swiss clinical trial organisation

swissethics

Schweizerische Ethikkommissionen für die Forschung am Menschen
Commissions d'éthique suisses relative à la recherche sur l'être humain
Commissioni etiche svizzere per la ricerca sull'essere umano
Swiss Ethics Committees on research involving humans

Investigator initiated trials (IITs) under ClinO: Annual Safety Report

Please complete the form by replacing all text modules in square brackets. Use "x" for check boxes.

The annual safety report[1] shall summarise the actual state of knowledge and describe the handling of identified and potential risks. The sponsor-investigator must submit the annual safety report for clinical trials once a year to the ethics committee (EC); for Category B and C additionally to the Agency.

General information

Title of the clinical trial
Crying, unsettled and distressed infants: Swiss arm of an international randomised controlled trial to test the effectiveness of osteopathic care

Annual Safety Report number	Trial code/ protocol number	BASEC number	SNCTP number	Swissmedic number	EC name (Lead EC and/or concerned EC)
2021-2022	IRAS_ID268925_CH_1.2	2021-00099	[no.]	n/a	CED-Vaud

Clinical trial with …			Category
[ ] Investigational Medicinal Product (IMP)	[ ] Medical Device		[X] A [ ] B [ ] C
[ ] Transplant Product	[X] Other		

Trial design			
[X] Randomised	[ ] Open	[X] Blinded	[ ] Others: [free text]

Product name / Intervention
Light osteopathic touch using techniques such as articulation, tension release (to ligaments, articular strains, fontanelles/cranial sutures), counter-strain/facilitated positional release, indirect functional techniques, myofascial release, soft tissue

Contact details of the sponsor-investigator
Paul Vaucher, paul.vaucher@hes-so.ch, +41 78 788 33 66

Name and address of institution
Haute Ecole de Santé de Fribourg, Route des Arsenaux 16A, 1700 Fribourg

Date of report	Reporting period
16.09.2022	01.09.2019 to 31.07.2022 The Swiss trial only began in September 2021 and ended in July 2022. Therefore, only a single annual safety report was planned. This report however covers the entire trial in all three countries in which it took place.

Details of the clinical trial

Please specify the numbers for Switzerland and overall in case of international trials.

Participating centre(s)			
Total:	Planned:	Open:	Closed:
84	30	0	84

Number of participants			
Target number:	Enrolled:	Completed:	Prematurely terminated:
112	66	66	0

[1] Refer to ClinO Art. 43

Participant's safety

Please include differences between study and control group if applicable. In case the trial is blinded, please add a comment, whether participants were unblinded.

Summary of the safety profile
During the reporting period, 2 of 66 participants (3 %) reported a total of 2 serious adverse events (SAEs; with possible relationship to the intervention). The most frequent SAEs documented were chest infections requiring hospitalisation (2x). Both infants were in the control group. SwissEthics was not informed as both these events took place in the UK (SwissEthics SEA reporting document specifies that only Swiss SAEs have to be reported). As required by ICH E6, SAE need to be reported as planned by national regulations. In the UK, SAE need to be reported to the sponsor within 14 days. Only if the SAE is deemed related and unexpected does it need to be reported to the ethical commission. Both SAE were reported to the principal investigator within 24h, they were then discussed by the trial management group and reported within 14 days to the Trial Steering Committee. Both events were evaluated as unrelated to the intervention. During the trial, SwissEthics only asks to report SAEs that have occurred in Switzerland. Including the two SAEs, ten adverse reactions were reported. Of the eight non-serious events, five included exacerbations in symptoms (three in the test group, two in the control group), two were likely unrelated to the trial (covid-19 in the control group; fever in the test group), and one involved regurgitation (test group) that could be related to the trial.

	Fatal cases	Serious Adverse Events[2], SAEs
Number of cases (during reporting period)	0	2
Number of cases (cumulative) since the start of the clinical trial	0	2

Summary of the safety evaluation

If relevant, please consider regulations as MedDev, CIOMS, etc.

Relevant safety measures (e.g. by sponsor, manufacturer/ marketing authorization holder, DSMB, agency, ethics committee) No particular measure was taken other than having put into place an independent physician to assess whether SAEs can or cannot be related to patient management within the trial. Both reported SAEs were deemed unrelated. However, following cases of fever and respiratory infections, all participating osteopaths were reminded to wear PPEs.
New findings related to the safety of the product The SAEs and other reported adverse events were balanced between groups. There were eight non-serious adverse events, five in the test group and three in the control, with six possibly related to the trial (exacerbation of existing symptoms and regurgitation).
Impact of new findings related to the trial conduct (changes to IB, Informed Consent form, contraindications, adverse events of special interest) No changes were made.
Risk-benefit ratio and conclusion The risk-benefit ratio does not favour osteopathic light touch manual treatment with intention over control touch on random regions without intent. However, this trial did not report more undesirable events in one group over the other. To note, the study was powered to detect MCID for benefit, not harm. The study can rule out 30-minute differences between arms but if an intervention were to increase crying time by less than 30 minutes this might still not be acceptable. Therefore, the study was planned as underpowered to detect minimal important clinical differences for harm.

[2] Refer to ICH GCP E6(R1) 1.50

Line listing

Line listing of SAEs, SADRs and SUSARs, including international cases
(code and version of used standard (e.g. MedDRA or CTCAE) should be indicated, details on SUSARs will be attached as appendices)
In case the line listing is generated automatically by your database, please replace the table below, considering all relevant information. For medical devices you may refer to MEDDEV 2.7/3.

SAE / SADR / SUSAR	Serious adverse event/ reaction No.	Participants ID	Age / Sex (F=female, M=male)	Country and site in which participant is/was enrolled (for multicentre, international trials)	Description of event/ reaction	Description of intervention (dosage, schedule, route, if applicable)	Date of onset	Date of treatment (start and stop)	Outcome (e.g. resolved, fatal, improved, sequel, unknown)	Comments, if relevant (e.g. causality assessment, relationship)
SAE	10047700 / 10013950	PNC0006	44 days of age / Female	UK (PNC)	Hospitalisation for chest infection (bronchiolitis) and feeding difficulties	Control	14.05.2021	29.04.2021 – 06.05.2021	Resolved	Deemed unrelated to test intervention
SAE	10047700	ESO0009	50 days of age / Female	UK (ESO)	Hospitalisation for chest infection	Control	15.09.2021	31.08.2021	Resolved	Deemed unrelated to control intervention

Signature and approval

Place / date	Name and signature of sponsor-investigator
Fribourg, the 16.09.2022	Paul Vaucher 

Appendix

SUSAR reports	If applicable, please list the reports including reference number
n/a	Attached is the Adverse Events log and both reports for each SAE.

Adverse Events log

Incident date	Reported by	ID and allocation	Incident	Outcome	TMG assessment	Comment
7.4.21	Andrew MacMillan	PNC0004 TTR	Extra medical care. Infant saw GP due to raised temperature. Aetiology unknown	Resolution spontaneous	Non serious AE, unrelated to trial	Reminder to all osteopaths to wear PPE
14.5.21	Andrew MacMillan	PNC0006 GTR	Unexpected hospital admission due to bronchiolitis and feeding difficulties	Hospital stay with NG feeding tube. Infant discharged and all OK.	Serious AE, unrelated to trial. Sponsor informed. No further action required.	Reminder to all osteopaths to wear PPE
29.7.21	Claire Piper	ESO0007	Mum involved in a car accident on way to appointment. Mother and baby OK but distressed. No medical help sought.	Baby was not enrolled or randomised but Mum had completed the baseline questionnaire prior to the consultation	Non serious AE, unrelated to trial treatment	Record not to be included in final dataset
15.9.21	Claire Piper	ESO0009 GTR	Unexpected hospital admission. Baby caught a cold from brother, which worsened, baby hospitalised with a chest infection for2 days	Chest infection resolved with hospital care.	Serious AE, unrelated to trial. Sponsor informed no further reaction required.	Mum continued recording crying time and will seek care at a later date
16.3.22	Claire Piper	ESO0017 GTR	Mother had COVID couldn't attend 2nd appointment	Isolating otherwise healthy	Non serious AE, unrelated to trial	Baby remains in study, follow up as normal
21.6.22	Dominque Vergnuad	CH10012 TTR	After 1st follow-up baby vomited and cried over a 2-3 hour period	Resolved within 24 hours	Non serious possibly related	
28.6.22	Dominque Vergnuad	CH10012 TTR	After 2nd follow-up infant did not sleep well afterwards during that night	Resolved within 24 hours	Non serious possibly related	

30.11.20	Laura	PO10002 GTR	After 2nd follow-up infant was very unsettled and colicky for 4-5 hours	Resolved with 24 hours	Non serious possibly related	
29.10.21	Natalia Herron	CH10008 TTR	After follow-up 2 infant had more episodes of incessant crying	Resolved with 24 hours	Non serious possibly related	
16.4.21	Alex Corsar	PNC0005 GTR	After 1st follow-up Infant crying increased for 2 days	Resolved with 48 hours	Non serious possibly related	

Total serious adverse events 2 unrelated to trial – Chest infections resulting in unexpected hospital admissions (both control group)

Total non-serious events 7,

4 events involved exacerbation in symptoms, possibly related to treatment (2 control, 2 test group)

2 involved new symptoms –1 x covid19 (control), 1 x raised temperature (test group), most likely unrelated to trial

1 involved new and exacerbated symptoms – 1 x vomiting and crying (test group) – possibly related to the trial

Total adverse reactions 9

CRYING, UNSETTLED, DISTRESSED INFANTS: EFFECTIVENESS STUDY

Adverse Events

Date: 13.5.21

Participant ID: PNC0006

Adverse Event: Hospital admission

Name of person reporting the event: Andrew MacMillan

Please describe in as much detail the nature of the adverse event or protocol deviation and email as soon as possible to dawn.carnes@uco.ac.uk

Should the event be serious: unexpected hospital admission, visit to A&E or death please contact Dawn Carnes immediately on 07720 868 337 and email.

Andrew MacMillan <Andrew.MacMillan@uco.ac.uk>

Thu 13/05/2021 11:21

Hi Dawn.

Baby 006 has been reported as an adverse event. She has Bronchiolitis and was admitted to hospital Sunday (09.05.21) due to feeding difficulties. She is being NG tube fed but is expected to be discharged this week.

She was in the GTR group and we will follow up with her, Sophie spoke to Alex yesterday on the phone and we reassured her and advised not to worry about the crying diary etc. I raised it as an adverse event on castor.

Thanks

Andrew

AM Followed up, baby discharged later in the week and is recovering well.

CUTIES

CRYING, UNSETTLED, DISTRESSED INFANTS: EFFECTIVENESS STUDY

Adverse Events

Date: 8.9.21

Participant ID: ESO0009

Adverse Event: Serious: unexpected hospital admission

Name of person reporting the event: Claire Piper

Please describe in as much detail the nature of the adverse event or protocol deviation and email as soon as possible to dawn.carnes@uco.ac.uk

Should the event be serious: unexpected hospital admission, visit to A&E or death please contact Dawn Carnes immediately on 07720 868 337 and email.

Mum of baby ESO 0009 rang to cancel her infants 2nd appointment today because the infant had been ill with a chest infection and was hospitalised, see email below.

Baby will continue to be in the study but will only have received one treatment as there are no clinic slots within the trial period available.

The infant will be continue to be treated outside the trial period in the normal ESO clinic.

EXTERNAL-- Cuties baby ESO0009
Claire Piper <ClairePiper@eso.ac.uk>
Wed 08/09/2021 10:08

Hi Dawn

I just spoke to mum and baby has been very unsettled since the session. She caught a cold from her brother which went onto her chest and turned into a chest infection. She was hospitalised for a few days and is now discharged and recovering.
Mum is happy to fill out the remaining paperwork and I advised her that she can book baby into the normal children's clinic where we can continue her care.
Many thanks
Claire

CRYING, UNSETTLED, DISTRESSED INFANTS: EFFECTIVENESS STUDY

Adverse Events

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Participant ID: PNC0006

Adverse Event: Hospital admission

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