Clinical trial results:
Perioperative complications in obese and non-obese patients: Prevention and treatment of wound infections and post-operative pain. Prospective, open, monocentric study to investigate perioperative tissue concentrations of antibiotics and regional analgesics using microdialysis in obese and non-obese patients.

Summary

EudraCT number	2012-004383-22
Trial protocol	DE
Global end of trial date	21 March 2017

Results information

Result version number	v1 (current)
This version publication date	05 July 2020
First version publication date	05 July 2020

Trial information

Trial identification

Sponsor protocol code	Mikrodialyse

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University of Leipzig
Sponsor organisation address	Ritterstr. 26, Leipzig, Germany,
Public contact	Clinical Trial Centre Leipzig, ZKS Leipzig - KKS, 0049 034116 254,
Scientific contact	Clinical Trial Centre Leipzig, ZKS Leipzig - KKS, 0049 034116 254,

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	13 September 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 March 2017
Global end of trial reached?	Yes
Global end of trial date	21 March 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The establishment of an optimized drug-dose-model based on tissue concentrations of antibiotics, analgesics and other substances in obese patients.

Protection of trial subjects:

The trial did not contain an intervention or subject the patients to additional risk.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 October 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	Germany: 125
Worldwide total number of subjects	125
EEA total number of subjects	125

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)	117
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Obese patients fulfilling the inclusion/exclusion criteria were all asked to participate. Matched non-obese patients were identified vial the electronic medical records and asked to participate.

Pre-assignment period milestones

Number of subjects started	125
Number of subjects completed	125

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Obese

Arm description:

Patients with BMI >= 35 kg/m^2

Arm type	Experimental
Investigational medicinal product name	Linezolid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

600 mg, single dose

Investigational medicinal product name	Meropenem
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

1000 mg, single dose

Investigational medicinal product name	paracetamol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

1000 mg, single use

Investigational medicinal product name	metamizol
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 1000 mg, single dose	
Investigational medicinal product name	tigecyclin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 100 mg, single dose	
Investigational medicinal product name	Cefazolin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 2000 mg, single dose	
Investigational medicinal product name	metronidazol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 500 mg, single dose	
Investigational medicinal product name	fosfomycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 8000 mg, single dose	
Investigational medicinal product name	piperacillin/tazobactam
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 4000 mg (piperacillin) / 500 mg (tazobactam), single dose	
Arm title	Non-obese
Arm description: Patients with 18.5 <= BMI < 30 kg/m^2	
Arm type	Experimental
Investigational medicinal product name	Linezolid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 600 mg, single dose	

Investigational medicinal product name	Meropenem
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 1000 mg, single dose	
Investigational medicinal product name	paracetamol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 1000 mg, single use	
Investigational medicinal product name	metamizol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 1000 mg, single dose	
Investigational medicinal product name	tigecyclin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 100 mg, single dose	
Investigational medicinal product name	Cefazolin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 2000 mg, single dose	
Investigational medicinal product name	metronidazol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 500 mg, single dose	
Investigational medicinal product name	fosfomycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 8000 mg, single dose	
Investigational medicinal product name	piperacillin/tazobactam
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

4000 mg (piperacillin) / 500 mg (tazobactam), single dose

Number of subjects in period 1	Obese	Non-obese
Started	65	60
Completed	65	60

Baseline characteristics

End points

End points reporting groups

Reporting group title	Obese
Reporting group description: Patients with BMI >= 35 kg/m^2	
Reporting group title	Non-obese
Reporting group description: Patients with 18.5 <= BMI < 30 kg/m^2	

Primary: Area under the time-concentration curve in ISF

End point title	Area under the time-concentration curve in ISF
End point description:	
End point type	Primary
End point timeframe: 0-8 hours after administration	

End point values	Obese	Non-obese		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13[1]	14[2]		
Units: mg/l*h				
log mean (standard deviation)	1052 (± 394)	1929 (± 725)		

Notes:

[1] - 15 obese patients received fosfomycin, 2 did not provide valid data in the ISF

[2] - 14 non-obese patients received fosfomycin, 1 did not provide valid data in the ISF

Statistical analyses

Statistical analysis title	Comparison of AUC between obese and non-obese

Statistical analysis description:

The linear-up/log-down trapezoidal rule was used for calculation of AUC. Extrapolation to infinity was based on the last predicted concentration. Comparison between the groups used a t-test with Welsh correction.

Comparison groups	Obese v Non-obese
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	877

Confidence interval	
level	95 %
sides	2-sided
lower limit	414
upper limit	1340

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Per Patient: From the administration of the study drug until 72 hours later	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	Obese
Reporting group description:	
Patients with BMI >= 35 kg/m^2	
Reporting group title	Non-obese
Reporting group description:	
Patients with 18.5 <= BMI < 30 kg/m^2	

Serious adverse events	Obese	Non-obese	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 65 (6.15%)	2 / 60 (3.33%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Investigations			
Transaminases increased			
subjects affected / exposed	1 / 65 (1.54%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Anastomotic leak			
subjects affected / exposed	1 / 65 (1.54%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 65 (0.00%)	1 / 60 (1.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 65 (1.54%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 65 (0.00%)	1 / 60 (1.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 65 (1.54%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 65 (1.54%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

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

Non-serious adverse events	Obese	Non-obese	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 65 (61.54%)	44 / 60 (73.33%)	
Investigations			
Mean arterial pressure decreased			
subjects affected / exposed	1 / 65 (1.54%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Transaminases increased			
subjects affected / exposed	1 / 65 (1.54%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
C-reactive protein increased			
subjects affected / exposed	0 / 65 (0.00%)	2 / 60 (3.33%)	
occurrences (all)	0	2	
Inflammatory marker increased			

subjects affected / exposed	0 / 65 (0.00%)	2 / 60 (3.33%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			
Anastomotic leak			
subjects affected / exposed	1 / 65 (1.54%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Procedural hypotension			
subjects affected / exposed	1 / 65 (1.54%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Hypotension			
subjects affected / exposed	37 / 65 (56.92%)	40 / 60 (66.67%)	
occurrences (all)	37	40	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 65 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Cardiac disorder			
subjects affected / exposed	0 / 65 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Sinus bradycardia			
subjects affected / exposed	0 / 65 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 65 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 65 (1.54%)	0 / 60 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Hypercapnia			
subjects affected / exposed	0 / 65 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Hypocapnia			

subjects affected / exposed	1 / 65 (1.54%)	1 / 60 (1.67%)	
occurrences (all)	1	1	
Pleural effusion			
subjects affected / exposed	0 / 65 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 65 (0.00%)	1 / 60 (1.67%)	
occurrences (all)	0	1	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 65 (0.00%)	2 / 60 (3.33%)	
occurrences (all)	0	2	
Pneumonia			
subjects affected / exposed	1 / 65 (1.54%)	1 / 60 (1.67%)	
occurrences (all)	1	1	
Septic shock			
subjects affected / exposed	1 / 65 (1.54%)	0 / 60 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 November 2014	New substances were included for investigation (Fosfomycin, Piperacilin/ Tazobactam) in 30 additional patients

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported