Pharmacokinetics of fosfomycin: a study in patients with prolonged treatment for urinary tract infection

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Ethical review	Approved WMO
Status	Completed
Health condition type	Bacterial infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON46751

Source
ToetsingOnline

Brief title
Pharmacokinetics of fosfomycin in prolonged treatment

Condition

- Bacterial infectious disorders
- Urinary tract signs and symptoms

Synonym
bladder infection, Urinary tract infection

Research involving
Human

Sponsors and support

Primary sponsor: HagaZiekenhuis
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Fosfomycin, Pharmacokinetics, Urinary tract infection

Outcome measures

Primary outcome

PK profile of fosfomycin, which includes:

- Maximum concentration (Cmax)

- Time to reach Cmax (Tmax)

- Area under the curve of fosfomycin (AUC)

- Elimination half-life (T¬¬¬1/2)

- Bio availability

Secondary outcome

Urinary concentration of fosfomycin in 24 hours urinary sample

Number of recurrent UTIs

Side effects of fosfomycin

Study description

Background summary

Multi-drug resistant bacteria (MDRB) are an increasing worldwide problem as recognized by the WHO. In clinical practice this leads to limited oral antibiotic treatment options for patients with urinary tract infection (UTI). Fosfomycin is one of the older antibiotics discovered in 1969 and is a broad spectrum antibiotic that includes effectivity against uropathogenic Enterobacteriaceae. As the majority of Enterobacteriaceae are still susceptible to fosfomycin, it is a potential drug to treat UTIs with MDRB.

There are two different administration variants available of fosfomycin, fosfomycin disodium for intravenous use and fosfomycin tromethamine and calcium for oral use. In the Netherlands, fosfomycin tromethamine is only registered as single dose treatment for uncomplicated urinary tract infections. Fosfomycin

disodium is recently approved in the Netherlands for treatment of systemic infections.

Because of the potential of fosfomycin in treating MDRB, studies are conducted to investigate the pharmacokinetics (PK) and pharmacodynamics (PD) of fosfomycin, especially with intravenous administration. However, robust data upon the PK of fosfomycin is lacking (the oral formulation in particular), due to difficulties in measuring fosfomycin levels. This leaves uncertainty about its potency to treat systemic infections with MRDB. Recently new methods to measure fosfomycin, including liquid chromatography * mass spectrometry, became avalaible.

Study objective

The aim of this study is to evaluate and describe the PK of fosfomycin in individuals receiving oral treatment with multiple dosages of fosfomycin for recurrent and/or complicatedurinary tract infection. The results of this study will be used to validate a recently published simulation model upon the PK of fosfomycin. In addition, the clinical and microbiological effectiveness of prolonged treatment with fosfomycin will be evaluated in this study.

Study design

Prospective open label, cohort study

Study burden and risks

With this study we can obtain data on the pharmacokinetics of fosfomycin. In our opinion this study provides us with the most information on the pharmacokinetics of fosfomycin with the least possible burden for the participants. The burden for participants are a day of visit to our clinic for drawing blood during the day. In case participants choose to also receive an intravenous dose of fosfomycin will this drug be the normale dose equivalent to the oral dose they already take as prescribed. The burden for the intravenous dose is the same as for oral except the fact that they receive the medication intravenously. Allergic reactions are not expected because they already take the drug.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Treatment of UTI with oral fosfomycin 3 gram every 3rd day for 14 days or longer as indicated by attending physician
2. Adults aged *18 years

Exclusion criteria

1. Proven allergy for fosfomycin
2. Pregnancy or breastfeeding
3. Usage of metoclopramide
4. Renal insufficiency defined as an estimated GFR <30 ml/minute calculated by MDRD method
5. Active malignancy

Study design

Design

Study phase:	2
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	17-04-2019
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Fomicyt
Generic name:	Fosfomycine disodium
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Monuril
Generic name:	Fosfomycin trometamol
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	18-12-2018
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	20-05-2019

Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	11-09-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2018-000616-25-NL
CCMO	NL62889.098.18

Study results

Date completed:	01-01-2020
Results posted:	17-09-2020
Actual enrolment:	12

First publication
26-07-2020