Clinical trial results:
Pharmacokinetics of Tigecycline in Patients Receiving Continuous Renal Replacement Therapy

Summary

EudraCT number	2012-005617-39
Trial protocol	DE
Global end of trial date	20 August 2018

Results information

Result version number	v1 (current)
This version publication date	21 January 2024
First version publication date	21 January 2024

Trial information

Trial identification

Sponsor protocol code	WS2030571

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University hospital Tuebingen
Sponsor organisation address	Hoppe-Seyler-Straße 3, Tuebingen, Germany, 72076
Public contact	Dept of Anestheseiology, University Hospital Tuebingen, 49 70712986900,
Scientific contact	Dept of Anestheseiology, University Hospital Tuebingen, 49 70712986900,

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	01 June 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 June 2018
Global end of trial reached?	Yes
Global end of trial date	20 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of the present study is to assess the pharmacokinetics of tigecycline in patients with acute renal failure receiving continuous veno-venous hemodialysis (CVVHD) with regional citrate anticoagulation or continuous veno-venous hemodiafiltration (CVVHDF) with conventional heparin-based anticoagulation. Particularly, the following parameters should be evaluated:

- Area under the concentration-time curve from 0 to 12 h (AUC0-12) in 8 patients each receiving CVVHD (citrate anticoagulation) or CVVHDF (heparin anticoagulation and predilution), respectively.
- Comparison of these AUC0-12 data with the values described in previous population kinetics.
- Total elimination half-life of tigecycline under CVVHD and CVVHD

All measurements will be taken under steady state conditions (on day 4 or later of intra-venous tigecycline treatment with an initial single dose of 100 mg iv and 50 mg iv b.i.d) after starting CVVHD or CVVHDF for at least 24 hours.

Protection of trial subjects:

Declaration of Helsinki
GCP

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 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: 11
Worldwide total number of subjects	11
EEA total number of subjects	11

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	5
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 11 patients were included in the study. the patients were treated with tigecycline due to cIAI (n=10) or infection caused by Acinetobacter baumanii (n=1)

Pre-assignment

Screening details:

Eleven patients mainly with intra-abdominal infections receiving either continuous veno-venous hemodialysis (CVVHD, n = 8) or hemodiafiltration (CVVHDF, n = 3) were enrolled, and plasma as well as effluent samples were collected according to a rich sampling schedule.

Period 1

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

Arms

Arm title	Tigecycline

Arm description:

Eleven patients mainly with intra-abdominal infections receiving either continuous veno-venous hemodialysis (CVVHD, n = 8) or hemodiafiltration (CVVHDF, n = 3) were enrolled, and plasma as well as effluent samples were collected according to a rich sampling schedule. Total and free tigecycline was determined by ultrafiltration and high-performance liquid chromatography (HPLC)-UV. Population pharmacokinetic modeling using NONMEM® 7.4 was used to determine the pharmacokinetic parameters as well as the clearance of CVVHD and CVVHDF. Pharmacokinetic/pharmacodynamic target attainment analyses were performed to explore the potential need for dose adjustments of tigecycline in CRRT

Arm type	Active comparator
Investigational medicinal product name	Tigecycline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for dispersion for injection
Routes of administration	Infusion

Dosage and administration details:

loading dose of 100 mg followed by 50mg twice daily

Number of subjects in period 1	Tigecycline
Started	11
Completed	11

Baseline characteristics

End points

End points reporting groups

Reporting group title	Tigecycline

Reporting group description:

Eleven patients mainly with intra-abdominal infections receiving either continuous veno-venous hemodialysis (CVVHD, n = 8) or hemodiafiltration (CVVHDF, n = 3) were enrolled, and plasma as well as effluent samples were collected according to a rich sampling schedule. Total and free tigecycline was determined by ultrafiltration and high-performance liquid chromatography (HPLC)-UV. Population pharmacokinetic modeling using NONMEM® 7.4 was used to determine the pharmacokinetic parameters as well as the clearance of CVVHD and CVVHDF. Pharmacokinetic/pharmacodynamic target attainment analyses were performed to explore the potential need for dose adjustments of tigecycline in CRRT

Primary: pharmacokinetic

End point title	pharmacokinetic[1]

End point description:

End point type	Primary

End point timeframe:

samples were collected before start of infusion (time 0) and after 1h; 1,25h; 1,5h; 1,75h; 2h; 4h;6h;8h; 12h

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: https://pubmed.ncbi.nlm.nih.gov/30558639/

End point values	Tigecycline			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: mg/dL				
number (not applicable)	11			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: read in abstract	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10

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

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: See the abstract, https://pubmed.ncbi.nlm.nih.gov/30558639/

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30558639