PHARMACOKINETICS AND PHARMACODYNAMICS OF ERTAPENEM IN PATIENTS WITH TUBERCULOSIS

Published: 23-08-2012
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The main objective is to evaluate pharmacokinetics of a maximum standard dose (2000mg) of ertapenem in TB patients.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Mycobacterial infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON43693

Source
ToetsingOnline

Brief title
Pharmacokinetics of ertapenem in TB patients

Condition

- Mycobacterial infectious disorders

Synonym
TB, tuberculosis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: ertapenem, Pharmacokinetics, tuberculosis

Outcome measures

Primary outcome

The main objective of this prospective clinical trial is to characterise the

pharmacokinetics of ertapenem in tuberculosis patients.

Secondary outcome

To evaluate T>MIC and AUC/MIC ratio

To evaluate limited sampling strategies based on a pharmacokinetic population

model to predict ertapenem AUC0-24h

To evaluate alternative blood sampling

Study description

Background summary

Treatment of multidrug or extensively drug resistant tuberculosis (MDR/XDR-TB) is a real challenge as failure in response to treatment and serious side-effects are frequently encountered. New, more effective drugs with less side effects are therefore urgently needed to solve this problem. Although several new drugs against TB are in the pipeline, physicians currently have limited treatment options for treatment of complicated MDR/XDR-TB cases. Therefore, drugs developed and labeled for other infectious diseases are evaluated for TB.

Study objective

The main objective is to evaluate pharmacokinetics of a maximum standard dose (2000mg) of ertapenem in TB patients.

Study design

In a prospective clinical trial the pharmacokinetic parameters of ertapenem will be evaluated.

This study is an pharmacokinetic study to characterise the pharmacokinetics of a single dose of ertapenem. Plasma samples (2 ml) will be taken at t= 0, 0.5, 1, 2, 3, 4, 8, 12, 24 hr post dosage. Also dried blood spot and mitra tip samples will be taken by fingerprick at timepoints 1 (peak), 4 (middle) and 12 (through) hr post dosage. MIC values for ertapenem will be determined if the specimen is cultured. The drug susceptibility test of the available M. tuberculosis isolates are performed with the Middlebrook 7H10 agar dilution method. The area under the concentration-time curve up to 24 hours post dosage (AUC0-24h) for plasma will be determined with a standard one-compartmental pharmacokinetic method using KINFIT module of MW Pharm 3.60 (Mediware, The Netherlands). To assure safety of the patients that will participate in the study the patients will be screened for a history of hypersensitivity or allergic reactions for carbapenems or *-lactam antibiotics (like penicillins and cephalosporins). As ertapenem is excreted primarily (80%) by the kidneys, renal function will be examined. Laboratory tests (clinical chemistry, urinalysis; including electrolytes (K, Mg, Na, Ca), transaminase values, serum creatinine and bilirubin) will be evaluated the day before the study drug is administered as part of routine treatment. During and after administration of ertapenem a physician will be available in the presence of the patient.

Study burden and risks

The risks of the use of ertapenem for patients are low, so far side effects occur in a low percentage and if present are of minor importance.
The patients may experience some minor discomfort due to the PK-sampling performed using an indwelling iv catheter. There is no benefit for the individual patient. Future patients with drug resistent tuberculosis (MDR-tb: multidrug resistant tuberculosis and XDR-tb: extensively drug resistant tuberculosis) may benefit from this study.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713 GZ
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713 GZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Patients with tuberculosis, caused by Mycobacterium tuberculosis or by M. africanum
- Adults: from 18 until 64 years of age

Exclusion criteria

o There are few adverse effects of ertapenem. The only absolute contra-indication is a previous anaphylactic reaction to ertapenem or other *-lactam antibiotic.
o Renal Insufficiency, defined by a eGFR of 30ml/min
o Pregnancy
o HIV
o Body weight < 40 kg

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-01-2017
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Invanz
Generic name:	ertapenem
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	23-08-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-01-2013
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-10-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2012-003386-18-NL
ClinicalTrials.gov	NCT01730664
CCMO	NL41380.042.12

Study results

Date completed:	13-07-2017
Actual enrolment:	12