Clinical trial results:
intraperitoneal microdialysis after server peritonitis

Summary

EudraCT number	2012-004398-22
Trial protocol	DK
Global end of trial date	01 October 2020

Results information

Result version number	v1 (current)
This version publication date	13 December 2021
First version publication date	13 December 2021

Trial information

Trial identification

Sponsor protocol code	1

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Odense University Hospital
Sponsor organisation address	dr Boulevadr 29, Odense, Denmark, 5000
Public contact	Afd. A, afd. A, anne_r_axelsen@hotmail.com
Scientific contact	Afd. A, afd. A, anne_r_axelsen@hotmail.com

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	10 April 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 April 2014
Global end of trial reached?	Yes
Global end of trial date	01 October 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Comparing the intraperitoneal concentrations og antibiotics (meronem, cefuroxim, tazocin, metronidazol og diflucan) with the patients clinic after operation for server peritonitis

Protection of trial subjects:

The project was approved by the Scientific Ethics Committee and all the patients could withdraw their commitment to participate if they did not want to participate.
The patients where given the same treatment as the ones WHO did not participate.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2013
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: 18
Worldwide total number of subjects	18
EEA total number of subjects	18

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	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients undergoing surgery acute surgery for secundary peritonitis due to bowel perforation og elective surgery for inflammatory bowel disease

Pre-assignment

Screening details:

The inclusion critieria were patients undergoing acute surgery for secondary peritonits due to bowel or gastric perforation.
15 patients were enrolled.
Patients undergoing elective surgery for inflammatory Bowel Disease. 11 patient were enrolled

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Peritonitis

Arm description:

Patients undergoing surgery because of peritonitis

Arm type	intervention (antibiotics and peritonits)
Investigational medicinal product name	cefuroxime
Investigational medicinal product code	SUB07433MIG
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

3 g peroperative

Investigational medicinal product name	cefuroxime
Investigational medicinal product code	SUB07433MIG
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1,5gx3 for 3 days

Investigational medicinal product name	Metronidazole
Investigational medicinal product code	SUB08922MIG
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

1,5g peroperative

Investigational medicinal product name	Metronidazole
Investigational medicinal product code	SUB08922MIG
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details: 500 mg x3 for 3 days

Arm title	Infalmmatory Bowel Disease
Arm description: Patients undergoing surgery for inflammatory bowel disease	
Arm type	Active comparator
Investigational medicinal product name	Metronidazole
Investigational medicinal product code	SUB08922MIG
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 500mgx3 for 3 days	
Investigational medicinal product name	Metronidazole
Investigational medicinal product code	SUB08922MIG
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous bolus use
Dosage and administration details: 1.5 g peroperative	
Investigational medicinal product name	cefuroxime
Investigational medicinal product code	SUB07433MIG
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 1,5 g x3 for 3 days	
Investigational medicinal product name	cefuroxime
Investigational medicinal product code	SUB07433MIG
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Bolus 3 g peroperative	

Number of subjects in period 1	Peritonitis	Infalmmatory Bowel Disease
Started	7	11
Completed	7	11

Baseline characteristics

Reporting groups	
Reporting group title	Peritonitis
Reporting group description:	
Patients undergoing surgery because of peritonitis	
Reporting group title	Infalmmatory Bowel Disease
Reporting group description:	
Patients undergoing surgery for inflammatory bowel disease	

Reporting group values	Peritonitis	Infalmmatory Bowel Disease	Total
Number of subjects	7	11	18
Age categorical			
Peritonitis group: mean age 62..9 years IBD grou: mean age: 46.6 years			
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)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
18-80	7	11	18
Age continuous			
Units: years			
median	62.5	46.6	
full range (min-max)	18 to 80	18 to 80	-
Gender categorical			
Units: Subjects			
Female	5	4	9
Male	2	7	9

End points

End points reporting groups

Reporting group title	Peritonitis
Reporting group description:	
Patients undergoing surgery because of peritonitis	
Reporting group title	Infalmmatory Bowel Disease
Reporting group description:	
Patients undergoing surgery for inflammatory bowel disease	
Subject analysis set title	Minimun Inhibitory Concentration of Metronidazole and Cefuroxi
Subject analysis set type	Full analysis
Subject analysis set description:	
At the end of surgery and before closure of the abdomen an intraperitoneal microdialysis catheter was placed in the intraperitoneal cavity in the most affected area. The following 3 days vials were collected every 8th hour. MIC values for Metronidazole at 4ug/ ml is considered efficient against anaerobe bacteria. MIC values for Ceruroxim at 4ug/ml is considered efficient against Gram -negativ bacteria.	

Primary: Metronidazol

End point title	Metronidazol[1]
End point description:	
End point type	Primary
End point timeframe:	
the 3 day sthey are followed	

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: There is not enough data to complete a statistic analysis for the endpoints.
The concentration of MTZ in the peritoneal cavity reached MIC in close to 100% of the time for both groups.
All of the samples collected in the peritonitis group and 99% of the samples collected in the IBD group concentration levels were well above MIC (4 µg/ml) for MTZ

End point values	Peritonitis	Infalmmatory Bowel Disease		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	11		
Units: ug/l				
number (not applicable)				
MIC above 4 ug/ ml	7	11		

Statistical analyses

No statistical analyses for this end point

Primary: Cefuroxime

End point title	Cefuroxime[2]
End point description:	

End point type	Primary

End point timeframe:

for the 3 days they were followed

Notes:

[2] - 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: There is not enough data to complete a statistic analysis for the endpoints.
In 88% of the time in the peritonitis group and 93% of the time in the IBD group concentrations reached MIC for CEF of 4 µg/ml. Concentrations reached MIC of 16 µg/ml 40 % of the time in the peritonitis group vs.only 23% of the time in the IBD group.All participants in the peritonitis group reached MIC (16 µg/ml) in at least one sample during the 3 days whereas 6 out of 11 participants from the IBD group reached MIC

End point values	Peritonitis	Infalmmatory Bowel Disease		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	11		
Units: ul/l				
number (not applicable)				
MIC above 4ul/l	6	10		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 27/7-2013 -22/7-2013	
Adverse event reporting additional description: 2 Serious adverse events was registered in 2 patients. None of them related the use of antibiotics	
Assessment type	Systematic

Dictionary used	
Dictionary name	ICD-10
Dictionary version	10

Reporting groups	
Reporting group title	Postoperative complications

Reporting group description: -

Serious adverse events	Postoperative complications		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Postoperative complications		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 18 (11.11%)		
Gastrointestinal disorders			
Postoperative wound complication	Additional description: 1 patient had a fascie rupture and had a new operation. 1 patient had a stomalhernia and had a new operation		
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		

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