Clinical trial results:
Does repeated administration of cefuroxime after orthopedic surgery provide a better prophylactic profile regarding postoperativ infection than a single administration of preoperative antimicrobial ?
- A micro dialysis study assessing the concentration of antibiotics in bone, synovial sheath, and subcutaneous tissue after trapeziectomy

Summary

EudraCT number	2019-001134-33
Trial protocol	DK
Global end of trial date	19 May 2021

Results information

Result version number	v1 (current)
This version publication date	22 October 2022
First version publication date	22 October 2022
Summary attachment (see zip file)	Results 2019-001134-33 (MANUS_Results T>MIC_2022.pdf)

Trial information

Trial identification

Sponsor protocol code	012329

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,
Public contact	Andrea René Jørgensen, Aarhus University Hospital, 0045 51955640, anjo@clin.au.dk
Scientific contact	Andrea René Jørgensen, Aarhus University Hospital, 0045 51955640, anjo@clin.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	26 September 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 May 2021
Global end of trial reached?	Yes
Global end of trial date	19 May 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objectives of the trial are to asses the penetration of cefuroxime when it is administered as either a single administration or as repeated administration, into bone, synovial sheath, and subcutaneous tissue with the use of the pharmacokinetic sampling method, micro dialysis. The primary endpoints are the time for which the concentration of cefuroxime is above the minimal inhibitory concentration (T>MIC) and penetration ratios. The secondary endpoints are standard pharmacokinetic parametres such as; half-life, Cmax, Tmax and AUC.

Protection of trial subjects:

Pain medication was given as in accordance with the normal treatment in relation to the surgery. Food and drink when needed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2019
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: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	7
From 65 to 84 years	9

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients requiring a trapeziectomy due to CMC1 osteoarthritis was asked.

Pre-assignment

Screening details:

Criteria for inclusion and exclusion, screened by medical doctor.

Period 1

Period 1 title	Intervention (overall) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	1x1500

Arm description:

Standard treatment.

Arm type	Active comparator
Investigational medicinal product name	PR1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

1,500 mg of cefuroxime given as a single bolus administration intravenously over 10 min.

Arm title	2x1,500

Arm description:

Repeat dose of cefuroxime.

Arm type	Experimental
Investigational medicinal product name	PR1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

2x1,500 mg of cefuroxime given as a single bolus administration intravenously over 10 min 4 h apart.

Number of subjects in period 1	1x1500	2x1,500
Started	8	8
Inclusion of all patients.	8	8
Surgery of all patients.	8	8
Data analysis of all patients.	8	8

Completed	8	8

Baseline characteristics

Reporting groups	
Reporting group title	1x1500
Reporting group description: Standard treatment.	
Reporting group title	2x1,500
Reporting group description: Repeat dose of cefuroxime.	

Reporting group values	1x1500	2x1,500	Total
Number of subjects	8	8	16
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	4	7
From 65-84 years	5	4	9
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	66	63	
full range (min-max)	51 to 80	56 to 74	-
Gender categorical Units: Subjects			
Female	6	7	13
Male	2	1	3

End points

End points reporting groups	
Reporting group title	1x1500
Reporting group description: Standard treatment.	
Reporting group title	2x1,500
Reporting group description: Repeat dose of cefuroxime.	

Primary: T>MIC	
End point title	T>MIC
End point description:	
End point type	Primary
End point timeframe: From time 0 and until end of the observation time (8h)	

End point values	1x1500	2x1,500		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: minute				
arithmetic mean (confidence interval 95%)				
Plasma	280 (251 to 308)	449 (421 to 478)		
Subcutaneous tissue	336 (308 to 365)	445 (414 to 475)		
Synovial sheath	315 (287 to 344)	446 (418 to 475)		
Bone	235 (206 to 263)	433 (405 to 462)		

Statistical analyses

Statistical analysis title	ANOVA
Comparison groups	2x1,500 v 1x1500
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	equivalence[1]
P-value	< 0.05
Method	ANOVA

Notes:

[1] - The pharmacokinetic parameters and mean fT>MIC were compared by the use of repeated measurements analysis of variance followed by pairwise comparisons by linear regression. A p-value < 0.05 was considered statistically significant

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
From the time of administration of cefuroxime (T = 0) and until 8 h after (first) administration.	
Assessment type	Systematic

Dictionary used	
Dictionary name	Produktresumé
Dictionary version	2016

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

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: There were no adverse events.

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Small sample size.

Notes: