



## Clinical trial results:

### Pharmacokinetic evaluation of fluoroquinolone antibiotics administered intravenously in intensive care patients with normal renal function and with renal hyperfiltration

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2010-019691-70   |
| Trial protocol           | BE               |
| Global end of trial date | 01 December 2013 |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 09 July 2021 |
| First version publication date | 09 July 2021 |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | AGO/2010/002 |
|-----------------------|--------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01109823 |
| WHO universal trial number (UTN)   | -           |

Notes:

##### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | University Ghent  |
| Sponsor organisation address | C. Heymanslaan 10 , Ghent, Belgium, 9000  |
| Public contact               | Universitair Ziekenhuis Gent   C. Heymanslaan 10   9000 Gent   Ingang 12, route 1280A<br>, Universitair Ziekenhuis Ghent, 0032 3326219,<br>Jan.DeWaele@UGent.be |
| Scientific contact           | Universitair Ziekenhuis Gent   C. Heymanslaan 10   9000 Gent   Ingang 12, route 1280A<br>, Universitair Ziekenhuis Ghent, 0032 3326219,<br>Jan.DeWaele@UGent.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                       | 01 December 2013 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 01 December 2013 |
| Was the trial ended prematurely?                     | Yes              |

Notes:

## General information about the trial

Main objective of the trial:

To describe the pharmacokinetics of fluoroquinolone antibiotics intravenously administered in intensive care patients with renal hyperfiltration, in comparison with patients with normal renal function.

Protection of trial subjects:

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

Background therapy:

At the intensive care unit (ICU) fluoroquinolone antibiotics, like levofloxacin, are frequently used for the treatment of infections. Efficient antibiotic therapy is very important in this setting, and more specifically, the spectrum of the antibiotic and the dosage are essential. It is almost impossible to change the spectrum of an antibiotic, but recent literature demonstrated that optimizing dosage improved the efficacy of therapy.

Adequate blood levels are required for a good efficacy of the antibiotic. Due to the fact that levofloxacin is almost completely eliminated renally, the blood levels for this antibiotic are strongly influenced by the renal function. This renal function can be normal in critically ill patients; however, hyperfiltration (due to an increased blood flow in the kidney) can also occur in this population. In a recent study from the department, up to 55 percent of patients receiving anti-infective treatment had some degree of hyperfiltration. The pharmacokinetics of intravenously administered levofloxacin has not yet been studied in patients with renal hyperfiltration. This study therefore aimed to evaluate the pharmacokinetics of levofloxacin in these patients, in comparison with critically ill patients with normal renal function.

Evidence for comparator:

In 20 patients of each group (patients with normal renal function and patients with renal hyperfiltration), the pharmacokinetics of levofloxacin will be studied. Blood sampling will be performed at 12 time points and for each sample 5ml blood will be taken. This study will be performed under steady state conditions (at least 32h after the first dose was given)

|   |             |
|---|-------------|
| Actual start date of recruitment                          | 19 May 2010 |
| 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: 14 |
| Worldwide total number of subjects   | 14          |
| EEA total number of subjects         | 14          |

Notes:

| <b>Subjects enrolled per age group</b>    |   |
|---|---|
| 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)                      | 7 |
| From 65 to 84 years                       | 7 |
| 85 years and over                         | 0 |

## Subject disposition

### Recruitment

Recruitment details:

14 patients were screened in the period from 19-May-2010 till 01-Dec-2013. 14 patients were included and completed the trial. End of trial notification was dated 01-Dec-2013 (last patient last visit) and submitted to EC and CA 31-Jun-2017.

### Pre-assignment

Screening details:

Patients hospitalized at the Department Intensive Care Unit who are being treated with Tavanic I.V. (500mg, twice daily) for an infection.

Exclusion criteria:

- Younger than 18 years
- No informed consent
- No arterial catheter
- Hematocrite  $\leq 21$
- Pregnancy and lactation
- Creatinine clearance  $< 80$  ml/min

### Pre-assignment period milestones

|                              |    |
|------------------------------|----|
| Number of subjects started   | 14 |
| Number of subjects completed | 14 |

### 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                                 |
| <b>Arm title</b>             | Patients with normal renal function |

Arm description:

Patients with normal renal function hospitalized at the Department Intensive Care Unit who are being treated with levofloxacin I.V. (500mg, twice daily) for an infection.

|  |                          |
|--|--------------------------|
| Arm type                               | Experimental             |
| Investigational medicinal product name | Tavanic                  |
| Investigational medicinal product code | BE192875                 |
| Other name                             |                          |
| Pharmaceutical forms                   | Suspension for injection |
| Routes of administration               | Infusion                 |

Dosage and administration details:

The commercially available Tavanic® I.V. 5mg/ml (100ml)

One milliliter of solution for infusion contains 5.1246 mg levofloxacin hemihydrate.

Dosing: 500 mg levofloxacin as a 1-hour infusion, twice daily

|                  |                               |
|------------------|-------------------------------|
| <b>Arm title</b> | Patients with hyperfiltration |
|------------------|-------------------------------|

Arm description:

Patients with hyperfiltration hospitalized at the Department Intensive Care Unit who are being treated with levofloxacin I.V. (500mg, twice daily) for an infection.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |                          |
|--|--------------------------|
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Dosing: 500 mg levofloxacin as a 1-hour infusion, twice daily

| <b>Number of subjects in period 1</b> | Patients with normal renal function | Patients with hyperfiltration |
|---------------------------------------|-------------------------------------|-------------------------------|
| Started                               | 8                                   | 6                             |
| Completed                             | 7                                   | 6                             |
| Not completed                         | 1                                   | 0                             |
| Protocol deviation                    | 1                                   | -                             |

## Baseline characteristics

## End points

### End points reporting groups

|  |                                     |
|--|-------------------------------------|
| Reporting group title  | Patients with normal renal function |
| Reporting group description:<br>Patients with normal renal function hospitalized at the Department Intensive Care Unit who are being treated with levofloxacin I.V. (500mg, twice daily) for an infection.   |                                     |
| Reporting group title  | Patients with hyperfiltration       |
| Reporting group description:<br>Patients with hyperfiltration hospitalized at the Department Intensive Care Unit who are being treated with levofloxacin I.V. (500mg, twice daily) for an infection.   |                                     |
| Subject analysis set title   | Creatinine Clearance                |
| Subject analysis set type  | Full analysis                       |
| Subject analysis set description:<br>A validated HPLC-method with fluorescence detection will be used for the analysis of the plasma samples at the Laboratory of Medical Biochemistry and Clinical Analysis, Faculty of Pharmaceutical Sciences, Ghent University |                                     |

### Primary: CL/TVCL

|   |                        |
|---|------------------------|
| End point title   | CL/TVCL <sup>[1]</sup> |
| End point description:<br>Blood samples will be taken before, during and after the administration of one dose of Tavanic. The present arterial catheter will be used for sampling.  |                        |
| End point type  | Primary                |
| End point timeframe:<br>Blood samples will be taken before (1), during (1) and after the administration (10) of one dose of Tavanic.  |                        |
| Notes:<br>[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.<br>Justification: No statistical analysis available |                        |

| End point values              | Patients with normal renal function | Patients with hyperfiltration |  |  |
|-------------------------------|-------------------------------------|-------------------------------|--|--|
| Subject group type            | Reporting group                     | Reporting group               |  |  |
| Number of subjects analysed   | 7                                   | 6                             |  |  |
| Units: ratio                  |                                     |                               |  |  |
| median (full range (min-max)) | 0.8 (0.6 to 1.3)                    | 1.3 (0.6 to 2.1)              |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

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### Adverse events information<sup>[1]</sup>

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Timeframe for reporting adverse events:

Overall study

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

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### Dictionary used

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|                 |       |
|-----------------|-------|
| Dictionary name | CTCAE |
|-----------------|-------|

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|                    |   |
|--------------------|---|
| Dictionary version | 5 |
|--------------------|---|

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

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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

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported