



## Clinical trial results:

### The RAS-study

### A reverse and anatomical prosthesis shoulder study

**Can we improve the prophylactic profile of antibiotic treatment in shoulder prosthesis surgery?**

**- A clinical microdialysis study assessing antibiotic concentrations in deadspace, bone, and soft tissue following weight-based cefuroxime dosage in both anatomic and reverse shoulder prosthesis surgery.**

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2020-003078-36  |
| Trial protocol           | DK              |
| Global end of trial date | 01 January 2023 |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 06 January 2024 |
| First version publication date | 06 January 2024 |

#### Trial information

##### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 727258 |
|-----------------------|--------|

##### Additional study identifiers

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

Notes:

##### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Aarhus University Hospital   |
| Sponsor organisation address | Palle Juul-Jensens Boulevard 99 , Aarhus N, Denmark, 8200                                |
| Public contact               | Sara Kousgaard Tøstesen, Aarhus University Hospital, 00 4542202469, 201510204@post.au.dk |
| Scientific contact           | Sara Kousgaard Tøstesen, Aarhus University Hospital, 00 4542202469, 201510204@post.au.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                       | 01 January 2023 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 15 October 2022 |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 01 January 2023 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

The main objective of this clinical cohort study is to determine local tissue concentrations of cefuroxime in deadspace, bone, muscle and subcutaneous tissue using micro dialysis in patients having either anatomic (ASA) or reverse (RSA) shoulder prosthesis surgery at Aarhus University Hospital.

Approximate 30 min. prior to surgery, a weight-based dose of cefuroxime (20 mg / kg) is administered as a bolus infusion over 10 min intravenously. At the end of surgery micro dialysis catheters are placed in the deadspace, in the coracoid bone process, in the deltoid muscle and in subcutaneous tissue. The second cefuroxime dose is administered 8 hours after the first dose.

Deadspace: At RSA, one catheter is placed in the large deadspace above the joint. At ASA, one catheter is placed in the prosthetic joint (intra-articular) and one above the rotator cuff (subacromial). In total, 4 catheters per patient in group 1 (RSA), and 5 catheters per patient in group 2 (ASA).

Protection of trial subjects:

Patients were provided with analgesic drugs concerning surgery following local guidelines. Food and drinks were also provided when needed. No patients experienced discomfort and no study-related adverse events were observed. A research assistant was with the patients during the study period.

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 01 October 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 | Denmark: 20 |
| Worldwide total number of subjects   | 20          |
| EEA total number of subjects         | 20          |

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)                      | 5  |
| From 65 to 84 years                       | 15 |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Patients having either anatomic (ASA) or reverse (RSA) shoulder prosthesis surgery at Aarhus University Hospital. Medical evaluation.

### Pre-assignment

Screening details:

In- and excluding criteria has to be fulfilled before assignment to the study. Screened by medical doctor.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall trial (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Not applicable                 |
| Blinding used                | Not blinded                    |

### Arms

|                              |   |
|------------------------------|---|
| Are arms mutually exclusive? | Yes   |
| <b>Arm title</b>             | Weight dosed cefuroxime (20 mg/kg) -in RSA patients |

Arm description:

Cefuroxime dosed by weight (20 mg/kg) was administered intravenously to all RSA patients preoperative and repeated 8 hours later.

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Cefuroxime                                   |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Powder and solvent for solution for infusion |
| Routes of administration               | Intravenous use                              |

Dosage and administration details:

20 mg/kg

|                  |  |
|------------------|--|
| <b>Arm title</b> | Weight dosed cefuroxime (20 mg/kg) in ASA patients |
|------------------|--|

Arm description:

Cefuroxime dosed by weight (20 mg/kg) was administered intravenously to all ASA patients preoperative and repeated 8 hours later.

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Cefuroxime                                   |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Powder and solvent for solution for infusion |
| Routes of administration               | Intravenous use                              |

Dosage and administration details:

20 mg/kg

| <b>Number of subjects in period 1</b> | Weight dosed<br>cefuroxime (20<br>mg/kg) -in RSA<br>patients | Weight dosed<br>cefuroxime (20<br>mg/kg) in ASA<br>patients |
|---------------------------------------|--|---|
| Started                               | 10   | 10  |
| Completed                             | 10   | 10  |

## Baseline characteristics

### Reporting groups

Reporting group title

Overall trial

Reporting group description:

Cefuroxime dosed by weight (20 mg/kg) was administered intravenously to all patients, both RSA and ASA, preoperative and repeated 8 hours later.

| Reporting group values                                | Overall trial | Total |  |
|---|---------------|-------|--|
| Number of subjects                                    | 20            | 20    |  |
| Age categorical<br>Units: Subjects                    |               |       |  |
| In utero  | 0             | 0     |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0             | 0     |  |
| Newborns (0-27 days)                                  | 0             | 0     |  |
| Infants and toddlers (28 days-23 months)              | 0             | 0     |  |
| Children (2-11 years)                                 | 0             | 0     |  |
| Adolescents (12-17 years)                             | 0             | 0     |  |
| Adults (18-64 years)                                  | 5             | 5     |  |
| From 65-84 years                                      | 15            | 15    |  |
| 85 years and over                                     | 0             | 0     |  |
| Gender categorical<br>Units: Subjects                 |               |       |  |
| Female  | 14            | 14    |  |
| Male  | 6             | 6     |  |

## End points

### End points reporting groups

|   |   |
|---|---|
| Reporting group title   | Weight dosed cefuroxime (20 mg/kg) -in RSA patients |
| Reporting group description:<br>Cefuroxime dosed by weight (20 mg/kg) was administered intravenously to all RSA patients preoperative and repeated 8 hours later. |   |
| Reporting group title   | Weight dosed cefuroxime (20 mg/kg) in ASA patients  |
| Reporting group description:<br>Cefuroxime dosed by weight (20 mg/kg) was administered intravenously to all ASA patients preoperative and repeated 8 hours later. |   |

### Primary: Cefuroxime concentrations

|   |  |
|---|--|
| End point title   | Cefuroxime concentrations <sup>[1]</sup> |
| End point description:<br>Mean cefuroxime concentrations over time in plasma, deadspace, bone, muscle, and subcutaneous tissue using microdialysis in patients having either anatomic (ASA) or reverse (RSA) shoulder prosthesis surgery at Aarhus University Hospital. |  |
| End point type  | Primary                                  |
| End point timeframe:<br>From time 0 h (preoperative cefuroxime dose) up to 16 h (end of the study period).  |  |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Raw data. See attached file: Mean cefuroxime concentrations in RSA and ASA patients

| End point values                     | Weight dosed cefuroxime (20 mg/kg) -in RSA patients | Weight dosed cefuroxime (20 mg/kg) in ASA patients |  |  |
|--------------------------------------|---|--|--|--|
| Subject group type                   | Reporting group                                     | Reporting group                                    |  |  |
| Number of subjects analysed          | 10  | 10   |  |  |
| Units: µg/mL                         |   |  |  |  |
| arithmetic mean (standard deviation) | 00 (± 00)   | 00 (± 00)  |  |  |

|                                   |   |
|-----------------------------------|---|
| <b>Attachments (see zip file)</b> | Raw data:/Mean cefuroxime concentrations in RSA and ASA |
|-----------------------------------|---|

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From time 0 h (preoperative dose of cefuroxime) to 16 h after first administration (end of study period/sampling) for each patient.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                 |               |
|-----------------|---------------|
| Dictionary name | produktresumé |
|-----------------|---------------|

|                    |      |
|--------------------|------|
| Dictionary version | 2020 |
|--------------------|------|

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | trial overall |
|-----------------------|---------------|

Reporting group description:

All 20 patient undergoing RSA og ASA

| Serious adverse events                            | trial overall  |  |  |
|---|----------------|--|--|
| Total subjects affected by serious adverse events |                |  |  |
| subjects affected / exposed                       | 0 / 20 (0.00%) |  |  |
| number of deaths (all causes)                     | 0              |  |  |
| number of deaths resulting from adverse events    | 0              |  |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events                            | trial overall  |  |  |
|---|--|--|--|
| Total subjects affected by non-serious adverse events |  |  |  |
| subjects affected / exposed                           | 1 / 20 (5.00%)   |  |  |
| Product issues  |  |  |  |
| Microdialysis error                                   | Additional description: Discontinuation of one microdialysis catheter failed and the biocompatible membrane was lodged in the deltoid muscle/subcutaneous tissue above |  |  |
| subjects affected / exposed                           | 1 / 20 (5.00%)   |  |  |
| occurrences (all)                                     | 20   |  |  |



## 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