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 Gentl | C. Heymanslaan 10 | 9000 Gent | Ingang 12, route 1280A , Universitair Ziekenhuis Ghent, 0032 3326219, Jan.DeWaele@UGent.be
Scientific contact	Universitair Ziekenhuis Gentl | C. Heymanslaan 10 | 9000 Gent | Ingang 12, route 1280A , Universitair Ziekenhuis Ghent, 0032 3326219, 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:

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)	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 ≤ 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
Arm title	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 levofloxacinehemihydrate.
Dosing: 500 mg levofloxacin as a 1-hour infusion, twice daily

Arm title	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

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

Number of subjects in period 1	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:	
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:	
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:	
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[1]
End point description:	
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:	
Blood samples will be taken before (1), during (1) and after the administration (10) of one dose of Tavanic.	
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	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

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