



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 receiving 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 (\pm 52.3) | 68.4 (\pm 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 adverse 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 ischemia or suspected dysfunctional 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