Clinical trial results:
Pharmacokinetics of small spectcrum beta-lactam antibiotics (Amoxicillin/Clavulanic Acid and Cefuroxime) on intensive care.

Summary

EudraCT number	2011-006107-35
Trial protocol	BE
Global end of trial date	21 January 2014

Results information

Result version number	v1 (current)
This version publication date	01 July 2021
First version publication date	01 July 2021
Summary attachment (see zip file)	Antimicrob Chemother 2013 (Population pharmacokinetics and dosing simulations of amoxicillin-clavulanic acid in critically ill.pdf) Antimicrob Chemother 2014 (Population pharmacokinetics and dosing simulations of cefuroxime.pdf)

Trial information

Trial identification

Sponsor protocol code	AGO/2011/012

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01581047
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ghent University Hospita
Sponsor organisation address	Corneel Heymanslaan 10, Ghent, Belgium, 9000
Public contact	Trial Bureau, Ghent University Hospital, 32 93320500, Trialbureau@uzgent.be
Scientific contact	Trial Bureau, Ghent University Hospital, 32 93320500, Trialbureau@uzgent.be

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	19 May 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 January 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the pharmacokinetics of Amoxicillin/Clavulanic acid and Cefuroxime antibiotics in patients hospitalized in the ntensive care.

Protection of trial subjects:

Ethics review and approval, informed consent, supportive care and routine monitoring.

Background therapy:

Adequate antibiotic therapy is very important in the treatment of infections. Spectrum and dosing of the antibiotics are two factors of the therapy: the spectrum of an antibiotic can't be changed, but the dosing scheme can be optimized. Recent studies proved that an optimized dosing scheme can improve the efficacy of the treatment. Broad-spectrum antibiotics have unpredictable pharmacokinetics in patients on intensive care units. This is due to the pathophysiologic processes in the patients on intensive care units: increased distribution volume, hypoproteinemia, organ failure… The investigators guess that similar processes influence the pharmacokinetics of small spectrum antibiotics (like amoxicillin and cefuroxime), but data lacks. Because the pharmacokinetics of broad spectrum antibiotics in seriously ill patients are better known, physicians are more confident prescribing these drugs. Studying the pharmacokinetic interactions of small spectrum antibiotics in seriously ill patients, can help to give the physician the confidence to prescribe these small-spectrum antibiotics.

Evidence for comparator:

In this study, the investigators will study the pharmacokinetics of amoxicillin/clavulanic acid and cefuroxime, in 60 patients on intensive care. 8 blood samples will be drawn via a central catheter on different moments after one administration of the antibiotic in the steady state phase. All the patients are prescribed the antibiotics for the treatment of their infections: they get the antibiotic therapy anyway. By measuring the concentrations on different moments after one administration, the investigators can reconstruct the pharmacokinetic function.

Actual start date of recruitment	15 March 2012
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	Belgium: 37
Worldwide total number of subjects	37
EEA total number of subjects	37

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)	22
From 65 to 84 years	14
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

59 patients were screened in the period from 15-Mar-2012 till 21-Jan-2014. 37 patients were included and completed the trial. End of trial notification was dated 21-Jan-2014 (last patient last visit) and submitted to EC and CA 02-Jun-2014

Pre-assignment

Screening details:

Male/Female >18 Years
Patients on the intensive care , who are treated with amoxicillin/clavulanic acid or cefuroxime for an infection
Exclusion Criteria:
informed consent lacking
haematocrit < 21 %
arterial catheter lacking

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	Amoxicillin/Clavulanic Acid

Arm description:

Patients in the intensive care unit, with an infection which will be treated with Amoxicillin/Clavulanic Acid.

Arm type	Experimental
Investigational medicinal product name	Amoxicillin/Clavulanic Acid
Investigational medicinal product code	J01CR02
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

1 g 4 x/day

Arm title	Cefuroxime

Arm description:

Patients in the intensive care unit, with an infection which will be treated with Cefuroxime.

Arm type	Experimental
Investigational medicinal product name	Cefuroxime
Investigational medicinal product code	J01D A06
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Solution for infusion

Dosage and administration details:

1,5 g 3 x/dag

Number of subjects in period 1	Amoxicillin/Clavulanic Acid	Cefuroxime
Started	16	21
Completed	16	21

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	37	37	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
median	65		
full range (min-max)	26 to 85	-	
Gender categorical Units: Subjects			
Female	9	9	
Male	28	28	

Subject analysis sets

Subject analysis set title	Area under the serum concentration versus time curve (AUC)
Subject analysis set type	Per protocol

Subject analysis set description:

Area under the serum concentration versus time curve (AUC) of Amoxicillin/Clavulanic acid. The concentrations of the antibiotic in serum samples, drawn at various times after one administration, will be measured. With these data, we can calculate the time above the minimal inhibitory concentration (MIC). [Time Frame: Before and at 15, 30, 45, 60, 120, 240 and 360 minutes after administration]

Subject analysis set title	Area under the serum concentration versus time curve (AUC)
Subject analysis set type	Per protocol

Subject analysis set description:

Area under the serum concentration versus time curve (AUC) of Cefuroxime. The concentrations of the antibiotic in serum samples, drawn at various times after one administration, will be measured. With these data, we can calculate the time above the minimal inhibitory concentration (MIC). [Time Frame: Before and at 15, 30, 45, 60, 120, 240 and 480 minutes after administration]

Reporting group values	Area under the serum concentration versus time curve (AUC)	Area under the serum concentration versus time curve (AUC)	
Number of subjects	16	21	

Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
median	62	69	
full range (min-max)	58 to 72	26 to 85	
Gender categorical Units: Subjects			
Female	3	6	
Male	13	15	

End points

End points reporting groups

Reporting group title	Amoxicillin/Clavulanic Acid
Reporting group description:	
Patients in the intensive care unit, with an infection which will be treated with Amoxicillin/Clavulanic Acid.	
Reporting group title	Cefuroxime
Reporting group description:	
Patients in the intensive care unit, with an infection which will be treated with Cefuroxime.	
Subject analysis set title	Area under the serum concentration versus time curve (AUC)
Subject analysis set type	Per protocol
Subject analysis set description:	
Area under the serum concentration versus time curve (AUC) of Amoxicillin/Clavulanic acid. The concentrations of the antibiotic in serum samples, drawn at various times after one administration, will be measured. With these data, we can calculate the time above the minimal inhibitory concentration (MIC). [Time Frame: Before and at 15, 30, 45, 60, 120, 240 and 360 minutes after administration]	
Subject analysis set title	Area under the serum concentration versus time curve (AUC)
Subject analysis set type	Per protocol
Subject analysis set description:	
Area under the serum concentration versus time curve (AUC) of Cefuroxime. The concentrations of the antibiotic in serum samples, drawn at various times after one administration, will be measured. With these data, we can calculate the time above the minimal inhibitory concentration (MIC). [Time Frame: Before and at 15, 30, 45, 60, 120, 240 and 480 minutes after administration]	

Primary: Area under the serum concentration versus time curve (AUC)

End point title	Area under the serum concentration versus time curve (AUC)[1]
End point description:	
The concentrations of the antibiotic in serum samples, drawn at various times after one administration, will be measured. With these data, we can calculate the time above the minimal inhibitory concentration (MIC).	
End point type	Primary
End point timeframe:	
Time Frame: Before and at 15, 30, 45, 60, 120, 240 and 360 minutes after administration Amoxicillin/Clavulanic acid Time Frame: Before and at 15, 30, 45, 60, 120, 240 and 480 minutes after administration Cefuroxime	
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: No statistical analysis available	

End point values	Amoxicillin/Clavulanic Acid	Cefuroxime		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	20		
Units: CL (L/h)				
number (not applicable)	10	9		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
Overall study	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	CTCAE
Dictionary version	5

Frequency threshold for reporting non-serious adverse events: 0.05 %

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: No non-serious adverse events were recorded for the participating patients

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