Clinical trial results:
Remifentanil tapering and post-adenotonsillectomy pain in children: a randomised, placebo controlled, double blind study

Summary

EudraCT number	2019-001677-81
Trial protocol	NO
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	03 November 2023
First version publication date	03 November 2023

Trial information

Trial identification

Sponsor protocol code	PTRS01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03994146
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Akershus Universitetssykehus
Sponsor organisation address	Sykehusveien 25, Lørenskog, Norway, 1478
Public contact	Principal Investigator, Akershus Universitetssykehus, william.james.morton@ahus.no
Scientific contact	Principal Investigator, Akershus Universitetssykehus, william.james.morton@ahus.no

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	18 October 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

Tonsillectomy is the commonest operation of childhood and results in considerable pain.
Remifentanil is a potent, ultra short acting opiod with a long- established safety record in paediatric anaesthesia that is used to provide intraoperative analgesia.
There is evidence from adult studies that remifentanil paradoxically increases postoperative pain, although this may be ablated if propofol (rather than inhalational anaesthesia) is used or if the remifentanil is tapered rather than abruptly discontinued at the end of surgery.
The analgesic effect of gradual withdrawl of remifentanil at the end of surgery has not been studied in children and may have significant clinical implications.
The primary measure of efficacy will be the dose of fentanyl rescue analgesia in the perioperative period (1 mcg.kg-1 bolus for >20% increase in pulse, blood pressure or movement intraoperatively or a FLACC(Face, Legs, Arms, Cry, Consolablity) score of >5 in the recovery unit.

Protection of trial subjects:

Independent clinician.
National data handling agreement.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 January 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Norway: 12
Worldwide total number of subjects	12
EEA total number of subjects	12

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	12
Adolescents (12-17 years)	0
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Trial prematurely terminated due to poor recruitment.

Pre-assignment

Screening details:

American Society Anaesthesiology I-II children (1 to 10 years)
Weight over 10.0 kg
Presenting for tonsillectomy / tonsillotomy or adenotonsillectomy / tonsillotomy at Akershus Universitetssykehus, Lørenskog, or Lovisenberg Diakonale Hospital, Oslo, Norway

Period 1

Period 1 title	Baseline (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

Blinding conducted by sealed envelop.

Arms

Are arms mutually exclusive?	Yes
Arm title	Remifentanil tapering / Placebo abrupt cessation

Arm description:

Syringe one contains Remifentanil 2 mg in 40 ml NaCl 9 mg.ml-1 = 50 µg.ml-1 which will be infused at a rate of 0.9 µg.kg-1.min-1 and Syringe two contains 40 ml NaCl 9 mg.ml-1 at an identical infusion rate. According to randomisation syringe one will then be tapered towards the end of surgery and syringe two abruptly stopped.

Arm type	Experimental
Investigational medicinal product name	Remifentanil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravascular use

Dosage and administration details:

Remifentanil 2 mg in 40 ml NaCl 9 mg.ml-1 = 50 µg.ml-1
infused at a rate of 0.9 µg.kg-1.min-1

Arm title	Placebo Tapering / Remifentanil Abrupt cessation.

Arm description:

Syringe one contains 40 ml NaCl 9 mg.ml-1 and Syringe two contains Remifentanil 2 mg in 40 ml NaCl 9 mg.ml-1 = 50 µg.ml-1 which will be infused at a rate of 0.9 µg.kg-1.min-1. According to randomization syringe one will be tapered towards the end of surgery and syringe two abruptly stopped

Arm type	Active comparator
Investigational medicinal product name	Normal Saline 0.9%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravascular use

Dosage and administration details:

40 ml NaCl 9 mg.ml-1

Number of subjects in period 1	Remifentanil tapering / Placebo abrupt cessation	Placebo Tapering / Remifentanil Abrupt cessation.
Started	6	6
Completed	6	6

Baseline characteristics

End points

End points reporting groups

Reporting group title	Remifentanil tapering / Placebo abrupt cessation

Reporting group description:

Syringe one contains Remifentanil 2 mg in 40 ml NaCl 9 mg.ml-1 = 50 µg.ml-1 which will be infused at a rate of 0.9 µg.kg-1.min-1 and Syringe two contains 40 ml NaCl 9 mg.ml-1 at an identical infusion rate. According to randomisation syringe one will then be tapered towards the end of surgery and syringe two abruptly stopped.

Reporting group title	Placebo Tapering / Remifentanil Abrupt cessation.

Reporting group description:

Syringe one contains 40 ml NaCl 9 mg.ml-1 and Syringe two contains Remifentanil 2 mg in 40 ml NaCl 9 mg.ml-1 = 50 µg.ml-1 which will be infused at a rate of 0.9 µg.kg-1.min-1. According to randomization syringe one will be tapered towards the end of surgery and syringe two abruptly stopped

Primary: Premature trial termination due to poor recruitment

End point title	Premature trial termination due to poor recruitment

End point description:

End point type	Primary

End point timeframe:

06.01-2020 to 22.12.2021

End point values	Remifentanil tapering / Placebo abrupt cessation	Placebo Tapering / Remifentanil Abrupt cessation.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[1]	6		
Units: 0	0	0		

Notes:

[1] - Premature trial termination due to poor recruitment

Statistical analyses

Statistical analysis title	Premature trial termination

Statistical analysis description:

No statistical analysis due to premature trial termination due to poor recruitment.

Comparison groups	Remifentanil tapering / Placebo abrupt cessation v Placebo Tapering / Remifentanil Abrupt cessation.

Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	< 0.05 [3]
Method	Kruskal-wallis
Parameter estimate	Odds ratio (OR)
Point estimate	10
Confidence interval	
level	95 %
sides	1-sided
lower limit	5
Variability estimate	Standard deviation
Dispersion value	10

Notes:

[2] - No statistical analysis due to premature trial termination due to poor recruitment.

[3] - No statistical analysis due to premature trial termination due to poor recruitment.

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 06.01.2020 to 22.12.2021	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	2.1
Reporting groups	
Reporting group title	Remifenatil Tapering

Reporting group description: -

Serious adverse events	Remifenatil Tapering		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Remifenatil Tapering		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 12 (8.33%)		
Surgical and medical procedures			
Surgical failure	Additional description: Surgical time to achieve haemostasis necessitated an unplanned overnight stay for the patient. Not related to trial.		
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported