Pharmacokinetics of posaconazole given as a single intravenous dose to obese subjects: Dosing Obese with Noxafil® Under a Trial (DONUT).

Published: 08-08-2017
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Primary objective:To determine the effect of obesity (BMI > 35 kg/m2) on the pharmacokinetics of posaconazole and develop a dosing regimen for obese patients.
Secondary objective:• To describe the pharmacokinetics of the augmented dose of 400 in...

Ethical review	Approved WMO
Status	Completed
Health condition type	Fungal infectious disorders
Study type	Interventional

Summary

ID

NL-OMON45475

Source
ToetsingOnline

Brief title
DONUT

Condition

- Fungal infectious disorders

Synonym
Fungal infection / aspergillose

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum

Source(s) of monetary or material Support: Merck Sharp & Dohme (MSD),MSD

Intervention

Keyword: Obese, Pharmacokinetiek, Posaconazol

Outcome measures

Primary outcome

A farmacokinetic model using Non Linear Mixed Effects Modelling (NONMEM). Model

validation using bootstrap

method. The final model will be used for Monte Carlo simulation for

multiple-dosing regimens and higher dosages.

Secondary outcome

NA

Study description

Background summary

The prevalence of obesity in adults and children is rapidly increasing across the world. Pharmacokinetic studies are necessary to determine the appropriate dosing regimen, as obesity and morbid obesity are associated with many physiological changes affecting pharmacokinetics.

Although posaconazole is approved for the prophylaxes and treatment of invasive fungal infections, specific dosing guidelines for posaconazole in (morbidly) obese patients are not specified [1]. There is clear evidence indicating that heavier patients are receiving a sub-optimal dose if the current guidelines are used [2]. Specifically in the setting of augmented prevalence of species with intermediate susceptible to posaconazole, adequate dosing is needed at start of treatment.

Therefore it seems prudent to conduct a trial in a cohort of obese patients who receive posaconazole (300mg or 400mg) and define the pharmacokinetics. These will then be compared to the pharmacokinetics in a normal-weight group receiving 300mg posaconazole.

This study aims to provide clinical information that will be used to compare with non-obese patients and determine an optimal dosing strategy thru modeling and simulation.

Study objective

Primary objective:
To determine the effect of obesity (BMI > 35 kg/m2) on the pharmacokinetics of posaconazole and develop a dosing regimen for obese patients.
Secondary objective:
• To describe the pharmacokinetics of the augmented dose of 400 in obese patients;

Study design

Prospective, open-label, non-randomized, multi-center, single-dose dose escalation trial.

Intervention

Placing a venous cathether for blood sampling.
Single dose of posaconazol, adminstered according to SPC.
Sampling of a total of 60ml blood (including, PK curve, lab and hematology)

Study burden and risks

The risk-classification is assessed as negligible to the patient population receiving study drug at the current regimen. The drug is licensed on the Dutch market for the 300 dosages administered in this trial. Although the 400mg dose in obese is not a registered dose but we expect similar exposure in this group compared to non-obese, based on the study of Miceli et al 2015 [2]. The medication will be administered as a single dose only and posaconazole is considered to be safe. Therefore ,there is no attributable risk for the application of the study protocol to the subjects.

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. Subjects BMI:
o obese groups: subject must have a BMI >=35 kg/m2 at the time of inclusion,
o non-obese group: subject must have a BMI >=18.5 and < 25kg/m2 at the time of inclusion.;2. Subject is at least 18 years of age on the day of screening and not older than 65 years of age on the day of dosing;
3. If a woman, is neither pregnant nor able to become pregnant and is not nursing an infant;;4. Subject is able and willing to sign the Informed Consent before screening evaluations.
For the non-obese subjects the following additional inclusion criteria applies:
5. Subject is in good age-appropriate health condition as established by medical history, physical examination, electrocardiography, results of biochemistry, hematology and urinalysis testing within 6 weeks prior to study drug administration. Results of biochemistry, hematology and urinalysis testing should be within the laboratory's reference ranges (see Appendix A). If laboratory results are not within the reference ranges, the subject is included based on the investigator*s judgment that the observed deviations are not clinically relevant. This should be clearly recorded;

Exclusion criteria

1. Documented history of sensitivity to medicinal products or excipients similar to those found in the posaconazole preparation;

2. History of, or known abuse of drugs, alcohol or solvents (up until a maximum of three months before study drug administration);
3. Use of medication that has known relevant interaction with study drug as determined by the investigator up to 1 weeks prior to study drug administration.
4. Donation of blood or plasma to a blood bank or in a clinical study (except a screening visit) within 4 weeks prior to study drug administration;
5. Blood transfusion within 8 weeks prior to study drug administration;
6. Any other sound medical, psychiatric and/or social reason as determined by the investigator.

Study design

Design

Study phase:	4
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	16-11-2017
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Noxafil
Generic name:	Posaconazole
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	08-08-2017
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-10-2017
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2017-002916-14-NL
CCMO	NL59354.100.17

Study results

Date completed:	01-09-2018
Results posted:	26-11-2020
Actual enrolment:	26

First publication
06-12-2019