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
Arm title	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

Arm title	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

Number of subjects in period 1	Weight dosed cefuroxime (20 mg/kg) -in RSA patients	Weight dosed cefuroxime (20 mg/kg) in ASA 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 Units: Subjects			
In utero	0	0	
Preterm newborn infants (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 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:	
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:	
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[1]
End point description:	
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:	
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)		

Attachments (see zip file)	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