Clinical trial results:
Efficacy of Perioperative Long-acting Anesthesia by Local Infiltration Following Median Sternotomy - The PAIN Trial

Summary

EudraCT number	2021-005886-41
Trial protocol	DK
Global end of trial date	16 April 2024

Results information

Result version number	v1 (current)
This version publication date	15 June 2025
First version publication date	15 June 2025

Trial information

Trial identification

Sponsor protocol code	AUH-PAIN-01

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Aarhus Universityhospital
Sponsor organisation address	Palle Juul-Jensens Blvd 99, Aarhus, Denmark, 8200
Public contact	Dept. of Cardiothoracic Surgery, Aarhus University Hospital, 0045 20990948, jonrau@rm.dk
Scientific contact	Dept. of Cardiothoracic Surgery, Aarhus University Hospital, 0045 20990948, jonrau@rm.dk

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	Final
Date of interim/final analysis	29 May 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 April 2024
Global end of trial reached?	Yes
Global end of trial date	16 April 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy and safety of long-acting local infiltration anesthesia in patients undergoing coronary bypass grafting through sternotomy.

Protection of trial subjects:

Intervention was performed under general anesthesia during surgery. A comprehensive follow-up of all participants were performed to ensure the safety of the intervention.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 November 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 113
Worldwide total number of subjects	113
EEA total number of subjects	113

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)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	43
From 65 to 84 years	70
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited at two danish univeristy hospitals: Aarhus Univeristyhospital and Aalborg universityhospital from november 2022 until october 2023.

Pre-assignment

Screening details:

All patients undergoing scheduled coronary artery bypass grafting surgery at the two sites were screened for eligibility to participate.

Period 1

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

Blinding implementation details:

All allocation of either active treatment or placebo were done using REDcap

Arms

Are arms mutually exclusive?	Yes
Arm title	Active intervention

Arm description:

Participants receiving active treatment

Arm type	Active comparator
Investigational medicinal product name	Bupivacaine w adrenaline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for injection
Routes of administration	Perineural use

Dosage and administration details:

60ml of 2.5mg/ml bubivacaine with 5ug/ml adrenaline

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Perineural use

Dosage and administration details:

2ml of 4mg/ml dexamethasone

Investigational medicinal product name	Clonidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Perineural use

Dosage and administration details:

0.5ml og 150ug/ml clonidine

Arm title	Placebo intervention

Arm description:

Participants recieving placebo intervention

Arm type	Placebo

Investigational medicinal product name	NaCl Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Perineural use

Dosage and administration details:

62.5ml of 0.9 NaCl

Number of subjects in period 1	Active intervention	Placebo intervention
Started	57	56
Completed	52	48
Not completed	5	8
Protocol deviation	5	8

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	113	113	
Age categorical Units: Subjects			
Adults (18-64 years)	43	43	
From 65-84 years	70	70	
Gender categorical Units: Subjects			
Female	12	12	
Male	101	101	

End points

End points reporting groups	
Reporting group title	Active intervention
Reporting group description: Participants receiving active treatment	
Reporting group title	Placebo intervention
Reporting group description: Participants recieving placebo intervention	

Primary: OME	
End point title	OME
End point description: Accumulated opioid consumption within the first 24 postoperative hours.	
End point type	Primary
End point timeframe: first 24 postoperative hours	

End point values	Active intervention	Placebo intervention		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	48		
Units: OME				
arithmetic mean (standard deviation)	68.7 (± 52.3)	68.4 (± 38.9)		

Statistical analyses

Statistical analysis title	OME
Comparison groups	Active intervention v Placebo intervention
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.971
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

the entire study period

Adverse event reporting additional description:

All participants electronic journals was read thoroughly once the adverese event period was terminated (4 weeks postoperative)

Assessment type	Systematic

Dictionary used

Dictionary name	See above
Dictionary version	1

Reporting groups

Reporting group title	entire population

Reporting group description: -

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: A threshold of 5% for non-serious adverse events were applied, and there were no non-serious events that was observed with a frequency higher than 5%

Serious adverse events	entire population		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 113 (8.85%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Coronary angio need	Additional description: participants needing postoperative angio for either suspected ishemia or suspected dysfynctional graft		
subjects affected / exposed	6 / 113 (5.31%)		
occurrences causally related to treatment / all	6 / 6		
deaths causally related to treatment / all	0 / 0		
Angina	Additional description: participants with postoperative angina not resulting in coronary angio.		
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Late pericardial efusion	Additional description: No need for intervention		
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Prolonged ICU need			

subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Need for cardial pacemaker			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Fascia defect resulting in need for redo surgery			
subjects affected / exposed	2 / 113 (1.77%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
affected kidney function			
subjects affected / exposed	1 / 113 (0.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	entire population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 113 (0.00%)		

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? Yes

Date	Interruption	Restart date
19 December 2022	Due to a national delivery stop of clonidine inclusion was paused from 19-dec-2022 until 03-feb-2023	03 February 2023

Notes:

Limitations and caveats

None reported