

immunopanel is lacking. We evaluated whether an immunopanel could reliably assess endometrioid endometrial cancer (EEC) outcome independent of clinicopathological information.

Method: A cohort of 306 EEC specimens was profiled using tissue microarrays (TMA). Immunohistochemical analysis of well-established tissue biomarkers (ER, PR, HER2, Ki-67, MLH1 and p53) and two new biomarkers (L1CAM and ASRGL1) was carried out. Statistical modeling with embedded variable selection was applied on the staining results to identify minimal prognostic panels with maximal prognostic accuracy.

Results: A panel including p53 and ASRGL1 immunohistochemistry was identified as the most accurate predictor of relapse-free and disease-specific survival. With this panel, patients were allocated into high- (5.9 %), intermediate- (29.5 %) and low- (64.6 %) risk groups. Cases in the high-risk group (aberrant p53, low ASRGL1) had a 30-fold risk ($p < 0.001$) of dying of EEC compared to low-risk group. The statistical modeling favored p53 over L1CAM for prognostic role in EEC.

Conclusion: P53 and ASRGL1 immunoprofiling stratifies of EEC patients into three risk groups with significantly different outcomes. This easily applicable panel could be a useful tool in EEC risk stratification and guiding the allocation of treatment modalities.

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Expression of DNA methyltransferases in ovarian tumours

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Objective: DNA methylation is responsible for gene silencing in various tumour types and is mediated by five DNA methyltransferases (DNMT1, 2, 3a, 3b, 3 L). The purpose of the present study was to explore the expression of DNMTs in borderline and malignant ovarian tumours.

Method: We examined the expression of DNMT1, DNMT2, DNMT3a and DNMT3b in 72 serous (12 borderline tumours, 15 low-grade carcinomas, 45 high-grade carcinomas) and 19 mucinous (12 borderline tumours, 7 carcinomas) primary neoplasms and in 16 relapsed serous carcinomas by immunohistochemistry. Nuclear staining was evaluated for all markers. Cytoplasmic staining was additionally evaluated for DNMT2 and DNMT3a. Intensity of staining (1–3) was multiplied by the % of positive cells. Mann-Whitney and Wilcoxon signed-rank tests were used for statistical analysis.

Results: DNMT1 expression was increased in high-grade compared to low-grade serous carcinomas and in relapsed tumours compared to their primaries ($p < 0.001$ and $p = 0.007$, respectively). Cytoplasmic expression of DNMT3a was lower and nuclear DNMT3a expression was higher in high-grade compared to low-grade serous carcinomas ($p = 0.04$ and $p = 0.004$, respectively). DNMT2 and DNMT3b expression did not show any correlation with tumour type or relapse.

Conclusion: Our results suggest a possible involvement of DNMT1 and DNMT3a in the pathogenesis and progression of high-grade serous carcinomas.

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Upfront pathology review in the randomised PORTEC-3 trial for high risk endometrial cancer

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Objective: In the PORTEC-3 trial, patients with high-risk endometrial cancer (HREC) were randomised to receive pelvic radiotherapy with or

without concurrent and adjuvant chemotherapy. The aim of this analysis was to evaluate the role of expert pathology review before randomisation.

Method: Six hundred eighty-six HREC patients were included in the PORTEC-3 trial; 184 (27 %) in the United Kingdom and 145 (21 %) in the Netherlands. A total of 1295 cases underwent central pathology review, of whom 1226/1295 (95 %) had available matching review and original reports. Inter-observer agreement was evaluated by the kappa value (κ).

Results: Among the 1226 potentially eligible patients, 6356 selected pathology items were evaluable for both original and review pathology. In 43.4 % of patients at least one pathology item changed after review. In 102 patients (8.3 %), this discrepancy led to ineligibility for the PORTEC-3 trial, most frequently due to differences in the assessment of histological type (34 %), endocervical stromal involvement (27 %) and histological grade (19 %).

Conclusion: Central pathology review by expert gynaecological pathologists changed histological type, grade or other items in 43.4 % of HREC patients, leading to ineligibility for the PORTEC-3 trial in 8.3 %. Upfront pathology review is essential to ensure enrolment of the target trial-population, and to avoid over- or undertreatment.

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Test p16/Ki67 twice-positivity and colposcopy with biopsy first-negativity: Detecting histologic HSIL-risk women in 12–18 months follow-up

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Objective: Current secondary cervical cancer prevention algorithms have limitations in detecting cancer precursors. p16/Ki67 test with simultaneous co-expression of anti-proliferative and proliferative proteins has been proposed as a biomarker of high-grade cervical intraepithelial lesions. We investigated whether twice-positive p16/Ki67 test—in first testing and in follow-up—will improve identification of these.

Method: 8350 automated processed LBC, including 1952 cotesting, have been performed in primary cervical cancer screening. Immunocytochemical p16/Ki67 double staining was done in 347 cases using automated preparation system. 181 women with ASC-H or higher or ASC-US/LSIL cytology and HPV-positive were referred to colposcopy with biopsy. 24 patients with histological LSIL or less (biopsy first-negativity), reached follow-up cotesting with p16/Ki67 test and biopsy in 12–18 months.

Results: Diagnostic value of twice-positive p16/Ki67 for histologic HSIL (hHSIL) for the second follow-up biopsy was evaluated. Follow-up p16/Ki67 was positive in 10 women – 8 hHSIL and 2 hLSIL cases were diagnosed in biopsy. 1 hHSIL was p16-Ki67 twice-negative. Sensitivity/specificity/PPV/NPV of p16/Ki67 for hHSIL in the second biopsy were 89/86/80/93 (CI 95 %) respectively.

Conclusion: Twice-positive p16/Ki67 test can be a precise biomarker in triage patients for hHSIL-risk groups. Also, it might be decisive in referring to 12–18-month follow-up biopsy without prior cytology or HPV testing.

OFP-04-011

Overexpression of SOX 9 protein in endometrial carcinoma

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Objective: Endometrial carcinoma is the most common gynecological malignancy in developed countries and the carcinogenesis is not fully understood. SOX 9 is a transcription factor involved in the tumorigenesis of a number of cancers, however its role in endometrial carcinoma is uncertain. This study is to examine the