR)	70 (65-74)	72 (68-74.5)	0.514
Body Mass Index, median (IQR)	27.2 (24.5- 31.9)	25.4 (23.5-29)	0.169
Rheumatic disease comorbidity index (RDCI), median (IQR)	2.0 (0.8-3)	2.0 (1.0-2.5)	0.916
GAD-7 score, median (IQR)	1.5 (0-4.2)	0 (0-1.5)	0.209
PHQ-9 score, median (IQR)	2.5 (0-7.2)	2 (0-3)	0.168
HAQ-DI score, median (IQR)	0 (0-0)	0 (0-0.1)	0.282
VAS pain score, median (IQR)	2 (0-4)	0 (0-1)	0.082
FACIT-F score, median (IQR)	44.5 (38-50)	47 (42.5-49.5)	0.443
C-reactive protein (mg/L), median (IQR)	3.8 (1.2-6.1)	3.4 (1.1-5.5)	0.835
Erythrocyte sedimentation rate (mm/hr), median (IQR)	10 (4-25)	8 (5.5-21)	0.915
Serum interleukin-6 levels (pg/ml) median (IQR)	6.8 (3.1-10.1)	6.7 (4.6-13.2)	0.539
Haptoglobin level (g/L), median (IQR)	1.7 (1.3-2.6)	1.7 (1-2.1)	0.414
Hemoglobin (g/dL), median (IQR)	13.2 (12.6-13.7)	13.7 (13.4-14.1)	0.234

Table 1: Patient Characteristics stratified by cognitive function.

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Disclosures: None.

P-166

Frailty and its impact on patient reported outcomes in Polymyalgia Rheumatica

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Background: Frailty is an increasingly important construct in the field of rheumatology, aiding the identification of individuals with increased vulnerability to accelerated clinical decline, and overall worse disease outcomes.

The aim of this research was to explore the prevalence of frailty, and its potential associated impact on patient reported outcomes (PROs) in a cohort of patients with polymyalgia rheumatica (PMR).

Methods: Patients with a diagnosis of PMR (fulfilling the 2012 EULAR/ACR Provisional Classification Criteria), who were in clinical remission and on active treatment with glucocorticoids were recruited from two centres. Patients were ³ 3 months and £ 12 months from diagnosis.

Frailty was defined by the 5 criteria of the widely validated Fried Phenotypic Frailty Index.

Patient reported outcomes included anxiety, using the Generalised Anxiety Disorder Assessment (GAD-7), mood using the Patient Health Questionnaire (PHQ-9), fatigue using the Functional Assessment of Chronic Illness Therapy – Fatigue Scale (FACIT-F), pain using the visual analogue scale (VAS) and overall health related quality of life using the Health Assessment Questionnaire- Disability Index (HAQ-DI). The associations between categorical variables were compared using the χ^2-test or Fishers exact test. The association between continuous variables and categorical variables was assessed using the Kruskal-Wallis test. Correlations were calculated using Pearson's r. All analyses were conducted using R (R Core Team, 2022). A p-value of <0.05 was considered as statistically significant.

Results: 51 consecutive patients were recruited, of which 56.9% (n=29) were female. Using the Fried Phenotypic Index, 64.7% (n=33) were classified as robust, 27.5% (n=14) as pre-frail and 7.8% (n=4) as frail. All patients classified as frail were female, and had a statistically significantly higher BMI (p=0.040) than those in the robust and pre-frail categories.

Compared to robust individuals, those who were frail had statistically significant higher median GAD-7 (p=0.003), PHQ-9 (p=0.001), VAS (p=<0.001) and HAQ-DI (p=<0.001) scores. FACIT-F scores were also worse in those who were frail versus robust (p=0.001).

Conclusion: Over one third of patients with PMR in this cohort were classified as pre-frail or frail.

Increased frailty status was significantly correlated with worse PROs, including mood, pain, fatigue and overall quality of life. As frailty is a potentially reversible state, accurately identifying frailty, and implementing appropriate interventions is of utmost importance to ensure improved clinical outcomes in those with PMR.

Table1. Baseline characteristics by frailty classification according to Fried Phenotypic Frailty Index

Characteristic	Robust (n=33)	Pre-frail (n=14)	Frail (n=4)	p-value
Sex, female, n(%)	18(54.5%)	7 (50%)	4 (100%)	
Age, median (IQR)	72 (69-76)	67 (59- 71.8)	66.5 (63-73.2)	0.049
Body Mass Index, median (IQR)	25.4 (23.8-28.4)	30.8(26.4-32.2)	34.1 (25.8-36.1)	0.040
Rheumatic disease comorbidity index (RDCI), median (IQR)	2.0 (1-3)	1.5 (0.2-2.8)	3.5 (2.5-4.2)	0.262
GAD-7 score, median (IQR)	0 (0-2)	0 (0-4.8)	11.5 (9-14.2)	0.003
PHQ-9 score, median (IQR)	1 (0-3)	3.5 (2.2-7.8)	1.45 (12.2-17.5)	0.001
HAQ-DI score, median (IQR)	0 (0-0)	0.6 (0-0.8)	1.4 (1.1-1.8)	<0.001
VAS pain score, median (IQR)	0 (0-0)	4 (2-4)	2 (2-2.5)	<0.001
FACIT-F score, median (IQR)	48 (45-50)	40.5(36.8-43.8)	18.5 (16-24.8)	0.001

Disclosures: None.

P-167

Fatigue in MPO-ANCA associated vasculitis: is long-term low dose steroid treatment the cause?

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Background/ Objectives: A large proportion of patients with ANCA-associated vasculitis (AAV) suffer from debilitating fatigue that mimics that described in patients with ME/CFS (1). Rates of ME/CFS are especially high in patients with MPO-AAV (up to 60%). In the ADVOCATE study, quality of life substantially improved after the use of Avacopan (2,3). Recently, we reported that mitochondrial markers could distinguish early systemic sclerosis (SSc) patients who suffer from ME/CFS, from SSc patients without ME/CFS. (4). Based on this observation, we postulated that prolonged steroid use in AAV patients may promote fatigue partly by virtue of promoting mitochondrial dysregulation.

Methods: We included MPO-AAV and PR3-AAV patients in clinical remission treated with or without chronic low-dose (<7.5mg) prednisone (P). ME/CFS and related symptoms were assessed by patient reported questionnaires. Mitochondrial gene expression (Dloop, ND4, CyB, Cox7C) was assessed through qPCR. Cell free mitochondrial DNA integrity was defined as the ratio of small to large fragments of 16S-RNA as determined by qPCR.

Results: The rate of ME/CFS was higher in MPO-AAV patients (72.2%) than PR3-AAV (36.3%) patients (p=0.05). Current P use was also higher in MPO-AAV patients than in PR3-AAV patients (27.7% vs 9%). Comparison of MPO and PR3 patients regardless of P use, showed a trend for reduced ND4 expression (p=0.05), and a significant increase in mtDNA integrity (p=0.02) in MPO-AAV patients. MPO-ANCA and PR3-ANCA patients not on P were similar; however, MPO-AAV patients on P showed a significant reduction in the expression of mitochondrially associated genes ND4 and CyB (ND4: 0.002 vs 0.347, p<0.001; CyB: -0.026 vs 0.252, p=0.001) compared to those not using prednisone.

Conclusions: Chronic low dose prednisone in MPO-AAV is associated with mitochondrial dysfunction. We postulate that this may promote increased fatigue in these patients. Future studies utilizing steroid-free regimens, perhaps with Avacopan replacing prednisone, may be associated with improved quality of life.

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Disclosures:

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Dr. Yacyshyn received advisory board honorarium from Otsuka.

P-168

Early Antibiotic Use in Patients Receiving Plasma Exchange for ANCA-associated Vasculitis

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Background/objectives: Plasma exchange (PLEX) is an adjunctive intervention in the treatment of severe anti-neutrophil cytoplasm antibody (ANCA)-associated vasculitis (AAV). Although the PEXIVAS trial did not demonstrate a reduction in the time to death or end-stage kidney disease (ESKD)[1], a meta-analysis suggested that PLEX decreased the risk of ESKD in AAV patients at greatest risk (serum creatinine >300 µmol/L), but increases risk of serious infection[2]. Our objective was to assess the effect of early antibiotic administration on serious infection rate or mortality in AAV patients treated with PLEX.

Methods: In this retrospective single centre cohort study, patients with AAV were included if they received PLEX from 2014 to 2022. Antibiotic courses were recorded if the antibiotic was regularly administered, with either therapeutic or prophylactic intent prior to and/or during PLEX, regardless of route of administration. The primary composite outcome was death or serious infection (life-threatening or requiring intravenous antibiotics or hospitalisation) within 30 days of the final PLEX session. A secondary outcome was the duration of hospital stay following the final PLEX session. The relationship between antibiotic courses and the primary and secondary outcomes were explored with odds ratios (OR) and independent samples t-tests, respectively.

Results: 100 patients were included, with 112 courses of PLEX administered. The mean duration of a PLEX course was 8 days. Death or serious infection occurred within 30 days of the completion of 33 PLEX courses (29.5%). Patients who received regular antibiotics within 24 hours of starting PLEX were less likely to die or develop a serious infection, within 30 days of completing PLEX, than those who received antibiotics later or not at all (OR 0.30, $p<0.05$). Furthermore, patients receiving antibiotics within 24 hours of PLEX had an average stay of 9 days after final PLEX compared to 13 days for those receiving antibiotics later or not at all ($p = 0.09$).

Conclusions: Our findings suggest that early initiation of regular antibiotics to AAV patients treated with PLEX reduces their combined risk of death or serious infection in the 30 days of starting PLEX. These conclusions should be interpreted with caution given that this study is retrospective and non-randomised, and due to the heterogeneity in choice and duration of antibiotic. However, the risk of severe infection in PLEX in AAV is well recognised[2] and this is the first study to suggest this risk can be mitigated by early antibiotic prescribing. A prospective study involving protocolised antibiotic administration during PLEX is required.

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Disclosures: RJ has investigator-initiated study collaboration with Roche and has received research grants from GSK, CSL Vifor, advisory board fees from CSL Vifor and GSK and Honoraria from Roche. DJ has received research grants from Roche/ Genentech and CSL Vifor.

P-169

Malignancy is increased in patients with antineutrophil cytoplasmic antibody-associated vasculitis in China

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Objectives: It has been reported that in western countries malignancy risk was higher in patients with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) compared with that in the general population [1]. Since the disease spectrum and serotypes of ANCA in Chinese AAV patients are different from those in western countries [2], and less cyclophosphamide exposure was reported in Chinese AAV patients [3]. Therefore, studies on malignancy in Chinese AAV patients were of great interest. In the current study, we investigated the incidence, spectrum and risk factors of malignancy in Chinese AAV patients.

Methods: AAV patients [4] diagnosed from 1995 to 2021 in Peking University First Hospital with a follow-up more than 12 months were recruited. Standardized incidence ratios (SIR) were calculated to describe the risk of malignancy, adjusted for sex, age and follow-up time [5].

Results: A total of 552 AAV patients were recruited, among which 23 patients had preceding or concurrent malignancies with AAV, and 43 of the rest 529 patients developed malignancies during a follow-up of 4.3±4.2 years (SIR: 2.24; 95% CI: 1.68-2.99; p<0.001). Among these 66 patients, twenty different sites of malignancy were observed, lung cancer being the leading one. To get exactly expected malignancies for the calculation of SIR, 529 patients without preceding or concurrent malignancies were included in the following analysis. Lung cancer was still the leading one with SIR of 5.01 (95% CI: 3.29-7.62), followed by malignancies in the kidney, bladder, ureter and prostate. Male gender (HR:2.84; 95%CI:1.36-5.96; p=0.006) and older age (per year, HR:1.04; 95%CI:1.00-1.07; p=0.038) were significantly associated with increased risk of malignancy. For patients with malignancy developed beyond 5 years after the diagnosis of AAV, significantly higher malignancy risk was observed in those with a cumulative cyclophosphamide dose over 20.0g (SIR: 11.54; 95% CI: 4.77-27.93; p<0.001). Within the first 2 years after the diagnosis of AAV, the risk of malignancy was still significantly higher than that in the general population, but the cumulative cyclophosphamide dose was not significantly associated with malignancy occurrence in this subgroup of patients.

Conclusions: Malignancy risk is higher in Chinese AAV patients than that in the general population, with a different malignancy spectrum from western countries. Both the use of cyclophosphamide and AAV *per se* might be associated with higher incidence of malignancy occurrence.

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P-170

Course of COVID-19 in patients with ANCA-associated vasculitis

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Background/Objectives: To determine the risk factors for COVID-19 hospitalization among patients (pts) with ANCA-associated vasculitis (AAV).

Methods: The retrospective study included medical histories containing information on the previous treatment of COVID-19 (outpatient or inpatient) of 53 pts with AAV (women (w) – 36, men – 17, age 53.94±14.26 years (yr), duration of disease 5.74±6.11 yr), who were on inpatient treatment at the V. A. Nasonova Research Institute of Rheumatology from September, 2021 to April, 2023.

The first group included 26 AAV pts (w – 19, ≥60 yr - 14) hospitalized with COVID-19. Among them 13 with granulomatosis with polyangiitis (GPA), 7 – eosinophilic granulomatosis with polyangiitis (EGPA), 6 – microscopic polyangiitis (MPA). The second group included 27 AAV pts (w – 17, ≥60 yr – 7, GPA – 15, EGPA – 9, MPA – 3) who received outpatient treatment for COVID-19.

In the first group before COVID arterial hypertension (AHT) was diagnosed in 20 (76.92%) pts, obesity (Ob) - 15 (57.69%), lung diseases - LD (including interstitial diseases, bronchial asthma, etc.) - 19 (73.08%), chronic kidney disease (CKD) - 14 (53.85%), coronary heart disease (CHD) or diabetes mellitus (DM) – 3 (11.54%), chronic heart failure (CHF) or cerebral vascular accident (CVA) in the medical history – 2 (7.69%), cancer – 1 (3.85%). 22 (84.62%) pts before COVID-19 was treated with glucocorticoids (GK), among them 18 (69.23%) used ≥ 10 mg of prednisolone equivalent (PE) per day. 4 (15.38%) pts used mycophenolate mofetil (MMF), 3 (11.54%) – azathioprine (AZT) or cyclophosphamide (CP), 2 (7.69%) – methotrexate (MTX). 14 (53.85%) pts received rituximab (RTM).

In the second group AHT was diagnosed in 7 (25.93%) pts, LD – 11 (40.74%), DM – 3 (11.11%), CKD or Ob – 2 (7.41%), CHD, CVA or cancer – 1 (3.7%). 17 (62.96%) pts before COVID-19 used GK, 6 of them in dose ≥ 10 mg/day of PE. 2 (7.41%) was treated with AZT, 1 (3.7%) – MTX, MMF or hydroxychloroquine. 7 (25.93%) pts received RTM, 4 (14.81%) – mepolizumab (MPLZ).

Results: We found that age over 60 yr (odds ratio (OR) 3.33, 95% confidence interval (CI) 1.05-10.59, p=0.038), AHT (OR 9.52, CI 2.72-33.38, p=0,0002), Ob (OR 17.05, CI 3.32-87.61, p=0,0001), LD (OR 3.95, CI 1.24-12.57, p=0,018) and CKD (OR 14.58, CI 2.85-74.71, p=0,002) were associated with higher odds of hospitalization. PE ≥ 10 mg/day (OR 7.88, CI 2.3-26.99, p=0,0006) and RTM treatment (OR 3.33, CI 1.05–10.57, p=0,038) were linked with higher odds of hospitalization. While AAV pts received MPLZ may have decreased odds of hospitalization (p=0.042).

Among 26 AAV pts hospitalized with COVID-19, 3 (2 – EGPA, 1 – MPA, w – 2, ≥60 yr – 2) of them required interleukin-6 inhibitors because of infection severity. All of them had LD and CKD, on of them had AHT and Ob, all was previously treated with PE ≥ 10 mg/day and RTM. CKD and RTM treatment probably associated with higher odds of extremely severe COVID-19 (p=0.007 and p=0.028 respectively).

Conclusions: According to our data COVID-19 severity in AAV pts was associated with variable risk factors, such as age, number of comorbidities, as well as some treatments.

References: No.

Disclosures: None.

P-171

Assessment of mental health in patients with Behçet's disease: Preliminary results from a non-endemic area

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Background/Objectives: Mental health disorders are prevalent in individuals with chronic and recurrent illnesses. Behçet's disease (BD), a multifaceted chronic condition, subjects patients to both emotional and physical stress. This study aimed to investigate the relation between mood disorders such as depression, anxiety, and clinical parameters, educational background, and socioeconomic status of BD patients in a non-endemic setting.

Methods: A cross-sectional investigation was conducted. Depressive symptoms were evaluated through the Beck Depression Inventory (BDI) and the Hospital Anxiety and Depression Scale (HADS), while anxiety symptoms were assessed using the HADS. The Health Assessment Questionnaire (HAQ) was used to measure the quality of life, and disease activity was obtained via the Brazilian Behçet Disease Current Activity Form Simplified Version (BRBDCAFs). Educational and socioeconomic status were determined using the "2014 Brazil Criterion for Economic Classification" by the Brazilian Association of Research Companies (ABEP). Statistical analysis was performed and $p < .05$ was considered as significant.

Results: In this study, involving 33 (60%) women and 22 (40%) men, the mean age was 48 ± 12.9 years, with a median BD duration of 15.6 (0.75-39) years. Krause's severity index and BRBDCAFs medians were 5 (2-8) and 0 (0-7), respectively. In our cohort, 45.5% and 27.3% of the 55 patients displayed depressive symptoms as per the BDI and HADS-D assessments, respectively. Anxiety, identified in 29% of patients via the HADS-A questionnaire, exhibited higher frequency in individuals aged 20 to 59 years ($p=0.026$). Female gender correlated with depression and anxiety according to the HADS form ($p=0.015$; $p=0.014$). Disease activity, as per BRBDCAFs, was associated with depression only when HADS-D was employed ($p=0.032$). Higher educational levels and single marital status were linked to depression ($p=0.012$; $p=0.013$). No statistical significance was observed between depression/anxiety and HAQ, Krause's severity index, social status, and ethnic groups. Remarkably, only cutaneous involvement was associated with depression ($p=0.032$).

Conclusion: This is the first study to assess depression and anxiety within BD patients in Brazil, a non-endemic area. A substantial prevalence of mood disorders in our cohort aligns with findings in endemic BD regions. While divergent results emerged from various assessment tools, disease activity correlated solely with anxiety. These findings significantly contribute to comprehending the mental health impact and quality of life in our BD patient cohort.

P-172

Risk factors for severe COVID-19 infection and the impact of COVID-19 infection on disease progression among patients with antineutrophil cytoplasmic antibody-associated vasculitis

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Objectives: To identify risk factors for COVID-19 infection and investigate the impact of COVID-19 infection on chronic kidney disease (CKD) progression and vasculitis flare in patients with antineutrophil cytoplasmic antibody (ANCA)-associate vasculitis (AAV).

Methods: This cohort study retrospectively analyzed the prevalence and severity of COVID-19 infection in 276 patients with AAV [1] who were followed up in our centre. The diagnosis of COVID-19 is based on the detection of SARS-CoV-2 using polymerase-chain-reaction (PCR) assay [2], as well as antibody, metagenomic testing, CT scan, laboratory assay or a presumptive diagnosis based on symptoms and epidemiological history by physicians.Logistic regression was employed to estimate the risk of COVID-19 infection as well as CKD progression [3] and vasculitis flare [4] upon COVID-19 infection.

Results: During the 6-month observation period, 213 (77.2%) of 276 patients had a diagnosis of COVID-19 infection. Of these 213 patients, 49 (23.0%) had a COVID-19-related inpatient admission, including 17 patients who died of COVID-19 infection. AAV patients with severe COVID-19 infection were more likely to be male (OR 1.921 [95% CI 1.020-3.619], P=0.043), suffered from worse kidney function (serum creatinine [Scr], OR 1.901 [95% CI 1.345-2.687], P<0.001; estimated glomerular filtration rate [eGFR], OR 0.976 [95% CI 0.958-0.994], P=0.009, respectively), had higher C-reactive protein (CRP) (OR 1.054 [95% CI 1.010-1.101], P=0.017) and less likely to have evidence of initial vaccination (OR 0.469 [95% CI 0.231-0.951], P=0.036), and Scr and COVID-19 vaccination were proven to be significantly associated with severe COVID-19 infection even after multivariable adjustment (adjusted OR 1.926 [95% CI 1.276-2.909], P=0.002; adjusted OR 0.212 [95% CI 0.046-0.969], P=0.045, respectively). Severe COVID-19 infection was significantly associated with subsequent CKD progression (OR 7.929 [95% CI 2.030-30.961], P=0.003) and vasculitis flare (OR 11.842 [95% CI 1.048-133.835], P=0.046) among patients with AAV.

Conclusions: AAV patients who were male, and with worse kidney function were more susceptible to severe COVID-19 infection, which subsequently increased the risk of CKD progression and vasculitis flare.

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Disclosures: None.

P-173

Prevalence and clinical impact of atherosclerosis in patients with Giant Cell Arteritis

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Background/Objectives: Giant Cell Arteritis (GCA) is the most frequent vasculitis in patients older than 50 years-old. GCA phenotypes may vary according to age of diagnosis [1]. Atherosclerosis is highly prevalent among patients with an advanced age. However, little is known about the coexistence of these two vascular diseases. The aim of this work is to describe the prevalence of atherosclerosis in patients with GCA.

Methods: Thirty-eight with GCA followed at our vasculitis clinic were included. GCA was diagnosed according to local imaging protocol with subsequent Vascular Ultrasound (VUS) followed by FDG-Positron Emission Tomography (PET-FDG). VUS protocol includes the systematic assessment of the following artery territories: common carotid, proximal internal and external carotid, vertebral, subclavian, axillary and temporal. VUS was also used to assess for the presence of carotid atherosclerotic plaques. Patients with GCA were compared with a 38 Polymialgia Rheumatica (PMR) patients and 80 controls, matched for age, sex and cardiovascular risk factors. GCA was also subclassified as Cranial (C-GCA, only cranial vessels involved), or Large-Vessel (LV-GCA when any degree of Large Arteries were involved).

Results: Patients with GCA included were diagnosed at age of 71 (65-79) years, 21/38 were male. GCA was newly diagnosed in 31 and relapsing in 7 patients at the time of VUS. Regarding disease phenotype, 27 (71%) of patients had LV-GCA and 11 (29%) had C-GCA. The prevalence of carotid atherosclerotic plaque in GCA patients was of 17/38 (45%), which was not different from PMR (53%, p=0,491) and from controls (59%, p=0,153). The presence of carotid plaques in C-GCA patients was of 9/11 (82%), whereas in LV-GCA was of 8/27 (30%, p=0,005). C-GCA was more frequent in older age >75 years-old 6/14 (43%) and LV-GCA in younger ≤ 75 years-old 19/24 (79%), although without statistical significance (p=0,142).

Conclusions: In our study cohort, the prevalence of carotid atherosclerotic plaques was considerable in GCA and only slightly inferior to PMR and controls. There was an association between the GCA phenotype and the presence of carotid plaques, and not with the age at diagnosis. These results should be validated in larger studies.

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P-174

Risk and rates of hospitalisation in patients with ANCA-associated vasculitis and polyarteritis nodosa: an Australian data linkage study

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Background/ Objectives: To determine risk and reasons for hospitalisation in West Australian (WA) ANCA-associated vasculitis (AAV) and polyarteritis nodosa (PAN) patients with controls.

Methods: Linked data for AAV/PAN patients and age-, sex- and temporally-matched controls were sourced from the WA Rheumatic Disease Epidemiological Registry (WARDER), containing population-level health data for public and private hospitalisations (1980 – 2015) and emergency department care (2002 – 2015) for rheumatic disease. International classification of disease codes were used to identify AAV/PAN patients from hospitalisation diagnoses. PAN and microscopic polyangiitis shared an ICD code until 2006 and was thus included.

Hospitalisations for AAV/PAN patients and controls were compared using random effects time-to-event model for recurrent events, using splines to model time-varying effects. Analyses compared risk of hospitalisation, pre-specified cause specific hospitalisations and length of stay for AAV/PAN patients and controls. All same day hospitalisations were excluded from analyses.

Results: In total, 616 AAV/PAN patients and 4474 controls were included in analyses. Crude hospitalisation rates per 1000 person years were 776 (5037/6489) for AAV/PAN patients and 284 (18895/66453) for controls.

Hospitalisations were more common in AAV/PAN patients compared with controls (proportional odds hazard ratio (HR) 2.53 (2.35, 2.74) and decreased over follow-up. This was observed for both elective (HR 1.66 (1.53, 1.81)) and emergency admissions (HR 3.98 (3.51, 4.51)).

Length of stay was longer for AAV/PAN patients (median days [interquartile range], AAV/PAN: 4.3 [2.0, 10.0] controls: 2.8 [1.6, 6.6] p <0.001).

Hospitalisations for vasculitis accounted for 632 (13%) of AAV/PAN patient admissions, concentrated in the first year after diagnosis.

Primary discharge diagnosis specific time-varying HRs are shown in Figure 1. HRs for renal disease, infection and non-infective respiratory disease hospitalisations were greatest early after diagnosis and decreased over time. In contrast, hospitalisations for malignancy increased over time. Hospitalisations for ischaemic heart disease and stroke were comparable between AAV/PAN patients and controls.

Conclusions: In this Australian population-based study, patients with AAV/PAN have more frequent and longer hospitalisations than matched controls, which remains over long-term follow-up. Patterns of cause-specific hospitalisation demonstrate some drivers of health care utilisation in AAV/PAN patients and help inform ongoing efforts to improve chronic disease management for these patients.

References: Nil.

Disclosures: JT/CH- research grant, CSL, outside of the submitted work.

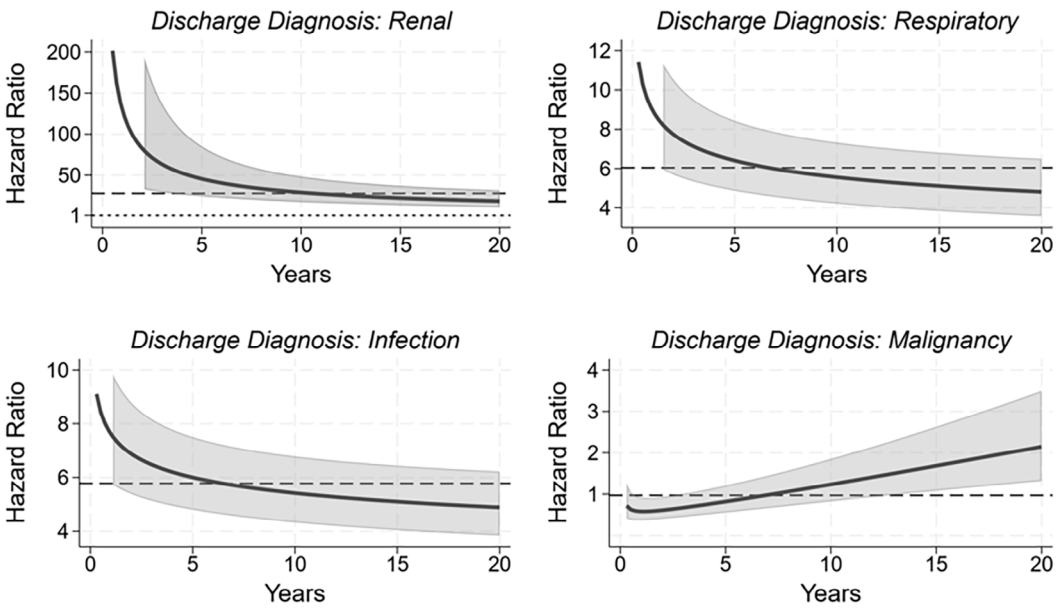

Figure 1: Primary discharge diagnosis specific HRs for AAV/PAN patients vs controls.

P-175

Gender differences in depression, anxiety and quality of life in patients with Behçet's disease: preliminary results from a non-endemic area

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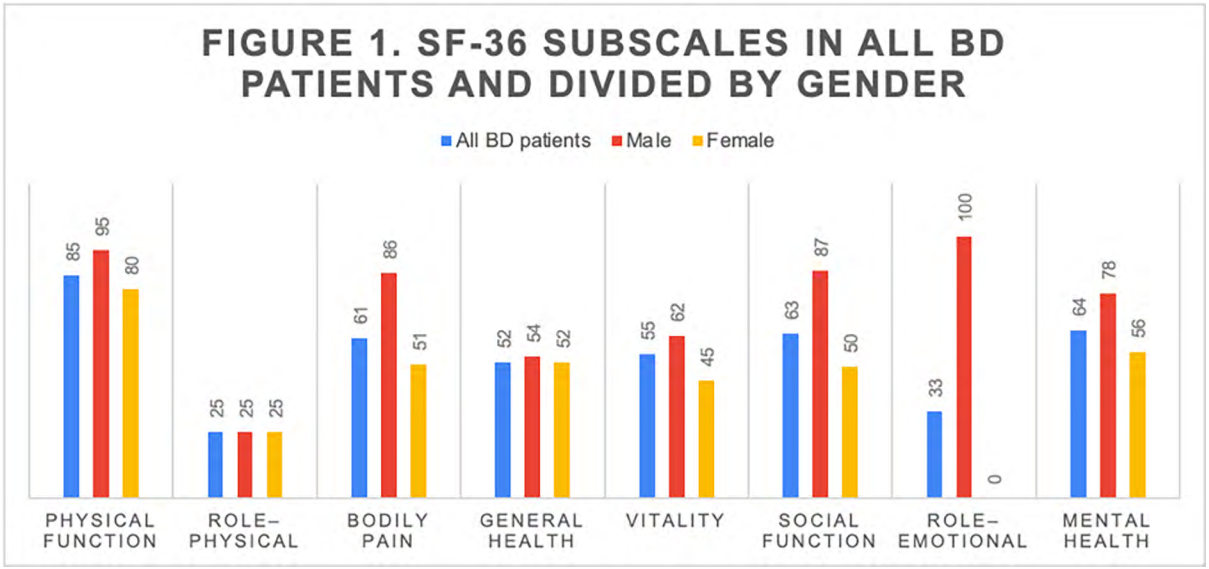
Background/Objectives: Behçet's disease (BD) is a systemic vasculitis with multiple organ involvement. Studies have reported a high prevalence of depression and anxiety among patients with BD, as well as their impact on health-related quality of life (HRQoL), and few data have added gender differences regarding these comorbidities. This study aimed to determine the frequency of anxiety and depression in patients with BD and evaluate the relationship between sex and disease activity, HRQoL, and mood disorders in patients with BD from a non-endemic area.

Methods: We conducted a cross-sectional study of 55 patients with BD in a single center in Brazil. All participants completed the Beck Depression Inventory (BDI) and the Hospital Anxiety and Depression Scale (HADS), through which humor disorders were assessed. HRQoL was assessed using the Short Form (36) health survey (SF-36). Disease activity and severity were obtained according to the Brazilian Behçet's Disease Current Activity Form Simplified Version (BRBDCAFs) and Krause's Severity Index, respectively. Statistical analyses were performed based on the characteristics of the variables. Multivariate analysis of covariance (MANCOVA) was performed to evaluate sex and the SF-36 subscales. Covariables included disease duration, activity and severity. All tests were performed at a significance level of $p < 0.05$.

Results: Sixty percent (N=33) of BD patients were female, with a mean age at diagnosis of 30.5±9.3 and median disease duration of 16.6 (0.75-38.6) years. Depression was present in 45.5% and 27.3% of the patients with BD according to the BDI and HADS questionnaires, respectively. A high frequency of anxiety was identified (29.1%). Women were more affected by humor disorders, as evidenced by the BDI (72% vs. 28%; p=0.097), HADS-D (86.7% vs. 13.3%; p=0.015), and HADS-A (87.5% vs. 12.5%; p=0.014). Depression was associated with disease activity when assessed using the HADS questionnaire (p=0.031) and disease duration when assessed using the BDI questionnaire (p=0.024). However, anxiety was not associated with age at diagnosis, disease duration, disease severity, or disease activity (p>0.05). Considering the SF-36, lower scores were found in female patients. Women had lower physical function (p=0.048), greater bodily pain (p=0.019), and worse mental health (p=0.015) (Figure 1). HRQoL and sex demonstrated significant differences in bodily pain (p=0.011) and mental health (p=0.010) after adjusting for disease duration, activity, and severity. This adjustment also showed a higher impact of disease activity on role-physical (p<0.001), vitality (p=0.004), and role-emotional (p=0.005). In addition, the disease duration was significantly different between role-physical (p=0.042), general health (p=0.036), vitality (p=0.002), and mental health (p=0.025). Disease severity assessed using Kraus's index did not have a significant impact.



Conclusion: In this group of patients with BD, depression, anxiety, and lower HRQoL were prominent, with females being the most affected. These findings highlight the importance of mental health care and targeted treatment.

1. CLINICAL SCIENCE
1.08. Pediatric vasculitis

P-176

The association between race/ethnicity and disease severity in pediatric patients with ANCA-associated vasculitis hospitalized in the United States

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The association between race/ethnicity and disease severity in pediatric patients with ANCA-associated vasculitis hospitalized in the United States.

Background: Race and ethnicity are societal constructs that contribute to health disparities. Small studies have found that patients of Hispanic ethnicity with ANCA-associated vasculitis (AAV) are more likely to present with severe features and complications, suggesting a relationship between race/ethnicity and severity of disease. However, racial/ethnic diversity is lacking in larger pediatric cohorts, a struggle that is pervasive in clinical research. The objective of this study was to examine the association between race/ethnicity and disease severity in a nationally representative and diverse sample of pediatric patients hospitalized in the United States (US).

Methods: This cross-sectional study used the Kids' Inpatient Database, the largest publicly available pediatric inpatient database in the US, to identify patients with granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA) using ICD-10 diagnoses. Severe disease was defined as a dichotomous variable comprised of illness in organ systems, complications, and interventions as previously defined. Multivariate logistic regressions were used to assess the overall odds of severe disease and specific severe disease features by race/ethnicity. Patients with missing race/ethnicity were excluded.

Results: A total of 701 AAV patients were identified, including 474 (68%) with GPA, 193 (27%) with MPA, and 34 (5%) with EGPA, with a median age of 16 years. Of the 701 patients, 438 (62.5%) were female, 394 (56.2%) identified as White, 69 (9.8%) as Black, 117 (25.2%) as Hispanic, 12 (1.7%) as Asian or Pacific Islander (AAPI), 13 (1.9%) as Native American, and 36 (5.1%) as Other. Of the 701 patients, 418 (60%) had severe disease; 56% White, 64% Black, 68% Hispanic, 67% AAPI, 38% Native American, and 53% Other had severe disease. Compared to White patients, Hispanic patients had 1.68 times the adjusted odds of having severe disease (p=0.021); after adjustments, older age, female sex, and elective admissions were associated with lower odds of severe disease, while those on Medicare and the West Coast had higher odds of severe disease. In subgroup analyses, patients identifying as Other had greater odds of sepsis (aOR 3.66, p=0.007) and Black patients had greater odds of hematologic (aOR 3.17, p=0.021), neurologic (aOR 3.66, p=0.008), and cardiac disease (aOR 8.09, p=0.011), stroke (aOR 18.75, p=0.020), and need for non-invasive ventilation (aOR 5.06, p=0.004).

Conclusions: To our knowledge, this is the first large, nationally representative study that has found an association between AAV disease severity and race/ethnicity among pediatric patients hospitalized in the US. Patients identifying as Hispanic had higher odds of severe disease, those identifying as Black had higher odds of specific severe features, including hematologic, neurologic, cardiac, stroke, and need for non-invasive ventilation, and those identifying as Other had higher odds of sepsis. These findings stress the need to boost recruitment of historically disenfranchised racial/ethnic minorities in research to understand and mitigate the effects of health care disparities.

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Disclosures: None.

Table 1. Adjusted odds of any severe manifestation by race/ethnicity among pediatric patients hospitalized with ANCA-associated vasculitis (AAV) in the Kids' Inpatient Database (KID) years 2016 & 2019.

	Total N=701	White N=394 (56%)	Black N=69 (10%)	Hispanic N=117 (25%)	Asian or Pacific Islander N=12 (2%)	Native American N=13 (2%)	Other N=36 (5%)
Severe	420	-	1.41 (0.68-2.94)	**1.68 (1.08-2.61)[a]**	1.86 (0.59-5.83)	0.55 (0.14-2.14)	0.93 (0.40-2.14)
RRT	225	-	1.68 (0.86-3.31)	1.62 (0.89-2.98)	0.86 (0.21-3.52)	1.32 (0.31-5.63)	0.77 (0.29-2.08)
Renal	149	-	1.50 (0.71-3.17)	0.77 (0.42-1.40)	1.67 (0.48-5.79)	1.14 (0.20-6.44)	1.69 (0.63-4.53)
Pulm. hemorrhage	91	-	0.83 (0.34-2.02)	1.24 (0.67-2.29)	3.69 (0.97-14.09)	0.47 (0.06-3.56)	1.01 (0.38-2.66)
Metabolic	64	-	0.84 (0.37-1.89)	0.64 (0.31-1.33)	2.31 (0.46-11.64)	1.42 (0.28-7.16)	0.47 (0.12-1.92)
Respiratory	62	-	1.07 (0.30-3.82)	1.01 (0.43-2.37)	/	0.97 (0.13-7.52)	0.56 (0.07-4.62)
Sepsis	60	-	0.64 (0.19-2.19)	1.16 (0.48-2.80)	1.90 (0.28-12.78)	5.17 (0.84-31.86)	**3.66 (1.44-9.33)[b]**
Plasmapheresis	46	-	2.38 (0.83-6.82)	0.78 (0.33-1.86)	2.27 (0.45-11.53)	1.77 (0.20-15.28)	0.97 (0.28-3.40)
Invasive vent.	46	-	2.40 (0.90-6.41)	1.20 (0.55-2.61)	/	3.06 (0.73-12.85)	0.68 (0.10-4.74)
Hematologic	41	-	**3.17 (1.19-8.44)[c]**	1.57 (0.54-4.57)	1.76 (0.19-16.28)	/	1.49 (0.29-7.71)
Neurologic	40	-	**3.66 (1.40-9.56)[d]**	1.26 (0.52-3.06)	/	4.43 (0.79-24.68)	1.39 (0.30-6.56)
Cardiovascular	39	-	1.40 (0.45-4.32)	0.63 (0.25-1.55)	/	1.23 (0.14-10.67)	1.83 (0.62-5.34)
Non-invasive vent.	20	-	**5.06 (1.67-15.32)[e]**	0.62 (0.18-2.19)	/	/	1.59 (0.28-9.07)
GI bleed	20	-	1.53 (0.25-9.20)	0.34 (0.07-1.76)	/	6.47 (0.37-112.40)	1.83 (0.49-6.79)
Cardiac	18	-	**8.09 (1.62-40.28)[f]**	1.49 (0.33-6.84)	6.36 (0.41-99.53)	/	3.60 (1.00-1.75)
ECMO	5	-	/	4.48 (0.43-46.45)	/	/	/
Stroke	3	-	**18.75 (1.58-222.38)[g]**	/	/	/	/
Hepatic	0	-	/	/	/	/	/

Adjusted for age, sex, estimated median household income by ZIP code, expected primary payer, hospital region, hospital teaching status, and type of admission (elective vs non-elective).

[a]p=0.021, [b]p=0.007, [c]p=0.021, [d]p=0.008, [e]p=0.004, [f]p=0.011, [g]p=0.020

Renal: acute kidney injury; metabolic: lactic or metabolic acidosis; respiratory: acute respiratory failure, acute respiratory distress syndrome, respiratory arrest; hematologic: defibrination syndrome, acquired coagulation factor deficiency, thrombocytopenia; neurologic: acute encephalopathy, altered consciousness, transient organic psychotic conditions, anoxic brain injury, coma; cardiovascular: hypotension, shock; cardiac: heart failure, acute myocardial infarction; hepatic: acute hepatic failure or necrosis, hepatic encephalopathy, hepatitis, hepatic infarction.

P-177

Concentration-dependent beneficial effects of anti-apolipoprotein A-2 in a mouse model of Kawasaki disease vasculitis

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Background/ Objectives: Kawasaki disease (KD) is usually treated with high-dose intravenous immunoglobulin (IVIg) as severe infectious and other diseases. Because of issues that are associated with immunoglobulin production, such as the risk of possible contamination by infectious agents and unknown target molecule, there is an urgent need to develop recombinant immunoglobulins. To date, we have developed a novel recombinant antibody drug candidate, "VasSF," based on the therapeutic effects it exerted on a mouse spontaneous crescentic glomerulonephritis model (SCG/Kj).[1,2)] As one of VasSF's target molecules Apolipoprotein A-2 (ApoA2) has been identified. In this study, we tested the potential of anti-apolipoprotein A-2 antibodies (anti-ApoA2) as a new therapeutic drug against KD by examining its effect on a mouse model, in which KD was induced via *Candida albicans* water-soluble fraction (CAWS).

Methods: CAWS was injected intraperitoneally into C57BL/6NCrSlc mice for five consecutive days. The incidence and histological severity of vasculitis in CAWS-induced coronary arteritis in mice administered anti-ApoA2 was examined. The following experimental groups were tested: solvent (only PBS); anti-ApoA2 antibodies at dosages of 0.05 to 0.5 mg/kg/day; human IgG at 0.1 mg/kg/day for 5 days.

Results: The group treated with anti-ApoA2 0.5 mg/kg/day showed a lower incidence of panvasculitis induced by CAWS, less inflammation of the coronary arteries and aortic roots in histological observations. And lower levels of serum IL-6, M-CSF, and MIP-1α and 32 cytokines/chemokines were observed compared with those in the solvent group.

Conclusions: The anti-ApoA2 treatment suppressed the development of coronary arteritis in an animal KD model and anti-ApoA2 shows potential as an effective therapeutic candidate for the treatment of KD vasculitis. The use of specific antibodies that display higher vasculitis-suppressing effects, such as anti-ApoA2, may attenuate KD as well as other infectious diseases, with less severe adverse side effects than treatment with IVIg.

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Disclosures: None.

P-178

S100A8/A9 as an indicator of disease activity in children with IgA vasculitis

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Background/ Objectives: S100A8/A9 molecule or calprotectin has a significant role in innate immunity. This heterodimer of two S100 proteins has cytotoxic and proinflammatory properties, monitors cell proliferation and differentiation, and it is also an indicator of monocyte and neutrophil activity. Although it plays a significant role in many inflammatory rheumatic diseases, little is known about the significance of S100A8/A9 in patients with IgA vasculitis (IgAV) (1).

Methods: Patients were diagnosed with IgAV according to the EULAR/PRES/PRINTO criteria. In a prospective study, serum S100A8/A9 values were monitored in patients with IgAV at the beginning of the disease, after 3 and 6 months from the onset of the disease, and were compared with the values in the control group of patients who did not have acute or chronic inflammatory disease. They were also compared with the values of other inflammatory markers, as well as the clinical manifestations of the disease itself.

Results: In patients with IgAV at the beginning of the disease, S100A8/A9 values were higher than in the control group (5740 ng/mL, CI 4982-6499; 1447 ng/mL, CI 1143-1751; $p<0.0001$). The values were also higher in patients with signs of active disease, regardless of the time of sample collection, compared to the control group ($p<0.0001$). Also, in patients who had an active disease after 3 months, higher values were observed compared to those in remission (4386±899.4 vs. 2294±1846; $p=0.0260$). Comparing the values of S100A8/A9 with other indicators of inflammation, a positive correlation was observed with the values of CRP ($p=0.0076$), ferritin ($p=0.0077$), C3 ($p=0.0065$) and fibrinogen ($p=0.0019$), while for the erythrocyte sedimentation rate we did not found statistically significant association, although it is possible that it exists ($p=0.0725$). It was also shown that the values of S100A8/A9 in the serum increase depending on the skin surface area covered by the rash ($p=0.0376$).

Conclusions: So far, the few studies of S100A8/A9 values in the serum of patients with IgAV suggested that S100A8/A9 could be a predictor of disease severity in patients with IgAV. This study showed that S100A8/A9 values were significantly higher in patients with active disease compared to the control group and patients in remission. Therefore, this molecule could serve as an indicator of disease activity and be useful in the clinical monitoring of patients.

SUPPORT: Croatian Science Foundation Project IP-2019-04-8822.

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Disclosures: None.

P-179

Pediatric Takayasu arteritis: a multicenter retrospective cohort study

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Objectives: Takayasu Arteritis (TA) is a chronic, inflammatory, granulomatous vasculitis that commonly affects the aorta and its major branches.[1] Diagnosis is difficult due to nonspecific symptoms at onset. Effective treatment is essential due to the high morbidity and mortality rates in follow-up. We aimed to identify demographic, clinical characteristics, and outcomes of pediatric TAK in a national cohort.

Methods: We conducted a multicenter retrospective cohort study in Turkey. The clinical data were collected from patients' charts provided by 9 prominent rheumatology centers. Patients who were diagnosed with TAK before 18 years of age were included in the study. All patients met the Ankara 2008 classification criteria.[2] ITAS 2010 score was used to evaluate disease activity.[3]

Results: Overall, 71 pediatric Takayasu Arteritis (p-TAK) patients were included (85.9 % female). The median age of symptom onset of disease was 13.2 (IQR,9-14.4) years, with a diagnostic delay of 5 (QR, 2-13) months, and a median follow-up time of 42 (IQR, 24-58) months. The most common symptoms at disease onset were neck, back, or abdominal pain (n=23,32.3%), fever (n=26,36.6%), and hypertension (n=13,18.3%). 62 patients had elevated acute phase reactants. The most common angiographic type at diagnosis was type III (16/71) and the least type was IIb (n=7). The others (I, IIa, III, V) were 15, 13, 15, and 15 in patients, respectively. ITAS2010 median at admission was 11 (2-25), ITAS2010 median at last control was 2 (0-14). At the last visit, there were 33 patients with an ITAS 2010 of less than 3 (ITAS 2010 <3), eight patients of them had a score of 0. Medications used included corticosteroids (n=68,95.7%), conventional (n=59,83.0%) and biological disease-modifying anti-rheumatic drugs (n=56, 78.8%), and other immunosuppressive therapies (cyclophosphamide (CYC) (n=35,49.2%)). The median duration of use of corticosteroids was 24 (6-96) months. There was a switch between biologic drugs in 20 (28.1%) patients. The first biologic drugs were tocilizumab (n=20), adalimumab (n=10), and infliximab (n=7), and the median time for the first biological drug use was 18 (2-70) months. Surgery procedures were required in 15 (21.1%) patients with severe disease refractory to medications. In follow-up angiographic imaging, there was deterioration in 21 (31.8%) patients, improvement in 10 (14.0%), and stable findings in 33 (46.4%) patients. 24 (33.8 %) patients had refractory disease. Only, 5 (7 %) patients had drug-free remission. Three patients died.

Conclusion: Notwithstanding aggressive immunosuppressive therapy and use of biologic agents, complete disease control was achieved in a small portion of p-TAK patients.

Disclosure of Interest: None declared.

Keywords: Takayasu arteritis, children, outcome, vasculitis.

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P-180

Nine-year Results of a Prospective Vasculitis Cohort from Eastern Mediterranean: Demographic Characteristics and Distribution of the Vasculitides Frequencies

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Background: Management strategies for most common diseases rely mainly on the results of randomized controlled clinical trials. However, implementing such an approach becomes extremely challenging for diseases with low prevalence such as vasculitides. To deal with these problems, large patient databases are required. In this assessment, we aimed to provide the current distribution and general characteristics of Hacettepe University Vasculitis Research Centre (HUVAC) and present the changes in the disease distribution of this tertiary center database over time.

Methods: HUVAC, the Vasculitis Registry of Hacettepe University, was established in 2014 with the aim of registering vasculitis patients in a database, managing the disease with a multidisciplinary approach, planning disease research in a more coordinated way and establishing training programmes. Since October 2014, all newly diagnosed/routine follow-up patients (adult/pediatric) are prospectively registered in the database. In 2016, the 2-year results of the database were reported (1). This evaluation analyzed the current distribution of patients in October 2023, including demographic characteristics according to the 2012 revised Chapel Hill nomenclature criteria, and also assessed changes in the distribution from 2016.

Results: A total of 2046 patients (female/male: 49.8%/50.2%) were newly diagnosed/followed during this period. 535 (26.1%) were paediatric patients. The leading vasculitis in adult patients was Behçet's disease (44.6%), whereas in paediatric patients it was IgA vasculitis (%50.4) (Table). Takayasu's arteritis (9.5%) was the most common large vessel vasculitis and there was a female predominance among adult patients with large vessel vasculitis (73.9%). Granulomatous with polyangiitis (7.7%) was the most common small vessel vasculitis in adults. Compared to 2016, there was an increase in the number of mimickers included in the database.

Conclusion: The trend in the distribution of patients did not show any remarkable changes, with similar rates of different types of vasculitis in adult and paediatric cases. It should be borne in mind that this is the result of a tertiary referral centre and that the predominance of Behçet's disease demonstrates the importance of the impact of geographical regions on the prevalence of these entities.

Reference: Omer Karadag et al, P1_145 Two-year Results of a Prospective Vasculitis Cohort from Eastern Mediterranean: Demographic Characteristics and Distribution of the Vasculitides Frequencies, *Rheumatology*, Volume 56, Issue suppl_3, March 2017, Pages iii88–iii95.

Table. Distribution of adult/ pediatric patients with vasculitides in 2016/2023 and current demographic data.

	ADULT PATIENTS				PEDIATRIC PATIENTS			
	April 2016 =734 (%)	September 2023 =2046 (%)	Current age in 2023 Mean (SD)	Female Rate in 2023 (%)	April 2016, n=205 (%)	September 2023, n=535 (%)	Current age in 2023 Mean (SD)	Female Rate in 2023(%)
Behcet's Disease	50.2	44.6	46.8 (12.4)	50.5	25.3	17	21.9 (5.4)	41.7
Giant Cell Arteritis	4.2	4.6	76.3 (9.6)	63.2	N/A	N/A	N/A	N/A
Takayasu Arteritis	11.5	9.5	46.4 (14.2)	84.6	2.9	2.9	21.6 (5.3)	75
Polyarteritis Nodosa	3.1	2.7	50.1 (17.9)	35.7	3.9	5.9	16.2 (5.4)	43.7
Kawasaki Disease	N/A	N/A			16.6	14.2	12.4 (3.4)	30.3
EGPA	2	2.7	51.9 (19.2)	49.1	0.6	0.6	16 (3.8)	66.7
GPA	8.2	7.7	56.8 (15.7)	40.1	1	1.7	21.4 (2.1)	44.4
MPA	0.8	0.6	55.9 (16.5)	33.4	N/A	N/A	N/A	N/A
AAV-Unclassifiable	NA	0.7	64.8 (11.6)	33.4	N/A	N/A	N/A	N/A
IgA vasculitis	6.1	4.3	40.5 (19.9)	47.7	44.8	50.4	15.5 (4.3)	44.8
Other (Cutaneous, Anti-GBM, Unclassified, Secondary)	2.3	9.5	53.1 (15.1)	58.7	0	4.2	20.3 (12.2)	52.2
Mimickers (IgG4-RD, DADA2, Buerger etc.)	11.6	13.1	60.9 (16.6)	49.8	4.9	2.8	24.6 (15.3)	46.7

EGPA: Eosinophilic Granulomatosis with Polyangitis, MPA: Microscopic Polyangitis, GPA: Granulomatosis with Polyangitis, AAV: Anca-associated vasculitis, GBM: Glomerular Basal Membrane, IgG4RD: IgG4 related disease, DADA2: Deficieny of Adenosine Deaminase
N/A: Not available

P-181

HMGB1, RAGE, Gd-IgA1 and PCDH1 - a possible biomarkers of IgA vasculitis (IgAV)?

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Background/ Objectives: Although various biomarkers have been considered in IgAV, the pathogenesis of the disease still remains unknown, nor it is elucidated which biomarker(s) could indicate active disease and predict possible damage. The aim of this study was to investigate high mobility group box 1 (HMGB1), receptor for advanced glycation end products (RAGE), galactose-deficient immunoglobulin A1 (Gd-IgA1) and protocadherin 1 (PCDH1) as a potential biomarkers in children with IgAV.

Methods: A prospective study conducted at the period from January 2020 until October 2023 included 86 children with IgAV and 70 children from the control group. HMGB1, RAGE, Gd-IgA1 and PCDH1 in serum and urine were determined by the enzyme-linked immunosorbent assay (ELISA) method at the onset of the disease and after six months interval.

Results: Concentrations of HMGB1, RAGE and PCDH1 in sera and concentrations of HMGB1, RAGE, Gd-IgA1 and PCDH1 in urine were statistically significantly higher in children with IgAV than in the control group ($p<0,001$). A statistically significant difference was observed in concentrations of HMGB1 (5573 pg/mL vs. 3477 pg/mL vs. 1088 pg/mL, $p<0,001$) and RAGE (309 pg/mL vs. 302,4 pg/mL vs. 201,3 pg/mL, $p=0,012$) in sera of children with IgAV at the onset of the disease compared to six months interval and between the control group. Serum HMGB1 significantly positively correlated with CRP ($\tau=0,161$, $p=0,029$), ferritin ($\tau=0,219$, $p=0,004$) and IgG ($\tau=0,147$, $p=0,045$). Cox regression analysis didn't reveal any of investigated biomarkers as a predictor of nephritis, although HMGB1, RAGE, Gd-IgA1 and PCDH1 in urine positively correlated with the urine albumine to creatinine ratio at the onset of the disease.

Conclusions: Our results imply a possible association of Gd-IgA1, HMGB1, RAGE and PCDH1 with IgAV development, with HMGB1 and RAGE showing elevated values during the disease follow up. Despite of indication of prolonged disease activity, none of them was a predictor of nephritis, the most important long term complication of IgAV.

SUPPORT: Croatian Science Foundation Project IP-2019-04-8822.

References: Bobek D, Grčević D, Kovačić N, Lukić KK, Jelušić M. The presence of high mobility group box-1 and soluble receptor for advanced glycation end-products in juvenile idiopathic arthritis and juvenile systemic lupus erythematosus. Pediatr Rheumatol. 2014;12(1):50.

Disclosures: None.

P-182

A Data-Driven Multiomic Approach Identifies Distinct Endotypes for Multisystem Inflammatory Syndrome in Children

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Background/ Objectives: Multisystem inflammatory syndrome in children (MIS-C) is a post-infectious hyperinflammatory condition temporally associated with SARS-CoV-2. Many lessons to treating MIS-C have been learned from Kawasaki Disease (KD), which it clinically resembles. However, due to the lack of a standardized diagnostic criteria for MIS-C and its clinical heterogeneity, there is currently limited and conflicting data describing the pathobiology driving MIS-C and its relation to KD. We aim to systematically characterize and compare children with MIS-C and KD using an unsupervised machine learning approach applied to multi-omic patient data.

Methods: A standardized set of clinical data and biospecimens from 31 treatment naïve MIS-C patients were collected prospectively within a tertiary center, and 35 pre-pandemic KD patients from a partner study. The expression of serum cytokines/ soluble cytokine receptors and interferon response genes (IRGs) were measured from biospecimens using Luminex and NanoString technologies, respectively. Data collected underwent dimensionality reduction by cross-validated probabilistic principal component analysis (PPCA). Sparsified PPCA scores were then used for patient clustering by Gaussian Mixture Modelling (GMM). The resulting patient groups were characterized by examining patterns in biological profiles, clinical phenotypes and treatment outcomes.

Results: Sparsified PPCA recovered 4 composite signatures capturing approximately 60% of dataset variation: 1) Elevated IRGs and cytopenias 2) Elevated cytokines and young age, 3) Hyperinflammation and cytokine antagonists, and 4) Platelet and endothelial Activation. GMM produced 4 patient clusters with distinct clinical and biological profiles that correspond to disease severity, treatment response and patient outcome. The clusters were summarized as unique phenotypes: Hyperinflammatory KD, Interferon (IFN)-mediated KD, Mild KD, and KD Shock (Figure 1). This stratification also revealed associations with genetic variants impacting the expression of cytokine responses. A p-value titration of response variables indicated that the cluster classification outperforms traditional clinical diagnoses, clinical phenotypes and institutional MIS-C case definitions in identifying homogeneous patient groups.

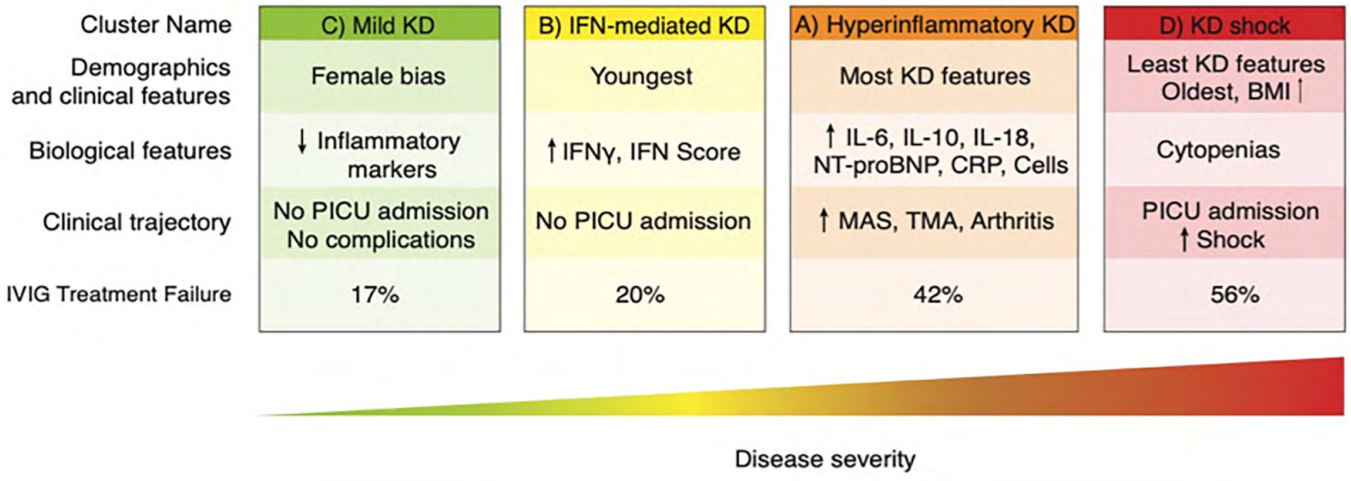

Figure 1. Unsupervised machine learning identified four distinct endotypes in children with post-infectious hyperinflammatory conditions. CRP = C-reactive protein; MAS = Macrophage activation syndrome; TMA = Thrombotic microangiopathy.

Conclusions: Data-driven machine learning approaches identified clinically and biologically meaningful patient subgroups in children with post-infectious hyperinflammation conditions that have clear associations with disease activity, treatment response and clinical outcomes, regardless of diagnosis. This contrasts with data using classic disease definitions and suggests that KD and MIS-C fit on the same disease spectrum.

Disclosures: None.

1. CLINICAL SCIENCE
1.09. Rare forms of vasculitis

P-183

Adult IgA vasculitis and cancer

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Background: Cancer has been reported as a potential trigger of adult IgA vasculitis (IgAV), however data on this topic is scarce. The aim of our single centre study was to evaluate the frequency and location of cancer in adult IgAV patients and to determine potential differences of cancer associated IgAV compared to non-cancer IgAV group.

Methods: We included 305 histologically proven adult IgAV patients, diagnosed between January 2010 and November 2022, and followed at our secondary/tertiary rheumatology centre of a median (IQR) 34.7 (13.1; 74.4) months. Cancer episodes were recorded and allocated into 3 groups according to their temporal relation to IgAV: 1) cancer diagnosed prior to IgAV diagnosis; 2) cancer diagnosed concurrently with IgAV; 3) cancer diagnosed during IgAV follow-up. Cases of non-melanoma skin cancer were excluded from analysis.

The term cancer associated IgAV (CA-IgAV) was defined as a cancer diagnosed within a 3-year period before or after IgAV diagnosis (the definition was adopted from the cancer associated myositis).

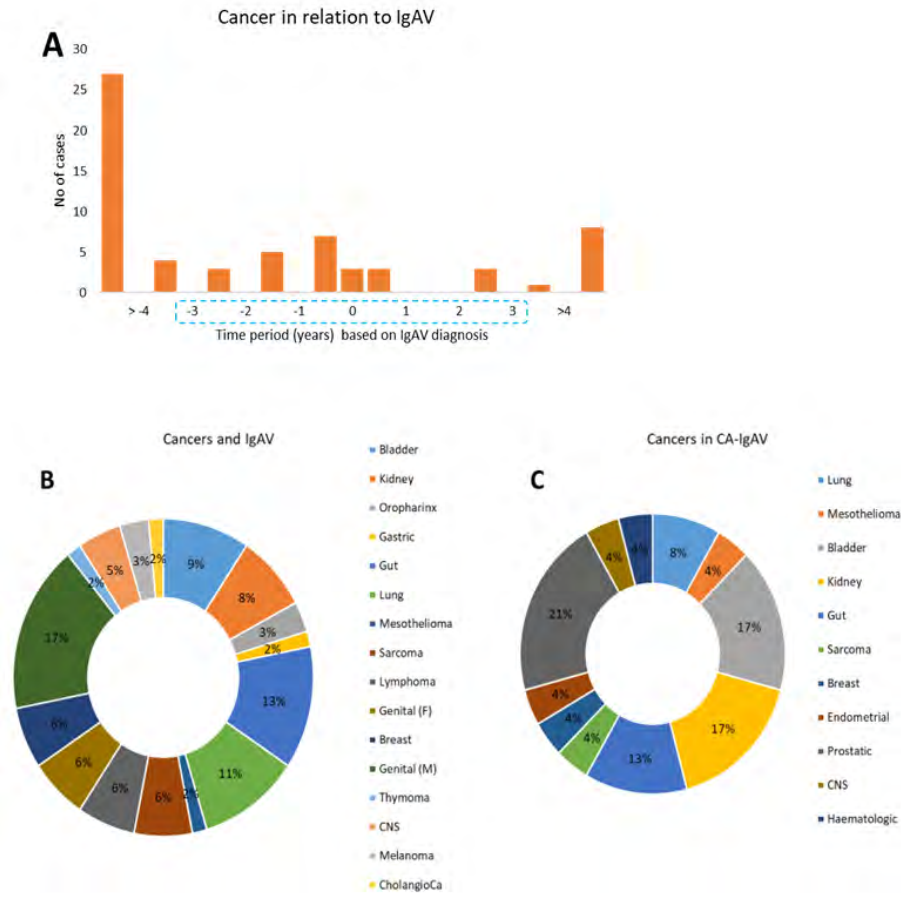
Differences in the baseline characteristics were compared between the CA-IgAV and IgAV patients without cancer.

Results: Fifty-four out of 305 IgAV patients (17.7%) developed in total 64 different cancer episodes (10 patients developed two different cancers). There were 46 (71.2%) cancers diagnosed prior to IgAV (and in three patients cancer was (still) active at the time of IgAV diagnosis), 3 (4.7%) cancers were diagnosed concurrently with IgAV, and 15 (23.4%) cancers were diagnosed during IgAV follow-up. Twenty-four (37.5%) cancer episodes (developed in overall 22 patients) fulfilled the temporal definition of CA-IgAV (Figure 1, panel A). Figure 1 also shows the location of all cancers recorded in IgAV patients (panel B), and cancers defined as CA-IgAV (panel C). The three most frequently diagnosed cancers in CA-IgAV group were prostatic cancer, renal cancer, and bladder cancer (together representing 55% of all CA-IgAV cases). Characteristics of CA-IgAV patients were compared to IgAV patients without cancer. Except of older age (median (IQR) age of 73 (64; 79) years vs. 60 (41; 73) years; p <0.001) none of IgAV's characteristics (sex, IgAV clinical presentation, severity of IgAV based on BVAS-3, relapses during follow-up) was associated with cancer. During follow-up 4 patients with CA-IgAV died due to cancer progression.

Conclusion: Urogenital tract cancers predominated in adults with CA-IgAV. Age but not IgAV's characteristics were associated with cancer in IgAV.

Disclosure: None.

Figure 1. Cancer type in IgAV patients: (A) unrelated to the time interval between diagnosis of IgAV and cancer; (B) in cancer associated IgAV (CA-IgAV); (C) temporal relation between IgAV diagnosis (time 0) to cancer diagnosis.



Legend: period of cancer associated IgAV (CA-IgAV).

P-184

Isolated ophthalmic artery arteritis: rare form of isolated vasculitis

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Presentation of Case: The case of a 50 year old man is presented, with history of recurrent episodes of scleritis in left eye since 2019, followed up by Ophtalmology. Due to the difficulty of managing, the patient was referred to Internal Medicine for study.

The anamnesis did not report any visual symptoms, headache, jaw claudication, scalp tenderness, morning stiffnes, fever or weight loss, arthralgias or myalgias, oral or genital sores nor skin lesions.

Physical examination did not reveal relevant data with normal temporal artery examination.

Diagnostic Testing: Initial patient evaluation focused on ruling out an infectious disease, so serologies and blood cultures were performed with negative results. Also autoimmunity study, including Anti-Neutrophil Cytoplasmic Antibodies (ANCA), was negative. Laboratory results did not show alterations with normal inflammatory markers.

Further study of the patient was reached with several imaging studies which were normal. Finally, it was decided to carry out a cranial angio-resonance with the result of enhancement in the wall of the left ophthalmic artery suggestive of vasculitis.

Differential & Final Diagnosis: Differential diagnosis of inflammatory vascular diseases is crucial. It should inlcude infectious diseases and also autoinmune disorders. When all these kind of disorders have been ruled out, the possibility of an isolated arteritis should also be taken into consideration.[1]

Patient clinical context suggested that it could be possible a Giant Cell Arteritis (GCA). However, there were no symptoms, physical examination nor imaging results suggestive of that. Therefore, he did not meet the GCA classification criteria according to ACR/EULAR 2022. He did not have any data suggestive of another type of systemic vasculitis.[2]

Finally, the diagnosis of isolated arteritis of the left ophthalmic artery was reached.

Discussion of Management: Regarding therapeutic management of the patient, scleritis episodes responded to oral Prednisone, but he presented new relapses after tapering.

Due to the severity and risk of blindness, induction treatment was performed in October 2021 with three IV boluses of 250 mg of Methylprednisolone with good response, and weekly 15 mg SC Methotrexate was iniciated. However, after 6 months the patient continued presenting scleritis. Due to this reason, in April 2022 it was decided to start treatment with Rituximab IV 1g every 6 months, with favorable response. Currently he is continuing with Rituximab, which allowed corticosteroid tapering.

Conclusions: Isolated ophthalmic arteritis is a rare condition. It generally appears as an associated manifestation of GCA. However, due to the risk of irreversible blindness because of ischemia of the optic nerve, it is an ophthalmological emergency that must be treated aggressively[1].

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Disclosures: None.

P-185

A Retrospective Study on the Clinical Characteristics and Outcomes of Isolated ANCA-Associated ILD

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Background/Objectives: Extensive research has highlighted the association between anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis and interstitial lung disease (ILD).[1-2] Cases of ANCA-positive ILD without systemic manifestations of vasculitis have been reported.[3] However, our understanding of the clinical outcomes of isolated ANCA-positive ILD remains limited.[3] This study aims to characterize the clinical, radiographic, and histopathologic features, in addition to the progression and prognosis of isolated ANCA-associated ILD.

Methods: This is a retrospective study of patients over the age of 18 who had positive ANCA and radiographic evidence of ILD seen at University of South Florida (USF) Clinics. Patients were only included in the study if they had isolated ANCA-associated ILD without evidence of any initial systemic manifestations of vasculitis. For all cases, ANCA mimics were excluded including autoimmune hepatitis, Hepatitis C, HIV, endocarditis, and drug-induced reactions. Patients were identified through review of USF's database Epic between 2016 and 2023.

Results: A total of 7 patients were examined in this study with a mean age of 55 years old (table 1). All 7 patients tested positive for anti-myeloperoxidase (MPO) antibody, while 1 patient was positive for anti-proteinase-3 (PR3) antibody. Imaging revealed a UIP pattern of ILD in 4 out of the 7 patients.

Among the cohort of 7 patients with ANCA-associated ILD, 4 individuals (57%) developed vasculitis during the course of the study. The average duration between the diagnosis of ILD and vasculitis was approximately 96 months, ranging from 17 to 288 months. Renal involvement was found to be the most prevalent manifestation of vasculitis with 3 patients exhibiting pauci-immune glomerulonephritis on biopsy. For all patients, treatment was initiated at the onset of systemic symptoms. The pulmonary fibrosis remained stable in all 4 patients with vasculitis following treatment. One of the patients who did not develop vasculitis passed away due to progression of ILD.

Table 1: Patient's Characteristics

Patient No.	Age (yrs.)	Sex	Duration between diagnosis of ILD and vasculitis (mo.)	Radiographic Pattern	Vasculitis Features	Serology		Therapy	Fibrosis Progression	Long-term oxygen (L)	Mortality
						Anti-MPO	Anti-PR3				
1	25	M	--	UIP	--	+	-	CTX, AZA, RIX, MMF	slightly progressed	--	alive
2	60	F	31	NSIP	renal, neurologic	+	-	CTX, MMF, PLEX	stable	3	alive
3	74	F	288	UIP	cutaneous	+	-	CTX, MMF, AZA	stable	3	alive
4	25	F	47	Unclassified	renal	+	-	RIX, MMF	improved	--	alive
5	60	F	--	UIP	--	+	-	MMF	worsened	3	deceased
6	79	F	17	UIP	renal	+	+	MTX, RIX	stable	--	alive
7	65	M	--	Unclassified	--	+	-	--	mildly improved	--	alive

s/p UIP, usual interstitial pneumonia; NSIP, Nonspecific interstitial pneumonia; CTX, cyclophosphamide; AZA, azathioprine; RIX, rituximab; MMF, mycophenolate mofetil; PLEX, plasmapheresis; M, male; F, female

Conclusion: Our study showed that over half of the patients with isolated ANCA-associated ILD developed vasculitis even after a significant period of time. This suggests that ILD can be an initial presentation for ANCA-associated vasculitis and highlights the importance of long-term monitoring and follow-up. Given the debilitating nature of the disease, early detection is critical to promptly initiate treatment, which as shown in our study can mitigate disease progression and improve patient outcomes.

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Disclosures: None.

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Safety and Efficacy of CT-guided Percutaneous Infra-Renal Periaortic Biopsies in Suspected Retroperitoneal Fibrosis

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Background/Objectives: Retroperitoneal fibrosis (RPF) commonly affects the infrarenal abdominal aorta (irAA) and manifests with periaortic soft tissue thickening (pASTT). RPF can be either idiopathic (primary) or secondary. Secondary causes include malignancy and infection and thus biopsy aids in differentiating etiologies. Data describing the safety and efficacy of pASTT biopsy sampling using computed tomography (CT)-guidance, the purpose of this study, is limited.

Methods: Patients undergoing CT-guided percutaneous pASTT biopsy from June 1, 1999 through September 30, 2022 were identified retrospectively within a large single institution RPF cohort. All patients were required to have radiographic evidence of soft tissue thickening/mass in direct contact with the irAA and have had CT-guided biopsy performed. Patients with biopsies of periaortic lymph nodes or the perivascular space of the iliac vessels or inferior vena cava were excluded. Routine laboratory screening thresholds prior to biopsy included INR <1.6 and platelet count >50 x10^9/L. Anticoagulation/antiplatelet agents were held prior to biopsy. Charts were reviewed by a physician abstractor. Demographics, biopsy features, and outcomes were collected. Complications were graded based on common terminology criteria for adverse events (CTCAE): categories 1 and 2 being minor, and categories 3-5 considered major.

Results: 83 patients (28 females, 55 males) with 84 biopsies of the pASTT at the level of the irAA were identified. Mean age at biopsy was 58 (range 31-83) years. Biopsy approach was paraspinal in 73 (87%) and anterior abdominal in 11 (13%). Mean number of passes was 5 (range 1-12). A 17/18 gauge needle size was most commonly used (67/84), followed by 19/20 gauge (15/84). One biopsy used a 15/16 gauge device and one report did not specify needle size. Local anesthesia only was used in 18 (21%) biopsies, moderate anesthesia in 61 (73%) and anesthesia type was not specified in 5 (6%). Three of 84 (3.6%) biopsy events had minor bleeding at entry site. One (1.2%) patient had a major bleeding complication with left rectus sheath hematoma requiring embolization of left inferior epigastric pseudoaneurysm. No post procedural infections were observed. Biopsy of the irAA soft tissue confirmed diagnosis following 73/84 (87%) biopsies (**Table 1**) with mean thickness at biopsy site 14.4 mm (range 3.4-27.9). In the 11 procedures where the diagnosis was not achieved by initial biopsy, 6 were due to insufficient tissue for histologic characterization [mean thickness 15.1 mm (range 5.2-25.4)] and 5 were due to concern for alternative etiology despite sufficient tissue.

Conclusion: In this study, percutaneous CT-guided infra-renal pASTT biopsy was considered safe and confirmed diagnosis in 87% of cases. Final diagnosis differed from pre-biopsy suspicion in 34%, highlighting benefit of this procedure.

References: (-)

Disclosures: K.J.W.: Kiniksa, Amgen, Sanofi, BMS, Eli Lilly; M.J.K.: Amgen; Others: none.

Pre-biopsy suspected diagnosis	Post-biopsy confirmed diagnosis	N=73
iRPF	iRPF	45 (54%)
iRPF	IgG4-RD	10 (12%)
iRPF	ECD	1 (1%)
IgG4-RD	IgG4-RD	2 (2%)
Malignancy	iRPF	9 (11%)
Malignancy	IgG4-RD	2 (2%)
Malignancy	Malignancy	1 (1%)
Other (Infection, Sarcoid)	iRPF	3 (4%)
ECD, Erdheim Chester Disease; IgG4-RD, immunoglobulin G subclass 4 related disease; iRPF, idiopathic retroperitoneal fibrosis		

Table 1: Pre-biopsy suspected diagnosis and post-biopsy confirmed diagnosis in patients where CT-guided infra-renal abdominal aorta periaortic soft tissue thickening biopsy was sufficient for diagnosis.

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Real-life data comparing the long-term outcome and treatment in adult and pediatric DADA2 patients: Single center experience over 10 years

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Background/Objectives: The deficiency of adenosine deaminase 2 enzyme (DADA2), a hereditary autoinflammatory condition due *ADA2* enzyme deficiency. Investigating real-world outcomes, our focus is on anti-TNF agents as a primary treatment for individuals with DADA2, acknowledging TNF's pivotal role in the disease.

Methods: This descriptive analysis encompassed all adult/ pediatric patients with DADA2 from our Vasculitis Research Centre prospective database. We documented demographics, clinical features, and treatment specifics. Among the entire cohort, we specifically examined patients who underwent anti-TNF therapy, analyzing the treatment details, and outcomes. Physicians' assessments determined treatment responses, categorized as full response (symptom-free state with normal acute phase reactants) or partial/no response.

Results: A total of 32 patients (adult/pediatric, n=19/13) were analyzed. The mean (SD) current age of the living patients was 27.4 (8.5) years in adults and 11.2 (3.5) years in children. The mean age at diagnosis was 14.9 (9.2) years. The *G47R* mutation was homozygous in 25/27 (92.5%) and heterozygous in 2/27 (7.4%) of the patients (Table). 28 of the 32 patients were prescribed anti-TNF agents (etanercept, n=26; adalimumab, n=2). During the median (IQR) 60 (66) months of follow-up on anti-TNF treatment, 10 (35.7%) of the patients showed a complete response who had received anti-TNF agents for predominant nervous system involvement (n=6), renal involvement (n=1), constitutional symptoms (n=1) or skin involvement (n=3). Nine, patients (32.1%) had a partial response and in 3 patients the outcome was not available. Two patients underwent bone marrow transplantation (BMT), with one patient dying and the other being cured and off treatment. Of the patients who received anti-TNF treatment, 20/28 are still on treatment. 13/20 (65%) patients are currently receiving tapered anti-TNF treatment according to their physician's decision. The first patient was diagnosed in 2013 and in the last 10 years 6/32 (18.75%) of the patients have died. Five out of 6 deceased patients received TNFi: One patient with haematological involvement did not respond to anti-TNF, died after BMT. The other patient died in 2015 after 3 months of anti-TNF. In one patient, anti-TNF was discontinued due to cardiomyopathy. One patient had resistant digital necrosis the last patient had a novel mutation with both haematological/immunological and neurological involvement, both died of sepsis.

Conclusion: In conclusion, although anti-TNF drugs are the main treatment for DADA2, hematological involvement does not respond. The clinical course of patients is diverse, with a mortality rate of up to 20% over a 10-year period. However, in certain instances, treatment tapering may be feasible, emphasizing the need for individualized decision-making in patient management.

Disclosures: None.

Table. Demographic and clinical characteristics of patients.

Patient ID	Current age, years/ Gender	Age at symptom onset, years	Age at diagnosis, years	Diagnosis date	Mutation details	All the treatments used	Initial organ involvement	Ever Anti-TNF use	Anti-TNF start date	Dosage	Still on Anti-TNF	Anti-TNF duration, months	Anti-TNF indication	Anti-TNF response	Exitus
ID-1 (Index case)	*-M	20	22	2013	p.Gly47Arg /p.Gly47Arg	CS, Colchicine, Tocilizumab, CYC, AZA, IVIG, FFP	Livedo reticularis, erythema nodosum, skin nodule strabismus, myelofibrosis, proteinuria , HSM, AA amyloidosis	No	N/A	N/A	N/A	N/A	N/A	N/A	Yes
ID-2	55-M	40	40	PAN; 2008 DADA2 2015	p.Gly47Arg /p.Gly47Arg	CS, CYC, AZA, Colchicine	Ischemia in mesencephalon, livedo reticularis, hypogamaglobulinemia, proteinuria	Yes	September 2015	50 mg/ week ETN	Yes	98	Neurologic (central) involvement	Full	No
ID-3	30/F	19	19	2013	N/A	CS, CYC, AZA	Polyneuropathy and left pontin hypo-hyperdense signal associated with vasculitic involvement, livedo reticularis, renal microaneurysms	Yes	N/A	40 mg/ biweekly ADA	No	N/A	Constitutional symptoms	N/A	No

Patient ID	Current age, years/ Gender	Age at symptom onset, years	Age at diagnosis, years	Diagnosis date	Mutation details	All the treatments used	Initial organ involvement	Ever Anti-TNF use	Anti-TNF start date	Dosage	Still on Anti-TNF	Anti-TNF duration, months	Anti-TNF indication	Anti-TNF response	Exitus
ID-4	25/M	22	22	2021	Gly47Arg /p.Gly47Arg	CS	Mononeuritis multiplex, livedo reticularis, recurrent abdominal pain	Yes	March 2021	50 mg/ week, ETN	Yes	32	Neurologic involvement (peripheral)	Partial	No
ID-5	31/M	7	29	2019	p.Gly47Arg /p.Gly47Arg	IVIG, CS	Livedo reticularis, digital necrosis, hypogammaglobulinemia, proteinuria, HT recurrent abdominal pain,	Yes	June 2020	50 mg/ week, ETN	No	24	Digital necrosis	Exitus (sepsis)	Yes
ID-6	30/F	14	23	2016	p.Gly47Arg/-	CS, CYC, MMF, AZA, Colchicine	Putamen hemorrhage, livedo reticularis, erythema nodosum, RP, proteinuria, HT, aneurysm, recurrent abdominal pain,	Yes	August 2016	50 mg/ week, ETN	Yes	87	Neurologic involvement (central)	Full	No
ID-7	29/F	11	21	2015	p.Gly47Arg /p.Gly47Arg	Colchicine	Livedo reticularis, vasculitic skin lesions biopsy suggesting PAN, proteinuria	No	N/A	N/A	N/A	N/A	N/A	N/A	No
ID-8	*/M	4	22	2014	p.Gly47Arg /p.Gly47Arg	CS, Colchicine, CYC, AZA, FFP	Optic neuritis, lacunar infarcts on MRI, deafness, livedo reticularis, digital ulcers, optic neuritis, proteinuria, FSGS (collapsing variant), aneurysm recurrent abdominal pain	Yes	December 2014	50 mg/ week, ETN	No	3	Digital necrosis	Exitus (NA)	Yes
ID-9	25/M	2	17	2015	p.Gly47Arg /p.Gly47Val	Colchicine	Hemorrhagic and ischemic stroke, lesion in pons and bilateral thalamus, peripheral neuropathy, diplopia livedo reticularis, horizontal nystagmus hypogamaglobulinemia , proteinuria, recurrent abdominal pain, HSM	Yes	February 2016	50 mg/ week, ETN	Yes	93	Neurologic involvement (central and peripheral)	N/A	No
ID-10	31/F	9	31	2021	p.Pro151GlnfsTer33/ p.Pro151GlnfsTer33	Colchicine, CS, AZA, EPO,	Ischemic lacunar infarcts, livedo reticularis, strabismus, pancytopenia, proteinuria, FSGS, HM	Yes	April 2021	50 mg/ week, ETN	No	31	Neurologic involvement (central) and hematologic involvement	Exitus (sepsis)	Yes
ID-11	25/M	3.5	18	2018	p.Gly47Arg /p.Gly47Arg	Colchicine, CS	Sensorimotor axonal polyneuropathy, livedo reticularis, proteinuria (mesangial proliferative glomerulonephritis), HT, recurrent abdominal pain, HM, testicular involvement	Yes	March 2016	25 mg/ week, ETN	Yes	91	Neurologic (peripheral), skin and renal involvement	Full	No
ID-12	23/M	12	17	2017	p.Gly47Arg /p.Gly47Arg	CYC, CS	Digital ischemia, ulcer and RP, lymphopenia, proteinuria, HT, aneurysm recurrent abdominal pain, HSM, superior mesenteric artery stenosis on angiography	Yes	February 2017	25mg/ week, ETN	No	24	Mesenteric vascular involvement and hematologic involvement*	Exitus(dilated cardiomyopathy)	Yes

Patient ID	Current age, years/ Gender	Age at symptom onset, years	Age at diagnosis, years	Diagnosis date	Mutation details	All the treatments used	Initial organ involvement	Ever Anti-TNF use	Anti-TNF start date	Dosage	Still on Anti-TNF	Anti-TNF duration, months	Anti-TNF indication	Anti-TNF response	Exitus
ID-13	25/M	8	15	2015	p.Gly47Arg /p.Gly47Arg	CYC, AZA,MMF, MTX, CS, Colchicine	Peripheral neuropathy, pontin ischemic lacunar infarct, livedo reticularis, MAS, recurrent abdominal pain, intestinal perforation	Yes	N/A	35mg/ week ETN	Yes	72	Neurologic involvement (central +peripheral)	Full	No
ID-14	23/F	7	14	2014	p.Gly47Arg /p.Gly47Arg	NSAID, Colchicine, MTX, CS, MMF	Livedo reticularis, recurrent abdominal pain, arthritis	Yes	February 2015	25 mg/10 days, ETN	Yes	105	Skin involvement	Full	No
ID-15	22/M	14	14	2016	p.Gly47Arg /p.Gly47Arg	Colchicine, CS	Sensorimotor axonal polyneuropathy on EMG, livedo reticularis, recurrent abdominal pain, HM	Yes	February 2016	25 mg/ week, ETN	Yes	93	Neurologic involvement (peripheral)	Full	No
ID-16	11/M	1	5	2017	p.Gly47Arg /p.Gly47Arg	CS	Fever episodes	Yes	October 2017	25mg/ biweekly, ETN	Yes	85	Fever attacks	Full	No
ID-17	20/F	4	10	2013	p.Gly47Arg /p.Gly47Arg	AZA, MTX, CS, FFP	Fever, arthritis, livedo reticularis, neuropathy, pontin ischemia on MRI	Yes	August 2013	35mg/ week, ETN	Yes	123	Neurologic involvement (central and peripheral)	Full	No
ID-18	11/F	1.5	2	2015	p.Gly47Arg /p.Gly47Arg	AZA	Fever, arthritis, livedo reticularis, neuropathy	Yes	March 2016	12.5mg/ week, ETN	Yes	92	Neurologic involvement (peripheral)	Full	No
ID-19	21/F	4 months	17	2019	p.Gly47Arg /p.Gly47Arg	-	Diamond Blackfan anemia and arthritis	Yes	January 2019	40mg/ week, ETN	Yes	58	Hematological involvement	Partial	No
ID-20	8/F	3 months	3	2019	p.Gly47Arg /p.Gly47Arg	-	Diamond Blackfan anemia and livedo reticularis	Yes	January 2019	10mg/ week ETN	No	29	Hematologic and skin involvement	Cure after BMT	No
ID-21	17/M	4	10	2016		CS	Cerebral infarct, arthritis, livedo reticularis	Yes	January 2016	25mg/ biweekly, ETN	Yes	94	Neurologic involvement (central)	Partial	No
ID-22	14/F	1 months	8	2018	p.Gly47Arg /p.Gly47Arg	-	Livedo reticularis, arthritis	Yes	November 2018	25mg/ week, ETN	Yes	62	Skin involvement and arthritis	Partial	No
ID-23	10/F	6	6	2017	p.Gly47Arg /p.Gly47Arg	CS, IVIG, Bone marrow trans.	Abdominal pain, lymphopenia, myalgia, fever, hypogamaglobulinemia,	Yes	January 2018	25mg/ week, ETN	No	6	Hematologic involvement, hypogamaglobulinemia, fever episodes	Exitus (NA)	Yes
ID-24	12/M	10 months	8	2019	p.Gly47Arg /p.Gly47Arg	IVIG, CS	Fever, arthritis, livedo reticularis, abdominal pain, myalgia, lymphopenia, Noonan syndrome	Yes	October 2019	25 mg/ week, ETN	No	20	Hematological involvement, hypogamaglobulinemia	Partial (parents did not continue treatment, after 2020)	No
ID-25	10/F	3	5	2018	p.Gly47Arg /p.Gly47Arg	Colchicine	Livedo reticularis, vasculitis on skin biopsy	Yes	March 2018	15mg/ week, ETN	Yes	68	Skin vasculitis	Partial	No
ID-26	12/F	11 months	9	2020	p.Gly47Arg /p.Gly47Arg	CS, AZA, colchicine	Fever, livedo reticularis, abdominal pain, myalgia, hypertension, optic neuritis, renal microaneurysms	Yes	July 2020	20 mg/ week, ADA	Yes	39	Neurologic (peripheral), skin involvement	Partial	No

Patient ID	Current age, years/ Gender	Age at symptom onset, years	Age at diagnosis, years	Diagnosis date	Mutation details	All the treatments used	Initial organ involvement	Ever Anti-TNF use	Anti-TNF start date	Dosage	Still on Anti-TNF	Anti-TNF duration, months	Anti-TNF indication	Anti-TNF response	Exitus
ID-27	9/M	4	4,5	2020	p.Gly47Arg /p.Gly47Arg	Hydroxychloroquine	Livedo reticularis, fever	Yes	**January 2020**	**17.5mg/ week ETN**	**Yes**	**47**	**Skin vasculitis**	**Full**	No
ID-28	7/F	6 months	5	2021	p.Gly47Arg /p.Gly47Arg	IVIG	Livedo reticularis, hypogamaglobulineia,	Yes	November 2021	15mg/ week, ETN	Yes	24	Livedo reticularis, hypogammaglobulinemia,	Partial	No
ID-29	16,5/F	9	15	2022	c.1143A>T/p.R381S homozygous	Prednisolone, IVIG	Anemia, lymphopenia, fever, hypogamaglobulinemia	Yes	March 2022	50mg/ week ETN	Yes	20	Hematologic involvement	Partial	No
ID-30	6,5/M	4	6	2023	c.1143A>T homozygous	-	sibling with DADA2 Recurrent fever	Yes	February 2016	50 mg/ week, ETN	Yes	93	Neurologic involvement (central and peripheral)	N/A	No
ID-31	26/F	NA	25	2022	Gly47Arg /p.Gly47Arg	ASA	Digital ischemia, livedo racemose	No	N/A	N/A	N/A	N/A	N/A	N/A	No
ID-32	27/F	NA	27	2023	Gly47Arg /p.Gly47Arg	CS, AZA, ASA, HQ, MMF	RP, livedo reticularis	No	N/A	N/A	N/A	N/A	N/A	N/A	No

PAN: Polyarteritis nodosa; ADA2: Adenosine deaminase 2; DADA2: Deficiency of ADA2; AZA: Azathioprine; CS: Corticosteroid; CYC: Cyclophosphamide; FFP: Fresh Frozen Plasma; FSGS: Focal Segmental Glomerulosclerosis; HM: Hepatomegaly; HSM: Hepatosplenomegaly; IVIG: Intravenous Immunoobulin; MTX: Methotrexate; MMF: Mycophenolate mofetil; RP: Raynaud phenomenon; AA Amyloidosis: Reactive amyloidosis, HT: Hypertension, MRI: Magnetic Resonance imaging, EMG: Electromyography, Anti-TNF: Anti-Tumor necrosis factor; ETN: Etanercept: ADA: Adalimumab
*Anti-TNF agent was stopped because of dilated cardiomyopathy

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Comparative Analysis of two Canadian and Turkish cohorts of patients with Behçet's Syndrome

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Background/ Objectives: Data regarding Behçet's syndrome (BS) in Canada, and in non-endemic regions in general, are limited. The purpose of this study was to describe the clinical spectrum, and treatment of BS patients in Canada with different ethnic backgrounds, and compare them with a cohort of patients from Turkey, where disease prevalence is high.

Methods: Retrospective study conducted between January 1, 2023 and March 30, 2023 at two specialized referral centers in Canada (Toronto and London), and one in Turkey. Patients' demographics, clinical characteristics, laboratory and imaging studies, treatment and outcomes were retrieved from medical charts and analyzed, including with a two-step cluster analysis.

Results: A total of 168 patients (73 from Canada and 95 from Turkey) were included. Two thirds of the Canadian patients were Caucasians (White/European descents; 58.9%); 62% of the Canadian BS patients were female, compared to only 43% of the Turkish patients. Canadian BS patients had more frequent musculoskeletal involvement (43.4% of non-Caucasian vs. 51.2% of Caucasian patients, vs. 27.4% of the Turkish patients, p=0.018). Ocular inflammation was numerically more common in Turkish patients (mostly posterior uveitis) and non-Caucasian Canadians (mostly anterior uveitis) than Caucasian Canadian patients (44.2% and 43.3% vs. 25.6%, p=0.102). Turkish BS patients had a higher rate of major vascular involvement, but less superficial thrombophlebitides than both non-Caucasian and Caucasian Canadian patients (Table 1).

Cluster analysis of the Canadian BS patients showed three main clusters based on five clinical involvements: Cluster 1 (n=30, Female 76.7%) were mostly Caucasian (76.7%), mostly with an Irish or Scottish background (43.4%), with predominantly musculoskeletal involvement (86.7%). Major organ involvement was less common in this Cluster 1 than in the other two Clusters (C1: 36.7%, C2: 67.9%, C3: 93.3%; C1 vs. C2 p=0.017, C1 vs. C3 p=0.001). Cluster 2 (n=28, Female 64.3%) had a dominant non-Caucasian background (64.3%), more frequent eye (C1 36.7%, C2 46.4%, C3 0%, C2 vs. C1 p=0.313, and C2 vs. C3 p=0.001) and neurological parenchymal involvement (C1 0%, C2 14.3%, C3 0%, C2 vs. C1 p=0.048, C2 vs. C3 p=0.166). Cluster 3 (n=15, Male 66.7%) showed highest prevalence of vascular involvement (C1 0%, C2 0%, C3:93.3%, vs. C1 p=0.001, C3 vs. C2 p=0.001), and one-third of patients had gastrointestinal involvement (33.3% vs 0% in C1, p=0.02). Intolerance to colchicine was more common in C1 and C3 (C1 56.7%, C2 22.7%, C3 60%, C1 vs. C2 p=0.014, C2 vs. C3 p=0.05), as well as failure of multiple conventional immunosuppressives in C1 (C1 50.0%, C2 21.4%, C3 20.0%, C1 vs. C2 p=0.023, C1 vs. C3 p= 0.012).

Conclusions: This study revealed some differences in disease presentation and response to treatments between patients with BS from endemic and non-endemic areas, and between patients with different ethnic backgrounds living in non-endemic areas. What explains these differences and whether they should impact disease classification or treatment remains to be determined.

Disclosures: None.

Table 1. Demographic features and clinical characteristics of patients with Behçet's Syndrome

	Canadian BS patients (n=73)		Turkish BS patients (n=95)		
	non-Caucasian (n=30)	Caucasian (n=43)		*P-value Group 1 vs. 2*	*P*-value overall
Female, n (%)	18 (60.0%)	28 (65.1%)	44 (46.3%)	0.420	0.090
Age, years (median, IQR)	39.0 (31.5-56.0)	38.0 (31.0-48.0)	46.0 (37.0-53.0)	0.498	0.025*
Age at diagnosis, years (median, IQR)	30.0 (21.5-39.5)	29.0 (22.0-39.0)	28.0 (21.0-35.0)	0.393	0.591
Ethnic ancestry					
Caucasian	-	55 (100.0%)	-	NA	NA
Asian	12 (16.4%)	-	-		
Others (including Turkish)	12 (16.4%)	-	-		
African American /Hispanic	6 (8.21%)	-			
Presence of HLA-B51, n/total (%)	5/10 (50.0%)	4/11 (36.4%)	22/37 (59.5%)	0.425	0.391
Oral ulcers	29 (96.7%)	42 (97.7%)	93 (97.9%)	0.656	0.928
Genital ulcers	20 (66.7%)	34 (79.1%)	69 (73.4%)	0.179	0.495
Skin involvement	16 (53.3%)	30 (69.8%)	63 (66.3%)	0.118	0.318
Musculoskeletal involvement	13 (43.3%)	22 (51.2%)	26 (27.4%)	0.337	0.018*
Eye involvement	13 (43.3%)	11 (25.6%)	42 (44.2%)	0.091	0.102
Vascular involvement	4 (13.3%)	10 (23.3%)	31 (32.6%)	0.227	0.096
Superficial thrombophlebitis	3 (10.0%)	6 (14.0%)	3 (3.2%)	0.450	0.059*
Central neurological involvement	5 (16.7%)	7 (16.3%)	11 (11.6%)	0.604	0.661
Gastrointestinal involvement	3 (10.0%)	6 (14.0%)	7 (7.4%)	0.450	0.473
Epididymitis/Orchitis, n (male) /total (%)	2/12 (16.7%)	0/15 (7.4%)	0/51 (0.0%)	0.188	0.004*
Presence of major organ involvement	22 (73.3%)	22 (51.2%)	63 (66.3%)	0.047*	0.110

*BS: Behçet's Syndrome, IQR: Interquartile range

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Intracranial Giant Cell Arteritis: A Comprehensive Systematic Review

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Objectives: The occurrence of intracranial vasculitis in cases of giant cell arteritis (GCA) has been increasingly recognized. While traditionally associated with stroke, its clinical significance is incompletely understood. We identified all reported cases of intracranial GCA to describe presentations, investigations, treatments, and outcomes reported to date.

Methods: We conducted a systematic review using MEDLINE, Embase and Pubmed to identify studies that reported cases of intracranial manifestations of GCA. The study was registered on a systematic review database (PROSPERO 42023412373). We defined intracranial involvement as any vessel cranial to the dura mater that was confirmed by either histopathology or imaging. Abstract screening, full text screening, and data abstraction were performed in duplicate with any disagreements adjudicated by a third investigator. Data was described using summary statistics.

Results: A total of 1554 papers were screened and 114 papers were included. We found 374 patients with intracranial GCA. The median age was 73.0 (interquartile range (IQR) 65.9-80.0) and 143 (38.2%) patients were female (Table 1). GCA diagnosis was made through a combination of clinical assessment, inflammatory markers, imaging and/or biopsy. One hundred eighty-seven (50.0%) patients presented with stroke, 128 (34.2%) presented with vision loss, and 69 (18.5%) presented with constitutional symptoms. The most common vessels involved were 159 (42.5%) internal carotid, 147 (39.3%) vertebrobasilar, and 49 (13.1%) ophthalmic arteries. Across patients with strokes, 113 (60.4%) had cerebral strokes, 44 (23.5%) had brainstem strokes, and 35 (18.7%) had cerebellar strokes. Of the 193 cases which reported treatment, the most common treatment was glucocorticoids, administered to 182 (94.3%) of patients. A further, 45 (23.3%) patients were treated with cyclophosphamide, 33 (17.1%) with methotrexate, and 30 (15.5%) with tocilizumab. Median follow-up was 12 (IQR 3-36) months during which 34 (9.0%) intracranial GCA patients experienced relapse of their intracranial or non-intracranial disease, 17 (4.6%) had a recurrent stroke, and 52 (14.0%) died.

Conclusion: This data suggests that intracranial vasculitis in GCA is not a rare occurrence. Most intracranial GCA is disease that extends from extracranial vessels, however about 15% has exclusively intracranial disease. Half of intracranial GCA presents with stroke, and 14% of patients with intracranial GCA die. These findings suggest that individuals with GCA who present with stroke should be evaluated for intracranial GCA. Optimal therapy for intracranial GCA is unclear, but these patients may benefit from more intensive therapy.

Disclosures:

SP, IO, SA, CS, JS, RT – None.

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MJ – Unrestricted educational support from Roche.

Table 1. Clinical and imaging features of intracranial GCA.
Findings are presented as counts and frequency unless otherwise specified.

Baseline Characteristic for Patients with Intracranial GCA	**Total**
Total number of patients	374
Age in years (median (IQR))	73.0 (65.9-80.0)
Female sex	143 (38.2%)
ESR (mm/hr) (median (IQR)) (data from 150 studies)	60.5 (40-94.25)
CRP (mg/dL) (median (IQR)) (data from 107 studies)	7.0 (2.5-14.25)
Positive temporal artery biopsy	146 (39.0%)
Past Medical History	
Hypertension	85 (22.7%)
Dyslipidemia	45 (12.0%)
Diabetes	32 (8.6%)
Atrial fibrillation	9 (2.4%)
Transient ischemic attack or stroke	4 (1.1%)
Clinical Presentation	
Stroke	187 (50.0%)

Vision loss	128 (34.2%)
Constitutional symptoms	69 (18.5%)
Jaw claudication	57 (15.2%)
Scalp pain or tenderness	33 (8.8%)
Altered level of consciousness	32 (8.6%)
Territories of intracranial vasculitis	
Internal carotid arteries	159 (42.5%)
Vertebrobasilar arteries	147 (39.3%)
Ophthalmic and branches	49 (13.1%)
All cerebral arteries	57 (15.2%)
Middle cerebral arteries	24 (6.4%)
Posterior cerebral arteries	20 (5.3%)
Anterior cerebral arteries	12 (3.2%)
Cerebellar (including anterior inferior cerebellar, posterior inferior cerebellar, superior cerebellar)	6 (1.6%)
Other	11 (2.9%)
Morphology of Vessel Changes on Imaging	
Stenosis or occlusion	138 (36.9%)
Enhancement or wall thickening	79 (21.1%)
Dissection	6 (1.6%)
Aneurysm or dilatation	5 (1.3%)
IQR = interquartile range	

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Clinical Features and Outcomes of Hydralazine-associated Antineutrophil Cytoplasmic Antibodies Associated Vasculitis: A Case-Control Study

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Background/Objectives: Hydralazine can induce ANCA-associated vasculitis (AAV). We aimed to describe clinical features and outcomes hydralazine-associated AAV in comparison to those of primary AAV.

Methods: We performed a retrospective case-control study (1:2) of patients with hydralazine-associated AAV and primary AAV, matched for age, sex, and dominant ANCA-type. Demographics, clinical features and outcomes were compared.

Results: Twenty-one patients (57% male; mean age at diagnosis 71.2±9) with hydralazine-associated AAV were included. Fifteen (94%) patients were using hydralazine for at least 1 year. Median hydralazine dose was 100 mg/day (range, 50-150). All 21 patients were p-ANCA positive. Fourteen patients (67%) had MPO-ANCA, and 7 patients (33%) had both MPO- and PR3-ANCA. Fifteen patients (79%) were positive for ANA, and 9 also for anti-ds DNA. Major organ involvement included kidneys (86%) and lungs (71%). Nineteen patients stopped hydralazine when they were diagnosed as hydralazine-associated AAV. For remission induction, glucocorticoids were used in all patients (19 patients received iv methylprednisolone, 2 patients received high dose oral prednisolone), either alone or in combination with rituximab (n=9), cyclophosphamide (n=5) or mycophenolate mofetil (n=3). Twenty patients received oral glucocorticoids after initial methylprednisolone or high-dose prednisolone. In follow-up, 14 patients had achieved remission within 6 months, 6 patients did not have enough follow-up period to assess remission, 1 patient did not reach remission, 2 patients who did not stop hydralazine suffered relapses. Diffuse alveolar hemorrhage (52% vs 17%; p= 0.007) and pleuritis (14% vs 0, p=0.03) were more common among patients with hydralazine-associated AAV compared to 42 matched patients with primary AAV, whereas nervous system involvement was more common in primary AAV (0 vs 24%, p=0.008). Patients with hydralazine-associated AAV had higher serum creatinine levels at diagnosis (median 4.4 vs 2.2, p=0.008) and more frequently required hemodialysis (43% vs 10%, p=0.006) and respiratory support (24% vs 2%, p=0.04).

Conclusions: Multiple autoantibodies are common in patients with hydralazine-associated AAV, and acute inflammation affecting lungs and kidneys seems to be more common compared to matched patients with primary AAV.

Table 1. Clinical characteristics and outcomes of patients with Hydralazine associated AAV and matched primary AAV group.

	Hydralazine associated AAV (n=21)	**Primary AAV (n=42)**	p
Symptoms and Organ involvements, n (%)			
Constitutional	5 (24)	20 (48)	0.06
Arthralgia /arthritis	3 (14)	9 (21)	0.74
Cutaneous	3 (14)	4 (9.5)	0.68
Pulmonary DAH Pleuritis ILD nodule	15 (71) 11 (52) 3 (14) 1 (5) 0	18 (43) 7 (17) 0 10 (24) 1 (2.4)	**0.037** **0.007** **0.033** 0.08 1.0
Renal	18 (86)	34 (81)	0.74
Nervous system	0	10 (24)	**0.02**
Laboratory results			
Serum creatinine, median (IQR25-75)	4.4 (2.4-5.6)	2.2 (1.1-4.0)	**0.008**
Hematuria, n (%)	16 (80)/20	20 (62.5)/32	0.23
Proteinuria, n (%)	16 (84)/19	13 (65)/ 20	0.27
Serum CRP level, median mg/l (IQR25-75)	51 (23-79)/14	38 (5.4-84)/18	1.0
Sedimentation level, median mm/h (IQR25-75)	62 (56-74)/ 13	56 (24.5-91)/23	0.95
ANA positivity, n (%)	15 (79)/19	8 (33)/24	**0.005**
Anti-ds DNA positivity, n (%)	9 (64) /14	2 (17)/12	**0.02**

	Hydralazine associated AAV (n=21)	**Primary AAV (n=42)**	p
Anti-histone Ab positivity, n (%)	2 (100) /2	N/A	
Anti-Sm Ab positivity, n (%)	0/12	N/A	
Anti-GBM positivity, n (%)	0/12	0	
Complement 3 (low), n (%) Complement 4 (low), n (%)	7 (50)/14 5 (36)/14	0/3 0/3	
BVAS/WG at diagnosis, median (IQR25-75)	6.5 (6-9)	6 (4-7)	0.1
Induction Therapy			
IV methylprednisolone	19 (91)	26 (62)	**0.02**
Rituximab, n (%)	9 (43)	14 (33)	0.59
Cyclophosphamide, n (%)	6 (29)	18 (43)	0.09
Plasmaspheres, n (%)	3 (14.3)	4 (10)	0.68
Hemodialyses, n (%)	9 (43)	4 (10)	**0.006**
Outcomes			
Respiratory failure, n (%)	5 (24)	1 (2)	**0.04**
ESKD, n (%)	6 (29)/11	2 (8.3)/24	**0.006**
Patients with relapse, n (%)	2 (10)/8	5 (29)/17	1.0

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Role of Frontline Chemoimmunotherapy in Treatment of Cryoglobulinemic Vasculitis associated with B-Cell Lymphoproliferative Disorders

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Introduction: Cryoglobulinemic vasculitis (CryoVas) is a rare cause of small vessel vasculitis. B-cell malignancies and autoimmune diseases have become the 2 major causes of CryoVas in countries were direct acting antivirals for hepatitis C infection are available.[1] There is a higher risk of death and poor outcome for patients diagnosed with CryoVas and associated B cell lymphoproliferative disorders.[2] Management of CryoVas patients is not standardized, as some prefer immunosuppressants like steroids and others chemoimmunotherapy as first line treatement.[3] We aimed to describe clinical presentation, risk of vasculitis relapse and outcome according to the chosen therapeutic strategy for CryoVas. Patients treated with chemoimmunotherapy as first line were included in group 1 and patients who received only immunosuppressive therapy as Rituximab or steroids alone were subsumed in group 2.

Methods: Retrospective analysis of 49 CryoVas patients associated with B-cell lymphoma from 16 French university and general hospitals. The primary endpoint was vasculitis relapse. Secondary endpoints were overall survival, risk factors for relapse, use of maintenance therapy, complications, infections.

Results: Median age at CryoVas diagnosis was 69 ±13 years. 21 patients had lymphoplasmacytic lymphoma, 20 marginal zone lymphoma, 4 chronic lymphocytic leukemia and 4 small B-cell lymphoma. In 86% cases CryoVas preceded the diagnosis of a B cell malignancy.

16 (32.7%) patients who received clone-targeted therapy never had vasculitis relapse. At last visit, 22 patients (64.7%) treated with chemoimmunotherapy had complete regression of vasculitis, compared to 8 (53.3%) patients treated with immunosuppressants alone.

25 patients (51%) had steroid or Rituximab maintenance treatment for CryoVas. Those treated with chemoimmunotherapy had the shortest duration of steroid maintenance therapy with a median of 16 months.

Acute kidney injury [HR 17.64 IC95% (3.27 -95.1), p <0,022] and skin necrosis [HR 7.57 IC 95% (1.33 - 43.02), p <0,001] were associated with CryoVas relapse. Longterm steroid use caused endocrinological complications and infections.

Conclusion: Diagnosis of CryoVas should incite to screen for B-cell malignancies. Patients who did not receive chemoimmunotherapy as first line treatment might be at higher risk of relapse. Maintenance therapy with Rituximab should be considered in CryoVas patients with acute kidney injury and skin necrosis, as those manifestations were highly associated with vasculitis relapse. Steroids should be tapered quickly to avoid longterm complications and infections.

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Disclosures: None.

P-192

Central Nervous System Involvement and Mimickers in ANCA Associated Vasculitis

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Background/ Objectives: Central nervous system (CNS) involvement is rare in ANCA associated vasculitis (AAV). On the other hand, AAV patients may develop complications or other conditions that mimic CNS involvement. We aimed to present the clinical, laboratory and imaging features of our AAV patients with CNS involvement and conditions other than CNS involvement that caused neurologic symptoms.

Methods: We surveyed the charts of 430 AAV patients in order to identify patients who were evaluated for neurologic symptoms suggesting CNS involvement. We extracted data on their demographics, types of AAV, neurologic symptoms, final diagnoses after neurologic work-up and their outcome.

Results: Of 430 AAV patients, 61 patients (14%) (41 GPA, 11 MPA, 9 EGPA; 27 women, 34 men; mean age: 51.6±15.4) with neurologic symptoms were identified. Among these, the cause of neurologic symptoms was CNS involvement of AAV in 7 patients, other AAV manifestations in 30, and secondary complications mimicking CNS involvement in 15 patients, whereas neurologic work-up did not lead to an underlying condition in 9 (Table). Among the 61 AAV patients with neurologic symptoms, the most common neurologic symptom suggesting CNS involvement was headache (n=20), followed by muscle weakness (n=17), numbness (n=17), and visual impairment (n=16). At the time of the occurrence of neurologic symptoms, all patients had active disease [median (IQR) BVAS=11.9 (7-15)]. 14 patients (22.9%) had accompanying peripheral nervous system (PNS) involvement. Regarding the outcomes, 6 of the 7 patients with CNS involvement of AAV recovered with sequelae, whereas one patient completely recovered. Among the 30 patients with other AAV manifestations causing neurologic symptoms, 21 recovered without sequela while the remaining 9 recovered with sequela despite treatment. Finally, among the 15 patients with conditions mimicking CNS involvement of AAV, one patient with spondylodiscitis complicated with aortic pseudoaneurysm, one with septic emboli and one with diabetic ketoacidosis complicated with pneumosepsis had died, one patient with skull base osteomyelitis recovered with a sequela of blindness, and the remaining patients recovered without sequela.

Conclusions: CNS involvement was uncommon, observed in only 1.6% of our 430 AAV patients. AAV manifestations other than CNS involvement such as ocular, orbital and nasopharyngeal involvement, as well as complications like infections and cardiovascular disease, may mimic CNS involvement in patients with AAV. These non-CNS entities account for almost 75% of the causes for any neurological symptom among AAV patients.

References:

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Table. Causes for neurologic sign or symptoms.

Variable, n (%)	61 AAV patients
CNS involvement of AAV	7 (11.4)
Meningeal involvement	3 (4.9)
Vascular involvement	2 (3.2)
Intracranial hypertension	1 (1.6)
Cerebral venous sinus thrombosis	1 (1.6)
AAV manifestations other than CNS involvement	30 (49.1)
PNS involvement	8 (13.1)
Sinonasal involvement	4 (6.5)
Nasal involvement	2 (3.2)
Associated with disease activation	2 (3.2)
Orbital and paranasal involvement, seconder CNS paralysis and PNS	2 (3.2)
Orbital involvement	1 (1.6)
Ocular involvement	1 (1.6)
Facial paralysis due to facial nerve involvement	1 (1.6)
Facial paralysis due to orbital involvement	1 (1.6)
Facial paralysis due to parotid gland involvement	1 (1.6)
Associated with disease activation and PNS involvement	1 (1.6)
Associated with disease activation and cervical hernia	1 (1.6)
Retinal vasculitis	1 (1.6)
Nasopharyngeal mass and PNS involvement	1 (1.6)
Parotid gland involvement	1 (1.6)
Cardioembolic CVA associated with cardiac mass	1 (1.6)
Cardiac thrombus	1 (1.6)
Secondary complications	15 (24.5)
Atherosclerotic CVA	5 (8.1)
Infection	4 (6.6)
Drug side effect	2 (3.2)
Cardioembolic CVA associated with atrial fibrillation and PNS inv.	1 (1.6)
PRES	1 (1.6)
Hemorrhagic CVA secondary to hypertension	1 (1.6)
Heart failure	1 (1.6)
Neurologic work-up did not lead to an underlying condition	9 (14.7)

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Patient with Scleroderma Renal Crisis and "Kidney-Limited" Systemic Sclerosis

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Presentation of Case: A 40-year-old woman presented with severe headache, vomiting and hypertension (225/120 mmHg). Past medical history was significant for primary Raynaud's phenomenon and uncontrolled hypertension of 1 month.

Diagnostic Testing: Laboratory findings revealed elevated creatinine (296 mmol/l), moderate proteinuria and erythrocyturia, and microangiopathic hemolytic anemia. An extensive workup was performed. Anti-nuclear antibodies (ANA) were elevated >1:640 with a fine-speckled and nucleolar pattern and negative extractable nuclear antigen antibodies (anti-ENA). A kidney biopsy demonstrated segmental active glomerular and vascular thrombotic microangiopathy (TMA).

Differential & Final Diagnosis: TMA is a rare disease with significant morbidity and mortality. Coupled with a broad differential, including accelerated hypertension, small-vessel vasculitis and complement dysregulation, this clinical presentation frequently poses a diagnostic challenge (1).

In this patient, a presumptive diagnosis of complement-related TMA was made, and complement inhibition with ravulizumab was started. Despite multiple antihypertensive drugs, high-dose diuretics and intensive hemodialysis, there was limited clinical improvement. A trial of methylprednisolone was initiated, and shortly after that, her illness progressed with vision abnormalities, acute respiratory insufficiency, and profound thrombocytopenia. A final diagnosis of scleroderma renal crisis was made, confirmed with additional testing, which disclosed positive anti-RNA polymerase III, although skin and other organ involvement has been excluded. After treatment with an angiotensin-convertase inhibitor, her symptoms and hypertension improved, but she remains on kidney replacement therapy.

Conclusions: The case presented is significant for an unusual cause of TMA: scleroderma renal crisis as the presenting feature of kidney-limited systemic sclerosis. Risk factors include the presence of anti-RNA polymerase III antibodies, which can be suspected in the setting of fine-speckled or nucleolar pattern of ANA and negative anti-ENA (2). Glucocorticoid treatment increases the risk of developing this complication in a dose-dependent manner (3). A close collaboration of nephrologists and rheumatologists enhances the management of these complex cases.

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1. CLINICAL SCIENCE
1.10. Vasculitis -related diseases: polymyalgia rheumatica, IgG4-related disease...

P-194

Clinical Manifestations and Immunomodulatory Treatment in Patients with Relapsing Polychondritis

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Background/Objective: Relapsing polychondritis (RP) is a rare, heterogeneous, multisystem inflammatory disease lacking standard treatment guidelines. This study aimed to describe clinical manifestations, current treatment trends and potential associations between clinical manifestations and immunomodulatory medication use.

Methods: This study included adults with physician-diagnosed RP enrolled in a multicenter prospective observational cohort. Baseline data included demographics, clinical manifestations of RP ever experienced, organ damage, and immunomodulatory drugs ever received. Immunomodulatory treatment was categorized into three groups: Group 1 = glucocorticoids (GC)/none; Group 2 = non-biologic immunosuppressive drugs (IS) excluding Janus kinase inhibitors (JAKi)±GC; and Group 3 = JAKi or biologic IS with/without non-biologic IS±GC. Chi square test was done to compare organ damage in three treatment groups. Logistic regression and multivariable regression models were used to evaluate correlation between demographics, and clinical manifestations vs three treatment groups.

Results: 195 patients with RP were included in the study, predominantly female (86%, n=167) and white (89%, n=174), mean age 49 (SD 13) years. Mean age of diagnosis of RP was 43 (SD 13) years and mean disease duration was 5 (3-8) years. All patients had ear-nose-throat involvement and majority (83%, n=163) had musculoskeletal manifestations. All patients had ≥3 clinical manifestations, with a median of 11 (3-19) symptoms. Many had organ damage (54%, n=80), including sensorineural hearing loss (26%, n=50), auricular deformity (12%, n=23), saddle nose deformity (12%, n=23), and subglottic stenosis (SGS) (9%, n=18). Among subjects who had dynamic chest CT (n=162), tracheomalacia and bronchomalacia were found in 31% (n=50) and 20% (n=32), respectively. Distribution of patients per treatment group is shown in **Figure 1**. Most common non-biologic was methotrexate (65%, n=126) and TNF inhibitors were most used biologics (29%, n=57). Most patients (95%, n=186) received GCs.

Organ damage was more likely to be associated with treatment group 3 (62% vs 22% and 15% in groups 2 and 1 respectively, P=0.02). Patients in treatment group 3 were more likely to have arthritis (OR 2.4; CI [1.2, 4.6], P<0.01) and SGS (OR 6.4, CI [1.3, 30], P=0.01); patients in group 1 were less likely to have nose pain (OR 0.36, CI [0.16, 0.79], p<0.01).

Conclusions: Patients with RP have heterogeneous clinical presentations, with widespread organ damage, almost universal GC use and diverse immunosuppressive prescriptions. Patients without organ damage, airway disease or arthritis were less likely to receive biologics and/or JAKi. Standardized multisystem assessment of RP is crucial for early detection and treatment initiation. Absence of a consensus approach to treatment underscore the need for clinical trials and treatment guidelines for RP.

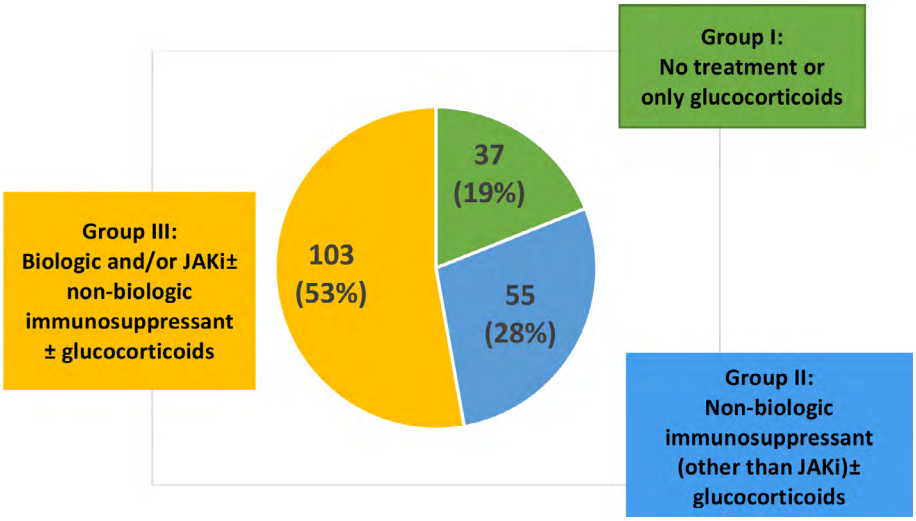

Figure 1.

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Polymyalgia rheumatica and giant cell arteritis following COVID-19 vaccination: Results from a nationwide survey

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Background/ Objectives: Some individuals experiencing the onset of PMR and GCA symptoms shortly after receiving COVID-19 vaccination have raised concerns about potential adverse events associated with immunization [1,2]. The aims of this study were to assess the risk and to determine the clinical profile of polymyalgia rheumatica (PMR) and giant cell arteritis (GCA) in COVID-19-vaccinated individuals over 50-year-old.

Methods: We conducted a retrospective national pharmacovigilance study including all French cases of PMR and GCA who developed their initial symptoms within one month of receiving the BNT162b2 mRNA, mRNA-1273, ChAdOx1 nCoV-19, and Ad26. COV2.S vaccines between 2020 and 2022. We determined the reporting rate (RR) of PMR and GCA cases per million vaccinated individuals, and then gathered clinical, therapeutic and follow-up data from individuals identified in the pharmacovigilance study by a nationwide survey.

Results: A total of 70 854 684 COVID-19 vaccine doses were administered to 25 260 485 adults, among which, 179 cases of PMR (RR 7, 1 cases/1 000 000 persons) and 54 cases of GCA (RR 2, 1 cases/1 000 000 persons) have been reported. The nationwide survey allowed the identification of 60 PMR and 35 GCA. Phenotype, GCA-related ischemic complications and -large vessel vasculitis as well as therapeutic management and follow-up seemed similar according to the number of vaccine shots received and when compared to the literature data of unvaccinated population.

Conclusions: Although cases of PMR or GCA following COVID-19 vaccination appear to be rare, the short time between immunization and the onset of initial symptoms suggests a temporal association. Physicians should be aware of this potential vaccine-related phenomenon; Re-challenging may be considered while maintaining vigilance.

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Disclosures: None.

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Clinical Phenotype Of Patients With Subclinical Giant Cell Arteritis In Polymyalgia Rheumatica

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Background: It has been reported that more than a quarter of patients with polymyalgia rheumatica (PMR) have subclinical giant cell arteritis (GCA) [1]. It remains unclear if all PMR patients should have ultrasound assessment for subclinical GCA.

Methods: Newly diagnosed PMR patients who met a clinical diagnosis for PMR, verified by two rheumatologists were examined with vascular ultrasound (US) of their temporal and axillary arteries. US of all 6 branches of the superficial temporal and both axillary arteries was performed using a GE P9 device. Sonographic abnormalities considered indicative of vasculitis in the temporal arteries included the halo sign and non-compressible arteries with a thickened intima-media complex. Clinical and laboratory characteristics were recorded. Halo scores were calculated for positive cases. Ultrasound findings were compared to a cohort of GCA patients.

Results: 91 patients with newly diagnosed PMR and 57 patients with newly diagnosed GCA were included. ACR/EULAR classification criteria were met in 67 of those with PMR (primarily due to prior corticosteroid use in primary care resulting in normal ESR/CRP) and all of those with GCA. Of the 91 patients with PMR, 16 were identified as having subclinical GCA on ultrasound (17.5%).

The mean age at time of diagnosis was 69 years for those with PMR, 70 years for those with subclinical GCA in PMR and 74 years for those with GCA. Males were more likely to have subclinical GCA in PMR, accounting for 12 (75%) of the subclinical GCA group compared to 27 (36%) of the pure PMR group (p=0.045). The mean ESR at baseline for those with subclinical GCA in PMR was higher than those with isolated PMR; 49mm/hr compared to 38mm/hr (p=0.18).

The extent of involvement of the temporal and axillary arteries of the 16 patients in the subclinical GCA group was compared to a cohort of 57 GCA patients. The total halo count was similar for both subclinical GCA in PMR and classic GCA patients at 4.33 and 4.36 respectively. However, GCA patients had higher halo scores in both temporal and axillary vessels of 13.17 and 13.28 respectively, compared to those with subclinical GCA with halo scores of 4.68 and 9.75. This suggests that patients with subclinical GCA in PMR have less vessel wall oedema than those with GCA. The subclinical GCA group had higher halo scores in the axillary arteries versus the temporal arteries, (p=0.0074) suggesting a predilection for extracranial vessels.

Conclusion: Patients with subclinical GCA had higher halo scores in the axillary arteries compared to the temporal arteries suggesting an extracranial phenotype. Male gender and a higher ESR at the time of PMR diagnosis appear to be risk markers for subclinical GCA though this requires analysis in larger cohorts of patients.

	PMR (75)	PMR with subclinical GCA (16)	GCA (47)
Age (mean and range)	69 (51-89)	70 (53-84)	74 (56-92)
Female	48 (64%)	4 (25%)	24 (52%)
Male	27 (36%)	12 (75%)	23 (48%)
Mean BMI	28.2	28.1	27.8
Mean ESR at baseline (mm/hr)	38	49	58
Mean CRP at baseline (mg/dl)	29	39.9	66
Mean halo count	0	4.33	4.36
Mean temporal artery halo count	0	4.68	13.17
Mean axillary artery halo count	0	9.75	13.28
Weight loss	18.5%	27.2%	29.2%
Hip girdle stiffness/pain	70.4%	90.9%	27.1%
Fever	3.7%	18.1%	10.4%

Table 1: Patient Characteristics.

References:

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P-197

Subclinical Aortic Inflammation in Patients with Polymyalgia Rheumatica

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Background/ Objectives: To investigate the clinicopathological features of patients with polymyalgia rheumatica (PMR) who had thoracic aorta repair surgery.

Methods: All patients evaluated at the Mayo Clinic in Rochester, MN, with at least one Current Procedural Terminology (CPT) code for thoracic aorta repair surgery between January 1, 2000, and December 31, 2021, were identified. All patients were screened for prior PMR diagnosis with diagnostic codes and electronic medical text search. Patients with a diagnosis of giant cell arteritis were excluded. The medical records of all patients were manually reviewed, and all the available aortic tissues were re-examined by an expert cardiovascular pathologist. Descriptive statistics were used to summarize the data.

Results: Of the 4621 patients with at least one CPT code for thoracic aorta repair surgery, 44 had an isolated PMR diagnosis in the absence of GCA (Table 1). Thirty-three (75%) were female, and the mean (SD) age at PMR diagnosis was 68.17 (6.91) years. Inflammatory markers (median [IQR]) were improved at aortic surgery compared to PMR diagnosis (erythrocyte sedimentation rate [mm/hr]: 48.50 [31.50- 85.25] vs. 18 [10.25- 20]; C-reactive protein [mg/L]: 22.90 [6.0- 35.60] vs. 3.0 [3.0- 3.98]). Thirty-five (80%) patients had thoracic aortic aneurysm and 9 (20%) had aortic dissection. All patients underwent ascending thoracic aorta repair surgery; in 2 patients descending thoracic aorta was also repaired concomitantly. Detailed histopathological evaluation revealed active aortic inflammation in 29 (66%) patients after a median (IQR) of 9.89 (4.87- 12.50) years. Healed aortitis was detected in 3 (7%) patients, and 12 (27%) had no evidence of active or healed aortitis.

Conclusions: A subset of patients with clinically isolated PMR have subclinical aortic inflammation that persists for years and leads to development of aortic aneurysm.

Disclosures: Kiniksa, Amgen, Eli Lilly, Sanofi, BMS.

Table 1: Characteristics of the patients with Polymyalgia Rheumatica who had thoracic aorta repair surgery.

	Total (n=44)	Active Aortitis (n=29)	Healed Aortitis (n=3)	No Evidence of Active or Healed Aortitis (n=12)
Age at PMR diagnosis, years, mean (SD)	68.17 (6.91) (n=39)	67.64 (6.24) (n=25)	65.47 (5.54) (n=3)	70.12 (8.64) (n=11)
Age at aortic surgery, years, mean (SD)	77.24 (4.48)	76.87 (4.61)	78.11 (3.72)	77.93 (4.58)
Sex, female	33 (75)	24 (83)	3 (100)	6 (50)
Race, white	41 (93)	27 (93)	3 (100)	11 (92)
Smoking, ever	18 (41)	9 (31)	1 (33)	8 (67)
Body mass index, mean (SD)	26.49 (3.89)	26.00 (3.22)	28.04 (1.36)	27.27 (5.50)
Hypertension	39 (89)	25 (86)	3 (100)	11 (92)
Diabetes mellitus	2 (5)	-	1 (33)	1 (8)
Hyperlipidemia	31 (70)	20 (69)	3 (100)	8 (67)
Length of time between PMR diagnosis and aorta surgery, years, median (IQR)	9.99 (4.63- 12.90) (n=39)	9.89 (4.87- 12.50) (n=25)	11.77 (11.56- 13.28) (n=3)	6.99 (0.47- 13.00) (n=11)
Initial prednisone dose at PMR diagnosis, mean (SD) mg	18.83 (11.57) (n=30)	22.10 (13.26) (n=19)	10 (0) (n=2)	13.88 (4.16) (n=9)
Duration of treatment with GCs prior to aortic surgery, years, median (IQR)	2.51 (0.94- 4.03) (n=33)	2.51 (1.25- 4.00) (n=21)	4.15 (2.20- 4.78) (n=3)	2.08 (0.33- 3.20) (n=9)
Number of patients on immunosuppressive treatment at aortic surgery	12 (27)	4 (14)	-	8 (67)
Prednisone dose at aortic surgery, mean (SD) mg	8.54 (10.61) (n=12)	3.25 (1.5) (n=4)	-	11.18 (12.32) (n=8)

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Pediatric and Adult Perspectives of Immunoglobulin G4-Related Disease: Results of a Multicentric Registry

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Background: Immunoglobulin G4-related disease (IgG4-RD) is an immune-mediated condition characterized by fibroinflammatory lesions that can develop in various anatomical locations. On the other hand, although IgG4-RD can be seen in pediatric and adult patients, no studies examine the differences between age groups.

Objectives: This study aimed to compare the involvement characteristics of IgG4-RD in the adult and pediatric population, to compare treatment choices, and to investigate the correlation of the IgG4 response index with the decision of remission according to the physician.

Method: Turkish Vasculitis Study Group Prospective Database (TRVAS) was screened for patients with IgG4-RD. Demographic and clinical features and treatments were obtained from Turkish Vasculitis Study registry data. A case report form assessing details of IgG4-RD Responder index and classification criteria for IgG4-RD was filled by the investigators, retrospectively. The involvement characteristics of adult and pediatric patients were evaluated by chi-square, and the correlation between IgG4 RD responder index and treatment response according to the physician in adult patients was assessed by Spearman correlation analysis.

Results: This study included 117 adults and 35 children with IgG4-RD. Of the adult and pediatric patients, 65 (55.6%) and 16 (45.7%) were male, respectively. The mean age for adult patients was 53.2 (±14.4) years, while for pediatric patients it was 14.7 (±4.3) years. Eye and musculoskeletal findings are prominent in pediatric patients, while periaortitis, retroperitoneum, and nephrological/genitourinary system (GUS) involvement are more common in adults. Similar rates of elevation in serum IgG4 levels were observed. Storiform fibrosis was observed more frequently in pediatric patients' biopsies, and the classification criteria were less fulfilled. While mycophenolate mofetil and azathioprine are preferred treatments in the pediatric age group, cyclophosphamide and rituximab are more commonly used in adults. (Table 1) According to the physician, the correlation between the final visit remission decision and the IgG4-RD response index showed a good correlation in the entire population (rho:0.69 p<0.001), While this situation was good in the evaluation of adult patients (rho: 0.70 p<0.001), it was low and moderate in the assessment of pediatric disease (rho: 0.40 p: 0.11).

Conclusion: IgG4-RD, more frequently seen with ocular involvement in pediatric patients, can affect various tissues and organ systems, especially the retroperitoneum and GUS, in adults. While serum IgG4 levels increased similarly, pediatric patients fulfilled the classification criteria less frequently. In children, the use of azathioprine and mycophenolate mofetil was more frequent. The physician's decision regarding disease remission showed high correlation with the response index in adults, but low correlation in pediatric patients.

Disclosures: None.

Table 1: Comparison of demographic, clinical characteristics, and treatment of IgG4-related diseases in adult and pediatric.

	Adult n:117	**Pediatric n:35**	**p**
Gender (male %)	65 (55.6)	16 (45.7)	0.30
Disease duration, months (IQR)	33 (51.5)	16.5 (28.5)	0.16
Constitutional symptoms (%)	42/104 (40.4)	11 (31.4)	0.34
Mucocutaneous involvement (%)	10/101 (9.9)	7 (20)	0.14
Musculoskeletal involvement (%)	20/106 (18.9)	12 (34.3)	**0.05**
Lymph node (%)	26/102 (25.5)	11 (31.4)	0.49
Eye involvement (%)	34/92 (37)	20 (57.1)	**0.04**
ENT involvement (%)	23/90 (25.6)	5/34 (14.7)	0.19
Respiratory system involvement (%)	17/101 (16.8)	5 (14.3)	0.72
Cardiovascular involvement (%)	19/98 (19.4)	4 (14.3)	0.53
Periaortitis (%)	10/101(9.9)	0	**0.06**
Pancreas and GI tract involvement (%)	29/104 (27.9)	6 (17.1)	0.20
Retroperitoneum (%)	38/101 (37.6)	2/33 (6.1)	**0.001**
Nephrological/GUS involvement (%)	33/106 (31.1)	5 (14.3)	**0.05**
CNS involvement (%)	10/90 (11.1)	6 (17.1)	0.38
Peripheral Nervous system involvement (%)	2/74 (2.7)	0	1
Biopsy (%)	94/111 (84.7)	31(88.6)	0.56
Disease confirmed on biopsy (%)	67/94 (71.3)	27/32 (84.4)	0.14
Dense lymphocyte infiltration in biopsy (%)	30/101 (29.7)	10/34 (29.4)	0.97
Obliterative phlebitis on biopsy (%)	7/102 (6.9)	4/34 (11.8)	0.46
Obliterative arteritis on biopsy (%)	3/102 (2.9)	0	0.57
Storiform fibrosis on biopsy (%)	16/102 (15.7)	13/34(38.2)	**0.005**
IgG4/IgG+ cell ratio (≥40%) on biopsy (%)	34/44 (77.3)	14/17 (82.4)	1
Serum IgG4 level (%) • normal/not checked • <2 fold • 2-5 fold • >5 fold	 59/100 (59) 17/100 (17) 16/100 (16) 8/100 (8)	 15/34 (44.1) 7/34 (20.6) 11/34 (32.4) 1/34 (2.9)	0.13
Probability of IgG4 diagnosis (%) • Probable • Possible • Definite	 20/83 (24.1) 5/83 (6) 58/83 (69.9)	 12/34 (35.3) 8/34 (23.5) 14/34 (41.2)	**0.004**
Fullfilled IgG4 classification criteria (%)	75/101 (74.3)	17/33 (51.5)	**0.01**
IgG level at diagnosis mg/dl (IQR)	1355 (595)	1265 (795)	0.50
CRP at time of diagnosis, mg/dl (IQR)	2 (6)	1.1 (14.4)	0.49
Sedimentation at the time of diagnosis mm/h (IQR)	23 (29.8)	35.5 (51)	0.30
Comorbidity (%)	82 (70.1)	8 (22.9)	**<0.001**
Malignancy (%)	8/112 (7.1)	0	0.19
Medical treatment (%)	103/109 (94.5)	35 (100)	0.33
Pulse steroids (ever) (%)	27/90 (23.1)	14 (40)	**0.04**
Oral steroid (ever) (%)	93 (74.4)	32 (91.4)	0.10
Cyclophosphamide (ever) (%)	20 (17.1)	3 (8.6)	0.21
Mycophenolate mofetil (ever) (%)	6 (5.1)	8 (22.9)	**0.004**
Azathioprine (ever) (%)	31 (26.5)	18 (51.4)	**0.006**
Methotrexate (ever) (%)	26 (22.2)	8 (22.9)	0.93
Colchicine (ever) (%)	6 (5.1)	1 (2.9)	1
Rituximab (ever) (%)	**39 (33.3)**	8 (22.9)	0.23
Infliximab (ever) (%)	3 (2.7)	0	1
Disease status at last visit (according to physician) (%) • Complete remission • Partial remission • Stable disease • Recurrence • Progression	 18/71 (25.4) 28/71 (39.4) 16/71 (22.5) 3/71 (4.2) 6/71(8.5)	 7/17 (41.2) 8/17 (47.1) 2/17 (11.8) 0 0	0,36
IgG4 response index at last visit (IQR)	2 (3)	0.5 (1)	**0.003**

ENT: ear, nose, throat GI: Gastrointestinal tract GUS: Genitourinary system CNS: Central nervous system CRP: C reactive protein

1. CLINICAL SCIENCE
1.11. Infectious vasculitis, vasculitis associated to autoimmune or haematologic disorders

P-199

Autoimmune pancytopenia as a clinical manifestation of Eosinophilic Granulomatosis with Polyangiitis

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Presentation of Case: A recent case of a 57 year old woman is presented, who is admitted to the Emergency Room due to a two months history of asthenia, along with respiratory symptoms of cough and wheezing. Initial analysis revealed hemoglobin of 5.5 g/L, 3700 leukocytes/L and platelet count of 84000/L. She is admitted to Internal Medicine for study.

Diagnostic Testing: Firstly, an etiological study of the anemia was carried out, performing an endoscopy study with normal result. Data of autoimmune hemolysis with positive Coombs test and reticulocytes elevation with persistence of pancytopenia was observed in laboratory test. An infectious cause was ruled out. In the autoimmunity study, positivity of Anti-Neutrophil Cytoplasmic Antibodies Anti Myeloperoxidase (MPO-ANCA) of 65 arb/mL stands out. In previous tests she already had eosinophilia of up to 1100 eosinophils/L. Moreover, abdominal ultrasound and thoracic computed tomagraphy tests were unremarkable.

She was evaluated by Otorhinolaryngology who identified nasal polyposis; and also by Pneumology with high suspicion of bronchial asthma.

Differential & Final Diagnosis: A complex clinical case is presented where we are faced with a clinical picture consisting of respiratory symptoms of possible bronchial asthma, eosinophilia, nasal polyposis and MPO-ANCA positivity. All of this is suggestive of a possible Eosinophilic Granulomatosis with Polyangiitis (EGPA) which meets the ACR/EULAR 2022 classification criteria (8 points).[1]

Autoimmune hemolytic anemia in Allergic Granulomatous Angitis (AIHA) is described as a very rare complication[2]. It is postulated that the AIHA is mediated or enhanced at least partly by high IL-4 and IL-5 production.

What is striking in the present case is an autoimmune pancytopenia, a fact that to date has not been recorded in the literature within the spectrum of EGPA.

Discussion of Management: Firstly, it is decided to perform a blood transfusion with a favorable initial response but subsequently the pancytopenia continues to worsen. This is why it is decided to start treatment with 60 mg/day IV Methylprednisolone with good response. After 10 days of treatment, it is decided to switch to oral 30 mg/day Prednisone. Due to stability of the clinical picture, she is discharged home with subsequent follow-up in Internal Medicine outpatient clinics, where she receives a weekly dose of 10 mg SC Methotrexate as a corticosteroid-sparing agent.[3] Currently, the patient is stable at a hematological level.

Conclusions: Autoimmune pancytopenia should be considered as a clinical manifestation of EGPA.

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Disclosures: None.

P-200

Biomarker VAP2 for vascular inflammation in serum of severe patients with COVID-19

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Background: In the present study we analyzed VasSF binding molecule VAP2 (aberrant APOA2) as a vascular inflammation marker in sera of the COVID-19 serious cases. VasSF has been developed as a recombinant clone of the artificial gamma globulin for the treatment of ANCA-related vasculitis (AAV) and its target antigen is aberrant APOA2 (K. Suzuki *et al*. DDDT. 2019 13:555, M. Koura *et al.* Clin Exp Immunol, in press). Furthermore, VAP2 has been demonstrated as a risk molecule for the vasculitis because treatment with anti-APOA2 antibody to a Kawasaki disease model mouse was effective (F. Ito, *et al*. Ped Rheu.2022;20:119). Recently, VAP2 was shown as 26kDa in AAV model mouse SCG/Kj (M. Koura *et al.* Clin Exp Immunol, in press), and APOA2 in HDL of serum of human AAV was shown as aberrant APOA2 in both 24kDa and 17kDa different molecular size of 10kDa of normal APOA2 (in preparation, J. Suzuki *et al*). On the other hand, severe cases of COVID-19 showed an association with vascular inflammation, and higher levels of serum cytokines and myeloperoxidase (MPO) (Kimura Y, *et al*. Sci. Rep. 2021; 11:206383).

Material and Methods: We analyzed VAP2 levels and reaction with anti-APOA2 antibody by Western Blot, and MPO activities and IL-6 in 59 patients with COVID-19 who agreed with consent to these analyses admitted to the Chiba University Hospital. Moreover, these levels were compared with various clinical parameters in serum during the clinical course.

Results: In the serious case group of COVID-19, levels of VAP2 and reaction with anti-APOA2 antibody were shown maximum scores at admission, and then these levels decreased at discharge time. These activities were corelated with CRP titer, but low value in HDL and higher levels in d-dimer remained until discharge. On the other hand, in the death discharge group with serious cases, levels of VAP2 and reaction with anti-APOA2 antibody did not decrease as remaining a higher activity, but CRP was low value and low titer of d-dimer during admission. MPO activity and IL-6 in the serum of the serious patient group showed high levels on admission and ICU, but slightly decreased at the time of discharge. On the other hand, in the death discharge group, these levels showed extremely higher at the time of admission.

Conclusion: Serum levels of VAP2 showed higher levels in serious case group of the COVID-19, indicating that vascular inflammation during the serious period is similarly to patients with AAV and Kawasaki disease. Based on these results, it is thought that VAP2 is useful as a severity marker for COVID-19 patients. In addition, VAP2 may be useful as an effective biomarker in the treatment of VasSF for COVID-19 such as AAV and Kawasaki disease.

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Tuberculosis: Lessons yet to be learned

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Tuberculosis is a multi-system infection with insidious onset that could mimic or coexist with various diseases. Such diverse clinical presentations often result in diagnostic challenges and delays. We herein present an example.

A 35-year-old male, with no medical history, presented with weight loss and painful facial papules. Physical examination revealed bilateral enlarged cervical lymph nodes and diffuse subcutaneous nodules. He had increased serum level of inflammatory markers. Tuberculin Skin test showed a phlyctenular reaction of 3 cm. Sputum testing for tuberculosis was negative. CT-TAP showed a heterogeneous spleen and liver with liver perfusion abnormalities, a partial portal vein thrombosis and multifocal renal infarctions. Investigations ruled out endocarditis, arrhythmia, thrombophilia, antiphospholipid syndrome, hyperhomocysteinemia and JAK2. Cryoglobulin test was positive.

Cutaneous biopsy showed granulomatous hypodermic lesions with necrosis and signs of vasculitis and thrombosis. Cervical lymph node biopsy showed epithelioid cell granuloma with necrosis.

The patient was diagnosed with cutaneous, lymph node, spleen and liver Tuberculosis, complicated by cryoglobulinemia vasculitis affecting the portal vein and renal arteries.

He received 6 months of fixed-dose combination antituberculosis therapy. Within the first two months, the papules, nodules and the swollen lymph nodes fully disappeared. Within 6 months, CT showed repermeabilization of the portal vein and disappearance of the renal infarctions. Cryoglobulin test became negative.

In conclusion, tuberculosis is a multifaceted disease that could potentially cause vasculitis, notably mixed cryoglobulinemia which may disappear after appropriate anti-tuberculosis therapy, as it occurred in our patient. Physicians should consider tuberculosis when clinical presentation is unusual, especially in endemic countries.

2. TRANSLATIONAL SCIENCE
2.01. Genetics and epigenetics. Alterations leading to monogenic vasculitis

P-202

An apolipoprotein L1 polygenic score is associated with giant cell arteritis susceptibility

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Background: Despite adverse effects, glucocorticoids remain central to the treatment of giant cell arteritis (GCA)(1). To improve patient outcomes, there is a need for more targeted therapies and improved risk stratification in GCA. Prior work suggests that evidence of genetic association can improve success rates from clinical trials and identify biomarkers for risk assessment, particularly when combined with other -omics data, including proteomics(2). Although evidence for a genetic component to GCA exists(3), few new treatment targets have emerged to date.

Methods: Polygenic scores (PRS) were optimized for 169 circulating plasma proteins using data from genome-wide association studies of protein levels(4). PRS were tested for association with GCA, utilizing the UK GCA Consortium and WTCCC population controls (cases *N*=729, controls *N*=2,619). Associated PRS were replicated in an independent dataset (cases *N*=1,129, controls *N*=2,654) and tested for causality using Mendelian randomization (MR). Finally, protein-protein interaction (PPI) network analysis was performed to evaluate relationships between proteins with associated PRS.

Results: The Apolipoprotein L1 (APOL1) PRS was significantly associated with GCA susceptibility (coefficient = -320.49; SE = 60.22; *p-value* = 1×10^{-4}). This observation was replicated in an independent cohort (coefficient=-27.43; *SE*=8.23; *p-value*=8.69×10^{-4}) and corroborated by evidence for causality in MR (beta = -0.093; SE = 0.02*; p-value* = 4.42×10^{-9}). PPI network analysis revealed enrichment for GO pathways “negative regulation of fibrinolysis” (pathway protein [PP] *N*=13, network protein [NP] *N*=2, *false discovery rate*[*FDR*]=0.04) and “negative regulation of blood coagulation” (PP *N*=46, NP *N*=4, *FDR*=2.8×10^{-4}).

Conclusions: Genetically higher APOL1 protein levels are associated with lower GCA susceptibility, which may implicate a role of reverse cholesterol transport and the trypanosome lytic factor in GCA. PPI network analysis also highlights a possible involvement of coagulation and fibrinolytic cascades in the development of GCA. Future studies will determine the potential for pharmaceutical targeting of the APOL1 pathway or it’s suitability as a clinical biomarker for risk stratification.

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Disclosures: None for the analyses performed in this study.

P-203

Characterization of alpha-1 antitrypsin function in ANCA-associated vasculitis

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Background/Objectives: Two separate genome-wide association studies demonstrated that polymorphisms in *SERPINA1*, encoding serine protease inhibitor alpha-1 antitrypsin (A1AT), are associated with increased risk of developing antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). It has been proposed that the functionality of A1AT is decreased in inflammatory conditions. This study aimed to gain insight into function of A1AT in AAV, including the relationships of A1AT genotype, and functional activity of A1AT, with targeted biomarkers and disease activity in AAV.

Methods: Clinical data and peripheral blood samples were examined from 250 participants with AAV in a longitudinal cohort, and 80 healthy control individuals. Among those with AAV, 170 with wild-type (WT) A1AT genotype (MM) and 80 with mutant (mut) A1AT genotype (MS, MZ, SS, SZ, or ZZ) with available samples during active disease and remission were selected. Comprehensive analyses were performed, including A1AT total and functional levels, markers of neutrophil activation, and cyto/chemokines.

Results: Participants with mut A1AT genotype were younger at diagnosis of AAV than those with WT A1AT genotype. Among participants with AAV and WT A1AT genotype, 66.5% were PR3-ANCA positive and 26.5% were MPO-ANCA positive during their disease course, as compared to 73.8% and 17.5%, respectively, among those with mut A1AT genotype. Birmingham Vasculitis Activity Score/WG with active visits were similar. Functional A1AT was higher with WT A1AT genotype than with mut genotype during both active disease ($p < 0.01$) and remission ($p < 0.01$), and higher among participants with AAV and WT A1AT genotype than among healthy subjects ($p < 0.01$). Total and functional A1AT aligned with genotype and were consistently lower among those with Z alleles. During active AAV, levels of proinflammatory cytokines IL-8 and IL-6 were similar across the A1AT genotype subgroups. The decline of these cytokines during remission of AAV was more distinct among those with WT A1AT genotype than those with mut genotype. In contrast, levels of IL-1α and IL-13 were more affected among those with mut genotype than those with WT A1AT genotype, resulting in significant increased levels during active disease ($p=0.05$ and $p < 0.01$, respectively). Levels of IL-8 and IL-6 among healthy control subjects were lower than those with WT A1AT genotype during remission ($p < 0.01$ and $p < 0.01$, respectively), but IL-1α and IL-13 were similar. During active AAV and remission, levels of the anti-inflammatory cytokine IL-10 were slightly higher among those with WT A1AT genotype than those with mut genotype ($p=0.07$ and $p=0.20$, respectively). By comparison, mean IL-10 among healthy subjects was lower than among those with WT A1AT genotype in remission ($p < 0.01$).

Conclusions: A1AT genotype among people with AAV is associated with differences in age at diagnosis, inflammatory markers, and several cytokines. Further analyses will explore the relationships among A1AT functional levels and disease characteristics and activity of AAV.

Disclosures: Some not all authors - Takeda consulting, research funds, or employment.

P-204

The impact of single nucleotide polymorphisms in glucocorticoid activation pathways genes on the outcomes of patients with Takayasu arteritis

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Background/objectives: Therapy for disease activity in Takayasu arteritis (TAK) is based on high-dose glucocorticoids (GC) in combination with immunosuppressive or biological agents. Long-term use of GC is common in TAK and may lead to several adverse events (AEs) (1). Single nucleotide polymorphisms (SNPs) in the GC receptor gene (*NR3C1*) or its co-chaperone (*FKBP5*) and in the enzyme involved in its metabolism (*HSD11B1*) may impact GC effects and toxicity (2). Therefore, this study aims to evaluate the influence of *HSD11B1, FKBP5,* and *NR3C1* SNPs on clinical phenotypes, therapy, and toxicity of GC in TAK patients.

Methods: A retrospective cohort study was carried out in TAK patients who met the 2022 ACR/EULAR classification criteria for TAK. Genotyping was performed to detect the SNP of interest, using the Sanger technique. The following SNPs were investigated: rs11119328 (*HSD11B1* gene), rs1360780 (*FKBP5* gene) and the following SNPs of the *NR3C1* gene: rs56149945 (N363S), rs41423247 (BclI), rs10052957 (TthIII1), rs6198 (9ß), rs6189 and rs6190 (ER22/23EK). *NR3C1* haplotypes were determined based on combinations of the SNPs using the software PHASE [ref] and were divided into five haplotypes (HT).

Results: Table 1 depicts the frequency of each SNP, and *NR3C1* haplotype, and their relations with clinical variables and GC toxicity in 81 TAK patients. No significant differences regarding study variables were observed between carriers and non-carriers of rs11119328 and rs1360780 of the *HSD11B*1 and *FKBP5* genes, respectively. Regarding the *NR3C1* gene HT, HT1 carriers had lower vasculitis damage index (VDI) scores compared to non-carriers (p = 0.016).

Conclusions: The SNPs rs11119328 of the *HSD11B1* gene, rs1360780 of the *FKBP5* gene and the HT1, HT2, and HT3 of the *NR3C1* gene are common in TAK patients. However, the carriage of these SNPs was not associated with a significant impact on TAK prognosis. HT1 carriers had lower VDI scores.

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Disclosures: None.

Table 1 – Genotypes and disease features of TAK patients.

Variables	All patients (n=81)	HT1 (n=16)	HT2 (n=12)	HT3 (n=12)	rs11119328 (n=27)	rs1360780 (n=44)
Females	73 (90.1%)	15 (93.8%)	11 (91.7%)	10 (83.3%)	25 (92.6%)	42 (95.5%)
Mean age at diagnosis, years	29.6 ± 11.4	27.6 ± 9.5	28.9 ± 10.8	30.2 ± 7.9	28.8 ± 12.0	29.4 ± 11.5
Type V	56 (69.1%)	13 (81.3%)	9 (75.0%)	9 (75.0%)	19 (70.4%)	31 (70.5%)
Sustained remission	49 (60.5%)	8 (50.0%)	9 (75.0%)	6 (50.0%)	16 (59.3%)	25 (56.8%)
Need for biologic therapy	45 (55.6%)	10 (62.5%)	5 (41.7%)	8 (66.7%)	18 (66.7%)	24 (54.5%)
Angiographic progression	42 (51.9%)	8 (50.0%)	6 (50.0%)	6 (50.0%)	15 (55.6%)	21 (47.7%)
Vascular intervention	27 (33.3%)	4 (25.0%)	6 (50.0%)	4 (33.3%)	9 (33.3%)	15 (34.1%)
Subclavian steal syndrome	13 (16.0%)	3 (18.8%)	2 (16.7%)	3 (25.0%)	6 (22.2%)	7 (15.9%)
Renovascular hypertension	19 (23.5%)	6 (37.5%)	4 (33.3%)	3 (25.0%)	7 (25.9%)	12 (27.3%)
Ischemic events	23 (28.4%)	5 (31.3%)	2 (16.7%)	4 (25.0%)	6 (22.2%)	11 (31.4%)
GC side effects	67 (82.7%)	12 (75.0%)	12 (100.0%)	9 (75.0%)	22 (81.5%)	36 (81.8%)

Variables	All patients (n=81)	HT1 (n=16)	HT2 (n=12)	HT3 (n=12)	rs11119328 (n=27)	rs1360780 (n=44)
Severe infections	7 (8.6%)	3 (18.8%)	0 (0.0%)	2 (16.7%)	3 (11.1%)	3 (6.8%)
Diabetes	16 (19.8%)	4 (25.0%)	2 (16.7%)	3 (25.0%)	4 (14.8%)	8 (18.2%)
Weight gain	11 (13.6%)	0 (0.0%)	1 (8.3%)	4 (33.3%)	3 (11.1%)	7 (15.9%)
Hyprlipidemia	41 (50.6%)	6 (37.5%)	6 (50.0%)	9 (75.0%)	15 (55.6%)	21 (47.7%)
Worsening or new-onset hypertension	22 (27.2%)	4 (25.0%)	3 (25.0%)	5 (41.7%)	9 (33.3%)	15 (34.1%)
Cataracts	3 (3.7%)	0 (0.0%)	1 (8.3%)	0 (0.0%)	0 (0.0%)	1 (2.3%)
Psychosis	1 (1.2%)	0 (0.0%)	1 (8.3%)	0 (0.0%)	0 (0.0%)	1 (2.3%)
Osteonecrosis	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GIOP	16 (19.8%)	3 (18.8%)	3 (25.0%)	2 (16.7%)	5 (18.5%)	8 (18.2%)

GC – Glucocorticoids; GIOP – Glucocorticoid-induced osteoporosis; HT – Haplotype; TAK – Takayasu arteritis.

2. TRANSLATIONAL SCIENCE
2.02. Exposome: climate, pollutants, triggering infectious agents...

P-205

Can diet influence the risk of giant cell arteritis and polymyalgia rheumatica? Data from the French E3N cohort study

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Background/ Objectives: Giant cell arteritis (GCA), is frequently associated with polymyalgia rheumatica (PMR), suggesting a common pathophysiological mechanism. Their etiological mechanism remains unclear. The occurrence of GCA/PMR shows a geographical pattern, with higher rates observed in North regions. Additionally, individuals with African, Asian, or Hispanic ancestry tend to have a lower incidence of these conditions. These differences could be explained partially by environmental and lifestyle factors, such as diet. The aim of this study was to assess the association between diet and the risk of developing GCA and/or PMR through a large prospective cohort.

Methods: The E3N cohort study (Etude Epidémiologique Auprès des Femmes de la Mutuelle Générale de l'éducation nationale) is a large prospective cohort study, conducted in France that has included 98,995 women since 1990. Dietary information was collected in 1993 through a validated food frequency questionnaire. Diet was analyzed using three approaches: food groups, dietary patterns via factor analysis, and the adherence to the Mediterranean Diet Score, using a 9-unit dietary score. Hazard ratios (HRs) and 95% confidence interval (95% CIs) for incident GCA and/or PMR were estimated using Cox proportional hazards regression models adjusted for age and the main potential confounders.

Results: Among 64,296 women, we identified 678 GCA/PMR cases, including 139 GCA, 278 PMR (261 were undifferentiated). Mediterranean diet adherence score was not associated with GCA/PMR nor GCA nor PMR (aHR 95%CI 1.01 [0.83 – 1.24], 1.04 [0.67 – 1.63] and 0.81 [0.58 – 1.13] for high score versus low score, respectively; *P* for trend > 0.05). Conversely, a Western diet was associated with an increased risk in GCA/PMR (aHR 95%CI 1.40 [1.07 – 1.85] for 4th quartile versus 1st quartile; *P* for trend = 0.01). The risk remained significant among PMR cases analyzed separately (aHR 95%CI 1.52 [1.00 – 2.32] for 4th quartile versus 1st quartile; *P* for trend = 0.04). However, no significant association was observed with GCA cases (aHR 95%CI 1.09 [0.58 – 2.03] for 4th quartile versus 1st quartile; *P* for trend = 0.67) (table 1).

Conclusions: We found a positive association between Western diet and the risk of GCA/PMR, mainly at the expense of PMR cases. This diet is characterized by high consumption of saturated fats, carbohydrates, salt and cholesterol, and low consumption of fiber, vitamins, and minerals. It is associated with chronic inflammatory state, at the origin of tissue inflammation, which has already been linked to a wide range of chronic diseases (cardiovascular disease, cancer, etc.). The pathophysiology of PMR, involving high concentrations of pro-inflammatory cytokines in the affected joints and muscles, could therefore be partly explained by this chronic inflammatory state mediated by the Western diet.

References:

Disclosures: None.

Table 1. Hazards ratios for GCA and/or PMR according to quartiles of dietary patterns in the study population.

Dietary pattern (quartiles)	1	2	3	4	*P for trend*
GCA/PMR (N=64,296)					
Prudent pattern					
Cases (N=678)	144 (21.24)	167 (24.63)	194 (28.61)	173 (25.52)	
M1 [HR 95%CI]	Reference	1.08 [0.86; 1.35]	1.21 [0.97; 1.50]	1.05 [0.83; 1.31]	0.6422
M2 [HR 95%CI]	Reference	1.07 [0.86; 1.34]	1.20 [0.96; 1.49]	1.05 [0.83; 1.32]	0.6353
Western pattern					
Cases (N=678)	172 (25.37)	168 (24.78)	169 (24.93)	169 (24.93)	
M1 [HR 95%CI]	Reference	1.11 [0.90; 1.38]	1.24 [0.99; 1.57]	**1.40 [1.07; 1.84]**	**0.0115**
M2 [HR 95%CI]	Reference	1.10 [0.88; 1.37]	1.23 [0.98; 1.56]	**1.40 [1.07; 1.85]**	**0.0124**
GCA (N=63,757)					
Prudent pattern					
Cases (N=139)	35 (25.18)	29 (20.86)	43 (30.94)	32 (23.02)	
M1 [HR 95%CI]	Reference	0.79 [0.48; 1.29]	1.15 [0.73; 1.81]	0.87 [0.53; 1.43]	0.9103
M2 [HR 95%CI]	Reference	0.79 [0.48; 1.29]	1.16 [0.74; 1.82]	0.89 [0.54; 1.46]	0.9730
Western pattern					
Cases (N=139)	44 (31.65)	34 (24.46)	35 (25.18)	26 (18.71)	
M1 [HR 95%CI]	Reference	0.94 [0.59; 1.48]	1.13 [0.69; 1.85]	1.03 [0.56; 1.92]	0.7912
M2 [HR 95%CI]	Reference	0.94 [0.59; 1.50]	1.15 [0.70; 1.90]	1.09 [0.58; 2.03]	0.6711
PMR only (N=63,892)					
Prudent pattern					
Cases (N=274)	62 (22.63)	66 (24.09)	76 (27.74)	70 (25.55)	
M1 [HR 95%CI]	Reference	0.99 [0.70; 1.41]	1.10 [0.78; 1.54]	0.96 [0.68; 1.37]	0.9107
M2 [HR 95%CI]	Reference	0.99 [0.70; 1.41]	1.10 [0.78; 1.54]	0.97 [0.68; 1.39]	0.9685
Western pattern					
Cases (N=274)	66 (24.09)	62 (22.63)	64 (23.36)	82 (29.93)	
M1 [HR 95%CI]	Reference	1.02 [0.72; 1.46]	1.13 [0.78; 1.64]	**1.56 [1.02; 2.37]**	**0.0302**
M2 [HR 95%CI]	Reference	1.01 [0.70; 1.43]	1.11 [0.76; 1.61]	**1.52 [1.00; 2.32]**	**0.0404**

HR: hazard ratio, CI: confidence interval
M1: Adjusted for total daily intake without alcohol (kcal/d)), and age (as the timescale)
M2: M1+ educational level (< High School, up to 2-level university, ≥ 3 level university), socio-professional category (teacher, higher managerial and professional occupations, intermediate occupation, unemployed, other, not available), body mass index at Q3 (< 18.5, [18.5 – 25[, [25 – 30[, ≥ 30), type 2 diabetes at Q3, smoking status at Q3 (non-smoker, current smoker, former smoker), and physical activity (metabolic equivalent hours/week)
Q3: third questionnaire (baseline)

P-206

Temporal clustering of ANCA-associated vasculitis occurrence

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Background: We hypothesised that observed annual incidence rates of ANCA-associated vasculitis (AAV) are driven by sporadic short-term, high-intensity rates characterised as clusters of diagnosis events in time. Using data from Ireland, Sweden and Spain, we performed a changepoint analysis to discover time intervals with high and low rates of vasculitis diagnosis.

Methods: We recruited 417 patients from the RITA-Ireland Vasculitis Registry. Adults (>16 years) diagnosed with AAV after 1/1/13 were eligible. Inclusion criteria were a definite diagnosis of microscopic polyangiitis or granulomatosis with polyangiitis. Patients with positive anti-GBM antibodies were excluded. The rate of diagnosis was modelled using a Poisson process changepoint model, which divides the timeline into intervals. Within each interval the time between diagnosis follows an exponential distribution with rate μ. Intervals with larger values of μ will have higher diagnosis rates. The number of changepoints was selected using cross-validation. We also applied this method to independent validation cohorts in Skåne (n = 351, Jan 1997 – Dec 2019, thus not including the pandemic period) and Barcelona (n = 82, Jan 2013 - present).

Results: A five changepoint model fit the Irish data best (Figure). We observed several diagnosis incidence rates, ranging from μ=22/year over 42 months (pandemic period) to μ=60/y over 41 months (2015-2018). We also observed a recent post-pandemic reset to a higher diagnosis rate. No clusters of diagnosis events in time were clearly identified by the model. No changepoints were identified for the Skåne data, with a consistent diagnosis rate of μ=16/y across the cohort time frame. For the Barcelona data, we observed one changepoint in 2021, with associated rates of μ=5/y and μ=10/y. Observed intervals between diagnoses closely matched simulations generated by the estimated models for the Irish data (Figure). However, very short-term intervals (<5 days) were underestimated by the model, possibly suggesting that these short intervals occur more frequently than expected by chance. We observed similar short interval results in the Skåne and Barcelona registries.

Conclusions: We observed little clear evidence for short-term, high-intensity diagnosis incidence rates across 3 independent cohorts. For both Barcelona and Ireland (inception cohorts without 100% ascertainment), changes in incidence rate can likely be explained by changes in registry recruitment strategy, particularly over the pandemic. Our findings suggest that much of the perceived volatile behaviour of diagnosis events are consistent with the expected rates using well-established Poisson process models. However, our models failed to fully account for very short-term diagnosis intervals.

Disclosures: None.

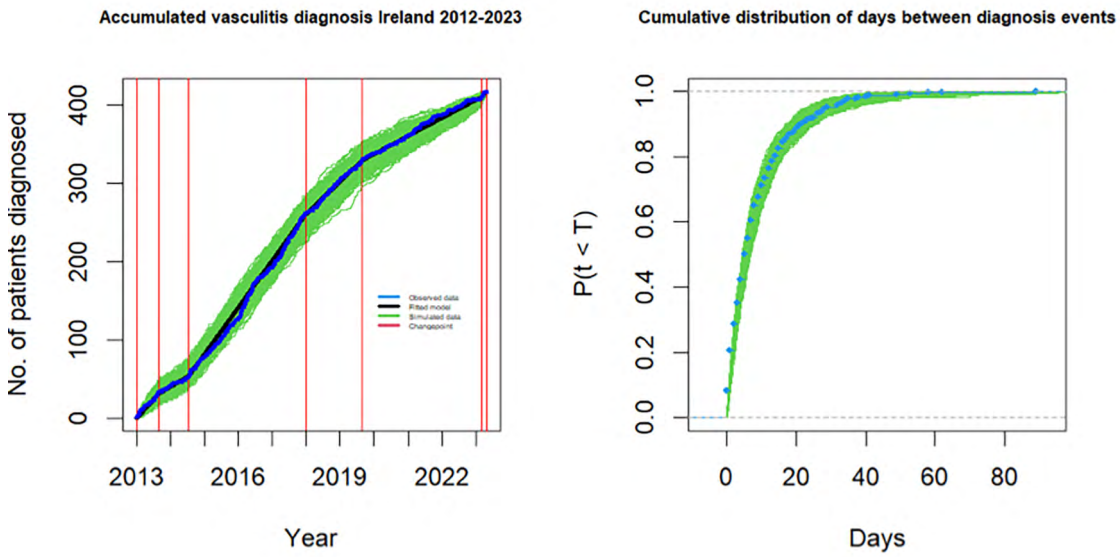

Figure: Irish data results, showing estimated changepoint locations (left) and cumulative distribution of time between consecutive diagnosis events (right). Data simulated from the fitted model resembles the observed data except for very low intervals (blue dots to the left of green simulated distribution).

2. TRANSLATIONAL SCIENCE

2.03. Cellular and molecular mechanisms of disease: B cells, T cells, macrophages, eosinophils, neutrophils, endothelial cells, stromal cells, complement, senescent cells...

P-207

Methylprednisolone pulse induced microcirculation disorders in a lupus-like murine model

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Background/ Objectives: Methylprednisolone (mPSL) pulse therapy is an essential option for patients with active systemic lupus erythematosus, but there is a risk of adverse events related to microcirculation disorders, including idiopathic osteonecrosis of the femoral head (ONFH) [1]. Recent studies have revealed that excessive neutrophil extracellular traps (NETs) are involved in microcirculation disorders [2]. This study aimed to demonstrate that mPSL pulse could induce NETs in lupus mice and identify the factors contributing to this induction.

Methods: Six mice with imiquimod (IMQ)-induced lupus-like disease and six normal mice were intraperitoneally injected with mPSL on days 39 to 41, and five mice with IMQ-induced lupus-like disease and six normal mice were injected with phosphate-buffered saline. Pathological examinations were conducted to evaluate the ischemic state of the femoral head and tissue infiltration of NET-forming neutrophils. Proteome analysis was performed to extract plasma proteins specifically elevated in mPSL-administered mice with IMQ-induced lupus-like disease, and their effects on NET formation were assessed *in vitro*.

Results: Mice with IMQ-induced lupus-like disease that received mPSL pulse demonstrated ischemia of the femoral head cartilage with tissue infiltration of NET-forming neutrophils. Proteome analysis suggested that prenylcysteine oxidase 1 (PCYOX1) played a role in this phenomenon. The reaction of very low-density lipoproteins (VLDL) containing PCYOX1 with its substrate farnesylcysteine (FC) induced NETs *in vitro*. The combined addition of IMQ and mPSL synergistically enhanced VLDL-plus-FC-induced NET formation.

Conclusions: PCYOX1 and related factors are worthy of attention to understand the underlying mechanisms and create novel therapeutic strategies for mPSL-mediated microcirculation disorders, including ONFH.

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2. Grayson PC, Kaplan MJ. At the Bench: Neutrophil extracellular traps (NETs) highlight novel aspects of innate immune system involvement in autoimmune diseases. *J Leukoc Biol* 2016;99:253-64.

Disclosures: None.

P-208

Tacrolimus with corticosteroid therapy reduces clinical disease activity, suppresses T helper subpopulations Th1, Th17, and Th17.1, and reduces type-I interferon related pathways in Takayasu arteritis

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Background/ Objectives: We evaluated serial changes in disease activity, circulating T-lymphocyte profile, and transcriptomics of peripheral blood mononuclear cells (PBMCs) in Takayasu arteritis (TAK) treated with tacrolimus (1) and corticosteroids.

Methods: Clinical disease activity (physician global assessment – active/inactive, ITAS2010, DEI.TAK), serial T-lymphocyte profile (%CD4+ T lymphocytes: Th1:Treg, Th17:Treg, Th17.1:Treg, PD1+Th17:Treg) using flow-cytometry, and PBMC transcriptome profile (n=13, comparing baseline with 3 months after treatment) using Affymetrix ClariomTM D human microarray of TAK treated with tacrolimus with corticosteroids before, 3 months, and 6 months after treatment were evaluated in a prospective cohort. Disease activity measures and T lymphocyte profiles (medians with IQR) were compared using Wilcoxon matched-pairs signed-rank test. Differentially expressed genes (DEGs) before vs after treatment were functionally annotated using DAVID and ClueGO. Protein-protein network of top up- and down-regulated coding genes was generated using the STRING database. Thereafter, the top clusters of hub genes were identified using the Cytohubba plugin of Cytoscape.

Results: 23 TAK [21 immunosuppressive-naïve, mean (SD) age of 31.70(10.76) years, 14/23 females] were recruited after obtaining written informed consent. At baseline, 22/23 TAK were active (2/22 and 1/20 were active at 3 months and 6 months, respectively). ITAS2010 (Fig. 1A), DEI.TAK (Fig. 1B), daily prednisolone dose (baseline dose initiated after sampling, Fig. 1C), Th1:Treg (Fig. 1D), Th2:Treg (Fig. 1E), Th17:Treg (Fig. 1F), Th17.1:Treg (Fig 1G), and PD1+Th17:Treg (Fig. 1H) all significantly reduced on follow-up at 3 months (vs baseline) and 6 months (vs baseline). 206/135750 genes (29 coding) were up-regulated before tacrolimus treatment, whereas, 1356/135750 genes (256 coding) were up-regulated after tacrolimus treatment. DAVID functionally annotated up-regulated DEGs to interferon-beta and tumor necrosis factor production pathways at baseline. ClueGO identified up-regulated immune processes pre-treatment related to T-cell differentiation, cytokine production, macrophage and mast cell activation (Fig. 1J). Protein-protein interaction (PPI) and analysis of hub genes revealed a significant reduction in genes involved in type I interferon signaling (IFI44, IFI44L, MX1, RSAD2, PLSCR1, Fig. 1K) following treatment.

Conclusions: Tacrolimus effectively suppresses T-lymphocyte activation and inflammatory pathways (including type-I interferon signaling-related pathways) in TAK concomitant with disease activity reduction.

References:

1. J Inflamm Res 2022;15:1521-41.

Disclosures: Funded by ICMR Grant 5/4/ 1-2/2019-NCD-II.

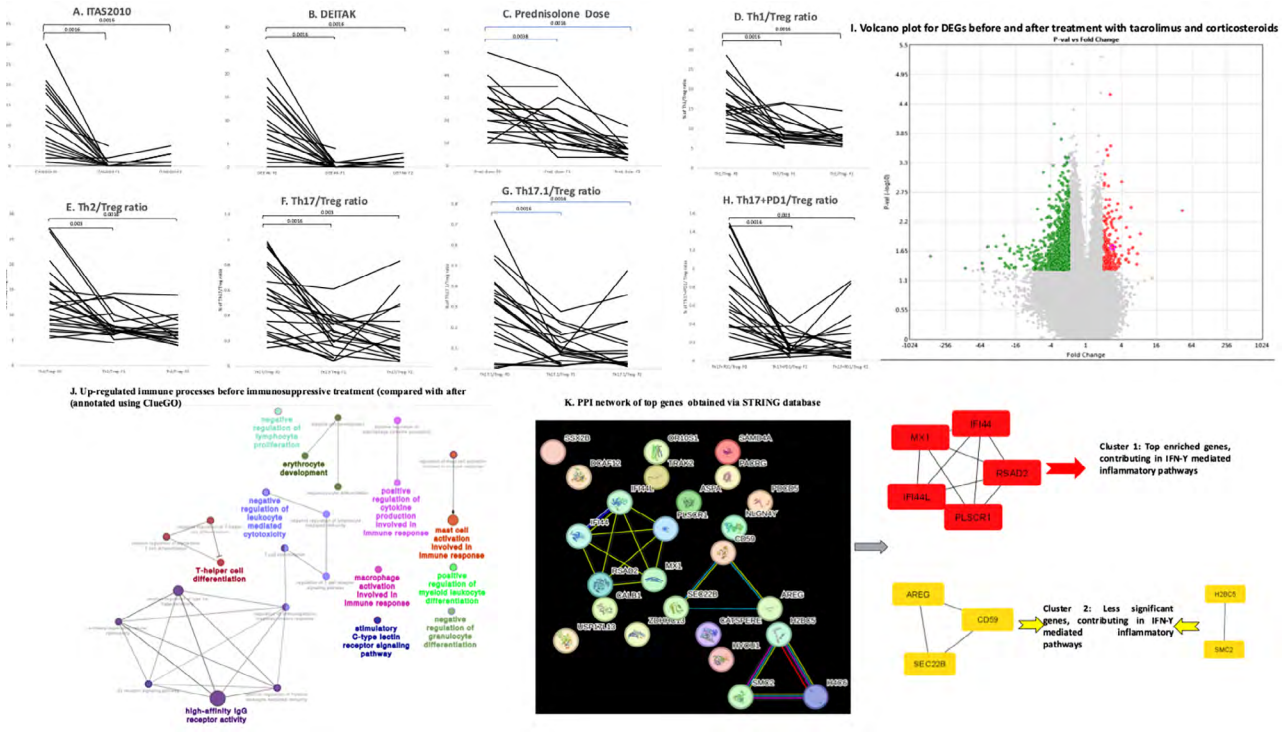

Figure 1: Serial changes in A.ITAS2010 B.DEI.TAK C.Daily prednisolone dose D.Th1:Treg E.Th2:Treg F.Th17:Treg G.Th17.1:Treg and H.PD1+Th17:Treg before, 3 months, and 6 months after treatment with tacrolimus and corticosteroid. I. Volcano plot of DEGs J. Up-regulated immune processes before immunosuppressive treatment K. PPI and hub gene analysis of proteins and genes following immunosuppressive treatment.

P-209

Rituximab treatment of ANCA-associated vasculitis is accompanied by changes in CD4⁺ T cell populations

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Background/ Objectives: B cell depletion by rituximab (RTX) is commonly used to treat anti-neutrophil cytoplasmic antibody associated vasculitis (AAV) but the mechanisms are not fully understood. The aim of this study was to elucidate the effect of RTX on T cell subpopulations in a large cohort of AAV patients.

Methods: Frequencies of the following T cell subpopulations were measured using flow cytometry: naïve, central memory, effector memory (EM) and effector cells of both CD4⁺ and CD8⁺ T cells, as well as Th1, Th2, Th17 and regulatory T cell (Tregs). Paired samples pre- and post-RTX from 20 patients constituted a discovery cohort. A validation cohort consisted of 31 treated and 62 untreated patients.

Results: The frequencies of Tregs increased after RTX treatment in both cohorts, from medium 3.2 to 3.9 % and 3.9 to 4.6 %, respectively (combined *p*=0.0037). There was also an increase in CD4⁺ EM (combined *p*=0.002). Post-hoc analysis suggests that the elevated levels of Tregs but not levels of CD4⁺ EM wane off with time. Maximum Tregs levels were seen 4-5 months after RTX (Figure 1). Other immunosuppressives given to non-RTX treated patients may explain some of the apparent RTX effect.

Conclusions: RTX seems to increase the number of Tregs and CD4⁺ EM cells, the change in Tregs is temporally associated with the clinical effect of RTX, but more research is needed before any conclusions can be made whether increases in Tregs mediate a beneficial effect of RTX in AAV patients and/or it can be used as a biomarker.

Disclosures: None.

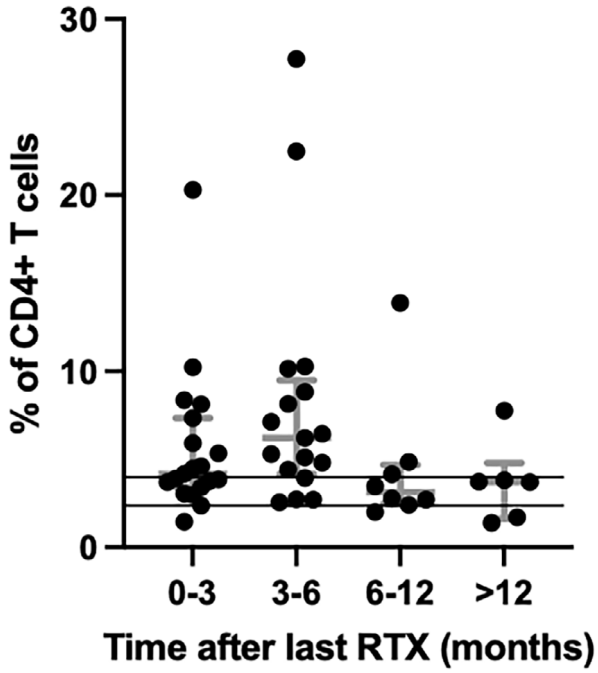

Figure 1. All samples taken after RTX are included and divided into four groups 0-3 months, 3-6 months, 6-12 months and >12 months after last RTX infusion. The horizontal lines in indicate the upper and lower 95% confidence intervals of healthy controls.

P-210

The Potential Role of Proinflammatory Cytokines IL-18 and IL-1B in Kidney Interstitial Damage in ANCA-Associated Vasculitis

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Background/ Objectives: Different components of the inflammasome system are quantitatively or functionally altered in ANCA-associated vasculitis (AAV), including the proinflammatory cytokines IL-18 and IL1B. IL-18 enhances neutrophil chemoattraction, whereas IL1B stimulates the release of other proinflammatory cytokines[1]. Interstitial damage in renal AAV is variable in incidence and grade, and influences the renal prognosis[2]. We aimed to investigate the distribution of three IL-18 and IL1B single nucleotide polymorphisms (SNPs) and the serum levels of these cytokines across the different grades of severity of interstitial lesions.

Methods: Patients with renal AAV were recruited and whole blood and serum were collected at diagnosis. Kidney biopsy was evaluated by an expert pathologist, and interstitial lesions—fibrosis, atrophy, and cell infiltrate—were graded according to their extension into: absent (<25%), mild (25-50%), moderate (50-75%), or severe (>75%). Serum IL18 (sIL-18) and IL1B (sIL1B) levels were measured by ELISA according to the manufacturer's instructions. DNA was extracted from whole blood and genotyped using the TaqMan assays (IL-18 rs187238 and rs1946518, and IL1B rs1143634).

Results: Ninety-two patients were recruited. sIL-18 levels were lower in patients with severe interstitial infiltrate (145.6 pg/mL (IQR 70.1-187.1) vs 307.5 pg/mL (IQR 129.7-652.7), p 0.049), and the grade of the interstitial infiltrate showed negative correlation with sIL-18 (rho -0.358, p 0.023). The IL-18 (rs187238) G-carrier genotype was associated with severe interstitial infiltrate (OR 4.033 IC95% 1.02-14.31, p 0.042). Additionally, G-carrier patients had lower sIL-18 levels compared to CC (145.5 pg/mL (IQR 60.2-514.5) vs 384.8 pg/mL (IQR 177.4-830.2), p 0.026). No differences were seen in the distribution of IL-18 (rs1946518) genotypes according to the extent of the interstitial lesions.

sIL-1B was higher in patients with absent to moderate interstitial fibrosis compared to patients with moderate to severe fibrosis (1.132 pg/mL (IQR 0.44-1.59) vs 0.13 (IQR 0-0.62), p 0.002). It was negatively correlated with the grade of interstitial fibrosis (spearman rho -0.467, p 0.005) and atrophy (spearman rho -0.381, p 0.034). However, no differences were observed in the distribution of IL-1B (rs1143634) genotypes.

Conclusions: Serum IL-18 and IL-1B levels were negatively correlated to interstitial damage in renal AAV. In addition, the IL-18 (rs187238) G-carrier was associated with less serum IL-18 and with a higher risk of developing severe interstitial infiltrates, confirming the role of both interleukines in the interstitial lessions.

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Disclosures: None.

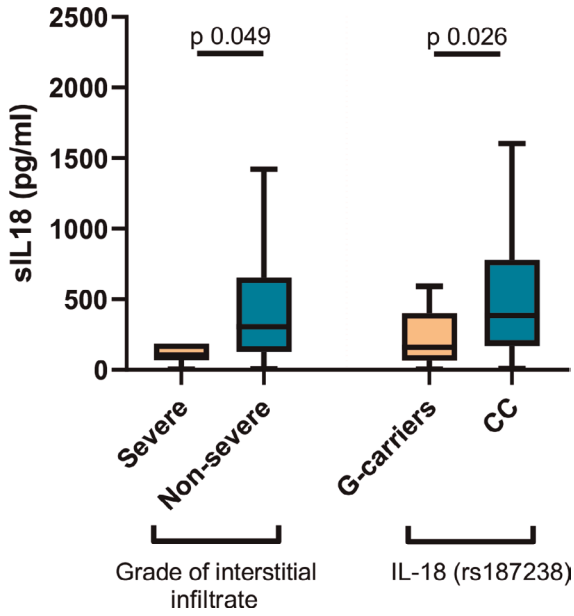

Figure 1. IL-18 levels were lower in patients with severe interstitial infiltrates in kidney biopsy and patients with IL-18 (rs187238) G-carrier genotype.

P-211

Interferon-alpha stimulatory capacity of phosphodiester double-stranded CpG-motifs in DNA

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Recognition of unmethylated CpG motifs by Toll-like receptor 9 (TLR9) is an innate immune mechanism that detects microbial DNA and leads to immune responses like interferon-alpha (IFNα) production. A similar mechanism may occur in inflammatory autoimmune diseases including Systemic Lupus Erythematosus (SLE) and ANCA-associated vasculitis. Most studies involving CpG utilise single-stranded phosphorothioate DNA (ssDNA) rather than double-stranded (dsDNA) phosphodiester motifs as found in genomic DNA. To address this gap, we evaluated the interferogenic potential of 136 different phosphodiester dsCpG motifs by systematically altering their CpG flanking bases, covering all possible combinations.

Method: Phosphodiester dsDNA sequences, each containing four identical repeats of CpG motifs were complexed with LL-37 for one hour. These complexes were incubated with PBMC samples from five healthy individuals, in six replicates, over 24 hours. We then measured supernatant IFNα concentration through ELISA in a high-throughput system.

Results: Each oligodeoxynucleotide demonstrated remarkable consistency in its stimulatory capacity. A strong stimulator in one responder is likely to be strong across all five healthy responders. Conversely, a poor stimulator is likely to be poor across all individuals. We calculated the mean stimulatory index for each oligodeoxynucleotide. All 136 double-stranded CpG-oligodeoxynucleotides were ranked starting from the motif with the highest to the lowest index. Remarkably, the conversion of the second strongest ds-CpG motif to ds-GpC motif rendered it worse than the weakest ds-CpG motif. This finding confirmed our experimental system was TLR-9 dependent. Our findings offer a potential tool to interrogate the stimulatory capacity of extracellular DNA in SLE and AAV.

Dislosures: None.

P-212

Aberrant oxidation of neutrophil myeloperoxidase in ANCA-associated vasculitis possibly relates to production of MPO-ANCA

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Objective: Mechanism of MPO-ANCA production, especially how myeloperoxidase (MPO) acquires the antigenicity, is still unknown. To address this issue, we analyzed post-translational modifications (PTMs) of MPO from MPO-ANCA-positive patients with ANCA-associated vasculitis (AAV).

Methods: MPO proteins were purified from neutrophil lysates obtained from 8 MPO-ANCA-positive patients with AAV and 8 healthy individuals by using Con A columns. The purified MPO proteins were digested with trypsin. Ion intensity and amino acid sequences including PTMs of MPO-derived peptides were comprehensively analyzed by nano-liquid chromatography-mass spectrometry.

Results: Ion intensity of 38 MPO-derived peptides was increased in the MPO-AAV group compared to that in the healthy group ($p<0.05$). 9 out of the 38 peptides included oxidation of Met, Phe, and Trp. Conversely, ion intensity of 10 MPO peptides was decreased in the MPO-AAV group compared to that in the healthy group ($p<0.05$). 4 out of the 10 peptides included glycosylation. Oxidized mouse MPO-immunized mice produced not only anti-oxidized MPO antibodies but also anti-MPO antibodies, whereas no preferential production of both antibodies was found in non-oxidized MPO-immunized mice ($p<0.05$).

Conclusions: The PTM profile of MPO of MPO-AAV patients was different from that of healthy individuals, including an increased oxidation. The oxidation of MPO may be a trigger of MPO-ANCA production.

Conflicts of Interest: None.

P-213

A novel cathepsin C inhibitor suppressed neutrophil serine protease activities and neutrophil extracellular trap formation *in vivo*

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Background/ Objectives: MPO-ANCA-induced neutrophil extracellular traps (NETs) are critically involved in MPO-ANCA-associated vasculitis (MPO-AAV) [1]. Neutrophil serine proteases (NSPs) such as neutrophil elastase (NE) and proteinase 3 (PR3) are granule-associated proteases primarily known for their roles in the intracellular killing of pathogens [2]. Cathepsin C (CatC) functions as a key enzyme in the maturation of NSPs and converts the inactive forms to the active forms by digesting dipeptides at the N-terminus during neutrophil differentiation in bone marrow [3]. Because NSPs, especially NE, are critically involved in the pathway leading to NET formation, targeting CatC to prevent the maturation and activation of NE could be a novel way to suppress NET formation. This study demonstrates that pharmaceutical inhibition of CatC can reduce the activity of NSPs including NE and inhibit MPO-ANCA-induced NET formation in vivo.

Methods: Human bone marrow (BM)-derived hematopoietic stem cells were cultured with G-CSF to differentiate into neutrophils under the presence of novel CatC inhibitor MOD06051 (0-10 μM). Eight days later, the NE activity and PR3 activity were measured. Normal rats were orally administered with MOD06051 (0, 0.3, 3, or 10 mg/kg, bid) for 2 weeks and the NE activity in bone marrow polymorphonuclear cells (PMNs) was determined. Normal rats were orally administered with vehicle or MOD06051 (3 mg/kg, bid) for 2 weeks. Peripheral blood neutrophils were primed with C5a or TNF-α, stimulated with MPO-ANCA immune complexes, and subjected for flow cytometry to detect NETs.

Results: MOD06051 suppressed NE and PR3 activities in in vitro differentiated human neutrophils. NE activity in rat bone marrow PMNs was decreased by MOD06051 dose-dependently. MPO-ANCA-induced NET formation in neutrophils derived from MOD06051-administered rats was low compared with vehicle controls regardless of priming factors.

Conclusions: MOD06051 suppressed NE activity and MPO-ANCA-induced NET formation in vivo. MOD06051 does not possess a direct inhibitory effect against NE, these inhibitions are considered to be caused by disruption of the CatC-mediated NE maturation that occurs during differentiation from bone marrow stem cells to neutrophils. MOD06051 is worth considering as a therapeutic agent for MPO-AAV.

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Disclosures: Modulus Discovery, Inc.

P-214

Mitochondrial-mediated inflammation and platelet activation in giant cell arteritis

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Background/Objectives: Mitochondria can be extruded via platelet activation and be immunogenic when misplaced extracellularly. As we discovered markers of extracellular mitochondria in patients with giant cell arteritis (GCA), we investigated whether extracellular mitochondria could activate peripheral blood mononuclear cells (PBMC) and platelets in GCA.

Methods: Pure mitochondria were isolated from HepG2 cells and opsonized with plasma from either GCA patients (n=58) or healthy controls (HC, n=10). Washed, opsonized mitochondria were then incubated with PBMCs or platelets to determine the capacity of opsonized mitochondria to promote inflammatory cytokine production and platelet activation.

Results: GCA plamsa promoted mitochondrial-mediated cytokine production (IL-1β, IL-6, IL-8, and TNF-α) by PBMCs as compared to HC (p=0.04, p=0.02, p<0.001, and p=0.002, respectively). Mitochondria opsonized with GCA plasma induced markedly higher platelet activation than mitochondria opsonized with plasma from HC (p=0.0015). Platelet activation as assessed by measuring levels of P-selectin via flow cytometry were associated with disease activity in GCA (r=0.34, p=0.01).

Conclusions: GCA patients have impaired ability to regulate the clearance of extracellular mitochondria, possibly contributing to excessive inflammation and platelet activation. Targeting key regulators of mitochondrial extrusion and/or their clearance could reduce inflammation and thrombosis leading to new therapeutic interventions in GCA.

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Disclosures: The authors have no relevant disclosures to disclose for this abstract.

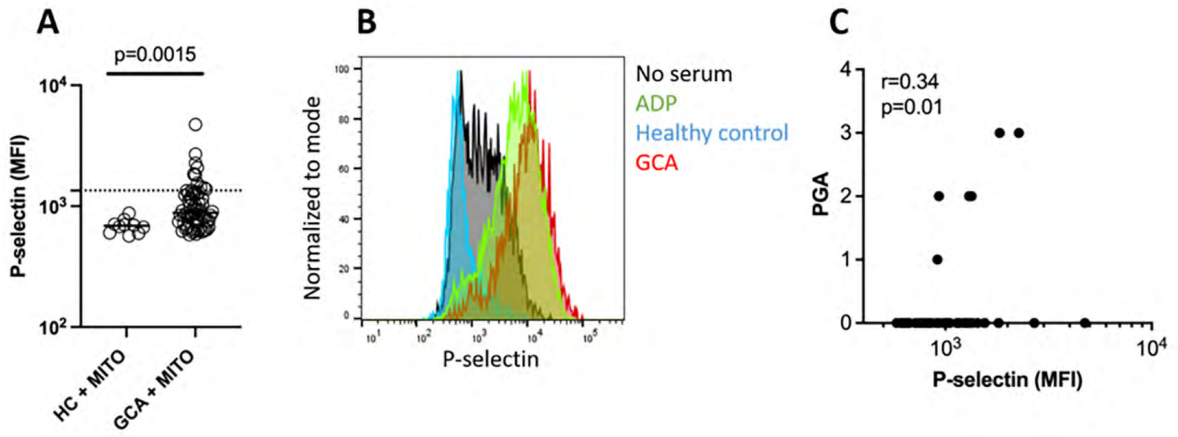

Figure 1. Mitochondrial-mediated platelet activation in giant cell arteritis. A) Platelet P-selectin was measured by flow cytometry after platelet-rich plasma from a healthy individual was exposed to mitochondria (mito) in the presence of plasma of GCA patients (n=58) or healthy controls (HC, n=10). B) Representative histogram illustrating platelet activation (P-selectin) upon incubation with ADP (green), or mitochondria opsonized with medium control (black), plasma from healthy control (blue) or from patient with GCA (red). C) Correlation between Physician Global Assessment (PGA) in patients with GCA and in vitro-induction of P-selectin on platelets from a healthy individual upon exposure to mito in the presence of GCA plasma. Statistical analyses by Mann-Whitney U test (A) and Spearman's correlation (C). The dotted line (A) represents the induction of P-selectin by non-opsonized mitochondria.

P-215

In Vitro Expansion of Regulatory T Cells Restores Suppressive Function in ANCA Vasculitis

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Background/ Objectives: Regulatory T cells (Tregs) are known to be functionally deficient in anti-neutrophil cytoplasmic autoantibody (ANCA) vasculitis. A major question has been how to restore suppressive function to Tregs in ANCA vasculitis patients.

Methods: Tregs defined as CD4+, CD127low, CD25high, and CD45RA+ were sorted from healthy controls and patients with ANCA vasculitis. Purified Tregs were then cultured *in vitro* using a 14-day expansion protocol. Expanded Tregs were analyzed by flow cytometry to determine any phenotypic changes and subjected to suppression assays with effector T cells to determine suppressive function.

Results: Tregs from both healthy controls and ANCA vasculitis patients expanded, on average, 1000-fold over the 14-day expansion period. Expanded Tregs maintained their phenotype (CD127low, CD25high, FOXP3+) in greater than 90% of samples. Interestingly, the mean fluorescence intensity of FOXP3 was highest in those patients in long-term remission off therapy when compared to other patients and healthy controls. In suppression assays, expanded Tregs were superior at controlling autologous effector T cell proliferation (range, 40-80% suppression).

Conclusions: *In vitro* expansion of Tregs is an effective approach to restore Treg suppressive function in patients with ANCA vasculitis. These studies are foundational for future clinical trials of Tregs as a therapeutic option in ANCA vasculitis.

References: None.

Disclosures: None.

P-216

The role of neutrophil-derived microparticles in complement activation in ANCA associated vasculitis

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Background: Recent studies emphasize the importance of the alternative complement pathway in the pathogenesis of AAV. Notably, the involvement of C5a and its interaction with neutrophil C5a receptors (CD88), leads to the recruitment of additional neutrophils (PMNs) (1). Moreover, it is well established that PMNs are pivotal in AAV pathogenesis, as they become activated by ANCA, releasing various inflammatory mediators. During this activation, PMNs release microparticles (MPs), the role of which in AAV pathogenesis is not fully understood (2,3).

This study aimed to stimulate PMNs from AAV and healthy controls (HC) with ANCA, to examine the expression of different complement proteins of the alternative pathway on the surface of MPs derived from PMNs from AAV patients and from HC and examine differences on the expression of these complement proteins between these groups.

Methods: PMNs from 5 AAV patients and 5 HC were isolated, primed, and stimulated with C5a and PR3-ANCA respectively. Two ELISA assays were used to measure MPO and lactoferrin, to verify the PMNs stimulation and degranulation. Both the supernatants from MPs and the unstimulated PMNs were incubated in two panels containing immunofluorescent antibodies of eight different proteins from the alternative complement pathway: C3, CD46, CD88, CD35 and C5L2, factor H, CD55, and properdin. Flow cytometry was performed to measure the expression of these proteins on the surface of the MPs originated from stimulated AAV-patient PMNs, from unstimulated PMNs from AAV patients, and from healthy controls. The Mann-Whitney U test was utilized for the statistical analysis.

Results: Unstimulated PMNs from AAV patients expressed higher levels of CD35 than from HC ($p=0,01$). CD88 was lower in PMNs from AAV patients than from HC ($p=0,0556$). Stimulation with PR3-ANCA did not cause greater degranulation of PMNs from AAV patients than of those from HC. MPs showed no significant complement factor expression differences between AAV patients and HC. However, MPO-ANCA-positive patients exhibited a slight increase in CD46 and C5L2 on MPs derived from MPO-ANCA-positive patients, suggesting that MPO-ANCA may influence complement factor expression on PMN-derived MPs.

Conclusions: This study unveils complement activation's potential role in AAV pathogenesis, focusing on PMN-derived MPs and their complement factor expression. Initial findings hint that CD35 could be a potential marker of previous inflammation or ongoing infection in AAV patients, and that MPO-ANCA patients influence the expression of CD46 and C5L2 on PMN-derived MPs.

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Disclosures: None.

P-217

Dysregulation of T cell interferon-gamma production in ANCA vasculitis

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Background/ Objectives: We have previously shown that B cells from patients with anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis during remission are unable to downregulate IFN-γ production by activated T cells from the same individual. This stands in contrast to healthy controls (HC) were a downregulation of IFN-γ was observed, despite similar levels of IL-10 (1). The aim of this study was to investigate the mechanisms related to the dysregulation of T cell IFN-γ production in patients.

Methods: T and B cells were isolated from patients with ANCA-associated vasculitis (*n=8*) in remission and from HC (*n=5*). T cells were activated by anti-CD3 and anti-CD28 antibodies and cultured with or without B cells for 4 days. To evaluate the effect of IL-10 on IFN-γ production by activated T cells from patients and HC, they were co-cultured with or without recombinant IL-10. Furthermore, T cells from HC were cultured with or without IL-10, together with plasma from HC, plasma from patients, IL-6, IL-15, or IL-18. IFN-γ levels in supernatants were measured with ELISA.

Results: IFN-γ production by activated $CD3^+$ T cells from HC were reduced when cultured with B cells. This regulation was attenuated when blocking IL-10 but not significantly with PDL1, CTLA4 or BTLA. Addition of recombinant IL-10 to $CD4^+$ T cells did, however, only suppress IFN-γ production in cells from HC (*p=0.013*) and not patients (*p=0.484*). The inhibitory effect of IL-10 on T cells from HC was also abolished if the cells were preincubated with patient plasma, IL-6, or IL-18 before activation (Fig. 1). Preincubation of HC T cells with plasma from HC or IL-15 did not affect the IL-10-mediated inhibition.

Conclusions: Suppression of T-cell IFN-γ production is mainly mediated by IL-10 in HC, but this regulatory mechanism appear to be absent in patients with ANCA-associated vasculitis. Our data suggests that T cell unresponsiveness to IL-10 is influenced by the local milieu rather than intrinsic differences between cells from patients and HC.

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Disclosures: None.

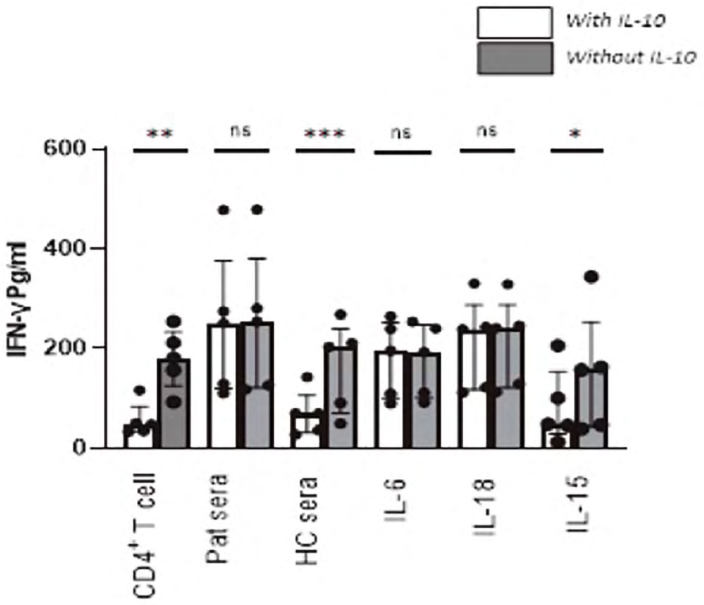

Fig. 1

P-218

Dysregulated NF-κB signalling in B lineage cells as potential therapeutic target in active ANCA-associated vasculitis

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Background: B lineage cells are critically involved in ANCA-associated vasculitis (AAV), as evidenced by alterations in circulating B cell subsets and beneficial clinical effects of rituximab (anti-CD20) therapy. This treatment renders a long-term, peripheral B cell depletion, but allows for the survival of long-lived plasma cells. Therefore, there is an unmet need for more reversible and full B lineage cell targeting approaches. The (non-)canonical NF-κB signalling pathways regulate fundamental B and/or plasma cell responses downstream of various surface receptors (B cell receptor, CD40, and TLRs) and may be suitable candidates.

Methods: Gene expression profiles from memory B cells (Bmem) obtained from AAV patients (active/remission) and healthy donors (HD) were generated by RNA-sequencing. Functional assays combined the stimulation of PMBCs from AAV patients and HD mimicking T cell-dependent (anti-CD40/IL-21/anti-IgM) and T cell-independent (CpG/IL-2) conditions, and the use of pharmacological inhibitors of Inhibitor-of-κB-kinase-β (IKKβ, canonical pathway) or NF-κB inducing kinase (NIK, non-canonical pathway). After 6 days, B cell proliferation and differentiation were determined by flow cytometry, and (auto)antibody production was detected by ELISA. Downstream NF-κB signalling was determined by Western blot.

Results: RNA sequencing of CD27+ Bmem of patients with AAV revealed an up-regulated NF-κB-associated gene signature in active disease, together with an up-regulated signature characteristic of plasma cells. Moreover, preliminary single-cell (sc) RNA sequencing of kidney biopsies in active AAV revealed the presence of distinct B and plasma cell populations in these target tissues. We demonstrated that small inhibitors of IKKβ and NIK could effectively block the canonical and non-canonical NF-κB pathways, respectively, while not affecting T cell responses. Moreover, both inhibitors significantly reduced B cell proliferation, differentiation and production of antibodies, including autoantibodies directed against proteinase-3 (PR3), by AAV B lineage cells.

Conclusions: RNAseq analysis of Bmem in active AAV patients exhibit upregulated NF-κB signalling and plasma cell associated genes, and scRNAseq of kidney biopsies revealed the presence of B and plasma cell populations in target tissue. Moreover, the reduction of key functional B cell responses, including autoantibody production by pharmacological NF-κB inhibitors while T cell responses were largely unaffected, highlight the potential of targeting NF-κB signalling as a novel B lineage-directed therapy for AAV.

Disclosures: Nothing to disclose.

P-219

Clinicopathologic associations between macrophage phenotype and topography in giant cell arteritis

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Background: Macrophages play a central role in the pathogenesis of giant cell arteritis (GCA), but few studies have correlated macrophage phenotype or topography from temporal artery biopsy specimens with clinical outcomes, such as the large vessel vasculitis index of damage (LVVID).

Methods/Objectives: Patients from the Vasculitis Clinical Research Consortium (VCRC) Longitudinal Study of GCA with linked temporal artery biopsy specimens in the VCRC Tissue Repository were included. Temporal artery tissue was stained using immunofluorescent antibodies to CD3 (T Cells), CD4 (T cells), FoxP3 (T Regs), CD68/CD86 (inflammatory "M1" macrophages), and CD68/CD163/CD206 (remodeling "M2" macrophages) using an Opal 7-Color Automation IHC Kit. The relative proportions of these cell types as a percent of the total number of cells in the adventitia and intima were calculated. Associations between macrophage location (adventitia, intima) and phenotype (M1 or M2) and the LVVID were evaluated using t testing and the Kaplan-Meier estimate.

Results: 40 patients had biopsy specimens available for analysis. The average age was 69.9 years (standard deviation [SD] 9.1), all patients were white, and 21/40 (52.5%) were male. The mean LVVID score was 1.4 (SD 2.2) at baseline; over the first year of observation 4 patients developed damage on the LVVID (4/40, 11.4%, mean follow up time 314 days, SD 118 days). In unadjusted analysis over the first year of observation, there was no association between developing damage on the LVVID and the relative abundance of intimal M1 macrophages (1.8% vs. 0.7% developed damage, p = 0.12), adventitial M1 macrophages (2.0% vs 1.2% developed damage, p = 0.53), intimal M2 macrophages (2.9% vs. 1.4% developed damage, p = 0.37), or adventitial M2 macrophages (3.7% vs. 2.4% developed damage, p = 0.61). There were also no associations identified for CD3+ or CD4+ T cells, but the relative abundance of adventitial FoxP3+ (TReg) cells was associated developing damage on the LVVID (2.8% vs. 1.0% developed damage, p = 0.04). When the analysis period was extended to include the entire observation period, half of patients developed damage on the LVVID (20/40, 50%, mean follow up time 1,109 days, SD 962 days. In unadjusted analysis over the entire observation period, there were no additional associations identified between developing damage on the LVVID and either macrophage location (intima or adventitia) or phenotype (M1 or M2). A time to event analysis using a Kaplan-Meier estimate supported these findings (**Figure**).

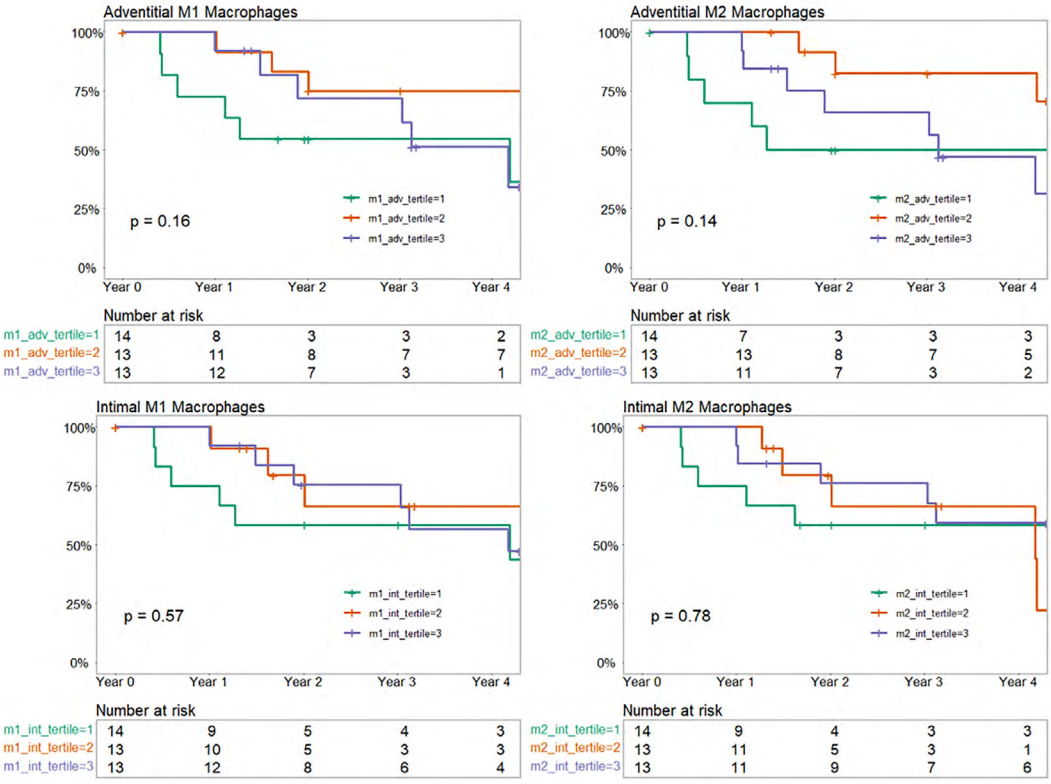

Figure 1: Estimate of time (days) to new damage on the Large-Vessel Vasculitis Index of Damage, stratified by macrophage phenotypes (n = 40) in temporal artery specimens from patients with giant cell arteritis.

Conclusions: Macrophage topography and phenotype from temporal artery biopsy specimens are not associated with the development of damage in patients with GCA.

References: None.

P-220

Phenotyping of senescent cells in giant cell arteritis and polymyalgia rheumatica biopsies using imaging mass cytometry

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Age is the most important risk factor for developing the inflammatory diseases Giant Cell Arteritis (GCA) and Polymyalgia Rheumatica (PMR). Ageing is also associated with the accumulation of senescent cells in the blood and tissues. Cellular senescence is a cell fate involving extensive changes to the functioning of the cell, including proliferative arrest and resistance to cell death. Importantly, senescent cells are not innocent bystanders; they release pro-inflammatory molecules. Recent studies have pointed at the presence of senescent cells in inflamed arteries of GCA patients. Here, we performed an in-depth characterization of senescence and phenotyping markers in GCA arteries, and expanded this analysis to PMR bursary biopsies.

We employed imaging mass cytometry (IMC) staining, using a 28-marker panel of metal-labeled antibodies, to phenotype senescent cells and their cellular lineage. Senescent cells were characterized by the expression of γH2AX, p16, p21 and GATA4, and the lack of Ki-67 and LaminB1 expression. We characterized immune and stromal cells using anti-CD45, CD14, CD68, CD3, CD4, CD8, CD20, MPO, CD31, CD34, vimentin and CD90 antibodies. We stained temporal artery biopsies (TABs) of GCA patients (inflamed, n=6), PMR patients (non-inflamed, n=4), and controls (n=5); subacromial bursa biopsies (SABs) of PMR patients (inflamed, n=6) and control (non-inflamed, n=1).

Inflamed TABs of GCA patients, and inflamed SABs op PMR patients, contain p16 or p21-expressing cells, which expressed γH2AX and GATA4, and lacked Ki-67 and LaminB1 expression (Figure 1). This definition was not fulfilled for all p16 and p21 expressing cells, particularly macrophages, indicating that a comprehensive antibody panel is required to identify senescent cells. Staining of p16 mostly overlapped with macrophage-rich areas (CD68+, CD206+), whereas most p21+ senescent cells lacked CD45 expression, and expressed Vimentin (mesenchymal cells). In GCA TABs, most senescent cells were found in the intima layer.

In this study, we identified and phenotyped senescent cells by IMC, which allows an in-depth characterization of the TABs and SABs. The presence of these senescent cells, that show signs of a DNA damage response (γH2AX expression) and transcription regulation of inflammatory cytokines (GATA4 expression), provides more information on the pathobiology of GCA and PMR. Further analyses will improve the quantification and phenotyping of the senescent cells in GCA and PMR, potentially allowing a rationale for the targeting of senescent cells by senolytics.

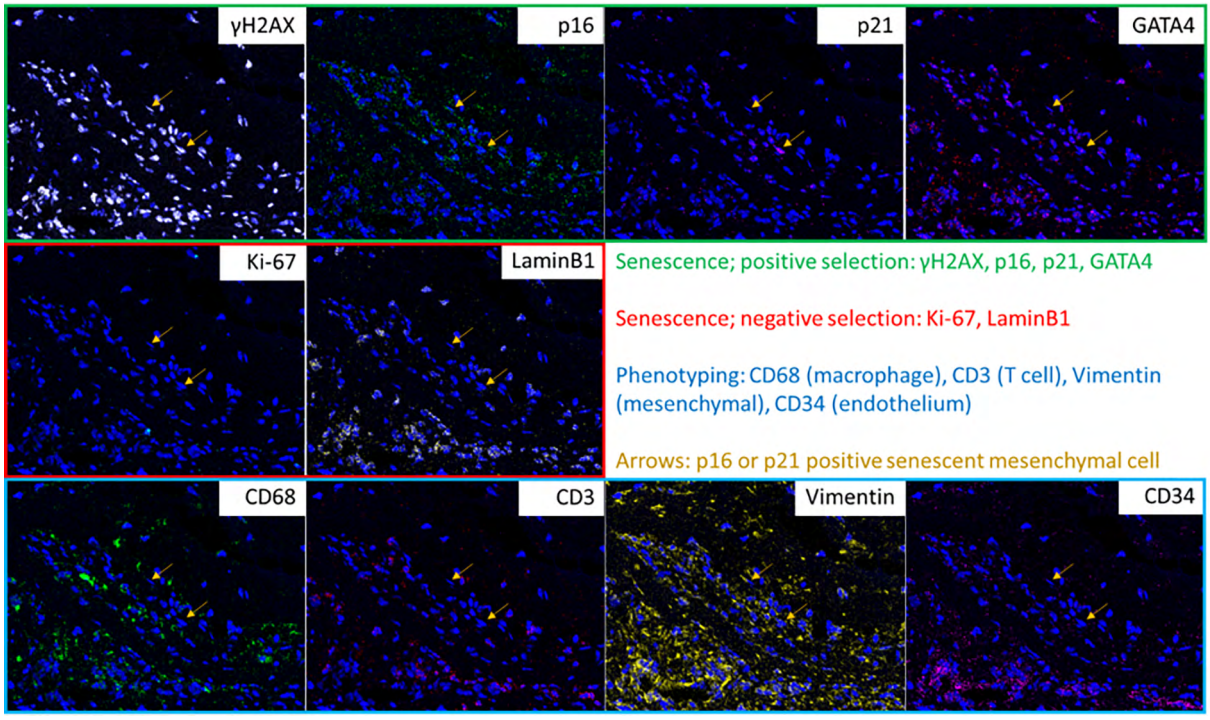

Figure 1: Identification of senescent cells in the intima region of the GCA TAB using IMC staining.

P-221

Abnormalities in Circulating Polymorphonuclear Cells in ANCA-Associated Vasculitis

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Background/ Objectives: In the pathogenesis of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), neutrophils play a crucial role, serving as both the target cells attacked by ANCA and the main participating cells in regulating the inflammatory process. [1]

Autoimmune and chronic inflammatory diseases can lead to abnormalities in leukocytes, particularly in polymorphonuclear cells (PMN), with neutrophils comprising the majority. Abnormal PMN morphologies may encompass hypo- and hyper-segmentation as well as immature forms. [2] There is a gap in the current literature regarding abnormalities in circulating leukocytes in patients in sustained remission.

The aim of this study is to investigate the different neutrophil phenotypes within three groups: granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA).

Methods: We collected blood samples from adult patients affected by GPA, MPA and EGPA, classified according to the EULAR/ACR criteria 2022, who attended the outpatients Vasculitis Clinic of Padua University. All patients were no longer taking steroid therapy and were in the remission stage, as per the EULAR/ACR definition. A control group of healthy subjects was enrolled. May-Graunwald-Giemsa (MGG) staining of peripheral blood smears was used for studying cellular morphology.

Results: Between may 2023 and November 2023, we enrolled 45 patients: 17 GPA patients, 12 MPA patients and 16 EGPA patients. Hence, we enrolled 13 matched healthy controls (HCs).

No differences were observed among the three groups of AAV patients with respect to female sex (GPA=47.5%, MPA=50%, EGPA=50%, p=0.982), age at sampling (median and IQR, GPA=54 [34-68], MPA=65 [52-78], EGPA=64 [54-71], p=0.139), disease duration at sampling (median and IQR, GPA=53 [41-143], MPA=87 [41-105], EGPA=65 [33-100], p=0.649), time from steroid discontinuation (median and IQR, GPA=33 [5-52], MPA=34[6-73], EGPA=33 [6-61], p=0.922), and ongoing immunosuppressive therapy at sampling (n and %, GPA=13 [76], MPA=9 [75], EGPA=9 [56], p=0.395).

A statistically significant increase in total PMN numbers was observed in AAV when compared to HC (HC 54.3 [50.8-58.6], GPA 73.4 [59.1-79.3], MPA 62.2 [52.4-67.5], and EGPA 59.6 [51.8-70.7], p=0.0139).

Hence, there was a statistically significant increase in the number of hypo-segmented in AAV patients (PMN: HC 7.6 [5.2-8.0], GPA 17.5 [14.8-20.8], MPA 12.15 [9.2-19.2], and EGPA 10.6 [8.8-13.2], p<0.0001). A statistically significant difference was observed between the EGPA and GPA groups, with p = 0.0302.

The number of hyper-segmented PMN was similar in the four groups. No differences were observed in monocytes, granulocytes, and lymphocytes.

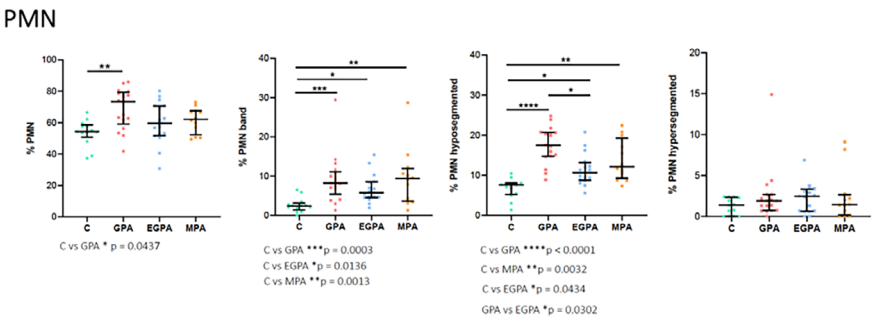
Conclusions: Patients with AAV exhibit statistically significant increase in the number of PMNs, particularly in the count of hypo-segmented PMNs. Further prospective studies involving larger cohorts are needed to confirm these differences and explore whether distinctions exist between active and inactive patients.

References:

1. Ge S et al.. *Front Pharmacol*. 2022;13:957660.
2. Baggio C et al.. *Int J Mol Sci*. 2023;24(6):5450.

Disclosures: None.

PMN



mediana ± IQR (%)	C	GPA	EGPA	MPA	p
PMN	54.3 (50.8-58.6)	73.4 (59.1-79.3)	59.6 (51.8-70.7)	62.2 (52.4-67.5)	0.0139
PMN band	2.4 (1.4-3.2)	8.2 (5.4-11.1)	5.8 (4.6-8.6)	9.4 (3.6-11.9)	0.0002
PMN hyposegmented	7.6 (5.2-8.0)	17.5 (14.8-20.8)	10.6 (8.8-13.2)	12.15 (9.2-19.2)	< 0.0001
PMN hypersegmented	1.4 (0.0-2.4)	1.9 (0.8-2.7)	2.5 (0.6-3.3)	1.5 (0.2-2.7)	ns

Kruskal-Wallis, HC *n* = 13; GPA *n* = 17; EGPA *n* = 16; MPA *n* = 12

P-222

Investigating the mechanism of anti-MPO driven pro-inflammatory cytokine release in monocytes

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Background/ Objectives: ANCA-associated vasculitides (AAV) are a group of rare systemic autoimmune diseases that affect small to medium sized blood vessels. Clinical and experimental data suggest that the pathogenesis of these diseases is driven by ANCA-mediated activation of monocytes and neutrophils. The objective of this research is to understand the molecular mechanism by which anti-MPO/PR3 antibodies drive pro-inflammatory cytokine release, focusing on Inflammasome activity, in monocytes and to explore novel inhibitors of this.

Methods: Monocytes were purified by positive selection from the peripheral blood mononuclear cells (PBMCs) of healthy volunteers using CD14 magnetic beads. Isolated monocytes primed for 1 hour with 1ng/ml of lipopolysaccharide (LPS) followed by stimulation for 4 hours with monoclonal anti-MPO or anti-PR3 antibodies. Supernatants were analysed by ELISA for IL-1β production, and cell lysates were lysed for Western blot analysis. Selected supernatants were also analysed using the O-link proteomic platform to provide insight into other ways in which anti-MPO and anti-PR3 stimulation affect the cytokine release from monocytes.

Results: We observed increase in IL-1α, ST1A1, IL-18, CSF-1 and various other proinflammatory cytokines following stimulation with a combination of LPS and anti-MPO. Stimulation of primary human monocytes with LPS and monoclonal anti-MPO (864pg/ml, 387.7-2062, IQR) / anti-PR3 (113.4pg/ml, 75.13-302.9, IQR) drives IL-1β secretion significantly in comparison to LPS and isotype control (56.09pg/ml, 39.50-143, IQR) (Figure 1). Western blot analysis of the lysates generated following stimulation have provided insights into the mechanistic role that anti-MPO plays in the induction, processing, and release of mature IL-1β. Using this system we have also investigated the capacity of novel anti-inflammatory, virus derived peptides that have been developed in house. Early findings have shown the potential therapeutic value of these peptides to decrease IL-1β production following stimulation.

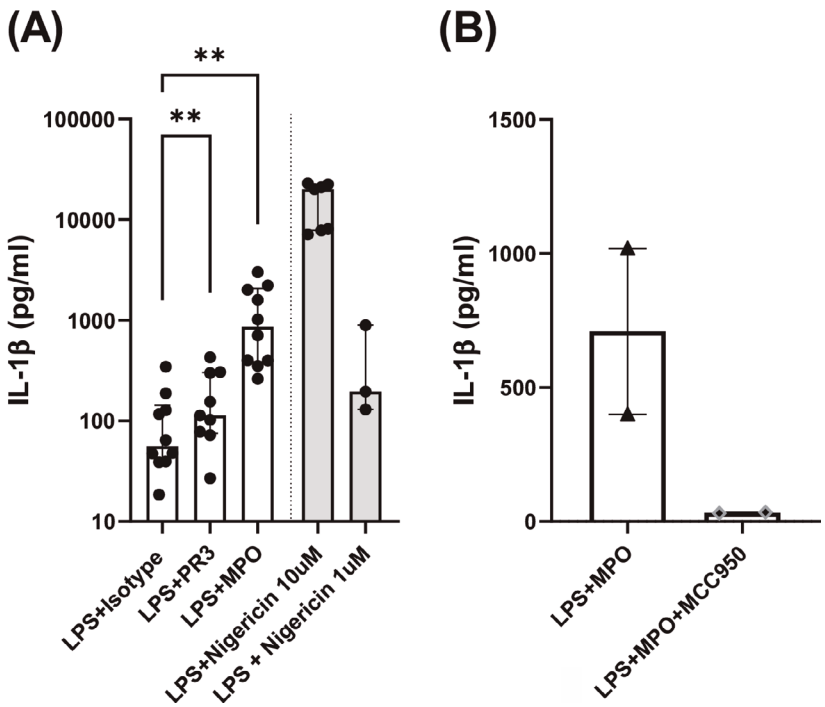

Figure 1. Monocytes isolated by CD14 positive selection were plated in 96 well plates and stimulated with a combination of LPS with either an isotype control, anti-MPO, anti-PR3 or nigericin. (**A**) Stimulation with LPS and either anti-MPO or anti-PR3 causes a significant increase in IL-1β production when compared to the isotype control. (**B**) Pre-treating of the monocytes with 1μM of MCC950, an NLRP3 inflammasome inhibitor, inhibits the production of IL-1β previously seen by stimulation with LPS and anti-MPO.

Conclusions: Anti-MPO cooperates with LPS to drive IL-1β release from primary human monocytes. The inhibition of IL-1β production when pre-treating with MCC950, a known NLRP3 inflammasome inhibitor, indicates that cooperatively LPS and anti-MPO are priming and activating the NLRP3 inflammasome.

References:

Disclosures: None.

P-223

Bruton's tyrosine kinase is a possible therapeutic target in MPO-ANCA-associated vasculitis

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Background/ Objectives: Bruton's tyrosine kinase (Btk) is an enzyme expressed in leukocytes other than T lymphocytes and plasma cells and involved in B-cell receptor- and Fcg receptor (FcgR)-mediated signal transduction [1]. Btk inhibitors potentially suppress autoantibody production due to the expected inhibitory ability of B lymphocyte differentiation into antibody-producing plasma cells and reduce FcgR-mediated neutrophil activation, including the release of neutrophil extracellular traps (NETs). Myeloperoxidase (MPO)-antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (MPO-AAV) is a systemic small-vessel vasculitis characterized by the pathogenic autoantibody, MPO-ANCA. MPO and MPO-ANCA immune complex (MPO-ANCA-IC)-induced FcgR-mediated NETs are critically involved in MPO-AAV pathogenesis [2]. This study aimed to demonstrate the therapeutic efficacy of the Btk inhibitor tirabrutinib on MPO-AAV.

Methods: Various doses of tirabrutinib or vehicle were orally administered to Sprague-Dawley rats daily. Four weeks later, the number of peripheral B lymphocytes was counted, and Btk phosphorylation in B lymphocytes was evaluated by flow cytometry. Human peripheral blood neutrophils were stimulated by MPO-ANCA-ICs, and Btk and its downstream Vav phosphorylation was assessed by western blotting. The effects of tirabrutinib on MPO-ANCA-IC-induced NET formation were examined *in vitro*. Wistar Kyoto rats were immunized with human MPO to induce MPO-AAV and given drug-free or tirabrutinib-containing feed (0.0037% or 0.012%) from day 0 or 28. All rats were euthanized on day 42 for serological and histological evaluation.

Results: Tirabrutinib inhibited Btk phosphorylation without decreasing B lymphocytes *in vivo*. Neutrophil Btk and Vav were phosphorylated when stimulated with MPO-ANCA-ICs. Tirabrutinib suppressed MPO-ANCA-IC-induced NET formation *in vitro* and ameliorated MPO-AAV in a dose-dependent manner. Although MPO-ANCA production was not affected, NET-forming neutrophils in the blood were significantly reduced by tirabrutinib.

Conclusions: The Btk inhibitor tirabrutinib suppressed MPO-ANCA-IC-induced NET formation *in vitro* and ameliorated MPO-AAV by reducing NET-forming neutrophils but not decreasing MPO-ANCA titer *in vivo*. This study suggests that Btk is a possible therapeutic target in MPO-AAV.

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2. Nakazawa D, Masuda S, Tomaru U, Ishizu A: Pathogenesis and therapeutic interventions for ANCA-associated vasculitis. Nat Rev Rheumatol 2019;15:91-101.

Disclosures: Ono Pharmaceutical Corp. Ltd.

2. TRANSLATIONAL SCIENCE
2.04. Mechanisms of tissue injury: oxidative damage, proteases, apoptosis, extracellular traps...

P-224

Western-blotting neutrophil extracellular traps (NETs): technical contributions to the study of the vasculitides

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Background/Objectives: The role of neutrophil extracellular traps (NETs) in some of the vasculitides seems undeniable. To gain a clearer understanding of their function, it is essential to unravel their intricate structure. They consist of a framework of DNA and proteins, and their composition and concentration can vary according to the environment (*in vitro* or *in vivo*)[1]. Therefore, there is no standard technique to quantitatively measure the presence and concentration of their proteins, and although Western blot could serve this purpose, there is wide variation in the methodology employed. In this study, we evaluated various aspects of the technique, such as stimulus duration, sample separation and loading controls.

Methods: Blood samples collected in ethylenediaminetetraacetic acid (EDTA) tubes were processed using Polymorphprep (Serumwerk) to isolate neutrophils. Their viability was assessed using trypan blue staining. The quality of the samples was evaluated by flow cytometry using the BD FACSAria II analyzer, with specific antibodies: CD66b-FITC, CD11b-PE, and CD16-APC. Neutrophils were stimulated with 20 nM Phorbol 12-myristate 13-acetate (PMA) for varying time intervals (0, 0.5, 1, 2, 3, and 4 hours). Antibodies against myeloperoxidase and Hoechst 33342 were used to stain NETs.

After stimulation, DNase1 was added, and proteins were precipitated with acetone. The precipitate was resuspended in radioimmunoprecipitation assay buffer, and cellular lysates were obtained. NETs and cellular lysates were separated by SDS-PAGE, transferred to polyvinylidene fluoride membranes, and probed with antibodies against human cathelicidin hCAP18/LL-37 (chosen as NETs associated protein), β-actin, and glyceraldehyde-3-phosphate dehydrogenase (GAPDH). Chemoluminescence imaging was used for band detection.

Results: For quantitative measurement of NET-associated proteins, it is essential to use a loading control with constant expression. Neither GAPDH nor β-actin proved suitable due to their expression. The blot revealed two hCAP18/LL-37 bands. The lower hCAP18/LL-37 band in cell lysates showed a decrement, becoming significant only at 4 h, while in NETs samples the upper band increased from 0.5 h to a peak at 1 h, gradually decreasing until 4 h (Figure 1).

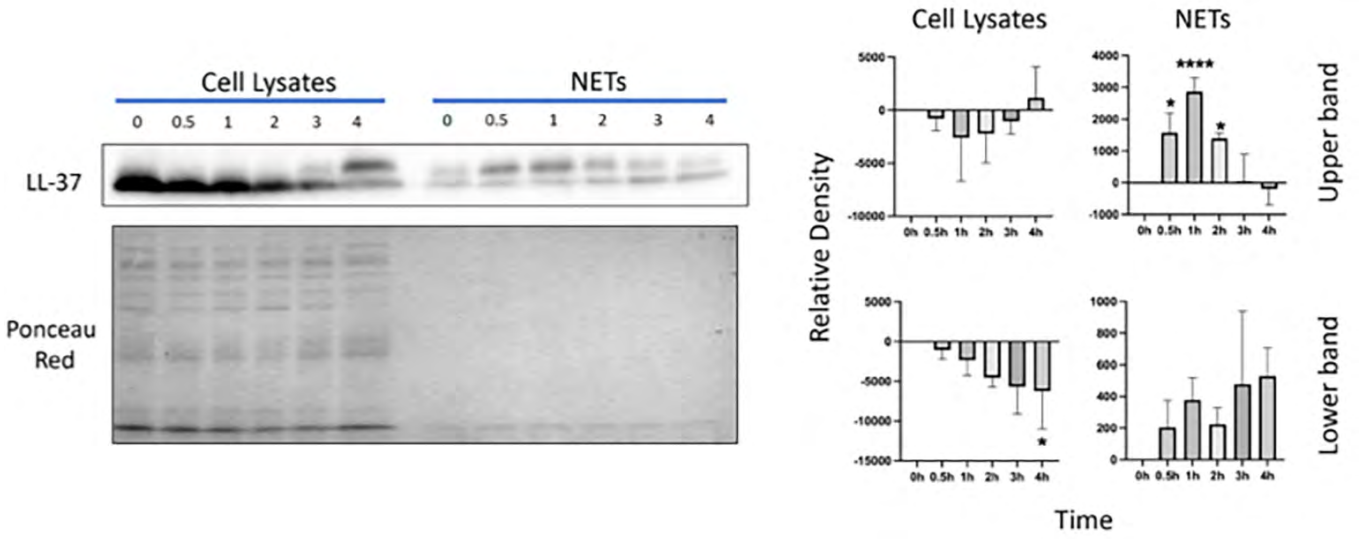

Figure 1: Evaluation of hCAP18/LL-37 as a NET-associated protein on NET-releasing neutrophil samples.

Conclusions: Our findings underscore the critical importance of segregating protein samples from cell lysates and those derived from NETs to prevent erroneous interpretations. This was evident for hCAP18/LL-37. While many articles examine proteins at 4 hours, our study revealed that concentration peaks may occur earlier.

References: Bruschi M *et al.* Neutrophil Extracellular Traps protein composition is specific for patients with lupus nephritis and includes methyl-oxidized α-enolase (methionine sulfoxide 93). *Sci Rep* 2019;9:7934.

Disclosures: Supported by Consejo Nacional de Humanidades, Ciencias y Tecnologías, Mexico. Project number: 304041.

P-225

Complement mRNA Expression in Patients with ANCA-associated Glomerulonephritis

Salem Almaani[1], Arnon Arazi[2], Huijuan Song[1], Pearlly Yan[1], Estela Puchulu-Campanella[1], Hubao Wang[1], Lynn Fussner[1], Brad Rovin[1], Samir Parikh[1].

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Background: The role of complement in patients with ANCA-associated vasculitis (AAV) has been increasingly appreciated and led to the use of complement system antagonists as a therapeutic strategy. However, it is unclear whether complement system activation occurs in affected organs such as the kidneys. This study aimed to characterize complement gene expression in patients with AAV with renal involvement (AAGN).

Methods: Whole-tissue RNA-sequencing was performed on kidney biopsy samples of 23 patients with AAGN, and 5 healthy kidney donors. After quality control, differential expression (DGE) analysis was performed using generalized linear models correcting for number of genes and batch effects. This abstract describes mRNA expression of 42 complement system proteins, receptors, and regulators. For this analysis, differential expression was considered statistically if the FDR-corrected p-value <0.05, and the absolute value of log2 fold change between groups was > 0.6 ($|\log_2 FC| > 0.6$).

Results: Patients' clinical and demographic characteristics are depicted in **Table 1**. Most patients were female (13/23), White (21/23), and had a median age of 58 years. Most patients had c-ANCAs and a granulomatosis with polyangiitis phenotype. DGE analysis revealed increased abundance of mRNA coding for proteins participating in the classical (C1q, C1r, C1s, C2, C4B), alternative (CFB, CFD), and common (C3, C7) complement pathways. In addition, there was an increase in abundance of the anaphylatoxin receptors (C3AR, C5AR). mRNA abundance of complement regulators (CFH, CD55, CD46, CR1) were not different compared to controls except for CR2 which was decreased in patients with AAGN.

Conclusion: Analysis of mRNA expression in kidneys of patients with AAGN reveals increased abundance of members of the classical and alternative complement pathways, anaphylatoxin receptors, without a concomitant increase in mRNA expression of complement regulatory proteins. Along with our previous finding of increased complement activation products in urine of patients with active AAGN, these data strongly suggest intra-renal complement system activation in patients with AAGN.

Disclosures: This work was supported by The Gilead Research Scholars in Rheumatology award.

Table 1. Patient and Disease Characteristics.

Age at biopsy, median (IQR)	58 (41-68)
% Female	59%
% White	95%
Newly diagnosed	95%
ANCA ELISA*	
anti-PR3	43% (10/22)
anti-MPO	43% (10/22)
both positive	5% (1/22)
negative	5% (1/22)
ANCA IIF	
c-ANCA	52% (12/23)
p-ANCA	30% (7/23)
*Negative***	17% (4/23)
Phenotype	
GPA	52% (12/23)
MPA	35% (8/23)
EGPA	13% (3/23)
Serum Creatinine, average ±SD	3.6 ±2.9

*not available in one patient
** all had detectable ANCAs by ELISA
Abbreviations: ANCA: antineutrophil cytoplasmic antibodies. PR3: proteinase 3. MPO: myeloperoxidase. c-ANCA: cytoplasmic ANCA. P-ANCA: perinuclear ANCA. GPA: granulomatosis with polyangiitis. MPA: microscopic polyangiititis. EGPA: eosinophilic GPA

P-226

C5a receptor 1/CD88 expression in ANCA-associated pauci-immune crescentic glomerulonephritis – a rationale for complement inhibiting therapy?

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Background/Objectives: Pauci-immune necrotizing crescentic glomerulonephritis (GN) is the histopathologic hallmark of ANCA-associated vasculitis (AAV). In AAV tissue damage is augmented by activation of the alternative complement pathway via the complement C5a receptor 1 (C5aR1, CD88). Complement inhibiting therapy with the oral C5aR1 blocker avacopan showed beneficial effects in AAV patients (1). Among patients with low eGFR avacopan improved kidney function even more in comparison to the standard glucocorticoid treatment regimen (2). Therefore, complement C5aR1/CD88 expression was studied retrospectively in routine kidney biopsy specimen from patients with acute ANCA-associated crescentic GN (AAGN).

Patients and Methods: We retrospectively included 15 patients (7x female, 8x male) with active AAGN (5x PR3-ANCA+, 8x MPO-ANCA+, 2x ANCA-). Mean age was 56,5 years and mean creatinine level was 4,3 mg/dl (min. 1,3 mg/dl, max. 13,9 mg/dl) at time of biopsy. Immunohistochemistry for CD88 was performed on remaining kidney biopsy specimens using a monoclonal rabbit anti-CD88 antibody.

Results: Compared to normal kidney tissue with only focal tubular expression of CD88, in AAGN CD88 was expressed in the glomerular (mesangial cells, glomerular epithelial cells, and endothelial cells) and interstitial compartment), whereas expression was scarce and weak in tubular cells and infiltrating neutrophils, respectively.

Conclusions: Using immunohistochemistry we demonstrate local expression of C5aR1 in the glomerular, vascular, and interstitial compartment in human kidney biopsies with AAGN. These data support the the known efficacy of C5a receptor blocking therapy of AAGN.

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Disclosures:

US: Study participation: Sanofi/Ablynx; Alexion/AstraZeneca; CSL Vifor/Chemocentryx; HansaBiopharma; Alentis Therapeutics. Advisory Board/Speaker fees: CSL Vifor; Sanofi; Alexion/AstraZeneca; Janssen.

2. TRANSLATIONAL SCIENCE
2.06. Biomarkers: diagnosis, prognosis, disease activity, predictors of response...

P-227

Activation of the overlooked classical complement pathway in Anti-neutrophil cytoplasmic antibody-(ANCA) associated vasculitis

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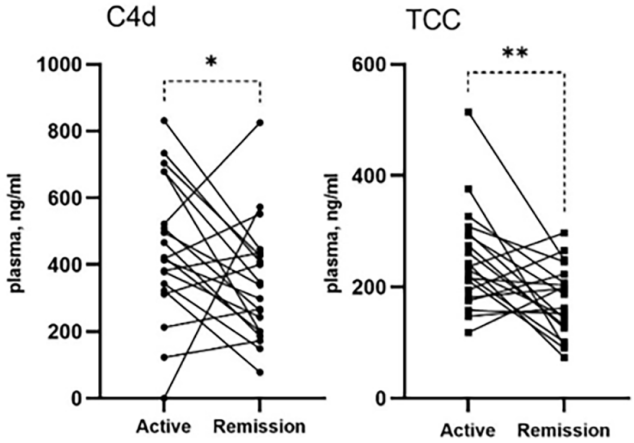
Background/Objectives: The alternative complement pathway is important in the pathogenesis of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). However, the evidence supporting the contribution of the classical or lectin complement pathway is less clear (1, 2). We aimed to investigate the involvement of the classical complement pathway in AAV in plasma by exploring the complement cleavage fragment C4d as a potential biomarker of AAV activity.

Methods: Plasma C4d was analysed by an enzyme-linked immunosorbent assay (ELISA) detecting an epitope that arises upon complement-mediated cleavage (SVAR Life Science). The plasma terminal complement complex (TCC) was analysed by ELISA. HLA-DRB1-typing and immunohistochemical staining of C4d in kidney biopsies were performed. Forty patients with active AAV were included (median Birmingham Vasculitis Activity Score, BVAS, 16). A follow-up sample obtained after induction therapy was available in 24 patients, of whom 20 had BVAS 0. Eighteen patients were males (45 %), and 24 (60 %) were anti-PR3 positive while 16 (40 %) were anti-MPO positive. The study included 27 (67.5 %) patients with GPA and 13 (32.5 %) with MPA. Thirty-three (82.5 %) patients had kidney involvement. For comparison 25 healthy controls were included.

Results: AAV patients with active disease had higher plasma levels of C4d and TCC compared to controls (median 420 ng/ml vs 209 ng/ml, p <0.001 and median 225 ng/ml vs 164 ng/ml, p = 0.005 respectively). A paired analysis revealed that levels of C4d and TCC were reduced in patients in remission (median 420 ng/ml vs 319 ng/ml, p=0.044 and median 233 ng/ml vs 174.5 ng/ml, p=0.009, n=20), Figure1. C4d levels in patients with active disease were higher in PR3-AAV patients than in MPO-AAV patients (median 522 ng/ml vs 361 ng/ml, p = 0.005). There was no difference in the frequency of HLA-DRB1*03 carriers between patients and controls or between patients based on diagnosis or serology. Patients with kidney involvement had lower levels of C4d than those without (median 400 ng/ml vs 679 ng/ml, p = 0.034). A positive correlation was seen between eGFR and C4d levels, r_s = 0.437, p = 0.005. C4d and TCC did not correlate with BVAS. Staining of C4d in kidney biopsies was negative.

Conclusions: The C4d assay revealed activation of the classical complement pathway in AAV, which reflected disease activity but not kidney involvement. This implies that the classical complement pathway may play a more significant role in AAV pathogenesis than previously thought and that plasma levels of C4d could potentially be used as a biomarker for disease activity.



Plasma levels of complement factors C4d, and Terminal Complement Complex (TCC)in AAV patients with active disease and remission, n=20.

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Disclosures: A.Blom: Patent on antibodies for C4d, WO2016038055A1.

P-228

Interstitial Fibrosis in ANCA-Associated Vasculitis: MPO vs PR3

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Background/Objectives: Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a necrotizing vasculitis characterized by inflammation of small blood vessels, being the kidney one of the most frequently affected organs. AAV has a high morbidity and mortality rate, leading to rapidly progressive renal failure that may lead to end-stage kidney disease. Its pathogenesis is a complex and multifactorial process involving inflammation and fibrosis. PR3-AAV and MPO-AAV have clinical-demographic differences and different renal phenotypes observed in kidney biopsy. The histopathological subgrouping into four classes (focal, crescentic, mixed, and sclerotic) is useful for predicting long-term renal survival, the worst being sclerotic class. Our aim is to determine whether interstitial fibrosis in AAV is at least as important as glomerular sclerosis in prognosis.

Methods: Retrospective single-center study of 80 AAV patients (66 MPO-AAV and 14 PR3-AAV) diagnosed by renal biopsy, with at least 1-year follow-up. Clinical and laboratory variables, type of ANCA, and renal/patient survival were evaluated. Histomorphometric quantification using MetaMorph® software on trichrome-stained biopsies slides was used to measure the degree of fibrosis in 67 patients. Data analysis performed under standard conditions. Statistical significance was defined as P values under 0.05. All P values were 2-sided.

Results: PR3-AAV population was predominantly male (70%, mean age= 62 years, mean follow-up= 54 months), while MPO-AAV population was mainly female (65.8%, mean age= 66 years, follow-up= 65 months).

Renal function was better in PR3-AAV patients at diagnosis and at the end of follow-up (p= 0.018 and p= 0.004, respectively) and improved in both groups throughout follow-up with statistical significance ($p<0.05$). Loss of renal function (need of renal replacement therapy) was greater in MPO-AAV population, without reaching statistical significance.

From a histological point of view: MPO-AAV manifests more interstitial fibrosis at diagnosis than PR3-AAV (p= 0.032). However, there were no statistically differences in the amount of glomerular sclerosis (p=0.26). It is noteworthy that PR3-AAV showed more crescentic proliferation at diagnosis (p= 0.03) but less fibrotic crescents than MPO-AAV (without reaching statistical significance).

Conclusions:

- The renal function in MPO-AAV population was significantly worse than PR3-AAV population at diagnosis and at the end of the follow-up.
- Renal function improved throughout the follow-up in both sub-groups, what could be explained as a consequence of a favorable response to treatment and clinical management.
- The method we used allows a quantitative assessment of renal fibrosis. Our data confirm that renal prognosis is better in PR3-AAV than in MPO-AAV. This could be explained by a greater interstitial fibrosis, as well as more fibrotic crescentic in MPO-AAV at diagnosis.

Disclosures: None.

P-229

SIRPα Expression in Systemic Vasculitis

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Background: Signal regulatory protein alpha (SIRPα) is primarily found on myeloid cells, including macrophages and neutrophils. Upon binding to CD47, SIRPa signaling regulates cellular functions such as phagocytosis, antigen presentation, cellular fusion, and migration (1). Therefore, SIRPa may be involved in the pathogenesis of autoimmune diseases including systemic vasculitis. This study aimed to assess SIRPa expression in tissue samples from patients with vasculitis.

Methods: Immunohistochemical staining for SIRPα was performed on kidney, lung, and temporal artery (TA) biopsy samples from patients with granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), giant cell arteritis (GCA), and patients without vasculitis. A semiquantitative estimation of SIRPα+ cells in monocytes/macrophages/ dendritic cells and neutrophils were reported using the H-score system based on a visual estimate of the percentage of SIRPα+ cells and the staining intensities classified from 0 to 3. Density of inflammatory infiltrate for individual cell categories was visually estimated and reported using an ordinal scale.

Results: 45 Samples from patients with different vasculitides (GPA, MPA, and GCA) were included: kidney from 11 and 8 patients with GPA and MPA respectively; lung from 11 patients with GPA; and TA from 15 patients with GCA. Most samples from patients with active vasculitis (15 of 15 TA, 16/19 kidney, 9 of 11 lungs) showed SIRPα staining. SIRPα staining intensity was less in kidneys compared to TA and lung samples.

Figure 1: Tissue Samples from Patients with Vasculitis Demonstrating SIRPα Expression.

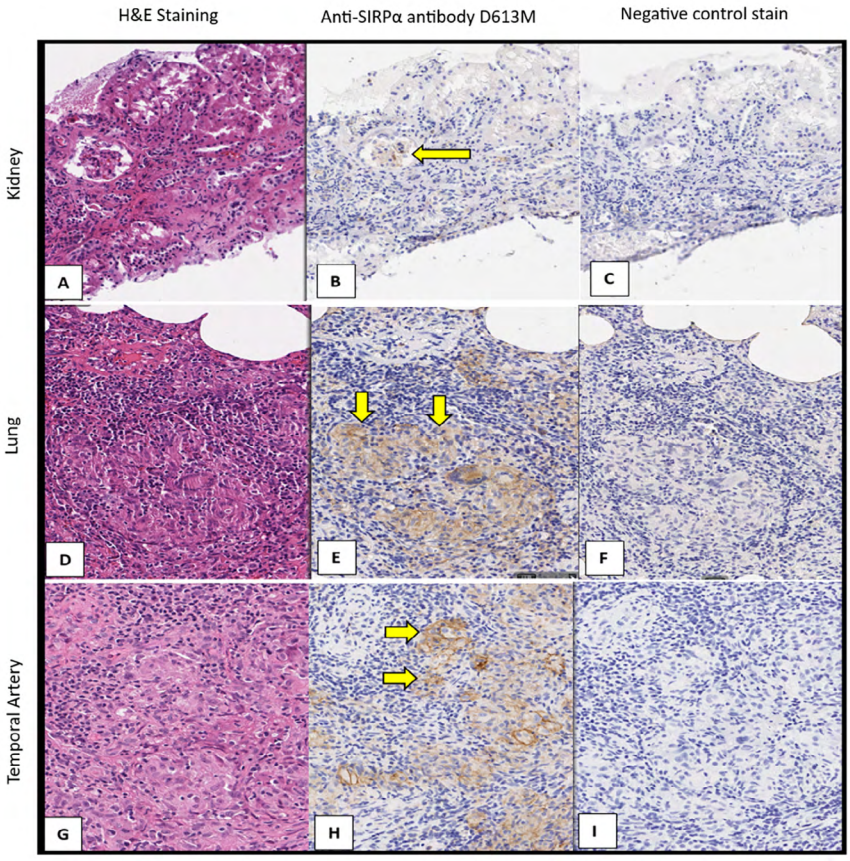

Figure 1: A-C: Renal biopsy (GPA); D-F: Lung biopsy (GPA): G-I: TA biopsy (GCA). Yellow arrows demonstrate areas of SIRPα stain. Magnification of all images was at 20X.

Due to absence of infiltrating immune cells, the kidney and TA control samples did not show SIRPα staining. Due to the presence of macrophages, monocytes, and dendritic cells in peri-bronchial lymphoid aggregates, control lung tissue showed SIRPα staining. **Figure 1** provides examples of SIRPα staining in tissue samples from patients with vasculitis.

Conclusions: This study demonstrates high-level expression of SIRPα in macrophages and monocytes in affected tissues in systemic vasculitis, particularly in TA and lung tissue. Some tissues had SIRPα+ neutrophils. These findings pave the way for further studies exploring the role of the SIRPα/CD47 pathway in the pathogenesis of systemic vasculitis and the potential for blockade of SIRPα pathway as treatment of systemic vasculitis.

References:

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Disclosures: Electra Therapeutics, AbbVie, Otsuka, Roche, Sanofi; Amgen, AstraZeneca, Bristol-Myers Squibb, Glaxo Smith Klein; Genentech, HI-Bio; AstraZeneca, GSK, Otsuka, Pfizer, Roche, Boeringher-Ingelheim, InflaRx, Takeda; ArGenx, Cabaletta, CSL Behring, Dynacure, HiBio, Janssen, Novartis, NS Pharma, Regeneron, Vistera; Eicos, Electra, Forbius, Genentech/Roche, Genzyme/Sanofi, Neutrolis; Kyverna, Q32, Sparrow, Royalties: UpToDate.

P-230

Serum biomarker profile explains heterogenity in patients with Takayasu arteritis

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Background: The clinical presentation of patients with Takayasu arteritis (TAK), a large vessel vasculitis, is heterogenous and absence on an ideal biomarker renders assessment of disease activity difficult (1). In the present study we determined the biomarker profile of patients with TAK and subclassified them based on the same.

Methods: Serum of consecutive patients with TAK and 36 controls were subjected to bead-based-multiplex assay or ELISA to quantify cytokines or chemokines or growth factors representing various pathophysiological pathways in TAK. The concentration of analytes between patients and controls and among various subsets of patients were compared. Unbiased clustering of patients was performed by dimensionality reduction methods and correlation networks were constructed.

The surgical arterial biopsies of a subset of patients were examined for the extent of inflammation, fibrosis and myxomatous changes in arterial wall and the changes were correlated with cytokine concentration.

Results: 85 patients with TAK [66 females, mean age: 28.8±8.9 years, symptom duration of 24 months (IQR: 8-48 months)] and 36 controls were recruited. Levels of B cell antigen (BCA-1) and Pentraxin-3 were higher in patients than controls after applying correction for multiple testing ($p<0.02$ for both). IL18 levels were highest in type 5 subtype ($p=0.015$) while angiopoietin-2 and BCA-1 levels were highest in type 4 disease ($p=0.015$, 0.003 and 0.009 respectively). The level of angiopoietin-2 was higher in patients with active disease (n=52) than stable disease at baseline ($p=0.007$) while IL6 and MMP-2 were paradoxically lower in patients with active disease ($p=0.029$ and 0.021 respectively). Serum IL18 and IL2Rα levels trended to correlate positively with intensity of inflammation in the studied samples of aortic tissues. Among treatment naïve patients, those with lower concentration serum IL15, IFNγ and IL12p70 separated into one cluster. The angiogenic factors, MMP-9 and pentraxin-3 demonstrated interconnectedness in patients with active disease and not in those with stable disease (figure-1).

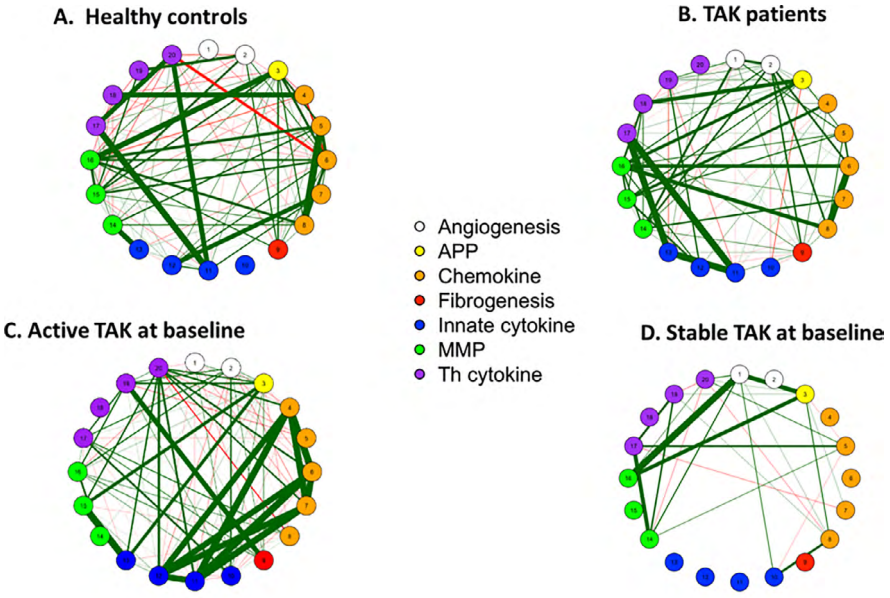

Figure-1 Inter-connectedness between different circulating biomarkers in patients with active and stable TAK and healthy controls.

Conclusions: Patients with TAK have varied biomarker profile that depends on angiographic type and intensity of inflammation. While serum BCA-1 and Pentraxin levels were higher in TAK as compared with controls, angiopoietin-2, Il-6 and MMP-2 levels differentiated active from stable TAK. IL-18 seemed to be associated with arterial tissue inflammation. The biomarkers interconnected among each other differently in active and stable patients.

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Disclosures: None.

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P-231

Deregulation of the endothelin-1 axis in adult IgA vasculitis patients

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Adult immunoglobulin A vasculitis (IgAV) is a small vessel leukocytoclastic vasculitis, characterized by variable clinical presentation and activation of endothelial cells, as one of the main features. Endothelial cells are the main source of endothelin-1, a potent vasoconstrictor peptide with pro-inflammatory action that binds to endothelin receptor (ET-R) located primarily in the vascular smooth muscle cells. Endothelin converting enzyme 1 (ECE1) cleaves endothelin precursors to biologically active peptides. Our aim was to identify deregulations in endothelin-1 axis by RNA sequencing of leukocytes and skin as well as ELISA serum measurement.

Peripheral blood leukocytes and skin biopsy samples were collected from treatment-naïve adult IgAV patients at the time of diagnosis with: 1) IgAV nephritis (n=3), 2) skin-limited IgAV (n=3), and age-/sex-matched healthy controls (HC) (n=3) for RNA sequencing analysis. ET serum levels were measured in 58 treatment-naïve adult IgAVs patients and 22 HC using ELISA (R&D Systems).

The expression of ECE1 was increased in the peripheral blood leukocytes of IgAV nephritis patients (FC= 0.74, p-adj= 9.8×10^{-3}), while the skin of the same group of patients exhibited an increased expression of ET-R ($\log_2$FC = 1.1, p-adj = 0.015). Endothelin-1 serum level was increased ($p < 0.0001$) in the sera of IgAV patients (Median (Q_{25}-Q_{75})= 3.18 (2.18-4.40)) as compared to HC (Median (Q_{25}-Q_{75})= 1.81 (1.63-2.17).

We observed elevated levels across multiple components of the endothelin-1 axis in IgAV patients' samples. Investigating the potential inhibition of the endothelin-1 axis warrants exploration through both in-vitro and in-vivo studies.

P-232

Study of pathogenic T-helper cell subsets in Asian Indian patients with Takayasu arteritis

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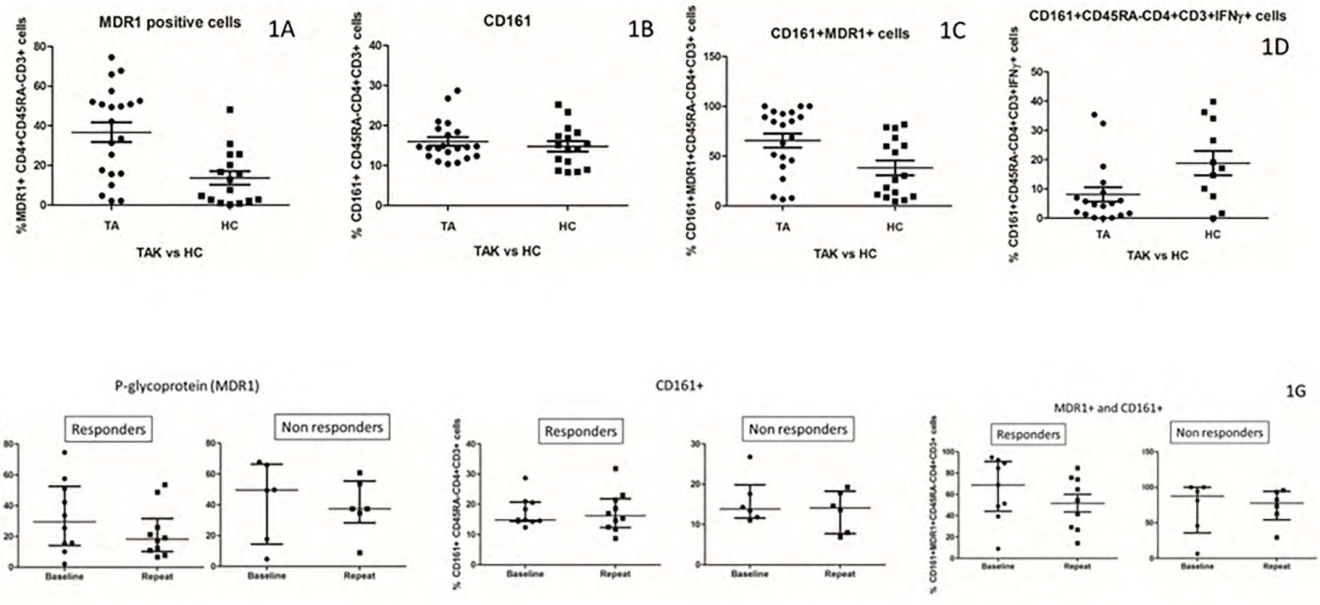
Background: Relapses and refractory disease are a challenge in management of patients with Takayasu arteritis (TAK). We quantified pathogenic CD4+memory T helper cells bearing surface markers CD161 and/or p-glycoprotein (MDR1) in patients with TAK.

Patients and Methods: Peripheral blood mononuclear cells of 21 patients with TAK and 16 age-matched controls were stained with anti-CD3, anti-CD4, anti-CD45RA, anti-CD161 and anti-p-glycoprotein antibodies and subjected to flow cytometry by FACS ARIAIII. 18 patients underwent follow up immunophenotyping. Intracellular staining for interleukin-17 and interferon-γ was performed for 18 patients and 11 controls. Surgical arterial biopsies of 6 TAK and 5 non-inflammatory controls were subjected to immunohistochemistry with anti-CD161 and anti-p-glycoprotein.

Results: At baseline MDR1+CD4+ and CD161+MDR1+CD4+memoryT cells frequency was higher in TAK than controls (p=0.002 and 0.01 respectively). After stimulation, IFN-y+CD161+cells frequency was higher in TAK than controls (p=0.028). Modal fluorescence intensity of CD161+MDR1+ CD45RA-CD4+ cells was higher in active as compared with stable disease (p=0.041).

At 6 months, MDR1+ and CD161+MDR1+ memoryCD4+Tcells decreased significantly only in patients who had complete/ partial response to treatment (p=0.047 and 0.02 respectively).

Immuno-histochemistry of arterial tissue showed staining with anti-CD161 and anti-p glycoprotein showed 2+ to 3+ staining intensity of 4 out of 6 patients while only one showed 1+ staining.



Conclusion: MDR1+ and MDR1+CD161+CD4+ memory T-helper cells are increased in patients with TAK. These cells decreased only in patients with response to treatment during subsequent follow up.

Disclosures: None.

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P-233

Low prevalence of neutralizing autoantibodies against type I interferons in ANCA-associated vasculitis

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Background: Dysregulated type I interferon (IFN) responses play crucial roles in the development of multiple forms of autoimmunity. Increased interferon regulated gene (IRG) has been found in the glomeruli and tubules of active anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) patients, and it has been also noted increased IFN-α concentrations in the serum of active AAV patients in comparison to AAV remission ones (1). In this sense, the gene expression profiles of MPA patients decrease in specific IFN regulated gene expression following remission induction treatment (2). In contrast, other studies suggest that IFN-I do not play an important role in the pathogenesis of AAV (3). Neutralizing autoantibodies (auto-Abs) against IFN-I are present in 5-15% of patients with type I IFN-mediated autoimmune diseases (e.g. systemic lupus erythematosus, Sjögren) and are related with lower disease severity (4). It is worth highlighting that it is not known whether these antibodies are present in AAV so we aimed to test for them and to determine relationship with the severity of the AAV.

Methods: Forty patients attended at a reference hospital who met the 2022 EULAR/ACR classification criteria for AAV were selected and their serum was collected. Auto-Abs against type I IFNs (IFN-α2, IFN-ω and IFN-β) were detected by an enzyme-linked immunosorbent assay (ELISA). Subsequently, we investigated the ability of these auto-Abs to neutralize high concentrations (10 ng/mL) of the three type I IFNs and also more physiological concentrations (100 pg/mL) of IFN-α2 and IFN-ω by a luciferase reporter assay (5).

Results: 31 microscopic polyangiitis and 9 granulomatosis with polyangiitis (GPA) patients were analyzed. Twenty-nine were women. Twenty of them had active disease at the time of sample collection. Only one (2.5%) GPA patient in remission showed auto-Abs with neutralizing activity against 100 pg/mL IFN- ω. Due to the low prevalence found, it cannot be analyzed whether there are clinical differences between patients with auto-Abs against IFN-I compared to the negative ones.

Conclusion: A low prevalence of auto-Abs with neutralizing activity against IFN-I has been found in patients with AAV, suggesting that IFN-I do not play a relevant role in this disease. AAV are rare diseases and therefore, being able to determine the presence of auto-Abs against IFN-I in 40 of them is of great value. Despite this, the presence of these antibodies should be analyzed in other series, especially GPA patients, to determine their true prevalence and its clinical significance.

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Disclosures: None.

P-234

Effects on circulating immune cells by ultra-short glucocorticoids followed by tocilizumab monotherapy in large vessel-giant cell arteritis patients

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Background/Objectives: Giant Cell Arteritis (GCA) is the most common vasculitis in the elderly, characterised by granulomatous infiltration of immune cells in medium and large arteries. A therapeutic protocol that combines ultra-short glucocorticoids (GC) followed by tocilizumab (TCZ) monotherapy has been proven effective in GCA patients with extracranial large vessel involvement (LV-GCA) [1,2]. Its effects on circulating immune cells are unknown. We aimed to analyse the effects of the above therapeutic protocol on circulating lymphocyte and monocyte subsets, and on monocyte receptors: CCR2, CX3CR1, HLA-DR in patients with LV-GCA. Monocyte subsets and the expression of CCR2 and CX3CR1 chemokine receptors have been reported deregulated in GCA [3].

Methods: We included 14 patients with active LV-GCA enrolled in the clinical trial NCT05394909. Patients received 500 mg/day of methylprednisolone intravenously for 3 consecutive days and weekly TCZ injections from day 4 until week 52. Patients in clinical remission at week 52 stopped TCZ and entered in a 24-week observational period. Peripheral blood samples were collected at baseline, at day 4 and, in 8/14 patients, also at week 24, 52 and 76. Peripheral blood mononuclear cells were stained with CD3, CD4, CD8, CD19, CD56 antibodies for lymphocyte profiling and CD14, CD16, CCR2, CX3CR1, HLA-DR antibodies for monocyte profiling by flow cytometry. Paired Student's t-test and mixed-model ANOVA were used for the comparison between and among groups, respectively. P values < 0.05 were considered statistically significant.

Results: GC increased the percentages of B lymphocytes (+8%) and reduced the percentages of T lymphocytes (-9%), whereas those of NK and NKT lymphocytes and the ratio between CD4+ and CD8+ T lymphocytes were not affected. TCZ did not impact the lymphocyte subsets. GC increased the percentages of classical monocytes (+12%) and reduced those of intermediate (-6%) and non-classical monocytes (-2%). TCZ had different effects reducing classical monocytes and increasing non-classical monocytes. Regarding monocyte markers, GC increased the expression of CCR2 (+4000, +11300, +11800) and decreased the expression of HLA-DR (-9200, -35000, -23500) and CX3CR1 (-2400, -9800, -15300) by all monocyte subsets (post-GC versus baseline mean differences in fluorescence intensities in classical, intermediate and non-classical monocytes are reported). Instead, TCZ monotherapy reduced the expression of CCR2 by classical and intermediate monocytes.

Conclusions: Ultra-short GC treatment followed by TCZ monotherapy showed effects mainly on monocyte subsets and their phenotype.

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Disclosures: None.

P-235

Prospective evaluation of usCD163 as a biomarker for active ANCA-associated glomerulonephritis in clinical practice

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Background: There is a need for a reliable non-invasive biomarker of ANCA-associated glomerulonephritis (ANCA-GN) to enable early diagnosis and treatment of active disease and prevent irreversible kidney damage. Several studies have investigated the use of urinary soluble CD163 (usCD163), a specific marker for M2 macrophages, as a potential biomarker of ANCA-GN with a proposed diagnostic threshold of 250 ng/mmol when normalised to urinary creatinine[1]. The aim of this study was to conduct a prospective evaluation of usCD163 as a biomarker of active ANCA-GN in clinical practice in a single-centre in London, UK.

Methods: A prospective observational longitudinal study of patients with ANCA-associated vasculitis (AAV) was conducted, with urine samples collected at time of diagnosis of ANCA-GN, extra-renal flare or from patients in stable remission. Urinary sCD163 levels were measured using a CE certified diagnostic-grade commercial ELISA from Euroimmun and normalised to urinary creatinine. Data are stated in median values ± IQR.

Results: Urine samples were collected from three cohorts from September 2022 to December 2023: 37 patients with ANCA-GN (biopsy-proven in 34 patients), 14 patients with active extra-renal AAV and 10 patients in stable remission.

The median value of usCD163 normalised to urinary creatinine was 252.2 (110.1-840.1) ng/mmol in those with active ANCA-GN, 43.87 (16.79-172.9) ng/mmol in patients with active extra-renal disease and 35.93 ng/mmol in those in stable remission (Figure 1). There was no statistically significant difference when samples were categorised according to the Berden histopathological classification[2], although the median value of usCD163 was highest in those with crescentic disease (870.7 ng/mmol).

The sensitivity of usCD163 in identifying active renal disease in this study of 61 participants with AAV was 51.3% with specificity of 95.9%. The positive predictive value (PPV) was 95.0% and negative predictive value (NPV) was 56.1%.

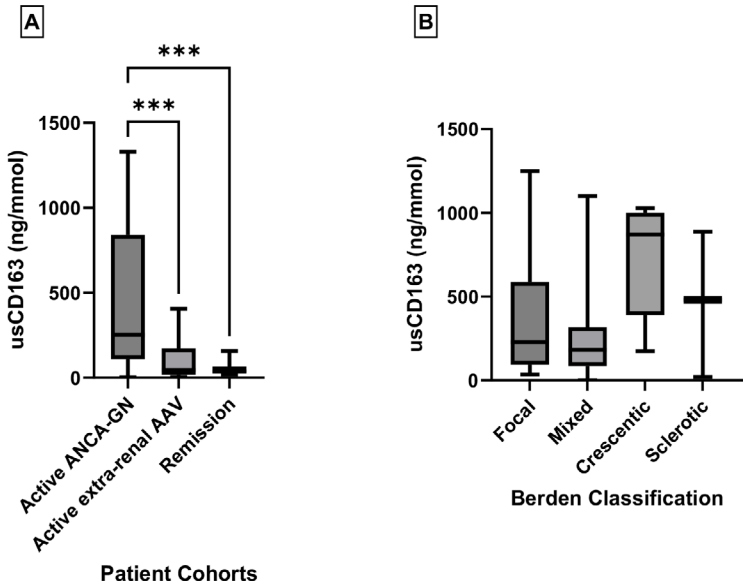

Figure 1. A: Normalised usCD163 in active ANCA-GN, active extra-renal AAV and stable remission, *** = p-value <0.0001; B: Normalised usCD163 levels according to Berden classification.

Conclusions: Urinary sCD163 has a high PPV for renal flare in patients with AAV and therefore has a valuable role as a rapid non-invasive test for early identification of patients who require kidney biopsy and/or treatment. However, a proportion of patients with active ANCA-GN in our cohort did not have normalised usCD163 levels meeting previously defined thresholds for renal flare (>250 ng/mmol), suggesting that this biomarker may not reliably identify patients with mild or focal disease. Kidney biopsy remains an important diagnostic tool when there is a clinical suspicion of active ANCA-GN.

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Disclosures: None.

P-236

Comparison of five different reagents for MPO and PR3 antibodies determination

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Background: Antibodies to myeloperoxidase (anti-MPO) and proteinase 3 (anti-PR3) are recognized as the only clinically relevant antineutrophil cytoplasmic antibodies (ANCA) specificities so far (

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Our aim was to compare the results of five different methods for anti-MPO and anti-PR3 in different hospital centers.

Methods: The study included 50 patients with history or suspicion of vasculitis. Anti-MPO and anti-PR3 were measured using 5 different reagents: anti-Myeloperoxidase ELISA (IgG) and anti-PR3-hn-hr ELISA (IgG) on Euroimmun Analyzer I-2P (EUROIMMUN AG, Lubeck, Germany), MPO and PR3 II chemiluminiscent immunoassay (CLIA) on IDS iSYS (IDS ISYS, Pouilly en Auxois, France), QUANTA Flash® MPO and QUANTA Flash® PR3 CLIA on BIO-FLASH® (Inova Diagnostics Inc, San Diego, USA), Anti-MPO and anti-PR3 hs on Alegria2 ELISA like method (Orgentec, Mainz, Germany), and Anti-MPO and anti-PR3 ELISA (Orgentec, Mainz, Germany).

Results were categorized as positive or negative and we calculated kappa statistics as well as intraclass correlation coefficient (MedCalc version 14.8.1).

Results: Intraclass correlation coefficient showed excellent degree of consistency in average measures (0.9778 (95%CI: 0.9665-0,9862)) for anti-MPO and and good reliability on single ratings (0.8981 (95%CI: 0.8522-0.9344). For anti PR3 intraclass correlation coefficient showed excellent degree of consistency in average measures (0.9257 (95%CI: 0.8873-0.9539)) but only moderate consistency in single ratings (0,7136 (95%CI: 0.6115-0.8053)) Cohen`s kappa testings revealed almost perfect agreement for reagent combination for anti- MPO (kappa from 0,825 to 0,958). For anti-PR3 we found moderate agreement between QUANTA Flash® PR3 and PR3 II IDS iSYS (kappa 0.520) but mostly substantial agreement for other combination of reagents (kappa from 0.629 to 0.865). We also found almost perfect agreement between two reagents (kappa=0.901).

Conclusions: Our results showed mostly almost perfect agreement for anti-MPO methods but moderate to almost perfect agreement for anti-PR3 methods suggesting higher variability of the results. Results showed that it is possible to obtain different results for anti-MPO and especially anti-PR3 for the same patient regardless of the standardisation of the methods. Considering that, it is important to follow up the patient with the same method, preferably in the same laboratory.

Disclosures: None.

P-237

Urine Immune Cells in Patients with ANCA Associated Vasculitis in Remission

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Background: ANCA-Associated Vasculitis (AAV) follows a relapsing-remitting disease path. The kidneys are often affected.(1) Measurement of urinary immune cells as a non-invasive prognostic marker has been demonstrated in another autoimmune renal disease, lupus nephritis.(2) Urinary T cell subsets have been identified as a possible indicator of disease prognosis in AAV patients.(3) We aim to use these cells as a non-invasive predictor of renal relapse to be applied when the patient is in clinical remission. This work seeks to define the urine immune cell phenotype during a period of stable remission.

Methods: Patients were recruited via the Irish Rare Kidney Disease Biobank. Inclusion criteria for this analysis was patients that had ≥ 6 months stable remission and were either anti-myeloperoxidase (MPO) positive or anti-proteinase 3 (PR3) positive. Patients with anti-glomerular basement membrane disease were also included for comparison. These patients provided urine that was processed fresh on the same day. Leukocytes were defined as being CD45+, T cells were defined as being CD45+CD3+, monocytes as CD45+CD3-CD14+CD16+, neutrophils as CD45+CD3-CD14-CD15+. Absolute cell counts per µL of urine were calculated using Countbright Plus Absolute Counting Beads.

Results: 26 patients across 32 encounters were included in the analysis. The cohort was divided between 53.8% female and 46.1% male, with a median age of 66.5 (±22.7%). Of these patients, 12 were anti-MPO positive, 11 were anti-PR3 positive and 3 were ANCA-negative. Despite all patients being in clinical remission at the time of sampling, we observed a median (IQR) of 515 (94 to 38700) CD45+ cells/ml of urine. Neutrophils were the most common subset found, with a median frequency of 69.5±44.1% (as a percentage of CD45+ cells). None of the participants had a positive urine culture. Monocytes were the least common leukocyte population (0.5±4.15%). We also found that the inclusion of dead cells dramatically skews the results because of autofluorescence.

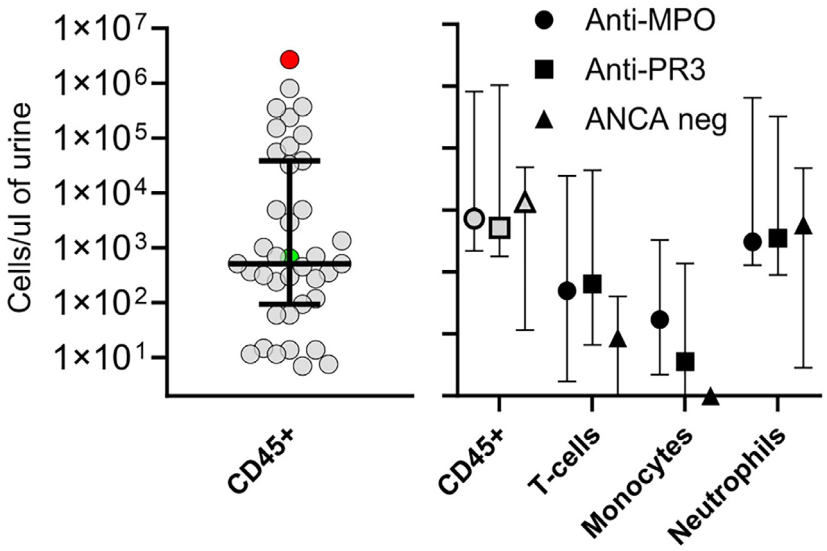

Figure 1: Neutrophils are the most common immune cell subset in urine of AAV patients in remission. The patient marked in red suffered a renal relapse 25 days after the sample was obtained.

Conclusions: Despite being in clinical remission, there is a subset of AAV patients that persistently have CD45+leukocytes in their urine. Neutrophils account for the largest proportion of these leukocytes, despite patients being negative for urinary tract infections at the time of sampling. Accurate flow cytometric analysis of urinary leukocytes relies on the exclusion of dead cells to remove excess autofluorescence and allow for appropriate gating.

Disclosures: None.

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P-238

Platelet blood count and complement alternative pathway activation in patients with AAV and renal impairment

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Background/ Objectives: ANCA associated vasculitis (AAV) is a small vessel- vasculitis characterized by higher mortality than general population and, higher rate of thrombotic complications because of platelet activation (1). Recently, low blood platelet count (BPC) has been shown to be a predictor of death in an AAV large cohort of patients from EUVAS RCTs. On the other hand, a recent work evidenced that platelets were activated via the thrombin-PARs pathway (2,3), triggering the alternative complement pathway in AAV patients. Hence, in this work we aimed to assess the relevance of platelet counts and systemic complement activation in a Spanish cohort of ANCA associated glomerulonephritis patients.

Methods: This is a retrospective cross-sectional study of patients with kidney biopsy proven AAV diagnosed from 2009-2023 at our Hospital. Demographic, clinical and laboratory tests including serum C3, BPC and C-Reactive Protein (CRP) were collected at patient debut flare. Renal function assessed by means of serum creatinine (sCreat) and dialysis dependence at baseline and 12 months were recorded. A descriptive analysis and a correlation test between potential immune biomarkers (serum C3, platelets and CRP) and kidney function was made.

Results: A total of n=76 AAV patients were recorded in the study period (87% MPO and 13% PR3). Mean baseline sCreat. was 3,7 mg/dl (IQR 4.2), and a total of 32.9% needed dialysis. Potential immune biomarkers at diagnostic were: CRP 25 mg/L (IQR 115), BPC 265.000/L (IQR 150.000) and C3 levels 118 mg/dl (+/-28). A correlation between sCreat. and C3 levels (r^2 Spearman= -0,34; $p<0.05$), and also a strong one between C3 levels and BPC (r^2 Spearman= -0,50; $p<0.0001$) was found. Nevertheless, we did not find any association between BPC and renal function. Moreover, an analysis based on median baseline platelets showed statistical significant lower serum C3 and CRP values in those in the lower BPC group (<258.000). Although there were no differences in mortality among the “higher or lower than the median” BPC groups, there it was a trend to a major need of dialysis at diagnosis in the lower group.

Conclusions: In our AAV cohort, we found that patients with lower serum C3 levels had worse renal function at diagnosis. A strong correlation between BPC and C3 levels was found, however we could not demonstrate a worse kidney impairment. A trend towards higher need of dialysis was seen in the patients in the lower BPC group with no differences in mortality.

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Disclosures: None.

2. TRANSLATIONAL SCIENCE
2.07. Emerging technologies and approaches: organoids, single cell RNA sequencing, spatial transcriptomics, data linkage and machine learning, personalized medicine...

P-239

HLA-DPA1*0103-HLA-DPB1*0104-transfected cells for antigen-presentation in GPA

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Background/ Objectives: Antigen-presenting cells (APCs) have a pivotal role in processing and presenting degraded proteins and pathogen-derived antigens internalized into endocytic vesicles via the MHC-II complex to cells of the adaptive immune system. Currently, the etiopathogenesis of granulomatosis with polyangiitis (GPA) is largely unknown, but is thought to involve the interaction of environmental factors with a genetically predisposed host. According to Heckmann et al., candidate gene studies suggest associations between GPA and the HLA-DPB1*0401 allele [odds ratio (OR) 3.91 and 3.01] [1]. Further analyses revealed an association between distinct SNPs in the HLA-DPA1*0103 gene and GPA [2]. We therefore aimed to generate artificial APCs expressing HLA-DPB1*0401 and HLA-DPA1*0103 alleles to study and modulate pathomechanistic principles in GPA.

Methods: K-562 cells, which do not express MHC-II complexes, were double transfected using Lipofectamin LTX Plus. The transfected plasmids used a p-SFFV backbone with inserted HLA-DPB1*0401 or HLA-DPA1*0103 coding sequence. Transfection efficiency was evaluated by flow cytometry using IVA12 pan-MHC-II antibody to detect formed MHC-II complexes on the surface of the transfected cells.

Results: Flow cytometric analysis demonstrated the ability of transfected K-562 cells to express HLADPB1*0401/HLA-DPA1*0103 MHC-II complexes. Twenty-six percent of the transfected cells expressed MHC-II complexes on the surface. In order to achieve a long-term stable and high expression rate of the MHC-II complex in K-562 cells, the gene segment CMV-HLA-DPA1*0103-2A-HLA-DPB1*0104 will be inserted into the AAVS1 locus using CRISPR-Cas9 technology. HLA-DPA1*0103-2A-HLA-DPB1*0104 will then be expressed under the CMV promoter.

Conclusions: By establishing a HLA-DPA1*0103-2A-HLA-DPB1*0104-transfected cell line, these cells will be a useful tool for the study of antigen-presentation with antigens of interest such as proteinase 3, the autoantigen in GPA, and antigen specific T cell assays.

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Disclosures: All authors declare no conflict of interest regarding this abstract.

3. CASE SERIES OR CASE REPORTS OF SPECIAL INTEREST

P-240

Plasma exchange for refractory IgA Vasculitis

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Background: IgA Vasculitis (IgAV) frequently has a relapsing/refractory course despite glucocorticoids and immunosuppressive therapies and the management of refractory disease remains controversial.[1] Plasma exchange (PLEX) has been used as a rescue treatment in other vasculitides, but little is known about its role in IgAV. Here we present outcomes of patients with refractory IgAV treated with PLEX at our centre.

Methods: Clinical records of patients who met 1990 American College of Rheumatology classification criteria and 2012 Chapel Hill Consensus Conference definitions for IgAV were analysed and those receiving ≥1 course of PLEX (5 sessions) identified from our PLEX database. We assessed demographic and clinical features and outcomes after PLEX therapy. Response was defined as an improvement in vasculitis activity measured with Birmingham Vasculitis Activity Score (BVAS) 1 month after PLEX course completion and classified as "partial" (BVAS<3 and prednisolone <10 mg/day) or "complete" (BVAS=0). Relapse was defined as an increase in BVAS after initial response. Early adverse events occurring during PLEX course or within one week after completion of this were recorded.

Results: Among 174 patients with IgAV, 12 (7%) received ≥1 course of PLEX. This was started a median of 15 months after diagnosis (interquartile range, IQR 3-40). All patients received glucocorticoids and immunosuppressive therapy prior to PLEX (**Table**). At the time of starting PLEX, 8/12 patients had active skin involvement (7/8 had purpura and 2/8 ulcers) and 10/12 nephritis, with a median eGFR 37 mL/min (IQR 33-71). PLEX was combined with glucocorticoids and various immunosuppressive agents, most commonly cyclophosphamide (42 %) or mycophenolate mofetil (33%). All but one patient had a response at 1 month, and this was "complete" in five (42%). Ten patients (91%) relapsed a median of 3 months (IQR 2-7) after completion of the PLEX course and 8/10 (80%) resumed PLEX and achieved response. Six patients (50%) continued a "chronic" regimen of PLEX (1-2 monthly sessions) for a median of 85 months (25-141), as this was the only therapy that could control skin and/or kidney manifestations. Three patients experienced infection within a week of PLEX discontinuation and two reported reactions to FFP/albumin, but all recovered completely. Three patients (25%) developed kidney failure during follow-up and two died (one of whom had kidney failure), with death occurring 9 and 146 months after discontinuation of PLEX.

Table Main features of patients with IgAV and clgAN

	N=12
Female, n (%)	8 (66)
Age at diagnosis, median (IQ) – y	40 (31-53)
Elevated IgA (>2.2g/L), n (%)	6 (50)
Immunosuppressive therapy before PLEX	
Glucocorticoids, n (%)	12 (100)
Cyclophosphamide, n (%)	4 (33)
Rituximab, n (%)	2 (17)
Mycophenolate mofetil, n (%)	5 (42)
Other, n (%)	5 (42)
Age at the time of PLEX therapy, median (IQR) - y	43 (28-54)
Months since diagnosis, median (IQR)	15 (3-40)
Active organ involvement at the time of PLEX start	
Skin, n (%)	8 (66)
Joint, n (%)	2 (17)
Gastro-intestinal tract, n (%)	1 (8)
Nephritis, n (%)	10 (83)
eGFR, median (IQR) - mL/min/1.73 m2	40 (33-83)
Other*, n (%)	2 (17)
BVAS, median (IQR)	10 (6-14)
Concomitant therapy	
Glucocorticoids, n (%)	12 (100)
Cyclophosphamide, n (%)	5 (42)
Rituximab, n (%)	1 (8)
Mycophenolate mofetil, n (%)	4 (33)
Other**, n (%)	2 (17)
Outcome at 1 month	
Response (all)	11 (92)
Complete (BVAS=0), n (%)	5 (42)
Partial (BVAS<5), n (%)	6 (50)
No response, n (%)	1 (8)
Relapse, n (%)	10 (83)
Time to relapse from PLEX discontinuation, median (IQR) - months	3 (2-7)
Number of PLEX sessions, median (IQR)	25 (9-42)
Chronic PLEX therapy (monthly for >3 months), n (%)	6 (50)
Number of sessions, median (IQR)	25 (9-42)
Early adverse effects, n (%)	5 (52)
Infections, n (%)	3 (25)
FFP/albumin reactions, n (%)	2 (17)
Follow-up after PLEX start, median (IQR) - months	49 (32-116)
Kidney failure requiring RRT, n (%)	3 (25)
Death, n (%)	2 (17)

*Peripheral neuropathy
**Bortezomib, dapsone

Conclusions: In this small cohort of adult patients with severe and refractory IgAV, PLEX was associated with improved disease control and few early adverse events. The clinical response to PLEX appeared temporary, but some patients maintained remission through a "chronic" PLEX regimen. As highlighted by the high risk of death or kidney failure, more effective therapies for IgAV are needed but PLEX should be considered as a rescue treatment in severe/refractory cases.

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Disclosures: None.

P-241

False positive findings of large vessel vasculitis on FDG-PET in patients treated with immune checkpoint inhibitors: A case series

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Objectives: FDG-PET is increasingly used in the diagnosis of large-vessel vasculitis (LVV). Cancer patients treated with immune checkpoint inhibitors (ICIs) frequently undergo FDG-PET for tumor monitoring. Findings of vessel-wall uptake in these patients may prompt concerns for ICI-induced LVV, which could lead unnecessary immunosuppression and premature ICI discontinuation.

Methods: We review four patients treated with ICI with probable false positive findings of LVV on FDG-PET.

Results: *Case One:* 68-year-old female with stage IIIC melanoma on combination nivolumab and ipilimumab, completed May 2019. Routine FDG-PET in July 2020 found circumferential uptake in the thoracic aorta. She had no symptoms with normal exam and CRP. She received high dose prednisone. Repeat scan in October 2020 was normal. On original scan review, prolonged tracer injection to scan delay was thought to be responsible for positive findings. Prednisone was stopped with no recurrence over 2 years.

Case Two: 52-year-old female with stage II squamous cell carcinoma treated with cepilimab monotherapy one week after FDG-uptake to the thoracic and proximal abdominal aorta and proximal great vessels on PET scan in February 2022. She was not treated with immunosuppression and did not develop any clinical features of LVV. Follow up scan in May 2022 had no features of LVV.

Case Three: 59-year-old female with stage IIIA melanoma treated with Nivolumab monotherapy. FDG-PET scan three months after stopping ICI found increased uptake in the thoracic aorta. There were no clinical features of LVV. She was not treated with immunosuppression. Follow up FDG-PET was normal.

Case Four: 60-year-old male with stage IV melanoma completed one-year of pembrolizumab in Dec 2021. FDG-PET scan in March 2022 found diffuse uptake in the thoracic and abdominal aorta, subclavian and common carotid arteries. There were no clinical features of LVV. CRP, temporal artery ultrasound and CT-angiogram were normal. He was not treated with immunosuppression. Follow up FDG-PET scan in Aug 2022 was normal.

Our analysis identified several technical factors that likely influenced the positive diagnosis of ICI-induced LVV. Three of the index FDG-PET scans (patients 1,2,4) had FDG uptake intervals that were higher than the recommended 60 minute (106, 113, and 185 minutes each), resulting in decreased mediastinal blood pool activity, and relative conspicuity of the vessel wall, interpreted as LVV. The index scan for patient 3 used an alternative attenuation correction algorithm due to FDG contamination in the tracer injection site at the antecubital fossa which resulted in artificially accentuated signal to the thoracic aorta, subsequently interpreted as LVV.

Conclusions: Incidental vascular wall uptake on FDG-PET scans may not represent typical LVV but may be due to technical error, which is essential to recognize to avoid false diagnosis of LVV in cancer and other patients. Although PET-FDG has modernized the ability to diagnose and monitor vasculitis, we must continue to use our clinical judgement when clinical symptoms do not correlate to imaging findings.

	Patient 1	Patient 2	Patient 3	Patient 4
Visual grade (SUVmax)				
Thoracic aorta	2 (3.7)	3 (3.7)	2 (2.9)	3 (3.7)
Abdominal aorta	1 (2)	2 (3.1)	2 (2.9)	1 (3.4)
Subclavian arteries	1 (2)	1 (3.1)	1 (2.3)	1 (2.2)
Axillary arteries	1 (1.5)	1 (2.8)	1 (1.5)	2 (2.3)
Carotid arteries	1 (2.3)	1 (3.4)	1 (2)	2 (2.6)
Iliac arteries	1 (2.2)	1 (3.1)	1 (2.2)	1 (2.2)
Femoral arteries	1 (1.6)	0 (2.3)	1 (1.9)	1 (2.5)
Total vascular score	8	9	9	11
Liver (SUVmax)	3.2	3.3	3	1.5
Blood pool (SUVmax)	1.9	2.6	1.9	1.5
PMR associations (grade)	Scapular (3) Ischial (2)	Scapular (3)	Lumbar (3) Trochanteric (2) Ischial (2)	Trochanteric (2)
Serum glucose (mmol/L)	4.8	4.3	4.2	-
FDG uptake Interval (min)	113	76	106	185
Subsequent PET FDG uptake interval (min)	81	66	62	59

Table 1 – Standardized FDG-PET scan analysis.

P-242

Eosinophils gone Wild, an ANCA-associated vasculitis Mystery

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Presentation of Case: A 45-years old male presented with exertional dyspnea over 3 days and six months history of fatigue. No other respiratory symptoms. He smoked 14 pack-years. He has no relevant family history. His vital signs were within normal limits, and BMI is 32.9.

He appeared comfortable and had late inspiratory rales in the bases on auscultation. There were no other abnormalities on physical examination.

Diagnostic Testing: Chest x-ray showed pulmonary vascular congestion**.** Echocardiogram revealed ejection fraction 15% of the left ventricle. The right ventricle was mildly dilated, with moderately decreased systolic function. At this point, he was treated for heart failure with medications.

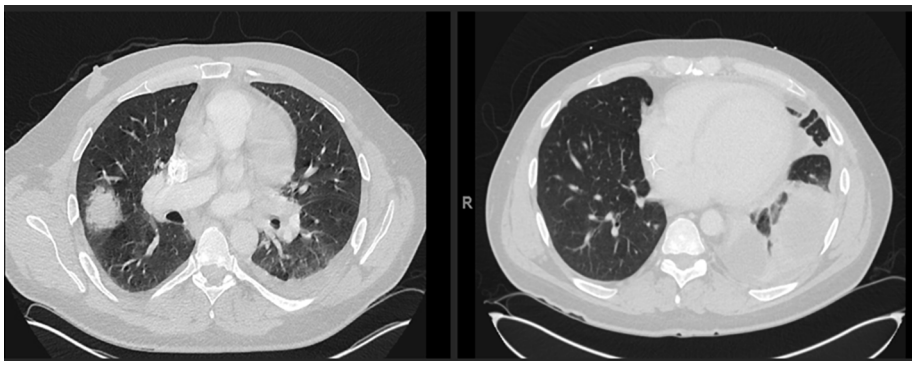
Six months later he re-presented with acute shortness of breath, hypoxic respiratory failure and acute renal failure. He also had a moderate left sided pleural effusion with a new right lower lobe lung mass on chest imaging.

Peripheral blood: Eosinophils 800 cells/ml, c-ANCA positive with titer 1:640, with PR3 positivity.

Pleural fluid: Nucleated cells 2422, Neutrophils 19%, Lymphocytes 25%, Eosinophils 49%, LDH 748, protein 4 g/dl.

Bronchoalveolar lavage:

Neutrophils 50%, Eosinophils 26%, Monocytes 20%. Negative infectious & cancer workup.



Kidney biopsy: Acute crescentic glomerulonephritis and focal arterial fibrinoid vasculitis, pauci-immune type. Segmental fibrinoid necrosis or a cellular crescent seen. Arteritis with fibrinoid necrosis.

Lung mass biopsy: Necrotic tissue insufficient for diagnosis. Rare multinucleated giant cells are present, which suggest a necrotizing granuloma. Negative infectious stains.

Differential & Final Diagnosis: Eosinophilic granulomatosis with polyangiitis (EGPA), granulomatosis with polyangiitis (GPA) and GPA with eosinophilic features were our three differentials. The latter being our final diagnosis.

Discussion of Management: Immunosuppression for vasculitis was initiated given ANCA positive and biopsy findings.

- Methylprednisonolone 1000 mg IV daily for three days.
- Cyclophosphamide initial monthly dose.
- He was then transitioned to rituximab two weeks later, with recovery in renal function and discontinuation of dialysis within 3 weeks of the development of renal failure. He returned home and follows in clinic.

Conclusions:

- In 1988, four cases were reported to manifest as GPA with eosinophilic infiltrates on open lung biopsy. [1] The cases differed from EGPA with lack of peripheral eosinophilia.
- ANCA-associated vasculitis (AAV) can manifest as EGPA, but very rarely as GPA with eosinophilic features. [1]
- Recent treatments in AAV include IL-5 inhibitor for EGPA, C5a receptor inhibitor for GPA & MPA, and recent evidence shows less benefit with plasma exchange. [2] In our rare variant of GPA we present, the use of these novel therapies is not studied and rituximab remains the mainstay of therapy.

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Disclosures: None.

P-243

Cyclophosphamide Resistant Granulomatosis with Polyangiitis (GPA)-Induced Acute Necrotizing Scleritis: A Non-Classical Clinical Presentation

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Background: The classical form of GPA primarily affects the blood vessels in the respiratory tract and kidneys, often leading to glomerulonephritis and lung cavities. While the exact cause of GPA is unknown, it is believed that various factors including microbes, genetics, and environmental triggers, contribute to its development. Notable genetic associations include alpha-1-antitrypsin, Cytotoxic T-lymphocyte-associated protein 4 and the Major Histocompatibility Complex class II, specifically DP alpha-1, among others. Furthermore, there are viral associations with GPA, including Epstein Barr, Cytomegalovirus, Parvovirus B-19, and Hepatitis C viruses. GPA is also associated with an increased risk of bladder cancer. Here we present a non-classical case of cyclophosphamide-resistant GPA with unilateral acute scleritis.

Case: A 63-year-old male, with a past medical history of shoulder osteoarthritis, presented with a six-month duration of persistent rhinorrhea, headaches, and left nostril congestion refractory to over-the-counter decongestants. A diagnosis of allergic rhinitis was made; however, the patient did not respond to subsequent anti-allergic medication or antibiotic therapy. Concurrently, the skin on the left nostril exhibited crust formation, and the patient experienced recurrent nosebleeds. Additionally, bilateral pterygium developed, necessitating surgical excision. The patient then reported acute left eye pain, diminishing vision, and was diagnosed with acute scleritis. A diagnostic workup revealed acute necrosis of the sclera, and a biopsy of a nasal lesion exhibited pathological features consistent with GPA. Laboratory investigations indicated elevated C-ANCA titers (1:80) and an increased proteinase-3 level (4.9 IU/mL). A chest Computed-Tomography scan revealed the presence of multiple mass-like densities with central cavitations, ranging in size from 4 to 7 cm. Pulmonary Function Tests and all other laboratory studies were unremarkable. Cyclophosphamide therapy provided no relief. Subsequently, treatment was transitioned to Rituximab and high-dose prednisone, resulting in complete resolution of scleral melting and termination of nosebleeds.

Discussion: GPA can affect the joints, eyes, gastrointestinal (GI) tract, heart, nervous system, and skeletal muscles. Research has indicated an increased risk of bladder cancer and non-Hodgkin Lymphoma among GPA patients. The GI manifestations of GPA often resemble chronic enteritis, presenting with bowel ischemia and an elevated risk of bowel perforation. In summary, the management of GPA necessitates a thorough evaluation of multiple organ systems and ongoing monitoring to reduce the risk of disease relapse.

Disclosures: None.

P-244

IL-1 inhibition as an example of implementation of Personalized Precision Medicine in Behçet's Disease

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Presentation of Case: Three patients are included (n=3), women (100%), between 40 and 42 years old, with Behçet's Disease (meeting ICBD criteria -Table 1) refractory to multiple immunosuppressive (TIS)/biological treatments who have carried out follow-up in the Systemic Autoimmune Diseases (SAD) Consultation of the Internal Medicine Service of the University Hospital of Navarra (HUN).**Case 1:** The patient received treatments with azathioprine, colchicine, mycophenolate mofetil, infliximab, adalimumab, golimumab, cyclophosphamide, cyclosporine, intravenous immunoglobulins, intereferon alfa, tocilizumab and anakinra from January 2011 to January 2016 with little response. Therefore, from January 2016 to the present, the patient is being treated with canakinumab with good disease control and no adverse effects.**Case 2:** The patient received treatment from March 2013 to April 2023 with salazopyrine, colchicine, methotrexate, adalimumab, infliximab, golimumab, tocilizumab, anakinra, rituximab and secukinimab with pooresponse. Treatment with canakinumab was started with good control and response to date.**Case 3:** The patient received the following therapies with insufficient response and adverse effects from November 2010 to October 2014: salazopyrine, methotrexate, azatiprine, mycophenolate mofetil, adalilumumab and cyclophosphamide. Subsequently, treatment with anakinra was started until December 2017, after losing efficacy, treatment with canakinumab was started until now, achieving adequate control of the disease.

Discussion of Management: The importance of IL-1 in the pathogenesis of BD is increasingly evident: its levels are elevated in patients with both active and non-active BD[1] and the pathways that connect this form of innate immunity with the clinical manifestations of BD are now of great clinical-therapeutic interest.There are already studies[2,3] that suggest the use of Canakinumab in refractory BD, with good clinical response (complete remissions, good control of ocular symptoms...) with few adverse effects and adequate tolerance.**Conclusions**: Canakinumab is an acceptable therapeutic alternative in patients with BE refractory to conventional treatment.

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Disclosures: None.

	Oral and genital aphthosis	Ocular disease	Skin lesions	Neurologic manifestations	Vascular disease	Patergia test positive	Others	HLA B51
Case 1	yes	Epiescleritis	Folliculitis Livedo reticularis	Headache	small intestine lymphangiectasias	yes	Fever, asthenia, anorexia Spondyloarthropathy Polyarthritis Diarrhea	+
Case 2	yes	Anterior uveitis	Folliculitis	Headache	Septal perforation 2nd to vasculitis	no	Spondyloarthropathy with sacroiliitis Inflammatory myopathy diarrhea	-
Case 3	yes	Anterior uveitis	none	none	Bilateral retinal vasculitis	yes	diarrhea	+

Table 1.

P-245

Rapidly evolving palatal perforation in a patient with granulomatosis with polyangiitis: a case report

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Presentation of Case: 41-year-old woman, smoker of 2-4 cigarettes a day, with a personal history of chronic sinusitis since November 2018, and endoscopic sinonasal surgery in June 2019. In October 2020, clinical worsening with scabs, epistaxis, purulent rhinorrhea, halitosis, anosmia and orthopnea, with a paranasal sinuses CT showing chronic pansinupathy, polyps, large septal perforation, exposed cartilage and scabs, treated with topical and oral corticosteroids and surgical reintervention.

In February 2023, she was referred to Rheumatology clinic due a positive anti-proteinase 3 (anti-PR3). No apparent extranasal symptoms were present. Physical examination revealed a saddle nose and tenderness in the maxillary sinuses. Biopsy of nasal tissue displayed chronic inflammation. Blood count, kidney function and urine were normal, without active sediment, and C-reactive protein (CRP) was slightly elevated (11.9 mg/L). In chest HRCT a mild emphysema was identified. Localized anti-PR3+ granulomatosis with polyangiitis (GPA) was suspected, and treatment was started with prednisone 20 mg/d and methotrexate. In August 2023, she went to the emergency room because she started 48 hours earlier with a hole in the palate through which liquids and food pass when swallowed; in addition, the patient perceived rhinolalia and fever. The examination revealed millimetric palatal perforation (figure 1), as well as nasal tenderness.

Diagnostic Testing: In emergency room, CRP of 65 mg/L and anti-PR3 of 12 Ua/mL stand out. Normal chest x-ray.

Sinuses CT showed occupation of paranasal sinus and erosion of the lower slope of the septum and turbinates, and nasopalatine fistula with a 6 mm communication.

Differential & Final Diagnosis: Main differential diagnosis is cocaine use[1], which our patient denied. In addition, local infections or tumors must be ruled out.

Final diagnosis was localized GPA.

Discussion of Management: Empirical antibiotic therapy with moxifloxacin was prescribed, but clinically the patient worsened and we observed progression of the palatal ulcer in just 6 days (figure 2).

Given the local aggressiveness of the clinical case, a treatment with intravenous pulses of methylprednisolone 250 mg x3 days, intravenous cyclophosphamide 1 g (single dose) and rituximab 1 g x2 separated by 15 days was instaured[2].

Currently, maintenance treatment with tapering of prednisone and rituximab 1g every 4 months with good evolution of the palatal ulcer (figure 3).

Conclusions: Palatal perforation is a rare manifestation of GPA but it can behave aggressively, greatly reducing the quality of life of patients, therefore it should be treated as a serious involvement of the disease.

References:

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Disclosures: None.

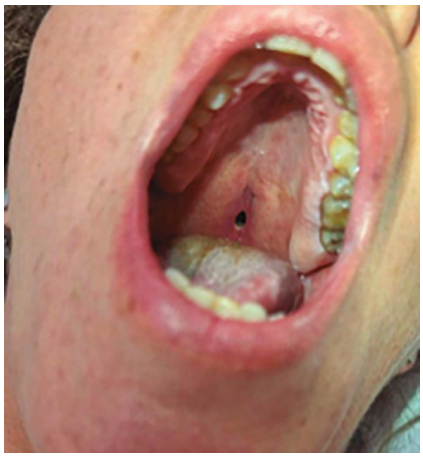

Figure 1. Palatal perforation 25/08/2023.

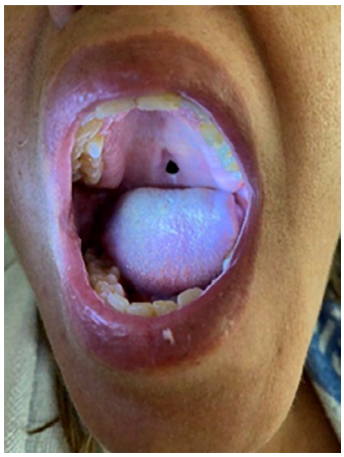

Figure 2. Palatal perforation 31/08/2023.

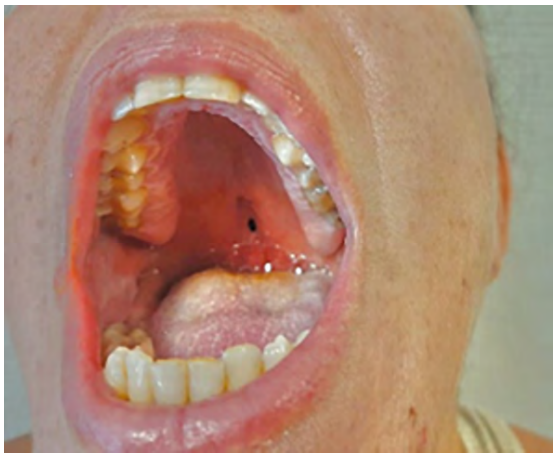

Figure 3. Palatal perforation 06/10/2023.

P-246

A Case of Spontaneous Remission of Interstitial Pneumonia in an MPO-ANCA Positive Chronic Hemodialysis Patient

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An 85-year-old female patient with a history of presumed chronic kidney disease due to nephrosclerosis had been receiving outpatient care for the past ten years. Although her renal function had been gradually declining, five years ago, she developed rapidly progressive glomerulonephritis associated with elevated MPO-ANCA levels at 295 EU. There were no signs of extrarenal vasculitis, and she was diagnosed with renal-limited microscopic polyangiitis (MPA). Consent for corticosteroid (CS) or immunosuppressive therapy could not be obtained, leading to the initiation of maintenance hemodialysis approximately three months later. Over the course of approximately five years, her MPO-ANCA levels remained consistently positive without any relapse. However, during a routine chest CT examination, infiltrative shadows on both sides, ground glass shadows, reticular shadows, and traction bronchiectasis were observed, suggesting interstitial pneumonia. Tests for bacterial, fungal and viral infections, including Mycobacterium tuberculosis, Mycoplasma, and Pneumocystis jirovecii, were negative, no antibiotic and antiviral treatment was given. Although she exhibited mild coughing and hypoxemia, raising concerns about interstitial pneumonia related to MPA, invasive testing and consent for immunosuppressive therapy including CS therapy were not obtained. Surprisingly, without any pharmacological intervention, she experienced spontaneous remission a few months later. Clopidogrel, an antiplatelet drug, was initiated for myocardial infarction treatment two months prior to the onset of interstitial pneumonia. However, the interstitial pneumonia had already begun to improve before discontinuation of this medication. Therefore, it is highly likely that the interstitial pneumonia in this case was related to MPA.

Discussion: Reports of untreated cases of acute interstitial pneumonia associated with MPA are rare, making this case a valuable contribution to the understanding of the pathophysiology of interstitial pneumonia in the context of MPA.

P-247

Incidence and prevalence of ANCA-associated vasculitis in a northern Spanish health region, between 2000-2022 a population-based study

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Background: Anti-neutrophil cytoplasmic antibodies (ANCA) associated vasculitis (AAV) is a group of vasculitis that affect small vessels. Includes Clinical phenotypes like Granulomatosis with polyangiitis (GPA), Eosinophilic granulomatosis with polyangiitis (EGPA) or Microscopic polyarteritis (MPA). Precise estimation of the incidence and prevalence of AAV has been difficult due to the absence of reliable diagnosis criteria.

Objectives: To estimate the incidence and prevalence of AAV in a Northern Spanish population-based cohort.

Methods: Population-based study of 171 patients diagnosed with small vessel vasculitis between 2000 and 2022. The diagnosis of AAV was made according to ACR/EULAR 2022 criteria. Incidence and prevalence were estimated by gender and year of diagnosis. Incidence and Prevalence were reported annually (on December 31st of every year) per 1,000,000 person-year and per 1,000,000 population respectively.

Results: A total of 171 (83 women /88 men) patients were included in the study. The mean age of the cohort at diagnosis was 69.1±13.7 years. The most frequent type of AAV was MPA with 66 (38.2%) patients followed by GPA, EGPA with 63 (36.4%) and 23 (13.3) respectively. The Indeterminate Vasculitis group had 21 (12.1%) patients.

Annual incidence of AAV in Cantabria area between 2000-2022 period was 15.7 (19.7-11.6) per 1,000,000 habitants. The incidence in male and female are 16.7 (21.5-12) and 14.6 (18.7-10.4) per 1,000,000 habitants, respectively. The incidence separated by the diagnosis of AAV was 5.8 (7.5-4.1) for GPA, 6.1 (8-4.2) for MPA and 2.1 (3.3-0.9) for EGPA. All the result are summarized in **FIGURE**. The prevalence of AAV in our series from 2000 to 2022 was 189.5 cases per 1,000,000 habitants. A comparison between different geographical areas is summarized in **TABLE**. Wide variations in annual incidence per million were observed. The highest annual incidence was in Nordic countries, The United States and central Europe while the lowest in Southern Europe.

Conclusion: There seems to be a progressive increase in incidence of AAV over the years in the studied population. Annual incidence in our population was like other regions.

Disclosures: None.

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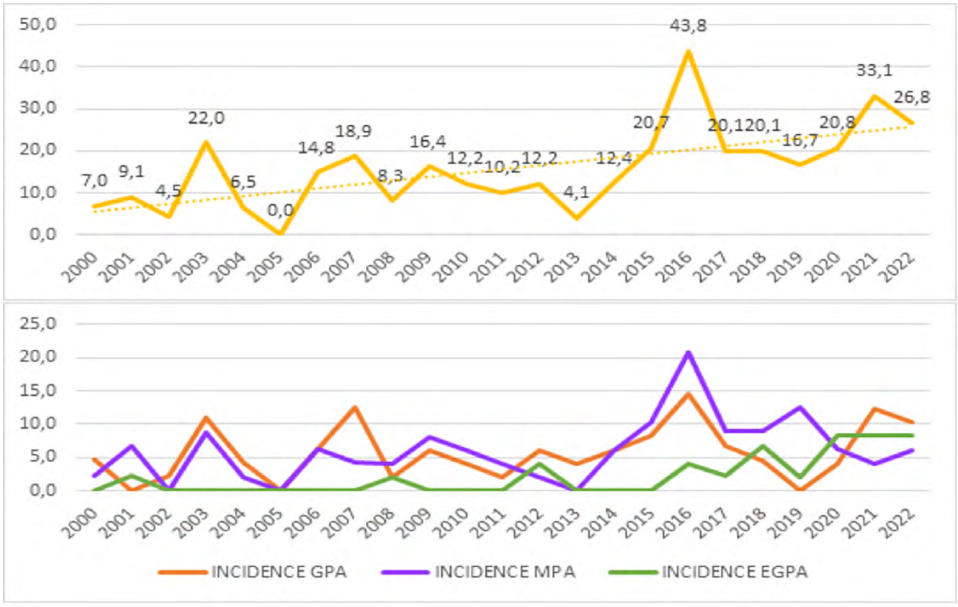

FIGURE.

Annual incidence of AAV in 171 patients between 2000-2022. Measured per 1,000,000 habitants/year. Comparison of Annual incidence of AAV in 171 patients between 2000-2022. Measured per 1,000,000 habitants/year.

Author, year.	Country, region	Time period	Diagnosis Criteria	N cases	Prevalence over 1.000.000 (CI 95%)	Incidence/ 1.000.000 habitants/ year (CI 95%)	Incidence GPA/1.000.000 habitants/year (CI 95%)	Incidence MPA/1.000.000 habitants/year (CI 95%)	Incidence EGPA/1.000.000 habitants/year (CI 95%)
Pearce FA, 2016	UK	2007-2013	EMA ACR90	107	ND	23.1 (18.9-27.9)	8.2 (5.8-11.3)	13.4 (10.3-17.2)	1.5 (0.6-3.1)
Nilsen AT, 2020	Norway	1999-2013	EMA ACR90	140	293 (246-346)	20.2 (17-23.8)	12.7 (10.2-15.6)	5.3 (3.7-7.3)	2.2 (1.2-3.6)
Mohamed AJ, 2009	Sweeden	1997-2006	EMA ACR90	140	ND	21.8 (18.2-25.4)	9.8 (7.4-12.2)	10.1 (7.7-12.6)	0.9 (0-0.17)
Helmich, B, 2021	Germany	2013-2016	ND	3054	256 (245-267)	46 (39-53)	34 (28-40)	13 (11-15)	ND
Dadoniene, J, 2005	Lithuania	1990-1999	ACR90	205	ND	43.8 (38.1-50.3)	2.1 (1.1-4.1)	ND	1.3 (0.5-2.9)
Panagiotakis SH, 2009	Greece	1995-2003	ACR90	67	ND	19.5 (15.7-23.4)	6.6 (3.7-9.6)	10.2 (5.8-14.6)	ND
Romero-Gomez C, 2015	Spain	1994-2010	ACR90	29	44.8 (25.5-66.1)	6.2 (3.9-8.4)	2.1 (0.8-3.4)	3.4 (1.7-5-.1)	0.6 (0-1.3)
Marh, 2004	France	2000	ACR90	68	149 (126-1749	ND	ND	ND	ND
Pamuk, 2016	Turkey	2004-2014	ACR90	50	69.3 (48.6-90)	8.1 (1-15.2)	4.8 (0-10.3)	2.4 (0-6.3)	0.8 (0-4)
Berti, 2017	USA	1996-2015	EMA ACR90	58	421 (296-546)	33 (24-41)	13 (8-18)	16 (10-22)	4 (1-6)
Fujimoto, 2011	Japan	2005-2009	EMA, ACR90	86	ND	22.6 (19.1-26.2)	2.1 (0.6-3.7)	18.2 (14.3-22)	2.4 (0.3-4.4)
Present studio, 2023	Spain	2000-2022	ACR/ EULAR22	171	189.5	15.7 (11.6-19.7)	5.8 (4.1-7.5)	6.1 (4.2-8)	2.1 (0.9-3.3)

TABLE. Epidemiological studies on AAV in other geographic regions.

Abbreviations (in alphabetical order): ACR: American college of Rheumatology; CI: Confidence interval; EGPA: Eosinophilic granulomatosis with polyangiitis; EMA: European Medicine Agency; EULAR: European Alliance of Associations for Rheumatology; GPA: Granulomatosis with polyangiitis; MPA: Microscopic polyangiitis; N: number; ND: No available data; UK: United Kingdom; USA: United States of America.

P-248

Anti-glomerular basement membrane disease developing 3 years after the development of Sweet syndrome and 1 year after the development of anti-neutrophil cytoplasmic antibody-associated vasculitis

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[1]Departments of Nephrology, Tokyo Metropolitan Geriatric Hospital and Institute of Gerontology, Tokyo, Japan; [2]Department of Nephrology and Endocrinology, Tohoku Medical and Pharmaceutical University Hospital, Sendai,Japan.

A 73-year-old Japanese woman, with a history of Sweet syndrome diagnosed 3 years earlier and anti-myeloperoxidase (MPO) antibody anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis diagnosed 1 year earlier, presented with an episode of rapidly progressive glomerulonephritis (RPGN) with anti-glomerular basement membrane (GBM) disease. At the time of diagnosis of the ANCA-associated vasculitis one year earlier, serological testing yielded a negative result for anti-GBM antibody. However, at the present visit, serology for anti-MPO antibody was negative, while that for anti- GBM antibody was positive. This is the first report of anti-GBM disease developing sequentially after Sweet syndrome and ANCA-associated vasculitis. This case may provide clues to the potential immunological links among these three distinct conditions.

P-249

A rare case of ANCA-associated Vasculitis and Scleroderma Renal Crisis in Mixed Connective Tissue Disease

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Presentation of Case: A 52-year-old woman with Mixed Connective Tissue Disease (MCDT), antinuclear antibodies (ANA) with a 1/1000 titer and strongly positive anti-U1 RNP antibodies, presented in the emergency department with a 1-month evolution of dyspnea, chest pain and visual disturbances.

On physical examination, she was diaphoretic, had blood pressure (BP) of 186/125mmHg and heart rate of 118bpm. Sclerodactyly and microstomia were evident. Blood tests revealed anemia (hemoglobin 11g/dL), thrombocytopenia, elevated serum creatinine (sCr 1.60mg/dL), urea (59mg/dL) and troponin I (1727ng/mL). Direct fundoscopy had signs of hypertensive retinopathy. The electrocardiogram had ST segment elevation in V4-V5 and the echocardiogram showed global akinesia and ventricular dysfunction. There was no evidence of coronary disease after percutaneous coronary intervention, compatible with Takotsubo Cardiomyopathy.

Considering scleroderma renal crisis (SRC) in the context of MCDT, presenting as a hypertensive emergency, captopril was progressively titrated with adequate BP control. However, despite improvement in hematologic, ophthalmologic and cardiac disturbances, renal function continued deteriorating (maximum sCr 5.02mg/dL).

Diagnostic Testing: 24-hour urine analysis was remarkable for proteinuria (1.24g/24h), blood tests with anti-double stranded DNA and complement levels were normal and antineutrophil cytoplasmic antibody (ANCA) testing was positive for PR3 (>200 U/mL).

A renal biopsy was performed and showed ischemic glomerular changes. Arterioles had intimal proliferation and thickening (onion-skin lesion) (Figure 1, A). Inflammatory changes in the medulla with leukocytoclasia of neutrophils and tubular necrosis were present, suggestive of medullar angiitis (Figure 1, B). There was no fibrinoid necrosis and no crescents. Immunofluorescence microscopy was unremarkable except for IgM+ mesangial deposition.

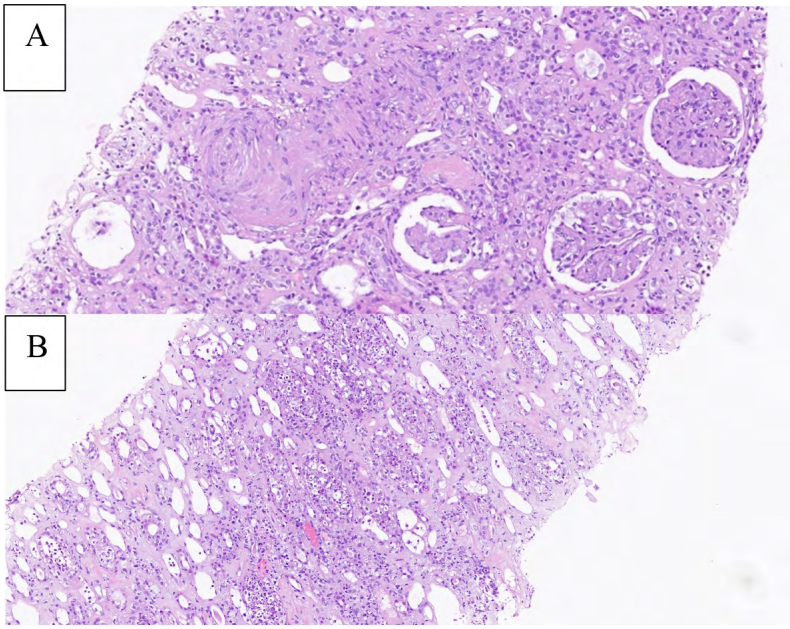

Figure 1 - Glomeruli with ischemic features and arterioles with intimal proliferation (A - HE 100X). Medulla with lesions characteristic of medullary angiitis (B – HE 200x).

Differential & Final Diagnosis: The renal biopsy findings were predominantly explained by SRC. However, the presence of medullar angiitis [1], ANCA-PR3 elevated titers and the progressive renal dysfunction with adequate BP control, led to the diagnosis of concomitant ANCA-associated vasculitis (AAV).

Discussion of Management: Treatment was started with 500mg intravenous methylprednisolone for 3 days, followed by oral prednisolone and rituximab two 1g infusions. Supporting a glucocorticoids (GC) reduction strategy, she was proposed for Avacopan [2]. Prior to therapeutical approval, she died.

Conclusions: SRC is a rare complication of MCTD with poor outcomes. Progressive renal dysfunction in patients with MCTD requires excluding other aetiologies, including AAV. The concomitant presence of the two entities creates a treatment challenge, particularly concerning GC, essential in AAV treatment but potentially deleterious in SRC.

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Disclosures: None.

P-250

VEXAS syndrome with microcytic anemia: what lies under this misleading feature?

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VEXAS syndrome standing for "Vacuoles, E1 enzyme, X-linked, Auto-inflammatory, Somatic," is a are autoinflammatory disease affecting mainly elderly individuals. It results from a mutation in the UBA1 gene on the X chromosome (1). It involves both rheumatologic and hematological manifestations usually represented by macrocytic anemia or macrocytosis caused by myelodysplastic syndrome.

This report presents the first case of VEXAS syndrome with microcytic anemia, contrasting with the typical observations (1–5).

Presentation of Case: A 61-year-old Sicilian man exhibited various symptoms, including skin lesions, recurrent fever, unintentional weight loss, venous thrombosis, and arthralgias.

Diagnostic Testing: Biological work-up revealed elevated inflammatory markers, deficiencies in vitamins B9 and B12 and anti-parietal cell antibodies. Despite appropriate supplementation, the anemia persisted. Hemoglobin electrophoresis indicated minor beta-thalassemia, categorizing the anemia as mixed, attributed to inflammation, beta-thalassemia, and vitamin deficiency. Further work-up revealed skin vasculitis in small and medium-size vessels, a pulmonary nodule, and vacuoles and dysplasia in myeloid progenitors of bone marrow (OGATA score: ¾, R-IPSS score: 1, IPSS score: 0; meaning a low risk MDS).

Differential & Final Diagnosis: Considering the symptoms, the MDS, and the presence of otherwise explained vacuoles, VEXAS syndrome was suspected and confirmed by highlighting a UBA1 gene mutation (p.M41T).

Discussion of Management: Initial treatment involved high-dose corticosteroids, later attempted to be tapered down using JAK-STAT inhibitors (tofacitinib, ruxolitinib), which was hindered by access-related issues. Currently, the patient maintains stability on methylprednisolone (8mg/day) with an improvement in microcytic anemia. Sarilumab (200mg every 2 weeks) has recently been initiated.

Conclusion: Microcytic anemia should not hinder clinicians from considering VEXAS syndrome when the clinical context is appropriate especially in areas where thalassemia is endemic.

Table 1 : Comparison of Macrocytosis and Mean Corpuscular Volume (MCV) among the largest cohorts of VEXAS Syndrome (1–5)

Cohort	Number of patients	Percentage of patients with Macrocytosis (%)	Mean of MCV (fL)
Beck et al. N Engl J Med 2020 (1)	25	96	NA
Beck et al. JAMA 2023 (2)	11	64	109,4
Georgin-Lavialle et al. Br J Dermatol 2022 (3)	116	NA	101
Ferrada et al. Blood 2022 (4)	83	97	NA
Van der Maede et al. J Allergy Clin Immunol 2022 (5)	12	75	99

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Disclosures: None.

P-251

Successful induction treatment of isolated pulmonary capillaritis with rituximab

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Presentation of Case: Isolated pulmonary capillaritis (IPC) is a rare autoimmune cause of diffuse alveolar haemorrhage (DAH), diagnosed by histopathological evidence of lung capillaritis in the absence of systemic vasculitis.

A 28-year-old healthy man presented to emergency department with two days history of dyspnoea and haemoptysis. His physical examination was entirely unremarkable except decreased oxygen saturation to 88 % on room air. The high-resolution chest computed tomography (HRCT) is described in (Figure 1).

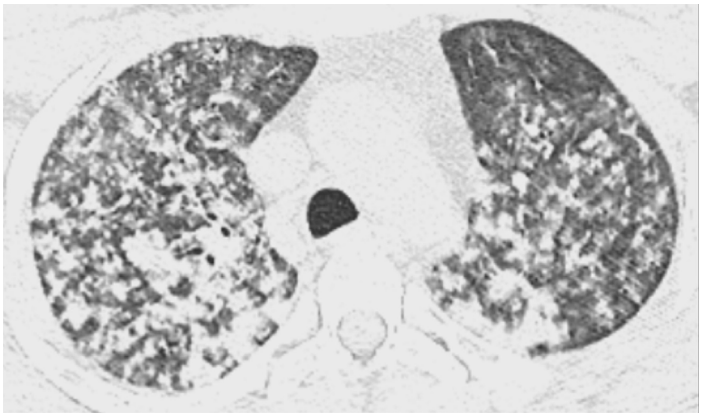

Figure 1. Representative image of chest (HRCT) showing extensive patchy alveolar consolidations with a peribronchovascular distribution, and areas of ground glass opacities (GGOs), in both lungs. The described lesions are mostly indicative of (DAH).

Diagnostic Testing:

1. Immunological profile was normal.
2. Normal urine analysis & negative blood cultures.
3. COVID-PCR test and serological profile for infections was negative.
4. Culture for Mycobacterium tuberculosis was negative.
5. Bronchoalveolar lavage fluid has revealed haemosiderin-laden macrophages.
6. There was no evidence of valvular heart disease on echocardiogram.

Differential and Final Diagnosis:

1. Hypersensitivity pneumonitis.
2. Anti-Neutrophil Cytoplasmic Antibodies (ANCA) associated vasculitis (AVV).
3. Vasculitis-associated with other systemic diseases and drugs.
4. Pulmonary and systemic infections.
5. Valvular heart disease such as mitral stenosis.

Video assisted thoracoscopy (VATS) with biopsy was performed and was consistent with pulmonary capillaritis.

Discussion of Management: Due to its rarity, treatment of (IPC) is adapted from therapies of (AVV). Patient during the hospital admission was put in high flow nasal cannula, he had received broad spectrum antibiotics and prednisolone 60 mg/day. After initial improvement had received 3 gr of methyl-prednisolone and two doses of rituximab 1 gr, two weeks apart with excellent clinical response. The rituximab was chosen over cyclophosphamide due to patient age and preference as well as due to the data for its efficacy coming from the treatment of (AAV). There are only a few case reports in the current literature for using rituximab in the treatment of (IPC). In these case reports the rituximab was used as rescue treatment, (1). Our case is the first suggesting the effectiveness of rituximab as induction therapy in adult patient with (IPC) and (DAH).

Conclusions: Rituximab may be effective first line treatment of (IPC) accompanying with (DAH).

References:

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Disclosures: None.

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Ileal tuberculosis masquerading as intestinal Behcet's Disease

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Presentation of Case: A 58 year old female with recurrent oral and genital ulcers and a positive pathergy test was diagnosed with Behcet's Disease (BD). She was given prednisone 0.5 millligram per kilogram per day (mkd), colchicine 1000 micrograms (mcg) and azathioprine 50 milligram (mg) daily for a year, had recurrent abdominal pain, and hematochezia.

Diagnostic Testing: She underwent colonoscopy with findings of nonspecific proctocolitis and irregularly shaped clean based ulcer in the distal ileum. Histopathology showed chronic active inflammation, lymphocytic vasculitis, granulation tissue, and negative for dysplasia. Ileal *Mycobacterium tuberculosis* Polymerase Chain Reaction (MTB PCR) was negative. Based on such findings, the impression was Intestinal Behcet's Disease. She was given prednisone 0.5 mkd, azathioprine 100 mg and mesalazine 3 grams daily.

2 weeks later, she had recurrent abdominal pain and hematochezia. Abdominal computed tomography scan showed distal ileum enteritis and acute appendicitis. She underwent laparoscopic appendectomy, and given intravenous methylprednisolone 500mg for 3 days for the refractory intestinal BD. Colonoscopy showed clean based ulcers at the distal ileum at the ileocecal valve. Repeat ileal MTB PCR tested positive and was started on quadruple anti-Koch's treatment, while prednisone 25mg and colchicine were continued.

Differential & Final Diagnosis: Intestinal BD ulcers are typically irregular, round, punched out, large, deep, single to a few numbers and majority affect the ileocecal region[1]. Similarly, gastrointestinal tuberculosis (GITB) majorly affect the same area to which the ulcerative form is the most common[2]. Those with GITB and intestinal BD, would commonly present with abdominal pain, anorexia, fever, and melena which the patient presented. Hence, ileal mucosa MTB PCR was done to differentiate between the two.

Discussion of Management: The possibilities here is that of the patient with BD having GITB from the onset or that the patient contracted GITB from the immunosuppression with steroid. Consequently, the diagnosis between GITB from BD remain a diagnostic challenge as the role of MTB PCR in intestinal biopsies has been less studied, with 8.1% sensitivity and 100% specificity[3].

Conclusions: Intestinal BD is associated with significant morbidity and mortality. GITB and BD exhibit similarities in clinical manifestations but treatment differs substantially. This highlights importance of suspicion of intestinal TB in Behcet's Disease with chronic steroid use. The case also demonstrates that with negative MTB PCR, the diagnosis of GITB should be considered despite colonoscopic features consistent with BD.

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Disclosures: None.

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Avacopan our experience in 1 year

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Presentation of Case: Male, 49 years old. Previous diseases: Diabetes Mellitus since he was 9 years old with associated proliferative retinopathy. He has always presented very poor glycemic control. Follow-up in our office since August 2002 where he was referred due to deterioration of renal function (Cr 1.5 mg/dl and proteinuria of 1.5 gr.) Previous normal renal function. Immunological study: positive ANCA (175), normal AntiMBG, normal immunoglobulins and complement levels (C3, C4).

Diagnostic Testing: Percutaneous biopsy was performed on August 22: 32 glomeruli were obtained with global sclerosis in 9 of them (28%) and segmental sclerosis in one (3%). Increase of mesangial matrix. There is glomerulomegaly in some of the glomeruli. In 16% of glomeruli there is evidence of fibrocellular crescents

Differential & Final Diagnosis: It was diagnosed as ANCA positive glomerulonephritis on diabetic glomerulopathy.

Discussion of Management: In view of these histological findings it was decided to start induction treatment with cyclophosphamide (according to RITUXVAS protocol)[1] and steroid pulse (500 mg each). Initially treatment was also started with Rituximab, which the patient did not tolerate due to allergic reaction. Given his history of diabetes mellitus with very poor glycemic control, it was decided not to maintain treatment with corticosteroids in the long term, so an association with Avacopan (30 mg/12h)[2] was proposed, starting in November 2022. Until he started receiving it, the patient was taking prednisone at a dose of 1 mg/kg/day (total 60 mg per day). The patient has been followed up for one year in consultation. During this time he has maintained stable renal function (Cr 1.6 mg/dl) with a decrease in proteinuria up to 500 mg/24 h, microhematuria and a decrease in ANCA (10). After completing 6 months of induction treatment with cyclophosphamide, and having presented previous reaction with rituximab, he currently maintains treatment with azathioprine and Avacopan. The patient has not presented any side effects due to the use of Avacopan and the transaminase controls have always been normal. He also maintains good glycemic control.

Conclusions: Avacopan can be considered a safe drug and an effective alternative for vasculitis management in those patients in whom prolonged use of corticosteroids should be avoided.

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Dislousures: None.

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When vasculitis is not your only problem

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Presentation of Case: 78-year old Caucasian male, smoker, with arterial hypertension, marginal splenic lymphoma (low risk, untreated) and blue finger syndrome 3 years previously (negative autoimmunity and infectious serologies).

Diagnosis of atrial fibrillation –rivaroxaban–. 1m later, non-palpable purpura in the lower extremities (normal kidney function, 0-5 red blood cells (RBC)/field, 80% dysmorphisms, no proteinuria), diagnosed as 2ry to rivaroxaban, changed to dabigatran. 1w later, he presented with acute perforated appendicitis with peritonitis. Complications included abdominal collections, suture dehiscence and psoas hematoma –stop anticoagulation–.

He developed hypoxic respiratory failure –orotracheal intubation–, AKIN III acute renal failure (GFR 28ml/min, S3 RBC/field, 30% dysmorphisms, UPCR 1.2g/24h) –furosemide pump and continuous venovenous haemofiltration–, new purpuric lesions, palpable and non-palpable (Fig. 1a), and minor hemoptysis.

Diagnostic Testing: Blood test: positive type-2 cryoglobulins (monoclonal IgM kappa + polyclonal IgG), low C3, C4 and CH50, RF 46 IU/mL, hb 7 g/dL (no hemolysis, normal platelets), occult hepatitis B virus (HBV) infection. Negative ANCA, anti-BGM, APL. CT angiography: Fig. 1b. Fibrobronchoscopy: diffuse bleeding signs without active bleeding. Bronchoalveolar aspirate: hemosiderophages. Skin biopsy: Fig. 1c and 1d. Renal biopsy not performed –instability–.

Differential & Final Diagnosis: Differential of renopulmonary syndrome: ANCA-associated idiopathic or drug-associated vasculitis, Good-Pasture syndrome, other autoimmune diseases (SLE, SSc, PM, DM, MCTD, IgA vasculitis, cryoglobulinemia) or thrombotic microangiopathy 2ry to APS, thrombotic thrombocytopenia, infections or malignancy[1]. Final diagnosis: cryoglobulinaemic vasculitis.

Discussion of Management: Treatment with 3 methylprednisolone boluses (500mg/24h), prednisone 1mg/kg/d PO, plasma exchange, rituximab (375mg/m^2, 1/w 4w), entecavir, cotrimoxazole. Complete recovery of kidney function and skin lesions, initial respiratory improvement –extubation– but subsequent worsening due to CMV and HSV1 pneumonitis treated with ganciclovir (stopped when undetectable CMV viral load) with 2ry pancytopenia and grade-4 neutropenia. Prophylactic bemiparin 3500 IU/d.

Excellent clinical evolution but 1m later he presented a left middle cerebral artery thromboembolic stroke, bronchial aspiration and died.

Conclusions: A high suspicion is needed to diagnose vasculitis when the first insidious symptoms start and repeat tests in case of inconsistencies. We must pay special attention to the patient's comorbidities, which can difficult diagnosis and management and, like in this case, be the cause of the patient's death.

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Disclosures: None.

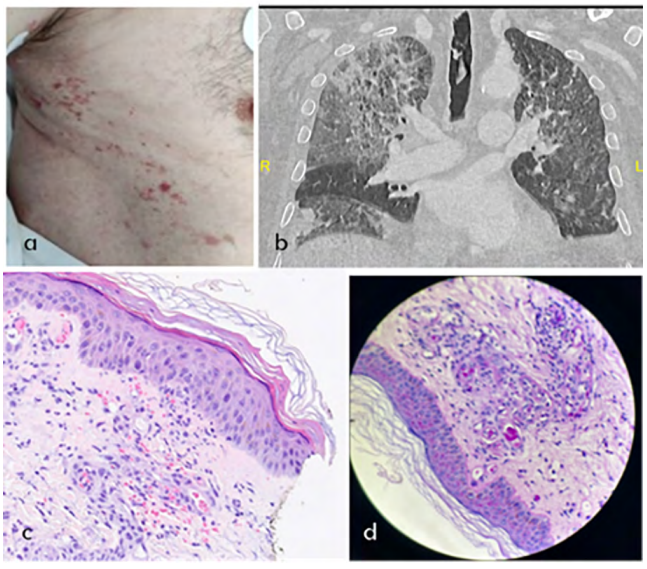

Fig. 1: a) purpuric lesions; b) lung CT angiography: bilateral septal ground-glass areas; c) hematoxylin eosin stain: leukocytoclastic vasculitis with subdermal neutrophil infiltrate; d) PAS stain: cryoglobulins

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Differential Diagnosis of Renal Deterioration in Patient with Multiple Autoimmune Overlaps

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Presentation of Case: 69-year old Caucasian woman with anti-Scl70+ diffuse systemic sclerosis (SSc) diagnosed 6 years before (untreated NINE ILD) and Sjögren's syndrome (SS).

Admitted due to weight loss, low-grade fever, night sweats and dysuria for 2 months despite outpatient UTI antibiotic treatment. Onset of high blood pressure. Persistent fever despite new antibiotic therapy and progressive worsening of renal function (hematuria, non-nephrotic proteinuria, no oliguria).

Diagnostic Testing: Blood test: GFR 7 mL/min, elevated APR and TSH, hb 7.6g/dL (micro-hypo, no hemolysis, normal platelets), positive ANCA anti-MPO, anti-TPO, negative IGRAs. Urinalysis: S2-3 red blood cells/field, UPCR 1.2g/24h, Ecoli+. Normal kidney ultrasound. Abdominal CT: lymphadenopathies <15mm. Lung CT: ILD. No amyloid in fat biopsy. Normal digestive endoscopies, no occult blood in stool. PPD-. Renal biopsy (Fig. 1a): type III extracapillary glomerulonephritis (GN) with activity.

Differential & Final Diagnosis: Differential: Lymphoproliferative syndrome/blood dyscrasias, neoplasms, tuberculosis, amyloidosis, autoimmune diseases' renal involvement (SSc, SS, SLE, cryoglobulinaemia, Goodpasture syndrome, IgA or ANCA vasculitis), postinfectious GN, IgA nephropathy, tubule-interstitial nephritis (nephrotoxic drugs)[1].

Final diagnosis (dx): renal-limited anti-MPO vasculitis, SSc, SS and Hashimoto's thyroiditis (HT) overlap. BBVAS 33.

Discussion of Management: Treatment: 3 methylprednisolone (MP) bolus (500mg/d), prednisone (PRED) PO, 1 dose IV CP, plasmapheresis, RTX 375mg/m^2 1st dose. At discharge: GFR improved –14 ml/min–, microhematuria persisted, BVAS 16, -ANCA.

Two days after: sudden dyspnea, hemoptysis, respiratory failure –NIVM and ICU– and anemization. Pulmonary CT: Fig 1b: ground glass and consolidative foci in both superior lobes. Bronchoalveolar lavage: macroscopic hematic appearance, hemosiderophages, +Rothia mucilaginosa. Plasmapheresis was restarted + RTX up to 4w doses + antibiotic + MPA at discharge (she had pancytopenia).

Dx: anti-MPO microscopic polyangiitis with renopulmonary syndrome, SSc, SS and HT overlap.

Evolution: Maintenance treatment was mostly with PRED achieving remission. Different immunosuppressants (IS) were tried but had to be withdrawn due to pancytopenia (normal bone marrow biopsy) and multiple infections. PRED was retired 5 years after dx. 3 years later she had a renal flare. Biopsy with mild activity –bolus MP + RTX– and high chronicity so no IS was added for maintenance. Current GFR 10ml/min pending hemodialysis.

Conclusions: Even though this patient had already different diseases that could explain the renal deterioration, she developed a new dx. Patients with autoimmune disease are more likely to present another one. The overlap SSc and ANCA vasculitis is not uncommon, and has a bad prognosis, so clinicians should maintain a high suspicion to early diagnose and treat it.

References:

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Disclosures: None.

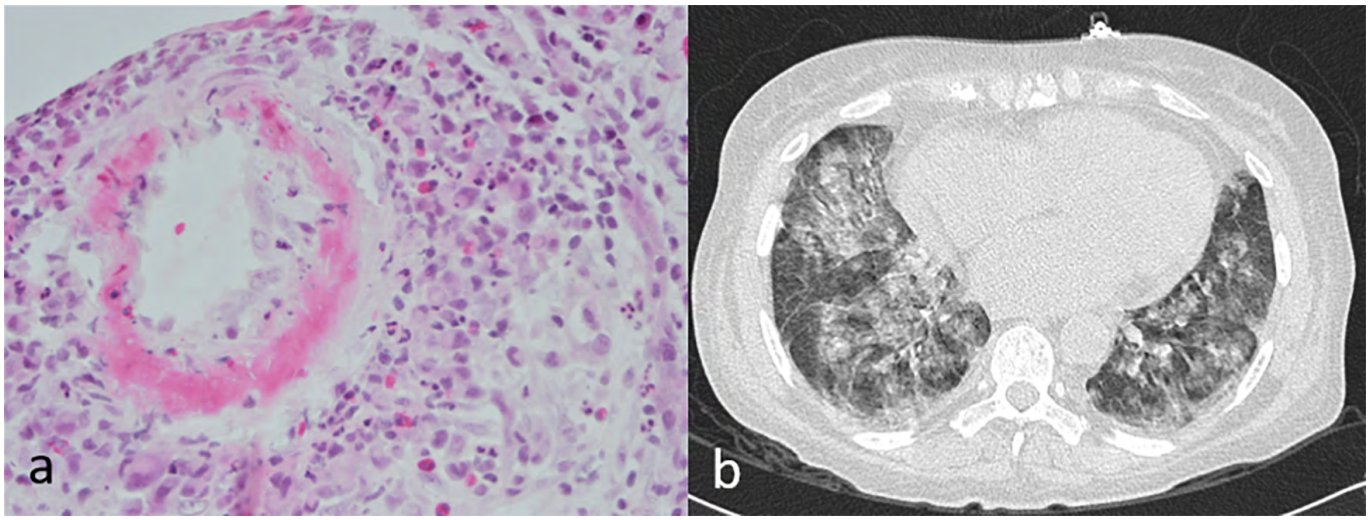

Figure 1. a) Renal biopsy: fibrinoid necrosis in the wall and karyorrhexis with acute inflammatory component in the periphery. b) Lung CT: ground glass and consolidative foci.

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Multifocal juxta-vertebral lesions in granulomatosis with polyangiitis

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Presentation of case: We report the case of a 60-year-old woman with a history of PR3-ANCA positive granulomatosis with polyangiitis (GPA) who complained of right basithoracic pain. GPA was diagnosed six years ago, on the basis of otorhinolaryngological symptoms, pachymeningitis, left apical pulmonary infiltrate and right hypoglossal nerve linked to retropharyngeal granulomatous infiltration encasing the carotids (1).

Reappearance of high titers anti-PR3-ANCA(523 U/ml) was noted. ANCA were negative during the remission period.

Diagnostic testing: A ^{18}F-fluorodesoxyglucose (^{18}F-FDG) positron emission tomography (PET) showed hypermetabolic infiltrates both at the level of Th4-Th5 and Th10-Th11 but also a well-defined hypermetabolic left pre-sacral mass (arrows on figure) without recurrence of the hypermetabolic spots which were observed during the initial flare six years ago.

Final diagnosis: We decided to avoid performing a biopsy to confirm a relapse of PR3-ANCA positive granulomatosis with polyangiitis GPA consisting in juxta-vertebral infiltrates without any other involvement.

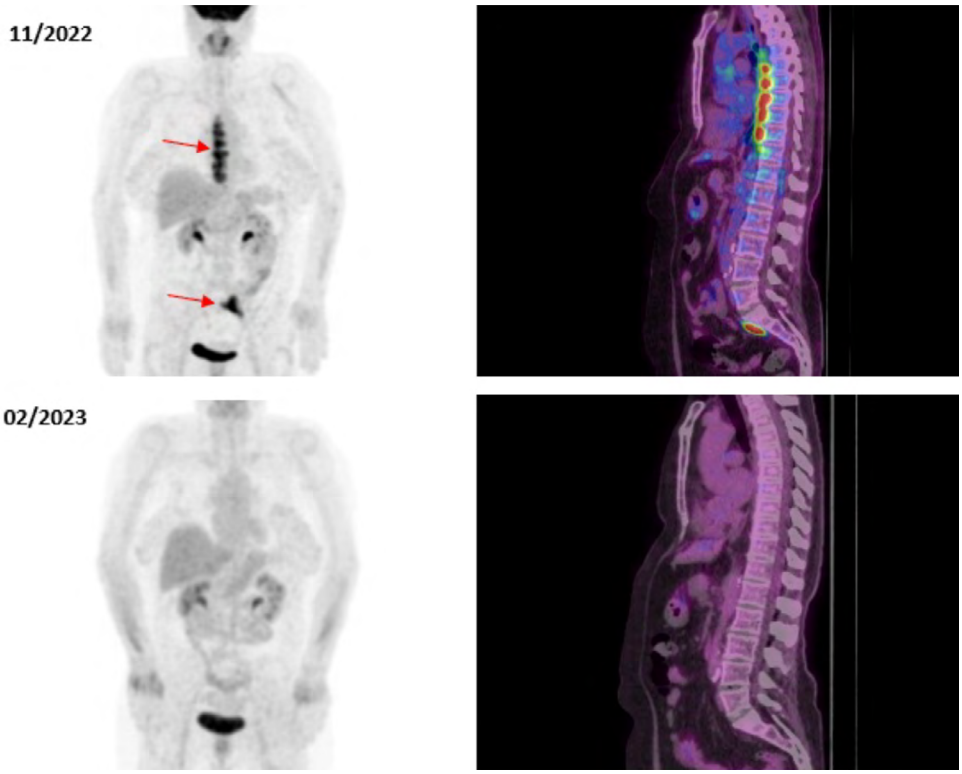
Management and discussion: The patient was treated with rituximab and steroids, which led to a complete clinical and metabolic remission.

Only 17 cases of juxta-vertebral lesions associated with GPA have been described (2).

Almost all of the reported cases had juxta-vertebral lesions located at the level of thoracic spine, with a constant pre-vertebral location, most of the time at the right side. Some authors have proposed to consider those infiltrates as a form of fibrosing mediastinitis. However, chronic fibrosing inflammation has been demonstrated on biopsy in only one case (3).

The sacral location of such juxta-vertebral has been reported only in one patient. This location can be assimilated to an atypical location of retroperitoneal fibrosis.

Another uncommon feature of our case is the complete clinical, biological and metabolic response after only three months of treatment with steroids associated with rituximab. Indeed, most of the patients in the series of Ramirez did not exhibit such a complete response.



Conclusion: We herein report for the first time a flare of GPA consisting in the concomitant occurrence of juxta-vertebral infiltrates both at the thoracic and sacral spine levels in a patient who has previously presented a first flare of GPA without those involvements.

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Disclosures: None.

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PR3 ANCA-positive vasculitis associated with myasthenia gravis

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Presentation of Case: In November 2020, a 73-year-old man presented with ptosis and dysphonia and was diagnosed with myasthenia gravis (MG). Antibodies against acetylcholine receptor (AChR) were positive, while imaging did not show a thymoma, thymic hyperplasia or malignancy. He responded well to intravenous immunoglobulins 2g/kg, prednisolone 60mg/day and pyridostigmine. Mycophenolate mofetil (MMF) (1250mg twice daily) was introduced to facilitate prednisolone taper, and this was completed in March 2023.

Four months following prednisolone withdrawal, he developed arthralgia. Blood tests showed raised inflammatory markers and creatinine 98µmol/L and he commenced prednisolone 15mg/dai for presumed polymyalgia rheumatica. Repeat assessment six weeks later revealed acute kidney injury (AKI) (serum creatinine 201µmol/L) with blood and protein in urine (**Table 1**).

Diagnostic Testing: AKI work-up identified a positive PR3 ANCA (19UI/L), but negative MPO ANCA, anti-GBM antibodies, and ANA. Kidney biopsy demonstrated a pauci immune glomerulonephritis with fibrocellular crescents in 5/19 glomeruli and mild parenchymal scarring. CT chest was negative for airway and lung involvement. There was no change in neurology and no signs of peripheral neuropathy at this time.

Final Diagnosis: History and findings were compatible with renal-limited PR3 ANCA-associated vasculitis (AAV) occurring in the context of MG well controlled on MMF immunosuppression.

Management: MMF was withdrawn and rituximab (2g) used for AAV induction therapy, which has shown positive results in refractory MG.[1] Prednisolone 60mg/day was commenced but rapidly tapered because the patient developed a severe urinary tract infection and myocardial infarction. In this context, his creatinine peaked at 430µmol/l. Avacopan 30mg twice daily was introduced. Two months later, his PR3 AAV is in remission, prednisolone has been withdrawn, and his renal function stabilised (creatinine of 230µmol/l).

Conclusions: Our patient presented with typical features of PR3 AAV which occurred within 3 years of diagnosis of anti-AChR-positive MG. Of note, he was receiving MMF immunosuppression at the time of AAV diagnosis, although prednisolone had recently been tapered and stopped. Both AAV and MG have been described associated with other autoimmune diseases, e.g. rheumatoid arthritis, but to our knowledge, this is the first report of their co-existence in the same patient. Shared genetic variations, such as in *HLA-DQ* and *PTPN22,* are likely to increase the risk of developing both diseases.[2,3] Importantly, both conditions exhibit autoantibodies as disease drivers and benefit from B cell-depleting therapy.

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Disclosures: None.

Table Main test results and immunosuppressive therapy

	Nov 2020 Diagnosis of MG	Mar 2023 Prednisolone withdrawal	Jul 2023 PMR-like symptoms	Aug 2023 Diagnosis of PR3 AAV	Sep 2023 Admission with UTI and NSTEMI	Nov 2023 Last follow-up
C-reactive protein, mg/L	37	<4	16	6	342	18
Serum creatinine, mmol/L	87	93	98	205	465	230
eGFR, mL/min/1.73 m^2	77	74	69	28	11	25
Haemoglobin, g/L	120	112	106	116	84	95
Anti-AChR Ab, nmol/L (ref. <0.2)	>20	13	14	16	n.a.	n.a.
MuSK Ab, nmol/L (ref. <1.5)	Neg	Neg	Neg	n.a.	n.a.	n.a.
PR3 ANCA, U (ref. <2)	n.a.	n.a.	n.a.	19	13	6
MPO ANCA, U (ref. <2)	n.a.	n.a.	n.a.	Neg	Neg	Neg
Anti-GBM Ab, UI (ref. <3)	n.a.	n.a.	n.a.	Neg	n.a.	n.a.
ANA, UI (ref. <2.5)	1.1	n.a.	n.a.	1.8	n.a.	n.a.
Urine ACR, mg/mmol	n.a.	n.a.	n.a.	15	72	84
Immunosuppressive therapy	IVIg+PDN	MMF	PDN+MMF	Rituximab+PDN	Avacopan	Avacopan

Abbreviations: AB, antibody; AChR, acetylcholine receptor; ANA, anti-nuclear antibody; ACR, albumin/creatinine ratio;GBM, glomerular basement membrane; IVIg, intravenous immunoglobulins; MMF, mycophenolate mofetil; MuSK, muscle-specific kinase; n.a., not available; NSTEMI, non-ST-segment elevation myocardial infarction; PDN, prednisolone

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Describing clinical diagnosis of pathological proven follicular bronchiolitis with focus on ANCA Associated Vasculitis (AAV)

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Background/Objective: Follicular bronchiolitis (FB) is a rare bronchiolar disorder associated with hyperplasia of the bronchus-associated lymphoid tissue (BALT). Whether there is a relationship between FB and vasculitis, however, is unknown.

Methods: We report a retrospective chart review of 23 biopsy-proven FB patients over a span of 24 years (1999 -2023). Demographics, underlying etiology, pulmonary symptoms, autoimmune serologies, and, when available, pulmonary function tests (PFTs) and high-resolution computer tomography (HRCT) chest, were recorded.

Results: The cohort included 18 (78%) females and 5 (22%) males. The average age at diagnosis was 50 years (range 19-79). Most (17/23,74%) had an underlying disease, including autoimmune (12), malignancy (5), immunodeficiency (2), and hypersensitivity pneumonitis (1). The remaining 6 (26%) were idiopathic. Among patients with autoimmune disease, 3/12 (25%) had Antineutrophilic Cytoplasmic Antibody (ANCA) associated vasculitis, 2/12 (16.7%) had Granulomatosis with Polyangiitis (GPA) and 1/12 (8.3%) had undifferentiated ANCA-associated vasculitis (AAV). Cough and dyspnea were more common complaints on presentation, 43% and 52% respectively. Among 20/23 patients with available PFTS, a non-specific pattern was the most prevalent (50%). HRCT was available in 22/23 patients. The most predominant findings were those suggestive of airway disease: bronchial wall thickening (17/22, 77%), centrilobular nodules (17/22, 77%), mosaic perfusion (13/22, 59%), and tree-in-bud nodules (9/22, 41%). Nodularity was also present in 68% of our study cohort in general, 83% in autoimmune, and 71% in malignancy. In ANCA-AAV patients, the most common radiologic findings were: centrilobular nodules (3/3, 100%), mosaic perfusion (2/3, 67%), tree-in-bud nodules (2/3, 67%), and bronchial wall thickening (2/3, 67%). More than half of FB patients with ANCA-AAV (66.7%) had lymphadenopathy on HRCT.

Conclusion: To the best of our knowledge, this is the largest cohort of follicular bronchiolitis patients ever described, and the first one to explore the association between FB and ANCA-AAV. Twenty-six percent of our patients were classified as idiopathic; however, it has been noted in the literature that an autoimmune disease might develop over time, requiring regular monitoring and annual autoimmune and ANCA serologies.[1] Clinicians should consider FB as a diagnosis when evaluating patients with ANCA-AAV. Further prospective studies are necessary to validate this correlation.

Reference:

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Description of clinical, serological and therapeutic characteristics of patients with crioglobulinemic vasculitis: a single hospital experience

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Objective: To describe the clinical and biochemical characteristics, treatment received, and outcome of patients with cryoglobulinemic vasculitis (CryoV).

Methods: Observational, retrospective and descriptive cohort study from a third level hospital. A chart review of patients diagnosed with CryoV between 1994-2022 was performed. Cases were classified according to CryoV preliminary criteria (De Vita S et al, 2011 & Quartuccio L et al 2014).

Results: Eleven patients were identified from whom 6 were positive for type II cryoglobulins (Brouet classification), being the most prevalent type (55%). The most frequent etiology was hepatitis C and B virus (55% and 18%, respectively), followed by systemic autoimmune diseases (27%). The latter group included 2 patients with Sjögren syndrome and 1 with systemic sclerosis, all of which were diagnosed with a low-grade B-lymphoma synchronously. Clinical manifestations consisted in constitutional symptoms in all of patients: fatigue (100%), fever (64%), and arthralgias or arthritis (67%). Necrotizing palpable purpura was the initial presentation in 8 patients (73%). This was complicated by severe ulcers in 4 (36%). One patient required the amputation of the left lower extremity due to ischemia. Four patients (36%) had associated renal involvement in the form of membranoproliferative glomerulonephritis (GMN), which progressed to chronic renal failure in two cases. One patient had gastrointestinal involvement (gastric ulcer) and 5 patients (45%) had peripheral neuropathy. The median baseline BVAS was 11.13 (SD 7.85). All patients, regardless of the type of cryoglobulinemia, presented with C4 hypocomplementemia and increased levels of rheumatoid factor at diagnosis. Median CRP was 10.76mg/dl (SD 7.93). The initial treatment consisted in high-dose oral glucocorticoids (0.5-1mg/kg/day prednisone or equivalent). Four patients (those with GMN) received intravenous methylprednisolone (250mg/day per 3 days) and rituximab (two doses of 1g 15 days apart). There were 4 relapses, two in the form of purpura and glomerulonephritis and two with worsening polyneuropathy. All relapses were treated with GC and rituximab. Three patients (27%) died, all by infectious complications.

Conclusions: CryoV is a complex and heterogeneous disease. According to the type of cryoglobulins identified, an infectious, hematological, or autoimmune etiology should be investigated. In agreement with previous publications, the most frequent organ-systems involved were the skin, the peripheral nerves, and the kidneys. Overall, clinical manifestations and outcome of this small series compare with large cohorts of patients [1].

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Anti-GBM disease in association with pembrolizumab

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Presentation of Case: A 75-year-old white man was referred to the nephrology team with a progressive decline in kidney function over a three month period. His medical history included a diagnosis of non-small cell lung cancer for which he had been undergoing pembrolizumab immunotherapy for the past 18 months (15 cycles). The patient was an ex-smoker and originally from Bosnia.

Diagnostic Testing: At referral, serum creatinine was 184µmol/L, eGFR 30 ml/min/1,73m^2. An autoimmune screen yielded a positive anti-glomerular basement membrane (Anti-GBM) result (23iu/L, normal range <7). The patient had normal urine output and did not have any clinical or radiographic evidence of pulmonary haemorrhage. He underwent kidney biopsy, which demonstrated focal and necrotizing crescentic glomerulonephritis with linear IgG deposition, and eosinophilic tubulo-interstitial infiltrate (Berden class - mixed).

Differential & Final Diagnosis: The differential diagnosis included acute interstitial nephritis (the most common kidney toxicity in relation to checkpoint inhibitors) diabetic nephropathy, monoclonal immunoglobulin deposition disease, fibrillary glomerulonephritis and anti-glomerular basement membrane (Anti-GBM) disease (the final diagnosis).

Discussion of Management: A diagnosis of Anti-GBM disease associated with pembrolizumab was established and the patient underwent treatment with corticosteroids, seven cycles of plasma exchange, oral cyclophosphamide (total dose 3.3g) and two intravenous doses of 1g rituximab. The patient achieved a negative anti-GBM status within 0.13 months of presentation. Despite treatment for anti-GBM disease and cessation of pembrolizumab, his kidney function continued to decline, and his cancer progressed. Further chemotherapeutic options were limited due to severely impaired eGFR.

Six months after diagnosis, he presented unwell to hospital and received treatment for a presumed chest infection. Unfortunately, his condition deteriorated during this inpatient stay. As he was not a suitable candidate for dialysis, or further lung cancer treatment, appropriate palliative care was provided, and he passed away peacefully (6.67 months after induction treatment).

Conclusions: Whilst immune checkpoint inhibitors have significantly improved the prognosis for patients with advanced malignancies, they can also be associated with diverse autoimmune organ toxicities, including those affecting the kidney[1]. This case demonstrates a rare but important diagnosis of anti-GBM disease in association with pembrolizumab therapy. It also highlights the challenges of managing immunosuppression and chemotherapy in patients who are frail and with impaired kidney function.

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IgA Vasculitis as an Initial Presentation of HIV in a Young Filipino Male: A Case Report

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Presentation of Case: A 29-year-old Filipino male presented with a one-month history of lower extremity purpura, joint pains, and abdominal pains. Past medical and family history were unremarkable, but he has been self-medicating on oral estrogen since he was 14 y/o, and has multiple sexual partners. He underwent an exploratory laparotomy due to suspected intussusception on imaging, but intraoperative findings only showed bowel wall erythema and edema. Persistent hematochezia and joint pains post-operatively led to rheumatology consult. Prednisone at 1 mg/kg/day (60mg) was started, and gradually resolved symptoms. However, new-onset paresthesia and progression of rashes to upper extremities led to further evaluation.

Diagnostic Testing: Pertinent laboratories showed the following: Hemoglobin of 82 g/L, Hematocrit 0.25, with a WBC of 11,400 (with 72% segmenters, 21% lymphocytes, and 7% monocytes), and platelet count of 273,000/ml. Bleeding parameters, serum creatinine, and electrolytes were all normal. Urinalysis showed hematuria and proteinuria, with an elevated urine protein-creatinine ratio of 6.07 g/g. Serology for syphilis, hepatitis B and C were normal. Testosterone and Estradiol levels were also normal. Anti-neutrophil cytoplasmic antibodies were negative, while an HIV ELISA screening was reactive. A baseline CD4 count showed levels of 87 cells/mm^3.

Differential & Final Diagnosis: IgA vasculitis was a primary consideration given the constellation of symptoms. However, the progression of his rashes and the development of paresthesia despite therapy prompted search for a secondary cause— hence HIV-associated IgA vasculitis was considered based on the work-up.

Discussion of Management: The therapeutic options for vasculitis are similar in both HIV-positive and HIV-negative patients, although no standardized protocol exists. Among those with IgA vasculitis, most are responsive to corticosteroids and antiretroviral therapy, as featured in case reports. This patient was managed with prednisone at 1mg/kg/day and enalapril at 5mg/day, to address his gastrointestinal, musculoskeletal, and renal manifestations. The use of Highly Active Anti-Retrovial Therapy (HAART) is integral in controlling the infection and preventing disease progression. In this case, steroids were gradually tapered, while HAART was initiated.

Conclusions: It is important to recognize vasculitis as an initial manifestation of HIV infection, since it can be seen at any stage of the HIV/AIDS spectrum.

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Acute kidney injury secondary to double positive MPO-ANCA and anti-GBM disease

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Presentation of Case: A 72-year-old male presented with acute kidney injury, history of microscopic haematuria for 6 months, constitutional symptoms and nasal crusting. He was known to have raised Myeloperoxidase anti-neutrophil cytoplasmic antibodies (MPO-ANCA) for 1 year without renal involvement.

Past medical history includes Cardiomyopathy, Psoriasis, Valvular heart disease, Ischaemic heart disease and Atrial fibrillation.

Diagnostic Testing: Urinalysis showed proteinuria and active sediments. Ultrasound scan showed normal kidneys with no obstruction. The immunology screen showed double-positive MPO-ANCA (62 IU/ml) and anti-glomerular basement membrane (anti-GBM) (54 U/mL). Native kidney biopsy showed crescentic glomerulonephritis with weakly positive IgG staining on Immunofluorescence.

Differential & Final Diagnosis: The patient was treated for acute kidney injury secondary to double-positive MPO-ANCA and anti-GBM disease.

Discussion of Management: Double-positive vasculitis is rare with poor renal survival. These patients experience early morbidity and mortality typical of anti-GBM disease and they carry the long-term risk of relapse typical of ANCA-associated vasculitis.

Our patient exhibited subacute disease with systemic symptoms and Acute Kidney Injury. He was treated with plasmapheresis, prednisolone, and cyclophosphamide. Reduction in antibody titres was noted with 7 sessions of plasmapheresis and creatinine was 350umol/L on discharge. No long-term dialysis was needed as renal functions did not reach end-stage failure.

The patient was re-admitted in 3 weeks with worsening renal functions. Required 4 more sessions of plasmapheresis due to raised anti-GBM titre (12 U/ml). Plasmapheresis was discontinued due to persistent hypotension. Cyclophosphamide was withheld due to pancytopenia. The patient succumbed to septicaemia from partial compliance and side effects of treatment.

Conclusions: Anti-GBM disease and MPO-ANCA-associated vasculitis are small vessel vasculitis that can lead to rapidly progressive glomerulonephritis and alveolar haemorrhage with a risk of organ failure and death. Serological testing and kidney biopsy are essential for diagnosis.

Double-positive cases require aggressive early treatment for anti-GBM disease (Plasmapheresis) and long-term follow-up with consideration of maintenance immunosuppression for ANCA vasculitis.

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Behçet's Disease and PR3 ANCA-Associated Vasculitis Overlap Successfully Treated with Rituximab

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Presentation of Case: We report the case of a previously healthy 21-year-old Caucasian male who presented with an acneiform rash, and penile and oral ulcers. He was seen in dermatology clinic, and papule biopsies revealed lymphoplasmacytic perivascular infiltration. Pemphigus vulgaris was ruled out. He then developed small volume hemoptysis, shortness of breath, and marked worsening of oral ulcers with odynophagia and 30 kg weight loss. He was admitted to hospital for nutritional support. Severe worsening of penile ulcers necessitated circumcision. Worrisome for Behçet's disease (BD), he was initiated on prednisone 60 mg and colchicine.

HLA-B51 was positive. Curiously, proteinase 3 (PR3) anti-neutrophilic cytoplasmic antibody (ANCA) (183 mean fluorescence units, normal <120) was also positive. Computed tomography (CT) revealed ground-glass opacities and micronodules. He was also found to have isomorphic hematuria without proteinuria. Palpebral conjunctival biopsies demonstrated ulcerative granulomatous conjunctivitis. Adalimumab and mycophenolate were added to support steroid-taper.

While initially stabilized, oral ulcers and shortness of breath re-emerged with prednisone taper prompting re-escalation to high-dose steroids and addition of apremilast. Repeat CT demonstrated extensive micronodular disease, and bronchoscopy revealed ulceration and friability. CT demonstrated sinusitis with ethmoid air cell mucosal thickening. Around this time, he also developed digital ulcers.

The patient was subsequently referred to vasculitis subspecialty rheumatology and diagnosed with a remarkable overlap of PR3 ANCA-associated vasculitis (AAV) and BD. Adalimumab and apremilast were discontinued. Rituximab was initiated resulting in sustained remission.

Diagnostic Testing: Anti-nuclear antibody (ANA) was also positive (1:80 AC-15, -16, -17, -19, -20, and -21). Myeloperoxidase (MPO) ANCA was negative.

Differential & Final Diagnosis: Ulcers, ocular disease, acneiform rash, and HLA-B51 supported BD [1-3]. Sinonasal and pulmonary disease, and PR3 favoured AAV [4]. The patient was diagnosed with a remarkable and exceedingly rare BD/AAV overlap.

Discussion of Management: There is limited evidence of the use of rituximab in Bechet's disease. The decision to use rituximab in this case was justified by the lack of response to mycophenolate and adalimumab, the patient's age, and his disease severity.

Conclusions: Patients with BD may rarely be seropositive for ANCAs [2], though to our knowledge, this represents only the second reported cases of BD/AAV overlap, and the first successfully treated with rituximab [3].

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Author 1: None.

Author 2: UCB, AbbVie, Novartis, Janssen, Sanofi, Otsuka.

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Avacopan in monotherapy for remission induction in ANCA-associated vasculitis: a case report

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Presentation of case: Here we describe the case of a severe ANCA-associated vasculitis (AAV) with pulmonary, ear-nose-throat (ENT) and renal involvement treated for remission induction with avacopan only after a short duration of methylprednisolone treatment.

A 68-year-old male was diagnosed with an AAV in 2002. His initial clinical presentation was a rapidly progressive glomerulonephritis, ENT involvement and high titers of anti-PR3 antibodies, allowing to diagnose granulomatosis with polyangiitis (GPA). His induction treatment consisted of methylprednisolone and cyclophosphamide followed by azathioprine and methylprednisolone therapy. He remained in remission during years with persistent anti-PR3 antibodies and with a chronic kidney disease stage G3bA2 according to KDIGO. Decision was made to stop azathioprine 10 years after the initial diagnosis because of the appearance of a cutaneous squamous cell carcinoma (cSCC) of the scalp region. Consecutively, methylprednisolone was interrupted in the beginning of 2023 because of osteopenia, skin atrophy and quiescent GPA.

End of march 2023 the patient presented with weight loss, fever, fatigue, ENT symptoms, lymphopenia and hypercalcemia. Pulmonary CT scan showed multiple excavated lung nodules and pleural effusions. Furthermore, microscopic hematuria appeared and glomerular proteinuria increased, but kidney function remained stable. Infectious and paraneoplastic causes were excluded. Anti-PR3 titers raised to values 4 times higher than baseline.

Final diagnosis: Relapse of anti-PR3 GPA. BVAS score at time of diagnosis was 27.

Management & discussion: Because of the past medical history of cSCC and the presence of severe lymphopenia (500/mm3), we decided not to treat the patient with cyclophosphamide or rituximab. We started corticosteroid therapy and avacopan in compassionate use. The high dose corticosteroid was rapidly tapered and stopped after 2 months of treatment. The patient remains in remission on avacopan monotherapy with a BVAS score of 0 at 6 months after treatment initiation. Avacopan has been shown beneficial for remission induction in AAV in adjunction with rituximab or cyclophosphamide instead of corticosteroids (1). However, no data have been reported on the therapeutic potential of this drug in monotherapy as an induction treatment.

Conclusion: The present case report demonstrates that avacopan in monotherapy can induce remission in a patient with a severe AAV. There was a high-unmet medical need in this patient where classic remission induction treatment was not suitable. Avacopan alone can be effective in treating severe or relapsing AAV in a selected patient population.

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Pauciimmune crescentic glomerulonephritis (PCGN) secondary to ANCA-associated vasculitis (AAV): therapeutic experience of a tertiary hospital

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Background/objectives: AAV is a rare disease and the different treatment's role of plasma exchange are still controversial. We evaluate the AAV outcomes of the last ten years of our centre.

Material and methods: We study AAV cases in our centre between 2013-2022. We included AAV flares with acute renal failure, positive ANCA-MPO or PR3 and renal biopsy with pauciimmune crescentic glomerulonephritis. We compared the presentation and evolution according to the type of ANCA, serum creatinine (SCr) and use of plasma exchange (PLEX). We included patients with a kidney biopsy, at least 6 months of follow-up and patients with positivity for both MPO and PR3, anti-GBM antibodies or did not meet inclusion criteria were excluded.

Results: Of 64 patients, 13 got excluded: 3 lack of follow-up, 3 absence of renal biopsy, 3 ANCA negative, and 4 presented concomitant anti-GBM antibodies. Finally, 51 patients underwent analysis (table 1): 28 women (54.9%), age 66.75±15.24 years, (64.7% over 65 years) and 44 (86.3%) with ANCA-MPO (+). Results comparing ANCA-MPO and PR3 in Table 1. The most frequent form of presentation was anaemia with haemoglobin 9.87±2.04 mg/dL, acute kidney injury (AKI) AKIN III (39.2%), median SCr 2.78 (1.58 -5.22) mg/dL, 41(80.4%) with microhematuria, proteinuria 2.62±2.7g/g and 8(15.7%) alveolar haemorrhage. 18 patients (25.3%) required hemodialysis, and 7 (13.5%) were transient (4 requiring <1 month). Rituximab was more used than cyclophosphamide (p<0.001). Of the patients treated with plasma exchange (PLEX, n=11), 6(54.5%) had an alveolar haemorrhage and/or 7(63.6%) SCr>5.6mg/dL, with no further infections or mortality at one year. Of the patients diagnosed with SCr>5.6mg/dL, 9(81.8%) were men (p=0.008), 7(63.6%) received PLEX(p<0.001) and 6(54.4%) died (p=0.003). There were 13 deaths (25.5%), 6 in the first year after diagnosis. The most used maintenance treatment was MMF (52.9%), SCr and glomerular filtration rates at 2 years were 1.5mg/dL and 45.36mL/min/1.72m² respectively.

Conclusions: The most common AAV in our centre are ANCA-MPO+, and they mainly affect people over 65 years of age, with rituximab being the most used treatment. ANCA-MPO+ patients have worse renal function at 18 months of follow-up. Mortality is higher in the case of serum creatinine greater than 5.6 mg/dL at diagnosis and in patients with ANCA-MPO +. PLEX therapy is more used in cases of alveolar haemorrhage or severe renal involvement, without presenting an impact in our cohort in incidence of infections or mortality at one year of follow-up.

Disclosures: None.

Table 1. Patients compared as ANCA-type.

	ANCA-MPO (n=44)	ANCA-PR3 (n=7)	p		
Gender (woman %)	25 (56,8)	3 (42,9)	0,491		
Age (years)	67,57±15,36	61,57±14,44	0,339		
Race (caucasic %)	37 (84,1)	6 (85,7)	0,913		
IMC (Kg/m²)	27,2±3,9	23±3,2	0,052		
Arterial hypertension (yes %)	26 (59,1)	3 (42,9)	0,421		
Dislypemia (yes %)	19 (43,2)	2 (28,6)	0,466		
Type 2 diabetes mellitus (yes %)	9 (20,5)	1 (14,3)	0,703		
Baseline serum creatinine (mg/dL)	0,85 (0,73-1,21)	0,87 (0,60-1,00)	0,502		
Hemoglobin (flare; g/dL)	9,88±2,11	9,83±1,70	0,952		
Serum creatinine (flare; mg/dL)	2,82 (1,74-5,21)	1,59 (1,29-5,79)	0,305		
Serum creatinine >5,6 mg/dL (yes %)	9 (20,5)	2 (28,6)	0,628		
Haematuria (yes %)	36 (81,8)	5 (71,4)	0,520		
Proteinuria (g/g)	2,75±2,83	1,68±1,07	0,369		
C reactive proteine(mg/dL)	3,93 (0,92-16,99)	6,78 (0,40-18,37)	0,834		

	ANCA-MPO (n=44)	ANCA-PR3 (n=7)	p		
Haemodyalisis (yes %) Transitient (yes %) Permanent (sí %)	14 (31,8) 5 (11,4) 9 (20,5)	4 (57,1) 2 (28,6) 2 (28,6)	0,193 0,299 0,772		
Alveolar haemorrhage (yes %)	7 (15,9)	1 (14,3)	0,913		
Infection at diagnosis (yes %)	10 (22,7)	0 (0)	0,160		
IS induction GC+CFM (%) GC+RTX (%) GC+CFM+RTX (%) GC+MMF (%)	 7 (15,9) 27 (61,4) 6 (13,6) 4 (9,1)	 2 (28,6) 3 (42,9) 2 (28,6) 0 (0)	 0,414 0,355 0,313 0,406		
PLEX (yes%)	9 (20,5)	2 (28,6)	0,628		
Infection after 12 months of follow-up (yes %)	19 (43,2)	4 (57,1)	0,491		
IS maintenance GC+RTX (%) GC+MMF (%) GC+AZA (%) GC (%)	 12 (27,3) 25 (54,5) 2 (4,5) 5 (11,4)	 2 (28,6) 2 (28,6) 2 (28,6) 1 (14,3)	 0,943 0,202 **0,028** 0,824		
Serum creatinine at 6 months (mg/dL)	1,90±0,90	1,39±0,48	0,223		
eGFR (CKD-EPI) at 6 months (mL/min/1,73m²)	40,2±22,8	54,8±24,0	0,194		
Serum creatinine at 12 months (mg/dL)	1,84±0,99	1,49±0,25	0,547		
eGFR (CKD-EPI) at 12 months (mL/min/1,73m²)	40,5±20,8	55,5±23,3	0,189		
Serum creatinine at 18 months (mg/dL)	1,74±0,75	1,21±0,46	0,183		
eGFR (CKD-EPI) at 18 months (mL/min/1,73m²)	39,9±16,8	61±23,0	**0,032**		
Serum creatinine at 24 months (mg/dL)	1,65±0,64	1,27±0,48	0,272		
eGFR (CKD-EPI) at 24 months (mL/min/1,73m²)	42,8±20,0	60,5±23,0	0,120		
Renal transplantation (yes %)	5 (11,4%)	1 (14,3%)	0,824		
	PLEX (n=11)		**NO PLEX (n=41)**		**p-valor (Chi-cuadrado)**
SCr greater/not 5,6 mg/dL					
Greater	7 (63,6%)		4 (9,8%)		**<0,005**
Minor	4 (36,4%)		37 (90,2%)		
Alveolar haemorrhage					
Yes	6 (75%)		2 (25%)		**<0,005**
No	5 (11,4%)		39 (88,6%)		
Infection afeter 12 months					
Yes	6 (26,1%)		17 (73,9%)		0,477
No	5 (17,9%)		39 (82,1%)		
Mortality during follow-up					
Yes	3 (23,1%)		10 (76,9%)		0,862
No	8 (21,1%)		30 (78,9%)		

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Muscle involvement in cryoglobulinemic vasculitis

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Presentation of Case: A 59-year-old woman consulted because of a palpable purpura on the lower extremities. Initial laboratory tests showed mild anemia, normal renal function and autoimmunity studies were positive for antinuclear antibodies (ANA 1:640, homogeneous nucleolar pattern), low complement C4 levels (normal C3), and positive detection of cryoglobulins (m*ixed cryoglobulinemia type III with polyclonal* IgG and IgM). *The patient referred a weight loss of 4Kg in 8 months, paresthesias, numbness and weakness in the lower extremities with difficulty in climbing stairs, without night sweats, gastrointestinal or respiratory symptoms, sicca syndrome, mouth sores, rash, fever or arthritis.*

Diagnostic Testing: The blood analysis showed increased rheumatoid factor, slightly elevated serum creatine kinase, negative serologies (HIV, HCV and HBV) and normal protein electrophoresis. Specific autoantibodies were all negative. Skin biopsy showed leukocytoclastic vasculitis. Nerve conduction study revealed a symmetric sensory axonal polyneuropathy and needle electromyography showed myopathic pattern with spontaneous activity at rest. A thoracoabdominal CT ruled out malignancy. Lower limb muscle MRI showed muscle edema without atrophy. Muscle biopsy revealed variability in fibre size with fibres of intermediate size and atrophic fibres, that were not grouped, with perivascular inflammatory infiltrate and MHC class I was up-regulated.

Differential & Final Diagnosis: The patient had a cryoglobulinemic vasculitis (CV). Mixed cryoglobulinemia (type II and III) can be seen in viral infections (mainly HCV or HIV), B-cell lineage hematologic malignancies and connective tissue diseases (CTD), especially in Sjogren's syndrome (1).

In our case, we consider undifferentiated CTD with CV as the final diagnosis. In the follow-up, we should look for new specific symptoms that could support the diagnosis of a specific CTD.

Discussion of Management: Treatment strategies should be individualized based on the underlying etiopathogenesis, severity of organ involvement, and underlying disease (1). In our case, hydroxychloroquine was started until the study was completed. After the study, we started treatment with prednisone 30mg/day and induction treatment with Rituximab. At 6-month follow up the patient had no purpura or weakness. Blood tests showed negative cryoglobulins and a depletion of CD19 B-cells.

Conclusions: To our knowledge, there are only two other case reports of muscle inflammation in the setting of CV (2, 3). In view of this, cryoglobulinemia should be considered in the differential diagnosis of inflammatory myopathies. On the other hand, patients with cryoglobulinemia should be questioned about weakness, and muscle involvement should be excluded by complementary investigations.

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Disclosures: None.

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A Case of Infective Endocarditis mimicking ANCA-associated vasculitis

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Presentation of Case: We report a clinical case of a patient who developed IE with systemic complications, viz, ANCA-associated rapidly-progressive glomerulonephritis, thrombocytopenia, and hepatosplenomegaly. A 37-year-old male patient with a history of hypertension and ischemic stroke presented with complaints of chills, subfebrile fever, dyspnea on exertion, lower-extremity edema, and visual deterioration in the right eye.

Diagnostic Testing: Initial examination revealed elevated creatinine levels (145-160 mcmol/L), trace proteinuria (0.3 g/L), and no changes in urinary sediment. Within the next three months the patient developed erythrocyturia (135,000/mL), anemia (hemoglobin 94 g/L), elevated ESR (53-74 mm/h), C-reactive protein (35.4 mg/L), and rheumatoid factor (128 U/L) levels. He was positive for anti-citrullinated protein antibody (21.7 U/mL); however, no signs of joint involvement were detected. Ultrasound examination showed hepatosplenomegaly and solitary kidney cysts. By the time of admission to our hospital he developed pronounced dyspnea, febrile fever, progressive deterioration of kidney function (creatinine 475 mcmol/L), severe anemia (hemoglobin 57g/L), and thrombocytopenia of $104x10^9$/L. ELISA was positive for proteinase-3-ANCA. CT scan showed ground-glass opacities in both lungs.

Differential and Final Diagnosis: Initial diagnosis of ANCA-associated vasculitis with rapidly-progressive glomerulonephritis was established, and the patient received methylprednisolone pulse-therapy 500 mg IV. However, on the second day of in-hospital stay echocardiography revealed severe mitral-valve insufficiency, and vegetations. Glucocorticoid treatment was immediately stopped. Several days later blood culture returned positive for *Enterococcus faecalis* and *Streptococcus oralis*.

Discussion of Management: The patient was diagnosed with IE and started on intravenous vancomycin in combination with meropenem. The patient underwent mitral-valve replacement with a mechanical prosthesis and was prescribed a 3-week course of antibacterial therapy consisting of ceftriaxone, ampicillin-sulbactam, and fluconazol. On therapy his fever and dyspnea completely resolved, ESR and CRP normalized, and creatinine level stabilized at 300 mcmol/L. During five years of follow-up, we have not registered any relapses of systemic autoimmune reactions.

Conclusion: The presented data suggest IE can lead to complications beyond heart valve involvement and mimic systemic autoimmune diseases, including ANCA-associated vasculitis. Multidisciplinary approach, close monitoring, early initiation of targeted therapy and potential surgical intervention are necessary to mitigate the impact of systemic complications and optimize the patient's overall prognosis.

Disclosures: None.

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Two cases of eosinophilic granulomatosis with polyangiitis and rheumatoid arthritis overlap

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Presentation of Case:

Case 1: A 42-year-old female patient presented with shortness of breath, cough, arthralgia, erythematous rash and fever >38°C. She was diagnosed with an acute asthma exacerbation and received a combination of oral and inhaled corticosteroids (CS) resulting in clinical remission. However, one year later her arthralgia became more severe, and she developed severe refractory asthma. Laboratory testing revealed elevated p-ANCA titer of 1:256. The diagnosis of Churg-Strauss syndrome (CSS) was established. Treatment with high-dose CS and cyclophosphamide was initiated. After remission was achieved, she was switched to maintenance therapy with azathioprine. Six years later she presented with erosive arthritis. Laboratory testing revealed high levels of rheumatoid factor (RF), anti-citrullinated protein antibodies (ACPA) and C-reactive protein (CRP). Rheumatoid arthritis (RA) was diagnosed. Azathioprine was canceled and she was treated with methotrexate (MTX) at a dose of 20 mg once weekly and prednisolone 10 mg/day followed by a dose reduction to 5 mg/day resulting in sustained remission.

Case 2: A female patient developed asthma with eosinophilia at the age of 13. Two years later, endoscopic sinus surgery was performed for chronic rhinosinusitis with nasal polyps. At the age of 16, she presented with arthritis, high levels RF and ACPA, and was diagnosed with juvenile idiopathic arthritis. She was treated with MTX and achieved remission. Two years later she stopped treatment by her own decision and soon developed arthralgia and palpable purpura. In-hospital investigation showed persistent eosinophilia up to 20% and high level of RF, CRP and ESR were within reference ranges, and ANCA were negative. Histological preparations which received from previous nasal intervention were re-evaluated and revealed pronounced lymphohistiocytic inflammatory infiltration with neutrophils and eosinophils, foci of necrosis and hemorrhages, and signs of necrotizing vasculitis. She was diagnosed with EGPA-RA overlap and re-treated with CS and MTX resulting in sustained remission.

Conclusions: It has been reported that AAV may coexist with RA. Most of the published cases describe the overlap of granulomatosis with polyangiitis (Wegener's) or microscopic polyangiitis and RA, and the evidence on EGPA-RA overlap remains anecdotal [1]. The possible explanation being the low prevalence of EGPA compared to the other AAV [2].

Discussion of Management: The reported cases show EGPA occurrence can either precede and follow RA. It should be noted that both DMARDs and systemic immunosuppressive therapy can delay and mask the presentation of the second condition. In both cases it is possible to assume a delayed diagnosis of the second diseases and it is impossible to accurately determine the time of their onset. These findings emphasize the importance of multidisciplinary approach to the patients with either EGPA or RA presenting with atypical symptoms.

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Disclosures: None.

P-269

Temporal arteritis revealing eosinophilic disease: A European multicenter retrospective study

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Background: Temporal arteritis (TA) is primarily associated with giant cell arteritis. In less than 5%, TA may be associated with other vasculitides or inflammatory diseases (1-3). Some of these conditions may be associated with blood and/or tissue eosinophilia (4,5). We aimed to describe the association of TA and blodd and/or tissue eosinophilia.

Methods: We performed a retrospective, descriptive, multicenter European study. Inclusion criteria were defined as follows: 1) confirmed temporal arteritis, either by histologic confirmation or by the presence of typical clinical symptoms together with inflammatory signs on imaging, excluding alternative diagnoses, 2) pretreatment blood eosinophilia levels greater than 1000/mm3.

Results: Thirty-eight patients from the European cohort and thirty-six patients from the literature review met the inclusion criteria. Of these, 30 (41%) patients were diagnosed with EGPA, 24 (32%) patients were diagnosed with hypereosinophilic syndrome (HES), 5 (7%) patients were diagnosed with Kimura's disease, and 15 (20%) patients were diagnosed with eosinophilic TA (EoTA). The median age [IQR] was 59 years [40.5; 69.5] with a male predominance. Clinically, constitutional symptoms were observed in 63% and typical cephalic manifestations in 80%. Osteoarticular signs were present in 35% of cases and ocular signs were reported in 21%.

In patients with EGPA, pulmonary, otolaryngologic, and multiple mononeuropathies were observed in more than 50% of cases. In contrast, patients with HES had predominantly cutaneous, cardiac, and vascular involvement in more than 30% of cases. Patients diagnosed with EoTA did not have systemic symptoms beyond those associated with temporal involvement.

CRP levels were significantly higher in patients diagnosed with EGPA (89 mg/l [34; 127]) compared to those with SHE and EoAT (5 mg/l [5;5] and 6.4 mg/l [5; 84] respectively p <0.001).

Histologically, 57 of 68 temporal artery biopsies were positive. In patients diagnosed with EoTA (n=15), findings revealed the presence of giant cells (36%) and eosinophilic infiltrate (73%). As expected, patients diagnosed with EGPA (n=30) showed features such as fibrinoid necrosis (36%), adventitial small vessel vasculitis (23%), eosinophilic infiltration (68%), and presence of giant cells (50%). In patients diagnosed with HES (n=7), findings included eosinophilic infiltration (84%), thrombosis (32%), and giant cells in 5% of cases.

The majority of patients received glucocorticoids between 0.6 and 1 mg/kg, resulting in remission in 69% of cases. In addition, 66% of patients received immunosuppressive agents, including cyclophosphamide (n=8), rituximab (n=8), methotrexate (n=7), and mepolizumab (n=5). Eosinophil evolution and clinical evolution paralleled each other in 84%.

Conclusion: This study, focusing on temporal arteritis presenting in association with blood and/or tissue eosinophilia, suggests that the three main entities are EGPA, HES, and single-organ eosinophilic temporal arteritis.

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Disclosures: None.

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Acute cholecystitis in granulomatosis with polyangiitis

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Presentation of Case: A 65-year old women presented with fever and generalized weakness, and was admitted to the Clinic for infectious diseases. Upon admission, physical examination revealed signs of dehydration, mild hypotension and tachycardia. There was no palpable tenderness in the abdomen, and Murphy's sign was negative.

Diagnostic Testing: Initial work-up revealed normocytic anemia (Hemoglobin 97 g/l), elevated markers of inflammation (C-reactive protein 122mg/l) and elevated biliary tract enzymes, with no signs of kidney damage. Urinalysis revealed larger amounts of protein and red blood cells. Blood and urine cultures were negative, and no signs of inflammation were identified on radiographic imaging. Due to persisting fever and unresolved inflammatory process despite the usage of parenteral antibiotic treatment, a computed tomography was also performed and revealed a calculous cholecystitis necessitating laparoscopic cholecystectomy. Histopathology of the resected gallbladder showed small-vessel vasculitis. On the fourth postoperative day the patient developed Coombs positive anemia (Hemoglobin 44g/l). Laboratory tests revealed positive proteinase-3- anti-neutrophil cytoplasmic antibody (PR3-ANCA), with an onset of renal dysfunction also set in (urea 32mmol/l, creatinine 354µmol/l). After having completed surgical treatment, the patient was transferred to the Clinic for Nephrology and Clinical Immunology.

Differential & Final Diagnosis: The preoperative diagnosis was calculous cholecystitis, but histopathology showed small-vessel vasculitis. The differential diagnoses that were taken into account were single-organ vasculitis and systemic vasculitis. Laboratory tests revealed elevated levels of creatinine and urea, microhematuria and proteinuria, and positive PR3-ANCA. These findings were consistent with a diagnosis of granulomatosis with polyangiitis (GPA).

Discussion of Menagement: Firstly she was treated with antibiotics but without improvement. After the histopathologic analysis, and having established the diagnosis she was started with glucocorticoids (GCs), the initial dose methylprednisolone of 1mg/kg daily (60mg in total), with gradual tapering. Also treatment with intravenous cyclophosphamide was initiated with a dose of 12,5mg/kg every two weeks for five months (700mg in total every two weeks). After this treatment, the patient's general condition stabilized and creatinine levels decreased to 161µmol/l, anemia resolved as well (Hemoglobin 110g/L), C-reactive protein levels decreased to 3.3mg/L. On the ambulatory check-up the patient was feeling well, no worsening of kidney function was noted and no other organ involvement was present.

Conclusion: GPA is a disorder that causes inflammation of blood vessels in various organs, primarily affecting the respiratory tract and kidneys. However, other organs such as the gall bladder may rarely be affected. We hereby present a case of a patient who presented with acute cholecystitis as the initial manifestation of the disease.

References: None.

Disclosures: None.

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Eosinophil-related vasospastic angina: a case report secondary to eosinophilic granulomatosis with polyangitis

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Presentation of Case: A 44 year-old woman had a past medical history of adult-onset bronchial asthma, pansinusitis, and transitory pulmonary infiltrates. In March 2021 she went to the Emergency Department because of chest pain, irradiated to the upper limbs. Given the increase in troponin levels, the ST elevation in V1-V2 and aVr and the reduced ejection fraction at echocardiogram (45%), she was admitted to the Cardiology Department. She underwent a coronary angiography that showed occlusion of the left anterior descending artery (LAD) and was treated with angioplasty and implantation of two drug-eluting stents. She was dismissed with the diagnosis of "ST-elevation myocardial infarction occurring during spontaneous dissection and occlusion of the LAD" and was given calcium antagonists and dual antiplatelet therapy. Afterwards, the woman kept presenting symptomatic episodes of *angina pectoris* and underwent another coronary angiography that resulted substantially normal. After seeking for a second opinion, she was admitted to our Rheumatological Unit.

Diagnostic Testing: The laboratory tests displayed eosinophilia >10%, and negative inflammatory indices. Cardiac enzymes were within normal values. Autoimmunity, including antineutrophil cytoplasmatic antibodies (ANCA), was negative. A cardiac MRI excluded signs of active or past myocarditis. The coronary angiogram images were reviewed in favour of vasospasm. During hospital stay the patient presented further episodes of chest pain that were partially controlled by nitrates and completely disappeared with oral glucocorticoid (GC) therapy [1 mg/kg/day of prednisone-equivalent].

Differential & Final Diagnosis: Coronary vasospasm related to eosinophils can be due to primary hypereosinophilic syndrome, allergic conditions, or drug toxicity. The past and present medical history of our patient, characterized by late-onset asthma, pansinusitis, transitory pulmonary infiltrates, and multiple findings of blood eosinophilia led to the diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA). Coronary vasospasm can be considered an eosinophilic manifestation of the disease and is consistent with the ANCA negative status of our patient.

Discussion of Management: Cardiac involvement in EGPA represents a negative prognostic factor (Five Factor Score = 1); therefore, we decided to induce remission with cyclophosphamide according to NIH scheme [0.5-1 g/m^2/month for 6 months].

Conclusions: Coronary vasospasm is a rare form of cardiac involvement compared to the more common presentation of eosinophil-related cardiac disease (i.e. endomyocardial fibrosis, thrombosis and myocarditis). It appears to derive from the release of vasoactive substances by eosinophils and to well respond to treatment with vasodilators and GCs. The cardiac involvement in EGPA represents an independent risk factor of mortality, thus requiring a major immunosuppressive treatment.

Disclosures: None.

P-273

Use of Avacopan in steroid-dependent refractory ANCA-vasculitis: A case series

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Background/Objectives: Avacopan is a novel small-molecule C5a receptor antagonist approved for use as a steroid-sparing adjunct during induction therapy for ANCA-associated vasculitis (AAV) (1). The utility of this medication as a steroid sparing agent outside the initial induction phase of treatment, such as in clinical situations where steroid tapering has been unsuccessful has not been described. In this case series, we present four patients with refractory disease who had been unable to taper prednisone and were subsequently initiated on avacopan as steroid sparing therapy. The objective of this series was to determine the potential role of initiating avacopan therapy outside of the window proposed by ADVOCATE.

Methods: Four patients from the University of Calgary Vasculitis Clinic were included in the case series. Each patient case demonstrated steroid dependence as defined as inability to discontinue prednisone without worsening of vasculitis symptoms.

Results: The four patients' clinical characteristics and disease progression are described in Table 1. All four patients had granulomatosis with polyangiitis and were PR3 positive. All were treated with rituximab as induction and maintenance therapy. All four had difficulty weaning prednisone due to refractory disease. Patient 2 had three serious infections in the one year prior to initiation. Once avacopan was initiated, two patients were able to completely stop prednisone following the introduction of avacopan and one was able to taper to 5 mg. Patient four experienced worsening gastrointestinal symptoms and prednisone was re-initiated at 50mg. He remained on avacopan but was switched to cyclophosphamide.

The three patients who stopped or significantly taper prednisone lost weight (range 1.6 to 11.9 kg) over the follow-up period (range 3-5 months). There were no documented infections. The only avacopan related side effects noted in our series was a transient increase in liver enzymes of one patient (ALT 120 U/L [ref: ULN 50 U/], decreased 50 U/L after 2 weeks) who remained on medication.

Table 1: Characteristics and outcomes of patients treated with avacopan

	Patient 1	Patient 2	Patient 3	Patient 4
Age	34	49	54	55
Sex	F	F	M	F
ANCA type	PR3	PR3	PR3	PR3
Year of diagnosis	2015	2013	2016	2023
Disease Profile	Sensorineural hearing loss Sinusitis Neuropathy Nephritis	Cutaneous ulcerations Arthritis Sinusitis Diplopia Dacryoadenitis	Mononeuritis Cutaneous ulceration and digital gangrene Sinusitis	Subglottic stenosis Sinusitis
Vasculitis Medications at time of avacopan initiation	RTX 1000mg q4m (Initiated 02/2022)	RTX 1000mg q6m (Initiated 11/2022)	Rituximab 1000 mg q4 months (Initiated 7/20)	RTX 500 mg q6m (Initiated 2/23)
		Avacopan Initiation		
Avacopan start	4/2023	4/2023	3/2023	7/2023
Prednisone exposure >10 mg for 6 weeks prior to start	Yes	Yes	No	No
Prednisone at avacopan start (mg daily)	30	25	0*	5
Prednisone related concerns	Weight gain Hypomania Hypertension	4 serious infections in 12 months prior to initiation.	Weight gain Osteoporosis	Weight gain
Vasculitis Disease Activity at time of avacopan initiation	Sinusitis Nasal crusting Arthralgia Fatigue Digital ischemia	Arthritis Epistaxis Nasal crusting Blurred vision	Ischemic bowel ulcers Arthralgia	Subglottic stenosis
		At last follow-up		
Duration of follow-up (months)	5	3	7	5
Disease Remission	Yes	Yes	No, patient switched in November 2023 to cyclophosphamide	Yes
Current prednisone dose (daily mg)	0	5	22.5	0
Time to prednisone d/c (weeks)	19.3	N/A	N/A	20

*Patient had been on prednisone 10 mg for >6 months, had stopped two months prior to flare.

Conclusions: From this case series we propose that there may be a role for late introduction of avacopan in steroid-dependent patients on RTX therapy. The safety profile of this intervention was good with no significant adverse events. This was a retrospective case series, so this data should be interpreted with caution. Future larger studies should consider employing prospective design with comparator group and may benefit from a modified tracking tool based on the abridged Glucocorticoid Toxicity Index (2).

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Diagnostic features of extracranial giant cell arteritis

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Presentation of Case: A 62-year-old female was referred with a 4-month history of low-grade fever, fatigue, upper extremity claudication and pain in proximal interphalangeal and metacarpophalangeal joints with 30-40 minutes early morning stiffness. Previously she was treated with sulfasalazine (1500 mg/day for three months) for suspected rheumatoid arthritis and levofloxacin for unspecified infection without any effect. She had no other medical history and took no medication. On examination she was subfebrile (37.3°C). Cardiovascular examination revealed an unequal brachial (right 120/90 mmHg, left 0/0 mmHg) and high ankle (right 200/90 mmHg, left 200/100 mmHg) blood pressure. There was no pulse on the left radial artery, while there were bruits over subclavian and axillary arteries. Other arteries were normal. There were no tender or swollen joints. Remaining examination showed no abnormalities.

Diagnostic Testing: Initial blood tests demonstrated a hypochromic microcytic anemia (hemoglobin 92 g/l), thrombocytosis (thrombocytes 453x10^9/l) and high erythrocyte sedimentation rate (ESR, 99 mm/h), while leukocytes and leukocyte formula were normal. Another inflammatory marker also was raised: C-reactive protein (CRP) 123 mg/l, fibrinogen 7.55 g/l. Antinuclear and anti-cyclic citrullinated peptide antibody, rheumatoid factor were negative. Urinalysis, biochemical blood and coagulation tests were unremarkable. Serial blood cultures were negative. An electrocardiogram showed right bundle branch block. Transthoracic echocardiography revealed no abnormalities. Abdominal and pelvis ultrasound were found to be normal. Hands X-ray showed no significant anomaly. CT angiography and Doppler ultrasonography demonstrating a stenosis up to 80% in right subclavian, 75% in right axillary, 90% in left subclavian and 85% in left axillary arteries.

Differential & Final Diagnosis: Differential diagnosis was carried out between large vessel vasculitis, polymyalgia rheumatica (PMR), rheumatoid arthritis (RA) and infection. The last one was excluded because of normal leukocyte formula and negative blood culture. Also, there were insufficient data to diagnose PMR and RA according to EULAR/ACR 2012 and ACR/EULAR 2010 diagnostic criteria respectively. Based on the clinical presentation, physical examination, laboratory findings and imaging results extracranial giant-cell arteritis (GCA) was diagnosed.

Discussion of Management: The patient was treated with 32 mg methylprednisolone, 150 mg ranitidine, 1000 mg calcium and 800 ME vitamin D3 daily. Because of arterial hypertension lisinopril and amlodipine were begun at a dose of 10 mg/day and 5 mg/day, respectively. Her symptoms and inflammatory markers (CRP 15 mg/l, ESR 20 mm/h) started showing improvement in the next few days.

Conclusions: Our case highlights the importance of considering GCA in adults presenting with constitutional symptoms and signs of inflammation in blood test results, even in those without cranial symptoms.

References: None.

Disclosures: None.

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Crescentic Pauci-immune Glomerulonephritis related to SLE and ANCA - case report

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Presentation of Case: This case concerns a melanodermic 45 year-old male with previous miopericarditis and fever of unknown cause, possibly related with undiagnosed auto-imune disease. In december 2022 he reported to the hospital with increased fadigue and peripheral edema, associated with increased NT-proBNP (>35000 pg/mL) and acute kidney disease (2.58mg/dL creatinine). His condition worsened with cardiogenic shock and he was admited to intensive care.

Diagnostic Testing: A CT scan showed a pericardial and pleural effusion and blood work showed positive anti-dsDNA (7.7UA/mL), ANA (antinuclear antibodies; >1/1280), MPO ANCA (myeloperoxidase anti-neutrophil cytoplasm antibodies; 248 UA/mL), and deplected C3 (66mg/dL), while urine tests showed hematoproteinuria (4045mg/g).

Differential & Final Diagnosis: Systemic Lupus Erythematosus (SLE) and ANCA vasculitis were considered (with a EULAR 2019 SLE score of 22 and due to positive antibodies). A renal biopsy showed fibrinoid necrosis and crescents, without endocapilar proliferative lesions and negative imunofluorescence (IgA, IgG, IgM, C1q, C3 and light chains). Considering the clinical and histologic findings a diagnosis of crescentic pauci-immune glomerulonephritis due to class III lupic nephritis and ANCA vasculitis was proposed.

Discussion of Management: Renal replacement therapy was started (14 days total) due to anuria. Despite not having an histologic diagnosis at the time corticotherapy was started with Metilprednisolone (1g/day for 3 days) and Prednisone (1mg/kg), and Mycophenolate Mofetil (MMF) instead of Cyclophosphamide due to the clinical severity. Afterwards anti-dsDNA became negative while ANCA remained positive, and the patient partially recovered his renal function while remaining treated with MMF.

Conclusions: Crescentic glomerulonephrities (GN) can be characterized by the deposition of immune complexes or their absence (pauci-immune), with SLE usually inserted in the first group and ANCA vasculitis in the second. However, despite their rarity there are some reports of necrotizing crescentic GN without subendotelial deposits with positive ANCA, anti-dsDNA and ANA[1, 2], possibly related to lupic nephritis with a ANVA vasculitis component.

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Disclosures: None.

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Cocaine-induced ANCA associated vasculitis (AAV)- a single centre perspective

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Background/ Objectives: Cocaine is one of the most commonly used illicit drugs in the UK. Cocaine causes direct local damage to the nose as well as triggering autoimmunity and ANCA associated vasculitis (AAV). This report describes the spectrum of disease seen.

Methods: A retrospective case series analysis between 2014-2023 from a single tertiary vasculitis centre. Thirty patients with a vasculitis phenotype and disclosure of previous or ongoing cocaine use or a positive urinary test for cocaine were identified. Prospective urinary cocaine screening is currently ongoing in our Vasculitis clinic to inform prevalence.

Results:

Characteristic	n=30
Age, median (IQR), years	44 (28-62)
Sex (M:F)	17:13 (57% : 43%)
Clinical phenotype	
Granulomatosis with polyangiitis (GPA)	28 (93%)
Microscopic polyangiitis (MPA)	0 (0%)
Eosinophilic granulomatosis with polyangiitis (eGPA)	2 (7%)
ANCA serotype	
PR3	28 (93%)
MPO	0 (0%)
Negative	2 (6%)
Median baseline creatinine (IQR), *µmol/l*	72.5 (44-141)
Urinary cocaine testing (positive: negative)	23:7 (77%:23%*)
Reported symptoms	
Epistaxis	15 (50%)
Fatigue	20 (67%)
Haemoptysis	2 (7%)
Nasal symptoms	29 (97%)
Sinusitis	26 (87%)

Table 1. Baseline clinical characteristics and demographics.

Nasal limited disease occurred in 63%, with nasal septal perforation in 67% (n= 20), oronasal fistulas in 7% (n= 2). Sinus symptoms were present in 90%, 67% had a sinus CT (n=18), with sinus mucosal thickening or sinonasal destruction seen in all patients. 80% had an ear, nose and throat (ENT) specialist review (n =24), a third underwent nasal biopsy. Typical findings were non-specific inflammation, ulceration and granulation tissue.

Patients with nasal symptoms only had treatment with topical therapies and corticosteroids; nasal douching (n= 21, 70%), naseptin cream (n= 10, 33%), and antibacterials (n=8, 27%). Oral co-trimoxazole was prescribed for 70% of patients (n= 21). 13% required intravenous antibiotics (n=4).

43% did not require additional immunosuppression, besides corticosteroids (n=13). Before starting immunosuppression all patients underwent nasoendoscopy where characteristic vasculitis inflammation was observed. 57% (n=17) received immunosuppression; 8 patients received rituximab alone, 4 received cyclophosphamide and 5 received rituximab cyclophosphamide combination. Of the 17 patients who received immunosuppression, indications included organ involvement besides ENT disease (n=5), pulmonary haemorrhage (n=2), severe new (n=5) or refractory ENT disease (n=5). 30% experienced relapse(s) (n= 9). 11 patients continue to use cocaine, 17 reported cocaine cessation, 1 continues to denies cocaine use and 1 patient was lost to follow up.

Conclusions: Cocaine induced vasculitis should be considered in younger patients with AAV, particularly those with nasal septal perforation, nasal limited disease or refractory disease. Topical therapies for isolated nasal symptoms and cessation of cocaine use should be encouraged first line, prior to systemic immunosuppression.

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P-277

Subdural Hematoma as a probable consequence of Giant Cell Arteritis

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Presentation of Case: A 71 year old Caucasian man presented with a 10 day history of a progressive left sided fronto-temporal headache. This was recently associated with scalp tenderness, transient visual blurring, photophobia and nausea. Despite multiple co-morbidities, notably preceding lung cancer and peripheral vascular disease, he had been systemically well and denied poly-myalgic symptoms. He was an ex-smoker and consumed 20 units of alcohol weekly. He denied significant head trauma.

On presentation, he had left-sided proptosis, bilateral temporal arterial tenderness and mildly reduced bilateral temporal artery pulsation.

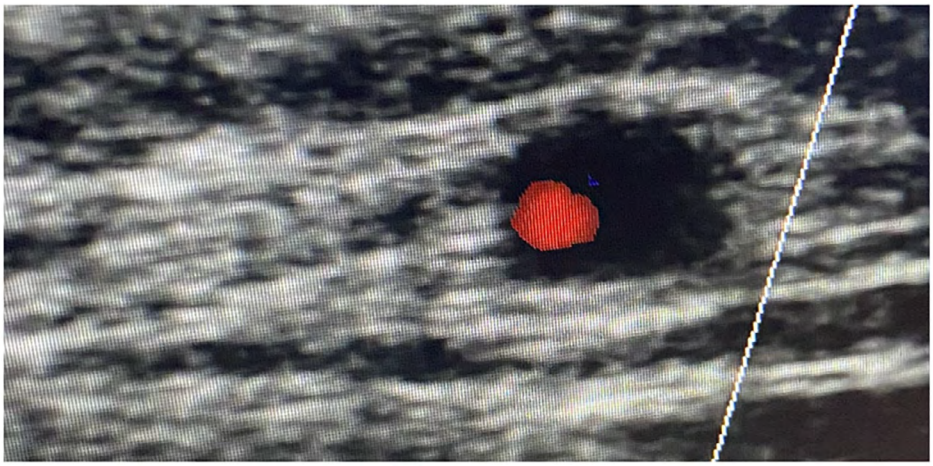
Diagnostic Testing: He had elevated inflammatory markers, Erythrocyte Sedimentation Rate (ESR) 124mm and C-Reactive Protein (CRP) 15mg/dl.

Computed Tomography (CT) Brain demonstrated an acute-on-chronic left sided subdural haematoma (SDH) measuring up to 10mm in depth. Mild mass effect with sulcal and left lateral ventricular effacement and midline shift of 5 mm were noted. Neurosurgical consultation confirmed no operative intervention was required.

Magnetic Resonance Imaging (MRI) of Brain, given his past history, excluded a mitotic lesion.

Given his presentation and inflammatory markers, temporal artery ultrasound was performed by an experienced Rheumatologist. This demonstrated a hypoechoic halo sign with increased intimal-medial thickness in the left and right frontal branches (Figure 1).

Figure 1 – Ultrasound of Right frontal branch demonstrating halo sign



Differential & Final Diagnosis: The clinical presentation of this gentleman was in keeping with both the final diagnoses of sub-dural haematoma and Giant cell arteritis (GCA). Prior to laboratory and radiological investigations, a wider differential of a mitotic lesion, infective process or migranous event could be considered.

While radiology confirmed a SDH, his clinical features, raised inflammatory markers, marked steroid responsiveness and abnormal temporal artery ultrasound led to the concomitant clinical diagnosis of GCA. The patient met 2022 American College Rheumatology / European Alliance of Associations for Rheumatology classification criteria for GCA with a total score of 14.

Given the lack of significant head trauma, we suggest that GCA was the primary cause of SDH in this interesting case. Mechanistically this may be explained by arteritis of the small subdural arteries which traverse the subdural space, a very rare phenomenon in GCA.

Discussion of Management: Given the transient visual symptoms, he received a loading dose of intravenous Methylprednisolone 500mg. He was then started on Prednisolone 60mg daily and tapered using the Giant Cell Arteritis Actemra (GiACTA) 26-week protocol. His headache promptly responded with full resolution of clinical symptoms within 48 hours and resolution of inflammatory response over the following week. He was commenced on Tocilizumab 162mg weekly. He was followed by the neurosurgical service with repeated imaging.

On follow up his symptoms have completely resolved. Interval CT brain has shown improvement with residual left-sided SDH.

Conclusions: We present a case of SDH as a probable consequence of Giant Cell Arteritis. This case highlights the importance of clinical history and the use of temporal artery ultrasound in diagnosing GCA.

References: None.

Disclosures: None.

P-278

Eosinophilic Granulomatosis with Polyangiitis vs IgA Nephropathy

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Presentation of Case: 44 yrs old male with history of asthma, sinusitis and HIV (undetectable viral loads). In 2015 presented muscle weakness, arthralgia, rhinorrhea and weight loss. Laboratory tests showed anemia (no hemolysis), Leukocytosis with eosinophilia, normal kidney function, PCR 630mg/d no hematuria. Chest CT and fibro-bronchoscopy demonstrated alveolar hemorrhage. Autoimmune panel positive p-ANCA, a muscular biopsy confirmed the diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA).

Induction therapy methylprednisolone IV and prednisone taper.

A renal biopsy (RB) showed focal segmental mesangial proliferation no extra capillary/ endocapillary proliferation. Positive immunofluorescence for IgA, probably a secondary cause (Vasculitis or HIV).

In 2018, presented acute kidney injury (Crs 2mg/dl, PCR 8g/d, & dysmorphic hematuria), increased MPO-ANCA (679). RB showed extra capillary focal and proliferative necrotizing glomerulonephritis (29% epithelial crescents) with mesangial IgA deposits. Induction therapy: prednisone & Rituximab (RTX) followed by maintenance RTX 500mg/6m.

He followed up with complete remission, however he presented severe infectious complications.

On Jan-23, he presented sinusitis, eosinophilia, increase proteinuria and MPO-ANCA (80) with preserved renal function. Due to the overlap of two histological expressions, we performed a new RB that showed same pattern of glomerulonephritis with persistence IgA deposits. Due to this anti IL-5 biologic therapy was started (Mepolizumab 100mg/4w). During follow up, there was an improvement in respiratory symptoms, and kidney function remained stable.

Diagnostic Testing: Muscle/renal biopsy and immunological study.

Differential & Final Diagnosis: EGPA with secondary IgA nephropathy.

Discussion of Management: Glucocorticoids (GC) had been the cornerstone in the treatment of EGPA followed by immunosuppressive (cyclophosphamide, azathioprine & RTX). The adverse effects secondary to therapy maintained at high doses of GC are known (not only as infectious complications but also as causes of organ damage), without maintenance therapy the risk of relapse is up to 85%. Multiple clinical trials have been carried out comparing the use of anti-L5 as treatment of ANCA-mediated vasculitis with favorable results given its efficacy and safety profile, reducing the risk of complications, and relapses (1,2).

Conclusions: EGPA is an ANCA-mediated vasculitis characterized by the presence of asthma, small and medium-sized vessel necrotizing vasculitis, rhino-sinusitis, and tissular and peripheral eosinophilia. Understanding the pathophysiology of EAGP and the role of eosinophils the use of anti-IL5 is approved agent for the treatment with less risk of complications.

Mepolizumab has a significant GC-sparing effect, reduced exacerbations, and improved control of asthma symptoms.

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Disclosures: None.

P-279

Hypertrophic pachymeningitis as GPA onset manifestation: a case report

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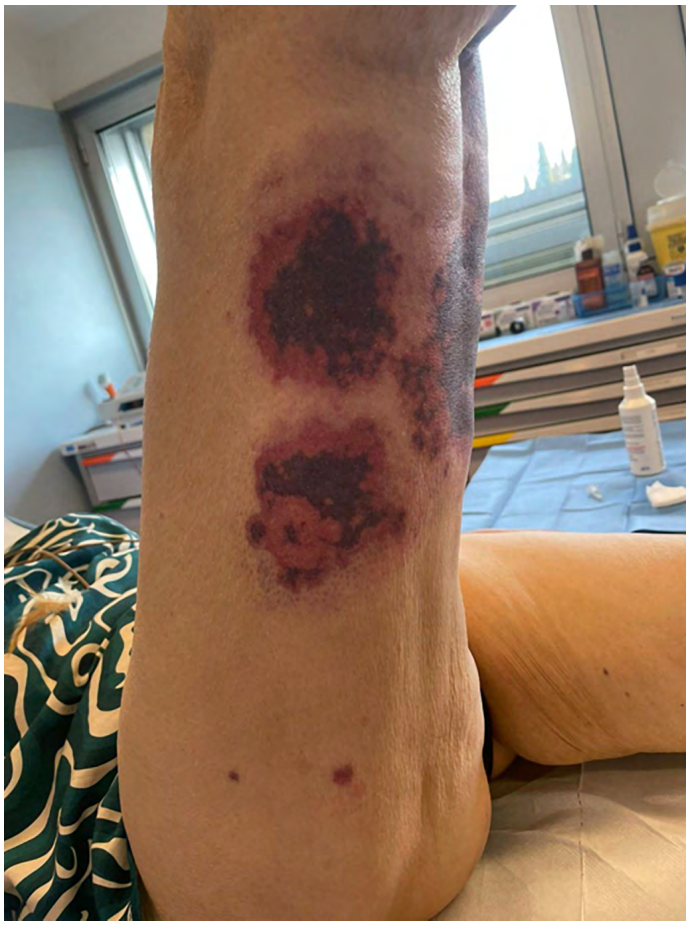

Presentation of Case: We observed a 74-year-old woman that developed granulomatosis with polyangiitis 20 years after the diagnosis of idiopathic granulomatous pachymeningitis. The onset of the clinical picture was confusion, headache and multiple cranial nerve palsy associated with significant MRI contrast enhancement and thickening of meninges, resolved after high-dose of intravenous corticosteroids. ANCA antibodies were repeatedly tested negative. After excluding infectious diseases and malignancies, the patient was treated with rituximab as induction treatment, and then every 6 months as maintenance for up to 2 years, then switched to mycophenolate. She maintained a good clinical response with this therapy for 10 years until she presented to our department with new acute onset of necrotizing lesions of the lower limbs associated with fever in the absence of other systemic symptoms.

Diagnostic Testing: Infectious and malignant disorders were primarily excluded, by means of a comprehensive serology testing, blood cultures, trans-thoracic echocardiogram, and 18FDG-PET. CRP and ESR were significantly increased. ANA, anti-ENA, cryoglobulins, APLs antibodies, RF tested negative, while ANCA resulted positive c-ANCA/PR-3, 3.5 UI/mL. No signs of renal involvement were detected, but pseudo-nodular pulmonary lesions were demonstrated by a chest CT. The ENT involvement was consistent with rhinitis and nasal crusting.

Differential & Final Diagnosis: After excluding an alternative aetiology, a diagnosis of GPA was made for the presence of c-ANCA/PR3positivity, ENT and pulmonary involvement and the result of cutaneous biopsy showing leukocytoclastic vasculitis.

Discussion of Management: The patient presented atypical cutaneous lesions that initially poorly responded to low-dose corticosteroid plus antibiotic therapy. After the diagnosis of GPA, we started high-dose intravenous corticosteroids and rituximab infusion (1000 mg). Central nervous system involvement is an uncommon manifestation of GPA, reported in 7%-11% of patients[1]. Hypertrophic pachymeningitis (HP) is a rare neurologic complication of GPA, presenting mostly with a persistent headache, although cranial neuropathies may develop[2]. Interestingly, HP is usually a presenting manifestation of GPA rather than a later complication of disease, with up to 60% of HP presenting at disease onset[3]; furthermore, several studies of patients with GPA indicate lower incidence of systemic manifestations in patients with HP[2].

Conclusions: We observed an atypical case of GPA with initial single-organ involvement and subsequent development of systemic vasculitis. This case report underlines the importance of monitoring this kind of patients over the time also.

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Disclosures: None.

P-280

Avacopan use in pediatric ANCA-associated vasculitis

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Background/ Objectives: Granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) are types of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) characterized by predominantly small vessel inflammation. GPA is a rare childhood vasculitis with severe multi-organ damage commonly presenting as pulmonary-renal syndrome with rapidly progressive necrotizing crescentic glomerulonephritis and pulmonary haemorrhage.

Standard treatment protocols involve immunosuppression induction treatment with high dose glucocorticoids and Rituximab or cyclophosphamide. Relapse rates are higher in childhood, and may occur once steroids are tapered. Broad immunosuppression may lead to severe toxicity adding to ongoing damage accrual. We present two patients; one with severe relapsing childhood-onset AAV and one with new onset AAV treated with a C5a receptor inhibitor, Avacopan.

Methods: Case 1. A 12 year old female is diagnosed with rheumatoid factor negative polyarticular juvenile idiopathic in remission after methotrexate therapy. She presents two years later with a severe disease presentation including otomastoiditis, ulcerative tracheitis, cavitating lung nodules, alveolar hemorrhage, vasculitic rash, facial nerve palsy, Horner's syndrome, and hypercoagulability resulting in a diagnosis of ANCA-associated vasculitis, PR3+, subtype GPA. Treatment includes methylprednisolone intravenous (IV) pulses, plasmapheresis, IV immunoglobulins, and rituximab. Once IV steroids are weaned severe bronchial stenosis occurs, necessitating recurrent bronchoscopic dilations. Due to the inability to decrease her oral steroids below 1.5 mg/kg, the C5a receptor inhibitor Avacopan 30 mg oral twice daily is added.

Case 2. A previously well 11 year old male presents with alveolar hemorrhage, palpable purpura, and renal failure secondary to crescentic glomerulonephritis. Investigation of his pulmonary renal syndrome leads to diagnosis of ANCA-associated vasculitis, PR3 positive. He is treated with PLEX, Rituximab and prednisone for maintenance therapy. Avacopan therapy 20mg twice daily is added at week 3 of disease to initiate quick taper of oral prednisone.

Results: In both cases, Avacopan allowed for tapering of high dose steroid without relapse of the disease.

Conclusions: Unmet needs remain for treatment of severe relapsing AAV in childhood. To minimize severe toxicity resulting from long courses of high dose steroids, biomarker-guided targeted treatment options are therefore needed. Complement inhibition is a promising treatment strategy in AAV. In both cases prednisone was tapered to stop without a recurrence of disease on Rituximab and Avacopan maintenance. Further studies in children are needed to address the application of Avacopan in childhood AAV.

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Disclosures: None.

P-281

Anti-neutrophil cytoplasmic antibody specificity switch associated with a change in disease manifestations in a patient with ANCA-associated vasculitis

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Presentation of Case: ANCA-associated vasculitis (AVV) is a group of diseases causing necrotizing inflammation of small-to-medium blood vessels and is associated with a presence of anti-neutrophil cytoplasmic antibodies (ANCA) against myeloperoxidase (MPO) or proteinase 3 (PR3) (1). Antibody specificity has been linked to specific disease phenotypes in AAV (1). A change in specificity is rare and the mechanisms behind it are not known (2). We present a case of a male patient who was diagnosed in 2003 at the age of 68 years with granulomatosis with polyangiitis (GPA). The patient first presented with fever, asthenia, weight loss, headache, partial visual loss (central retinal artery branch occlusion), chronic sinusitis and episcleritis; serological testing for ANCA was negative and a temporal artery biopsy showed granulomatous inflammation in a small artery branch. PR3-ANCA were identified in the patient's blood in 2005, with a subsequent negativization in 2006. In 2007, the patient presented with an acute exacerbation of AAV including pulmonary infiltrates and positive MPO-ANCA. In 2008 the patient was diagnosed with interstitial lung disease (ILD) following progressive dyspnoea. In April 2009 membranous nephropathy (MN) was diagnosed based on a kidney biopsy for nephrotic-range proteinuria.

Diagnostic Testing: Chest CT in 2007 showed small consolidation areas in both lung fields compatible with GPA pulmonary involvement, whereas the chest CT in 2008 showed peripheral ground glass infiltrates with a reticular pattern related to ILD. Autoantibodies related to primary MN were not available at that time.

Differential & Final Diagnosis: Due to atypical clinical and histopathologic manifestations and incomplete response to glucocorticoids (GC) in 2003, the final diagnosis was GPA instead of giant-cell arteritis and the diagnosis was supported by transient PR3-ANCA detection. ILD and MN, known to be infrequently associated with AAV (3,4), developed around the switch to MPO-ANCA specificity and predominated the clinical course thereafter.

Discussion of Management: He was first treated with GC and methotrexate (MTX). After his first GPA exacerbation the dose of GC was increased. Following the diagnosis of ILD, MTX was switched to azathioprine (AZA). After development of MN, AZA was switched to mycophenolate mofetil with complete remission. His clinical picture with predominant sinus and lung involvement turned into ILD and MN when developing MPO-ANCA.

Conclusions: Although rare, a change in ANCA specificity may underline a change in clinical phenotype and influence patient management. There is a need for better understanding of the mechanisms behind this phenomenon for more efficient patient care.

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Disclosures: Lecturing/consulting fees from GSK (MCC and GEF) and AstraZeneca (MCC).

P-282

How to classify ANCA-negative patients with glomerulonephritis using the 2022 ACR/EULAR classification criteria?

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Background/Objectives: Recently, new classification criteria for the diagnosis of granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA) were proposed by the American College of Rheumatology (ACR) and the European Alliance of Associations for Rheumatology (EULAR) (1,2). In contrast to previous criteria the incorporation of ANCA specificity (PR3-ANCA or MPO-ANCA) represented a cornerstone for the discrimination of GPA from MPA. Pauci-immune necrotizing crescentic glomerulonephritis (PIGN) is the histopathologic hallmark of kidney involvement of ANCA-associated vasculitis (AAV), commonly in GPA and MPA. However, 5-10% of GPA and MPA patients are ANCA-negative, and in renal-limited PIGN ANCA-negativity may occur in 20-30% of patients. The aim of this study was to evaluate the ACR/EULAR 2022 criteria for classification of AAV with the results of the European Medicines Agency (EMA) algorithm classification (3) in ANCA-negative patients with PIGN.

Patients and Methods: We retrospectively identified ANCA-negative patients within our cohort of 180 patients with ANCA-associated vasculitis diagnosed with GPA or MPA with predominant kidney involvement. Patients with a diagnosis of EGPA were not included. We compared the ACR/EULAR 2022 criteria for classification of AAV (1,2) with the results of the European Medicines Agency (EMA) algorithm classification (3).

Results: We found 7 ANCA-negative patients within our cohort (3x female, 4x male). All patients presented with active PIGN in the kidney biopsy. Renal-limited vasculitis was present in 5 patients, skin vasculitis was present in 2 patients, arthritis in 1 patient, while ENT- or lung-involvement was absent. Mean age was 53,6 years and mean creatinine level was 4,8 mg/dl (min. 1,1 mg/dl, max. 7,4 mg/dl). According to the EMA algorithm all patients were classified as MPA (5/7 with renal-limited manifestation). Using the 2022 ACR/EULAR criteria all patients could not be classified as GPA or MPA.

Conclusions: The new 2022 ACR/EULAR classification criteria have a strong focus on the presence of PR3-ANCA and granulomatous manifestation (ENT or lung) for the diagnosis of GPA and the presence of MPO-ANCA and the combination of lung- and kidney involvement for the diagnosis of MPA. In the case of renal-limited vasculitis and the lack of ANCA-positivity no attribution to a specific diagnosis of GPA or MPA is possible. Therefore, there is a need for a uniform diagnosis for this patient subgroup.

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Disclosures: US and MF: Study participation: Sanofi/Ablynx; Alexion/AstraZeneca; CSL Vifor/Chemocentryx; HansaBiopharma; Alentis Therapeutics. Advisory Board/Speaker fees: CSL Vifor; Sanofi; Alexion/AstraZeneca; Janssen.

P-283

Experience with Avacopan in anca vasculitis (VAA) at Hospital Universitario Torrecardenas (Almeria)

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Activation of the complement pathway plays an important role in the pathogenesis of AAV. Avacopan is a C5aR1 antagonist.

Case 1. 64-year-old male, overweight, dyslipidemia, CKD stage 3 (Cr 1.8 mgr/dl): bilateral episcleritis, turbinate hypertrophy, chronic sinusitis and polyarthritis.

Treatment: corticosteroids, azatypine and methotrexate. Referred to Nephrology Consultation due to Cr 1.82 mg/dl, proteinuria 3.64 grams/24h. ANCA-PR3: 416. Kidney biopsy= AAV. Tto: CE+CF+RTX+ Avacopan. At 12 months Cr 2.6 mg/dl, proteinuria 0.42 gr/24h, normal sediment.

Case 2. 47-year-old male, diagnostic of NINE, for which he received CE + CF and then Azathioprine+MMF. Previous normal kidney function. He was admitted due to fever, asthenia, hyporexia, weight loss, arthralgias, myalgias, O2 saturation 88%, hemoptysis, paresthesias and kidney involvement (Cr 3.39 mgr/dl, proteinuria 1.68 gr/dl). 24h). ANCA – MPO positive. Kidney biopsy: VAA. CE + CF + RTX + PF + Avacopan. At 12 months Cr 0.9 mg/dl, proteinuria 0.72 gr/24h, normal sediment.

Case 3. 54-year-old woman, HBP, CKD stage 3 (Cr 1.8 mgr/dl), chronic liver disease, heart failure, vertebral crushes and depression. Diagnosed with AAV-MPO, with lung, kidney, skin, peripheral nervous system (polyneuropathy), peripheral nervous system and vestibular neuritis involvement. Tto: 1st AVV outbreak CE+CF, then Az+RTX - 2nd AAV outbreak CE+CF+RTX. 3rd AAV outbreak: Lung-kidney syndrome, Cr 1.8 mg/dl, proteinuria 1.5 gr/24h, and nodular skin lesion on the forearm that required plastic surgery. ANCA-MPO: 420 U/ml. Treatment: EC + CF + PF + Avacopan. At 9 months Cr 1.3 mg/dl, proteinuria 0.7 gr/24h and normal sediment.

Case 4. 65-year-old woman, overweight, HBP, IgG4-related disease. Burst fracture of the L3 vertebra and osteoarthritis. Previous normal kidney function. He was admitted due to hemoptysis and deterioration of kidney function (Cr 3.5 mg/dl) and proteinuria 1.52 gr/24h. ANCA-PR3 positive. Tto: CE+CF+PF+Avacopan. At 6 months: Cr 2.03 mg/dl, proteinuria 0.2 gr/24h, normal sediment.

Case 5. 57-year-old man, IDDM, CKD stage 3 (Cr 2 mgr/dl). Bilateral episcleritis, arthromyalgias. He was admitted due to asthenia and weight loss with Cr 2.5 mgr/dl, proteinuria 1 gr/24h and active sediment. ANCA MPO gt; 500. Tto: CE + CF + RTX + Avacopan. At 6 months Cr. 1.65 mgr/dl, proteinuria 0.5 gr/24h, normal sediment.

In all cases, doses of steroids lower than those we prescribed when administered were used. The addition of Avacopan to the standard treatment of AAV contributes to controlling clinical activity, maintaining remission and minimizing organ damage due to the adverse effects of CE.

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Clinical features of ANCA-associated interstitial lung disease in five patients

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Background: The anti-neutrophil cytoplasmic antibodies (ANCA) are an established biomarker for a distinct group of systemic vasculitides that predominantly affect small vessels, commonly referred to as ANCA-associated vasculitis (AAV). Interstitial lung disease (ILD) is a rare (1-30%) AAV manifestation. However, recent reports have demonstrated that idiopathic interstitial pneumonia (IIP) can also be associated with serum ANCA (ILD-ANCA). Here, we present the clinical features of several patients with ILD-ANCA.

Methods: Patients who had undergone treatment at our clinic and were diagnosed with ILD were tested for rheumatoid factor, anti-cyclic citrullinated protein antibodies, anti-nuclear antibodies, proteinase-3 and myeloperoxidase ANCA, chest computed tomography (CT) were performed. The CT were reviewed by a chest radiologist and were classified using the radiologic patterns described in the ATS/ERS classification 2013 [1].

Results: Five patients with ILD, not fulfilling criteria for diagnosis of any systemic autoimmune disease, were found to be serologically positive for any of the performed tests, of which five were ANCA positive and considered as ILD-ANCA. Table 1 lists the characteristics of the ILD-ANCA patients. Median forced vital capacity in ILD-ANCA group was 60 (56.0; 62.0) %, diffusion capacity for CO was available in 4 patients with median 50 (39.5; 59.8) %. One lethal outcome of ILD acute exacerbation was registered. None of the patients developed systemic AAV.

Conclusions: ANCA in circulation in patients with idiopathic ILD could be an additional autoimmune feature of the disease even in absence of extrapulmonary manifestations.

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Disclosures: None.

Table 1. Characteristics of patients with ILD, positive for ANCA.

Patient	Age of onset, sex	ANCA type and titre	Other laboratory findings	CT pattern	Histology pattern	Lung function tests	Treatment	Outcome
1	67, f.	PR3, 5x ULN		nonUIP	N/A	FVC60%, FEV1 64%,	GC, CYC, AZA, MTX	Progression
2	67, f.	MPO, 2x ULN	RF 7x ULN	nonUIP	IIP	FVC56%, FEV1 50%, DLco 62%	GC, MMF, HCQ, RTX	Low activity, non-progressive
3	42, m.	PR3, 2x ULN	HEp-2 ANA 1:320 (AC-4), Eos. 12% ($1.0x10^9$/l)	nonUIP	HP	FVC40% FEV1 44% DLco 35%	GC, AZA, MMF, MTX	AEILD, lethal outcome
4	67, f.	PR3, 2.5x ULN	M-gradient5.5%	Possible UIP	N/A	FVC 72% FEV1 75% DLco 59%	MMF	Low activity, non-progressive
5	76, f.	MPO, 2x UNL		Possible UIP, CPFE	N/A	FVC 62% FEV1 69% DLco 41%	GC, MTX, LEF, RTX	No follow-up data is available to the moment

f. – female, m. – male, N/A - not available, AEILD – acute exacerbation of ILD, PR-3 - antibodies to proteinase-3, MPO - antibodies to myeloperoxidase, ILD - interstitial lung disease, HP - hypersensitive pneumonitis, IIP - idiopathic interstitial pneumonia, ANA - antinuclear antibodies, Eos. - eosinophilia, RF - rheumatoid factor, UNL - upper limit of the reference interval, UIP – usual interstitial pneumonia, FVC - forced vital capacity, FEV1 - Forced expiratory volume in 1 second, DLco - diffusing capacity of the lungs for CO, GC - glucocorticoids, CYC - cyclophosphamide, AZA - azathioprine, MTX - methotrexate, MMF - mycophenolate mofetil, HCQ - hydroxychloroquine, RTX - rituximab.

P-285

HIV infection misdiagnosed as a Behcet disease

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Presentation of Case: A 34 years old patient presented with a three months history of recurrent oral ulcers.

On initial examination the patient was apyretic. Cardiopulmonary auscultation and neurological examination were without abnormalities. No lymphadenopathy was found. The mucocutaneous examination revealed oral ulcers. No genital ulcers or pseudo-folliculitis were observed. The diagnosis of Behçet's disease was likely and treatment with colchicine was started.

A partial improvement with a reduction in the frequency of episodes of ulcers was noted.

One year later, the patient presented with a four month history of anorexia, weight loss, night sweats, dyspnea and diarrhoea. Physical examination was normal apart from bilateral subcentimeter cervical lymphadenopathies.

His complete blood count showed lymphocytes at 670 × 10^6/L and leukopenia at 3290 × 10^6/L. CRP was at 6 mg/l. Renal and liver tests were normal.

Diagnostic Testing: The thoraco-abdominopelvic computed tomography (CT) scan showed a mosaic attenuation pattern in both lungs with mediastinal lymphadenopathies.

CT Enterography revealed a focal and segmental parietal thickening of the ileocecal valve and the last ileal loop, moderately enhanced by the radiocontrast agent, without obvious extension to the ceacum, suggestive of an inflammatory disease flare. The colonoscopy showed a lower cecal ulcer and congestive and ulcerated valve. Human immunodeficiency virus blood serology was positive.

Differential & Final Diagnosis: Diagnosis was revised to HIV infection instead of BD.

Discussion of Management: Treatment with colchicine was discontinued and the patient was referred to the infectious diseases department.

Conclusions: It is true that oral ulcers are highly suggestive of Behçet's disease. However, other causes, mainly infectious, can also cause this symptom. A more detailed patient interview during the first examination regarding sexual behaviour could have led to the correct diagnosis.

References: None.

Disclosures: None.

P-286

Corticosteroid -induced central serous chorioretinitis in granulomatosis with polyangiitis: Between the devil and the deep sea

Houssem Abida[1], Thara Larbi[1], Zeineb Meddeb[1], Cherifa Abdelkefi[1], Bochra Ben Romdhane[2], Jihen Brour[2], Sana Toujeni[1], Amira Ouni[1], Kamel Bouslama[1], Saloua Hamzaoui[1].

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Presentation of case: A 55 year old man was diagnosed with Granulomatosis with polyangiitis with Ear, nose and Throat (ENT), pulmonary and renal involvement. He was treated with CS, cyclophosphamide and cotrimoxazole.

Six weeks after treatment was started, he presented with acute bilateral blurry vision. On admission, the patient was apyretic. Neurological examination was normal. Ophthalmological examination revealed a decreased visual acuity (VA) to logMar 0.9 in both eyes. The anterior segment proved to be normal . fluorescein angiography (FA) revealed segmental vasculitis.

His complete blood count, renal, hepatic blood tests and C-reactive protein rate were normal.

Diagnostic Testing: Blood serological tests ruled out syphilis, Virus Herpes simplex and cytomegalovirus infections. Serology for *Toxoplasma.gondii* serology was in favour of an old infection. Anterior chamber paracentesis was refused by ophthalmologists. Ocular involvement of the vasculitis was diagnosed and CS dose was increased.

ALL symptoms showed marked improvement after four months of treatment,except vision that worsened. VA was logMar 0.25 in both eyes. FA revealed extension of the retinal vasculitis with exudative retinal detachment (RD). Optical Coherence Tomography (OCT) showed a choroidal thickening. Treatment with three-days solumedrol infusions then with high doses of CS was restarted.

Examination upon two months showed a severe choroiditis with a giant inferior RD.

Differential & Final Diagnosis: The diagnosis was revised to CS induced central serous chorioretinitis (CSCR).

Discussion of Management: CS were rapidly tapered then stopped. Follow-up examination after two months revealed stabilisation of VA and complete resolution of the RD. Multiple areas of subretinal fibrosis were also found (figure 1).

Azathioprine was started as remission maintenance therapy in addition to cotrimoxazole. The patient didn't show any signs of relapse or new ocular complications during the following ten years of follow-up.

Conclusions: CS toxicity is a mechanism every clinician should consider when the patient develops CSCR after ruling out infections. That said, its treatment that consists of discontinuation of CS can expose the patient to relapses. In such cases, avocapan can be a great therapeutic alternative.

References:

Disclosures: None.

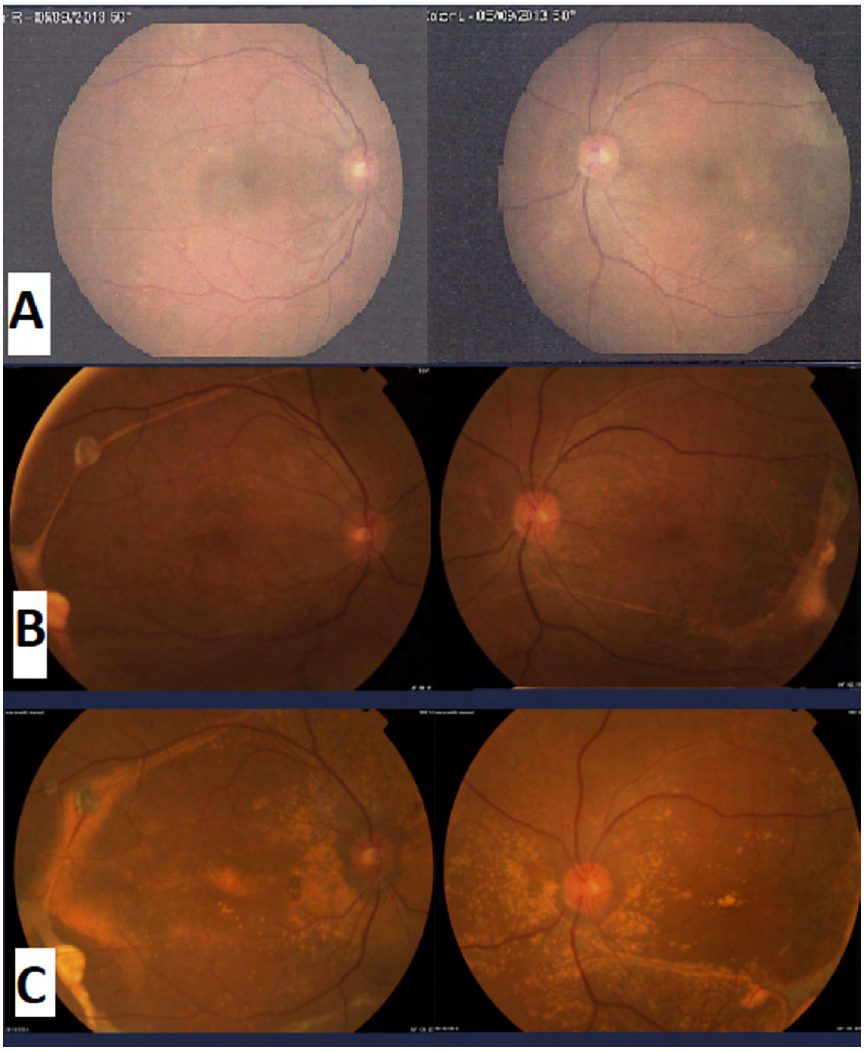

Figure 1: Evolution of the funduscopic examination: A: After 6 weeks of treatment with CS; B: After 4 months of treatment with CS; C: After 2 months of corticosteroids discontinuation.

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When on the silk road, he met Robert

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Presentation of case: A 50 year old man was diagnosed with Behcet Disease (BD) and treated with colchicine, corticosteroids (CS) and infliximab for retinal vasculitis for two years.

The patient presented with a three week history of fever. On initial assessment, he had a high-grade fever. Cardiopulmonary auscultation, neurological and vascular examinations were normal. No lymphadenopathy was found. Investigations showed lymphopenia at 869 × 10^6/L, C reactive protein of 257 mg/L, D-dimers of 2370 ng/L and Procalcitonine of 3,5 ng/ml.

Cyto bacteriological studies of urine and blood cultures were negative. Quantiferon and Acid-Fast Bacillus (AFB) Tests were negative. Virus serology blood testing. Thoraco-abdominopelvic Computed Tomography (CT) scan, transthoracic ultrasound, cerebral Magnetic resonance imaging (C-MRI) and bronchial fibroscopy (BF) were normal.

Polymerase chain reaction for the detection of Tuberculosis (TB PCR) on bronchoalveolar lavage (BAL) negative. Bone marrow biopsy refuted any malignant cells. A flare of the vasculitis was diagnosed and CS dose was increased. Stable apyrexia was initially obtained and the biological inflammatory syndrome improved.

Three-months later, the patient presented with a 2-weeks history of fever, anorexia, headaches and cough. Examination revealed crackles at the left lung base, steppage gait, monoplegia and hypoesthesia of the lower left limb.

Diagnostic Testing: C-MRI showed multiple abscess with perilesional edema (figure 1). The chest CT scan showed centrilobular, diffuse and bilateral micronodular pulmonary infiltrates. BF was repeated. Alveolitis was detected with hypercellular BAL, due to an increase of macrophages. BAL was negative for AFB by culture, while TB PCR was positive.

Differential & Final Diagnosis: Pulmonary and cerebral TB was diagnosed.

Discussion of Management: Oral anti-tuberculosis drugs combined with dexamethasone were started. Apyrexia was obtained, appetite resumed and headaches and cough showed marked improvement. Follow-up neurological examination showed persistence of the right lower limb's monoparesis. Biological inflammatory syndrome elements decreased. C-MRI after a month of treatment showed a worsening of the lesions and edema. Treatment was continued. Neurological signs resolved (figure 1). MRI at six months showed regression of the edema and a reduction in the size of the abscesses (figure 1).

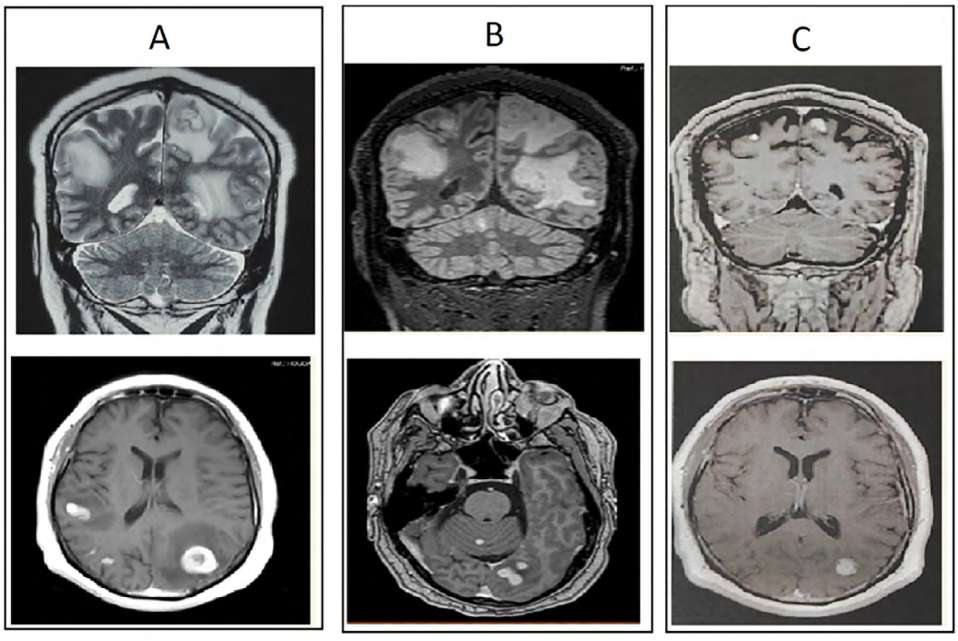

Figure 1: Evolution of the MRI abnormalities: A: At diagnosis of TB, B: After one month of treatment, C: After 6 months of treatment.

Conclusions: Infliximab was probably the TB reactivation factor in our case. Repeated tests were the clue to adjust diagnosis. Latent infections should always be considered for patients receiving immunosuppressive therapy.

References:

Disclosures: None.

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Small Vessel Vasculitis - Patient Journey

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Background/ Objectives: In the European Reference Network for Rare Immunological Disorders (ERN RITA) we recognise that a patient journey represents the entire sequence of events that a patient experiences from first appointment to treatment and prophylactic measures to prevent complications. Early diagnosis and timely access to treatment for people living with Small Vessel Vasculitis (SVV) is essential to avoid irreversible organ damage.

The Patient Journey is a visual, educational tool describing the experiences of patients living with SVV. Created by patients, it facilitates identifying gaps in care and adapting care pathways. It is a useful resource for patients' families, non-specialist clinicians, policymakers, and the public to understand the care needs of those living with SVV. The patient journey concept has become increasingly important as healthcare systems are focusing more on patient centricity.*

We aim to improve care through patient engagement, involving the patient in the design, evaluation, and designation of healthcare services, improving the relevance and quality of the services, and ability to meet patient needs**.

Methods: Our initial meetings focused on:

- developing patient journeys to benefit patients.
- existing literature & resources
- common elements to our diseases of interest
- potential challenges
- developing a common framework for all SVV conditions
- principles of meaningful, accessible and reusable work for our stakeholders.

The patient journey was divided into four stages (Symptoms, Diagnosis, Treatment, Follow Up and Aging), identifying the issues and gaps in care with suggestions as to what would have improved the experience. We used this framework to develop a handbook to guide the workshops, ensuring consistency for collection of reliable, unbiased information. All comments and suggestions were included and shared with workshop participants, in their local language to ensure inclusivity.

We held 2 online workshops, in English and French. The evidence from these was compiled and validated by patient groups and clinicians from the Czech Republic, Poland, Italy, France, Netherlands, Ireland, UK, and Sweden.

Results: The SVV Patient Journey was published on the ERN RITA website in March 2023 as a PDF document. The individual stages are available to download and been accessed 569 times.

Conclusions: Our work is available via the ERN RITA website This has been accessed by patients, families, patient organisations, researchers, and healthcare professionals. It is now being used by clinicians to provide information to patients, new healthcare staff and in developing care services.

References: *Bolz-Johnson, M., Meek, J. & Hoogerbrugge, N. "Patient Journeys": improving care by patient involvement. Eur J Hum Genet 28, 141–143 (2020). https://doi.org/10.1038/s41431-019-0555-6

** Beleffi E Mosconi P Sheridan S (2020) 'The patient journey' Textbook of Patient Safety and Clinical Risk Management pp 117–127 https://doi.org/10.1007/978-3-030-59403-9_10

Disclosures:

JP Honorariums from Vifor Pharma and Argenx.

ZA Honorarium from CSL Vifor Pharma.

AE is study group member for AZ.

P-289

Hepatic granuloma heralding Eosinophilic Granulomatosis with Polyangiitis (EGPA) overlapping with Sjögren's syndrome (SS)

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Background: Anti-Neutrophil Cytoplasmic Antibodies (ANCA)-associated vasculitides (AAVs) encompass a group of rare auto-immune diseases characterized by granuloma formation and inflammation of small vessels. The clinical spectrum of AAV varies widely. The liver location is exceptional leading to diagnostic challenges. Moreover, AAV can co-occur with other systemic diseases, further complicating the diagnosis. We herein present a unique case of AAV overlapping with Sjögren's syndrome (SS), with an uncommon mode of revelation.

Case report: A 47-year-old female was admitted for hiatal hernia surgery. During the intervention, nodular hepatomegaly was discovered. A liver biopsy was performed showing non-necrotizing epithelioid and central giant cell granulomas (figure 1). Computed-Tomography (CT) scan showed perilymphatic pulmonary micronodules with bilateral hilar lymphadenopathies, raising the suspicion of sarcoidosis. Minor salivary gland biopsy (MSGB) revealed lymphocytic infiltrates with a focus score of 1. That along with the patient's dry eye and mouth symptoms confirmed SS. Immunological workup showed negative Antinuclear antibodies (ANA) and positive anti-myeloperoxidase (MPO) antibodies. A year later, the patient presented with asthma flare-ups and ENT symptoms. A nasal biopsy was performed showing signs of Eosinophilic Leukocytoclastic Vasculitis, confirming the diagnosis of Eosinophilic Granulomatosis with Polyangiitis (EGPA). Oral steroid therapy was initiated, resulting in clinical improvement.

Discussion: There have been rare reports of hepatic granulomas associated with AAV, most of which are about Granulomatosis with Polyangiitis (GPA). Grigoriou et al. reported a case of a 22-year-old female with a history of asthma presenting with severe abdominal pain and vomiting, elevated transaminases, positive ANCA antibodies, patchy areas of liver attenuation on CT, and liver biopsy consistent with EGPA [1]. Darnall et al. reported a case of a 66-year-old female with history of EGPA who presented with abdominal fullness and lower limb edema, liver cirrhosis on CT-Angiography, and whose liver biopsy revealed granulomatous formation, eosinophilic infiltration and vasculitis [2].

Conclusion: We present a case highlighting the diversity of EGPA presentation. It can possibly mimic or occur with other auto-immune disorders. Thus, the importance of considering the differential diagnoses and carefully monitoring for any new symptom or organ dysfunction.

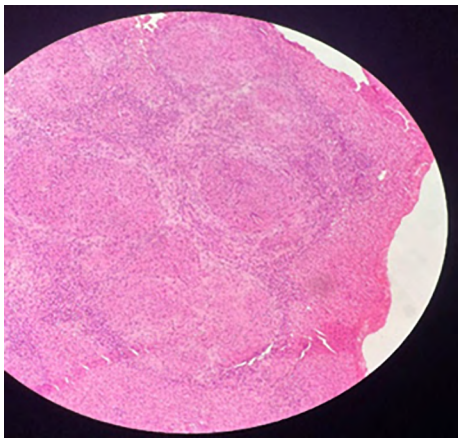

Figure 1: non-necrotizing epithelioid and central giant cell granulomas of the liver.

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P-290

Lower limb large vessel vasculitis: a case series

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Background/Objectives: Two subtypes of large-vessel vasculitis (LVV) are recognised; Takayasu arteritis (TAK) occurring in young people and giant cell arteritis (GCA) presenting later in life[1]. Both conditions are associated with significant morbidity. Prompt recognition and early treatment improve outcomes.

Arterial inflammation in LVV can result in intimal thickening, vessel injury, stenosis, and aneurysmal disease following myofibroblast proliferation[2]. Six angiographic subtypes have been defined in TAK within the Numano classification, based on phenotype of arterial involvement[3]. Subtype nomenclature in GCA is less well defined; largely divided into cranial GCA (C-GCA), and large-vessel GCA (LV-GCA)[4].

Positron emission tomography (PET) and angiography by computed tomography (CTA) and magnetic resonance (MRA) have superseded conventional angiography in the hierarchy of imaging modalities for diagnosis and surveillance of LVV[5]. Utilising these modalities, we describe an additional radiological subtype involving the lower limbs that fails to fulfil both American College of Rheumatology (ACR) & European Alliance of Associations for Rheumatology (EULAR) classification and represents an overlooked form of LVV that responds well to treatment.

Methods: Retrospective single-centre review of a database of 221 individuals with LVV.

Results: 5 patients with lower limb LVV were identified: 4 with TAK, 1 with LV-GCA (Table 1). Claudication was a frequent symptom at presentation, occurring in all TAK patients. Additional systemic symptoms included fever and malaise that usually predominate in LVV. The extent of fluorodeoxyglucose (FDG) avidity did not always correlate with the acute phase response and there was significant diagnostic delay in most cases.

Conclusion: Extracranial disease is common in LVV; however, involvement of lower limb vessels is much less frequently reported. It is critical to differentiate active vasculitis from peripheral vascular disease secondary to atherosclerosis as management varies considerably, with immunosuppression necessary prior to surgical revascularisation in the former context. A combination of clinical features and inflammatory biomarkers aid diagnostic certainty, in addition to PET and CTA/MRA imaging that elucidate active inflammation and extent of disease. Increased awareness of this lower limb LVV subtype is imperative in reducing the associated morbidity. We therefore propose a new subtype (VI) to the existing Numano classification for TAK and suggest revision of LVV classification criteria to include such cases.

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Disclosures: None.

Table 1. Characteristics of patients with lower limb LVV.

	Case 1	Case 2	Case 3	Case 4	Case 5
Sex	Male	Female	Female	Female	Male
Ethnicity	White	Indian/Asian	White	Indian/Asian	Asian
Age at symptom onset	20	21	17	Unknown	60
Age at diagnosis	23	22	20	32	60
Diagnostic delay (years)	3	1.5	3	-	0.1
Lower limb claudication	Yes	Yes	Yes	Yes	No
Smoker at time of presentation	Yes	Yes	Yes	No	No
Hypercholesterolemia	No	No	No	No	Yes
Other risk factors	-	OCP	-	-	Recent surgery – CABG
CRP at presentation (mg/L)	< 5	8	32	< 5	389
Arteries involved	IIA L PA R ATA R PTA	IRA Bilateral CIA	R ATA R PTA L PTA	IRA Bilateral RA SMA L CIA	Bilateral FA Bilateral PA
Numano subtype	IV + VI	VI	VI	IV + VI	VI
PET	Positive	Positive	Positive	-	Positive
ABPI (right/left)	0.67/0.62	-	-	-	1/1
Immunosuppression	-	CS MTX	CS AZA	CS MTX	CS MTX
Surgical Intervention	-	Bilateral CIA stents (in-stent stenosis 4 months later), Aortobifemoral graft	-	R CIA and R RA angioplasty	-

ABPI, ankle-brachial pressure index; ATA, anterior tibial artery; AZA, azathioprine; CABG, coronary artery bypass graft; CIA, common iliac artery; CRP, C-reactive protein; CS, corticosteroids; FA, femoral artery; IIA, internal iliac artery; IRA, infrarenal aorta; L, left; MTX, methotrexate; OCP, oral contraceptive pill; PA, popliteal artery; PET, positron emission tomography; PTA, posterior tibial artery; R, right; RA, renal artery; SMA, superior mesenteric artery.

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Nintedanib in ANCA-associated vasculitis-interstitial lung disease (AAV-ILD): Early experience from a UK centre

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Introduction: Interstitial lung disease (ILD) is a severe manifestation of ANCA-associated vasculitis (AAV). Nintedanib, an antifibrotic medication, has been licenced for use in diseases causing progressive fibrotic-ILD (PF-ILD) following the publication of the INBUILD study (*NEJM*, 381:1718-1727). However, only one patient included in this trial had AAV and patients with eGFR <30mL/min were excluded. Therefore, the efficacy and tolerability of nintedanib in AAV-ILD is uncertain.

Aim: We aimed to describe the clinical characteristics and drug tolerability of patients with AAV-ILD started on nintedanib in a single tertiary centre in the UK.

Methods: We performed a retrospective analysis of patients with AAV-ILD initiated on nintedanib since the UK licencing in February 2022.

Results: We identified five patients with AAV-ILD commenced on nintedanib (three females, mean age 77± 5 years). All patients were anti-MPO antibody positive. Three patients had biopsy confirmed kidney involvement with kidney dysfunction and one patient with an eGFR < 30 ml/min on starting nintedanib. Four patients had a UIP pattern of ILD and one had a fibrotic NSIP pattern. The mean forced vital capacity (FVC) % predicted at baseline was 87.5±6.6 and the transfer capacity of the lung for carbon monoxide (TLCO) % predicted was 42.3±24.1. The median time on treatment was 200 days (range 53-565). Three patients reported side effects associated with nintedanib use, with appetite loss and diarrhoea being the most frequently reported. One patient discontinued nintedanib due to side effects after 213 days of treatment. No deterioration in renal function was observed during therapy with nintedanib. No significant decline in FVC was noted.

Discussion: We found nintedanib similarly well tolerated in patients with AAV-ILD compared to those reported in other forms of ILD. Side effects and discontinuation rates were similar. Further data is needed to confirm the longer-term efficacy and tolerability in AAV-ILD.

Disclosures: CH has received honorarium from Boehringer Ingelheim for delivery of educational content.

P-292

A single-center case series of anti-GBM disease

See Jian Peng[1], Artemii Alekseev[1], Nikolay Bulanov[1], Mayra Bulanova[2], Mariia Litvinova[1].

[1]I.M. Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation; [2]Vladimir Regional Clinical Hospital, Vladimir, Russian Federation.

Background: Anti-Glomerular Basement Membrane (anti-GBM diseases) is a rare small-vessel vasculitis characterized by rapidly-progressive crescentic glomerulonephritis, with or without pulmonary hemorrhage.

Methods: We report three cases of anti-GBM disease followed between 2016 and 2023 by the department of nephrology at the regional clinical hospital in Vladimir, Russia. Diagnosis was established on the basis of clinical presentation and elevated levels of serum anti-GBM antibodies.

Results: Three patients were included in the study. The patient's initial characteristics, presenting symptoms, treatment and outcomes are summarized in Table 1. Among them, one presented with isolated lung involvement (Patient 1), one with severe pulmonary-renal syndrome (Patient 2), and one with isolated kidney involvement (Patient 3). All patients were negative for anti-neutrophil cytoplasmic antibodies (ANCA), antinuclear antibodies (ANA) and markers of antiphospholipid syndrome (APS). According to the current guidelines they were treated with methylprednisolone pulses 500-1000 mg IV for 3 days followed by prednisolone 60 mg/day for at least two weeks, with a gradual tapering of corticosteroid (CS) dose until complete withdrawal in 3-6 months. All patients received oral cyclophosphamide (CYC) 100-150 mg/day for 1.5-3 months. Plasma exchange (PE) procedures were also given to all the patients with exfusion of up to 60 ml/kg daily for 7 (Patient 1), 8 (Patient 2), and 10 days (Patient 3), till the level of anti-GBM antibodies normalized. Remission was achieved in all patients. Patient 2 remained dialysis-dependent. Patient 3 developed chronic kidney disease (CKD) stage 4. The following adverse events were registered on treatment: sepsis (Patient 1), leukopenia and QT prolongation (Patient 2), leukopenia and herpes virus infection (Patient 3).

Conclusion: Strict adherence to the standard-of-care resulted in the survival of all our patients with anti-GBM disease, despite life-threatening presentation at onset. However, kidney function has not fully recovered.

Table 1. Patients' characteristics, diseases onset, treatment, and outcomes.

	Patient 1	Patient 2	Patient 3
Year of observation	2016-2023	2017-2023	2018-2023
Sex	Male	Female	Female
Age at onset, years	24	27	30
Possible trigger	Smoking	Disinfectants	Not defined
First symptom	Hemoptysis	Macrohematuria	Macrohematuria
Dialysis dependent at onset	No	Yes	Yes
Kidney biopsy	Not performed	Extracapillary glomerulonephritis Type 1 (100% crescents)	Not performed
Creatinine, mcmol/L	91	535	1068
Alveolar hemorrhage	Yes	Yes	No
Hemoglobin at onset, g/L	86	64	82
ESR, mm/h	50	72	64
Anti-GBM antibodies level, IU/mL	>200	>200	>200
ANCA, ANA, APS markers	negative	negative	negative
Treatment	CS+CYC+PE	CS+CYC+PE	CS+CYC+PE
Outcome	Remission	Remission, CKD G5d	Remission, CKD G4

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Interstitial lung disease in a patient with eosinophilic granulomatosis with polyangiitis

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[1]FRCB-IDIBAPS, Barcelona, Spain; [2]Hospital Clinic Barcelona, Barcelona, Spain.

Presentation of Case: Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare, multisystemic, immune-mediated disease belonging to the group ANCA associated vasculitides (AAV). It is characterized by eosinophil-rich, necrotizing granulomatous inflammation and necrotizing vasculitis affecting small blood vessels (1,2). Patients with EGPA can present with of anti-neutrophil cytoplasmic antibodies (ANCA), predominately against myeloperoxidase (MPO) (2). Interstitial lung disease (ILD) has been associated with MPO-ANCA, however, only a few cases of ILD have been reported in EGPA patients (3). We present a case of a male patient who was first diagnosed with EGPA in 1998 in another hospital at the age of 47. He presented with severe bronchospasm, eosinophilia, positive c-ANCA and bilateral alveolar lung infiltrates seen on a CT scan. The diagnosis was confirmed by lung biopsy. In November 2022 he was admitted to the hospital due to progressive dyspnoea at minimal exertion and coughing, which was attributed to residual EGPA activity and ILD. After glucocorticoid (GC) increase the patient still reported high functional limitations. After discussion with the multidisciplinary committee in May 2023 mepolizumab was started for better control of EGPA, mainly due to long-term corticosteroid-dependent asthma with many exacerbations, and nintedanib to slow down the progression of ILD.

Diagnostic Testing: Chest CT in November 2022 showed EGPA exacerbation and interstitial involvement related to ILD. Lung function tests revealed restriction and an impaired diffusing capacity. Moreover, MPO-ANCA were detected. Following GC increase a chest CT in April 2023 showed a reduction in opacities, the remaining opacities suggested an infectious component. Bronchoscopy showed mucosal impaction of the right bronchial segments, microbiological testing of the aspirated mucosa came back positive for S. pneumoniae.

Differential & Final Diagnosis: Due to low inflammatory markers, lack of systemic signs of infection and reduction of opacities after GC increase the patient's dyspnoea was attributed to a poorly controlled asthmatic and vasculitis component of EGPA and restriction of ventilation due to ILD.

Discussion of Management: Although the patient did not present with signs of infection, clindamycin was prescribed due to a positive culture before starting treatment with mepolizumab. The patient started receiving mepolizumab in May 2023 and nintedanib in November 2023.

Conclusions: Dyspnoea in EGPA patients needs careful investigation and its management needs to be individually adapted to the patient. This case showcases combined treatment with mepolizumab and nintedanib to improve patient's lung involvement in EGPA with ILD.

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Disclosures: Lecturing/consulting fees from GSK (MCC, GEF, EA) and AstraZeneca (MCC).

P-294

Analysis of rituximab pharmacokinetics and efectiveness in patients with vasculitis

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[1]Vall d'Hebron Hospital, Barcelona, Spain; [2]Vall d'Hebron, Barcelona, Spain.

Background: Rituximab (RTX) is an antibody used to treat vasculitis. There is interpersonal variability in RTX pharmacokinetics (PK) (1), RTX could be aberrantly excreted in urine in case of proteinuria (2). We aim to describe RTX PK profile and effectiveness in a case series.

Methods: The trial (EUDRACT2020-000484-23) included patients with vasculitis and renal alterations receiving RTX, who had not received RTX at least 6 months.

RTX was administered in day(d) 1, dose was 1g or 0.5g and could be repeated in d14. Blood was collected d1, d7, d14 and d28. RTX and anti-RTX plasma concentration was determined by ELISA (Lisa-Traker®). *FCGRT* gen polymorphisms were analyzed by PCR.

Clinical data was collected during 1 year (y).

RTX PK analysis was done using non-lineal regression (Winnolin®). RTX maximum concentration (Cmax), distribution volume (Vd), clearance (Cl) half-life (t1/2) and area under the curve (AUC) were determined.

Quantitative data is expressed as median (range). SPSS® was used for multiple linear regression.

Results: Five patients were included. All were wild type for the *FCGRT* polymorphism (VNTR3/3) and received corticosteroids at the time of RTX initiation. Basal biochemical results: albumin 3.9 (3.7-4.5) g/dL, creatinine 1.5 (0.9-2.7) mg/dl, glomerular filtrate 45 (21-90) ml/min, reactive protein C 0.16 (0.07-0.31) mg/dl, 24h proteinuria 0.8 (0.6-4.1) g. CD19 cell count was normal prior to RTX initiation and they were depleted after RTX.

PK parameters: Cmax 12.2 (106.2-357.1) µg/ml, Vd 49.15 (45.17-105.09) ml/kg, Cl 0.12 (0.06-0.49) ml/h/kg, t1/2 17.0 (4.7-22.2) days, AUC 8,333.3 (1020-33,333.3) µg·h/ml. No anti-RTX antibodies were detected. A correlation between Log-proteinuria and RTX Cl was detected (p=0.080), 47.2% of RTX Cl variability is justified by proteinuria.

No infections or infusion reactions were reported.

Sex, age (y)	Diagnose	Weigh (kg)	Height (cm)	Previous exposure to RTX	Dose d1 (g)	Dose d14 (g)	RTX AUC (µg·h/ml)	Proteinuria 24h d1 (g)	Proteinuria 24h d180 (g)	Proteinuria 24h d365 (g)	ANCA d1 (U/mL)	ANCA d28 (U/mL)	ANCA d180 (U/mL)	ANCA d365 (U/mL)	Time until CD19 recovery	Complete remission 1y
Man, 74	ANCA PR3	65	166	Yes	0.5	-	8,333	0.6	0.4	0.6	0	0	0	0	>1y	No
Woman, 28	ANCA MPO	49	153	No	1	1	7,142	0.8	4.2	2.7	135.92	NA	NA	NA	6m	Yes
Woman, 72	ANCA MPO	96	159	Yes	1	1	25,000	0.8	0.5	0	158.8	NA	NA	NA	45d	No
Man, 49	ANCA MPO	93	164	Yes	0.5	-	1,020	4.1	5.1	NA	50.64	30.63	17.57	22.94	>1y	Yes
Woman, 86	ANCA MPO	61	154	No	1	-	33,333	1.4	2.6	NA	>200	37.8	22.4	NA	>1y	No

Patients characteristics, PK and outcomes (ANCA: Anti-neutrophil cytoplasmic antibody, d: day, h: hour, NA: not available, m: month, MPO:myeloperoxidase, PR3: proteinase 3, RTX: rituximab, y:year).

Conclusions: No alterations in the *FCGRT* gen or anti-RTX antibodies were detected. RTX PK was similar to those described for patients affected by immflamatory diseases. Proteinuria affects RTX Cl, the correlation was not significant potentially due to the small sample size.

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Disclosures: None.

AUTHORS' INDEX

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LAST NAME, FIRST NAME, PRESENTATION CODE

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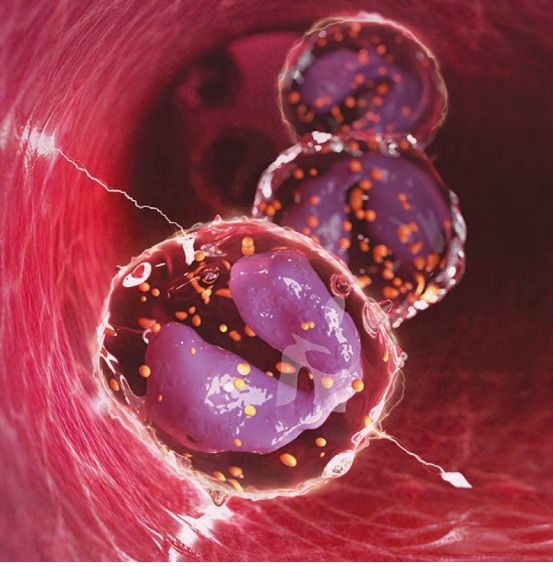
The Role of Eosinophilic Inflammation in EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (EGPA)

The eosinophil is a potent effector cell and a key contributor to inflammation across a number of debilitating diseases, including EGPA.[1-3]



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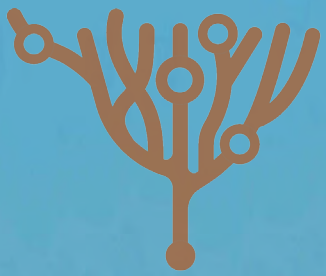

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