



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

Summary

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|--------------------------|----------------|
| 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 Anesthesiology, University Hospital Tuebingen, 49 70712986900, |
| Scientific contact | Dept of Anesthesiology, 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 CVVHDF

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 baumannii (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 | Tigecycline (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

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|-----------------|--------|
| 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>