Clinical trial results:
Plasma and intrapulmonary population pharmacokinetics of piperacillin/tazobactam in critically ill patients

Summary

EudraCT number	2011-004470-28
Trial protocol	GB
Global end of trial date	31 July 2014

Results information

Result version number	v1 (current)
This version publication date	11 April 2020
First version publication date	11 April 2020
Summary attachment (see zip file)	Trial publication (clpt.2014.131.pdf)

Trial information

Trial identification

Sponsor protocol code	2011RM010

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Manchester University NHS Foundation Trust
Sponsor organisation address	Oxford Road, Manchester, United Kingdom,
Public contact	Lynne Webster, Manchester University NHS Foundation Trust, 0161 2764125, lynne.webster@mft.nhs.uk
Scientific contact	Lynne Webster, Manchester University NHS Foundation Trust, 0161 2764125, lynne.webster@mft.nhs.uk

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	31 July 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 July 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary object of this study is to investigate changes over time in blood and lung concentrations of piperacillin and tazobactam in critically ill patients.

Protection of trial subjects:

The initial approach will always be made by a member of the clinical team who will ask permission for the researcher to visit the patient. If permission is not granted anonymous details of the patients will be entered into the screening log. Any patient presenting with significant side effects from piperacillin/tazobactam will not have any further piperacillin/tazobactam administered. Patients may withdraw or be withdrawn by PerLR or ProfLR from the trial at any time.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 November 2011
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	United Kingdom: 17
Worldwide total number of subjects	17
EEA total number of subjects	17

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)	14
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

June 2012 to July 2013
Single UK centre

Pre-assignment

Screening details:

Intubated and mechanically ventilated patients who received piperacillin–tazobactam for suspected or documented pulmonary infection

Period 1

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

Blinding implementation details:

No blinding

Arms

Arm title	Pharmacokinetic

Arm description:

Plasma and intra-pulmonary PK

Arm type	Experimental
Investigational medicinal product name	piperacillin-tazobactam
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

piperacillin 4 grams
tazobactam 0.5 grams

Number of subjects in period 1	Pharmacokinetic
Started	17
Completed	17

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	17	17	
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	56.0		
full range (min-max)	31.4 to 80.8	-	
Gender categorical Units: Subjects			
Female	9	9	
Male	8	8	
Missing	0	0	
APACHE II score Units: none			
median	15		
full range (min-max)	8 to 24	-	

Subject analysis sets

Subject analysis set title	PK analysis
Subject analysis set type	Full analysis

Subject analysis set description:

PK analysis conducted for all trial participants

Reporting group values	PK analysis		
Number of subjects	17		
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 full range (min-max)			
Gender categorical Units: Subjects			
Female Male Missing	9 8		
APACHE II score Units: none median full range (min-max)			

End points

End points reporting groups

Reporting group title	Pharmacokinetic
Reporting group description:	
Plasma and intra-pulmonary PK	
Subject analysis set title	PK analysis
Subject analysis set type	Full analysis
Subject analysis set description:	
PK analysis conducted for all trial participants	

Primary: Lung penetration

End point title	Lung penetration[1]
End point description:	
End point type	Primary
End point timeframe:	
Day 5	

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: This is a pharmacokinetic study to investigate the plasma and lung concentration of piperacillin and tazobactam in critically ill patients. The outcome involves the development of a pharmacokinetic model. There is a single arm and no statistical comparisons are made.

End point values	PK analysis			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: percent				
median (full range (min-max))	49.3 (2.0 to 515.9)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 28 days	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	17
Reporting groups	
Reporting group title	Pharmacokinetic
Reporting group description: Plasma and intra-pulmonary PK	

Serious adverse events	Pharmacokinetic		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 17 (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	Pharmacokinetic		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 17 (5.88%)		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea at rest			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 July 2012	1. Study of first dose and/or steady-state pharmacokinetics 2. Addition of Cardiothoracic Intensive Care Unit (CICU) 3. Adverse event reporting and exempt events 4. CRF as source data 5. Changes to consent at end of study 6. Removal of three medical qualified individual who are not longer involved in the study 7. Additions of comment regarding timing of steady-state
05 December 2012	1. Patient numbers changed to a range of 25 to 40. 2. Raising of the upper age limit from 75 to 85 3. Removal of "suspected pulmonary infection" from enrolment criteria 4. Removal of requirement for 48 hours intubation and mechanical ventilation prior to commencing IMP 5. Translation research facility now Clinical Research Facility
22 July 2013	1. Patient numbers changed to a range of 20 to 40.

Notes:

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.

None.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/24926779