Micafungin (Mycamine®) pharmacokinetics given as a single intravenous dose to obese patients (MICADO).

Published: 25-04-2016
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Primary objective:To determine the effect of obesity (BMI > 40kg/m2) on the pharmacokinetics of micafungin and develop a dosing regimen for obese patients. Secondary objective:* To describe the pharmacokinetics of the approved dose of 200mg in...

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

Summary

ID

NL-OMON43057

Source
ToetsingOnline

Brief title
MICADO

Condition

- Fungal infectious disorders

Synonym
Fungal infection / Candidiasis

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum

Source(s) of monetary or material Support: Astellas Pharma,Astellas Pharma B.V.

Intervention

Keyword: Micafungin, Obese, Pharmacokinetics

Outcome measures

Primary outcome

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

Een farmacokinetisch model met de hulp van non-lineaire mixed effect modelleren zal de data beschrijven. Met behulp van bootstrap zullen we dit model valideren. 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. Several general (patho) physiological alterations associated with obesity have been described, but the specific impact of these alterations on drug metabolism and elimination and its consequences for drug dosing remains largely unknown.

Although micafugin is a well studied drug, little is known about the farmacokinetic profile in morbidly obese. In a study with 12 obese patients it was found that patients with an increased body mass had a significant lower exposure of micafungin. Using Monte Carlo simulations these researchers found that a higher dose is justified. However, a large portion of unexplained

variation in the calculated AUC was found and these investigators also neglected to include sever significant covariates like gender, in their models.

We intend to investigate the exposure of micafungin and compare 2 obese groups (1 group will receive 100mg and 1 group will receive 200mg) with a group of non-obese subjects receiving 100mg micafungin. We expect to see a linear relation between 100 mg and 200 mg micafungin en this allows us to extrapolate to higher dosages. Using Monte Carlo simulations we will simulate a multiple dosing regimen en investigate an optimal strategy in an obese population.

Study objective

Primary objective:
To determine the effect of obesity (BMI > 40kg/m2) on the pharmacokinetics of micafungin and develop a dosing regimen for obese patients.

Secondary objective:
* To describe the pharmacokinetics of the approved dose of 200mg in obese patients;
* To determine optimal dosing strategy (multiple dose) in obese patients trough Monte Carlo simulations based on the developed PK model.

Study design

Prospective, open-label, non-randomized, multi-center, single-dose dose escalation trial (using 100 mg and 200 mg micafungin).

Intervention

Placing a venous cathether for blood sampling.
Single dose of micafungin, adminstered according to SPC.

Sampling of a total of 75ml blood (including, PK curve, lab and hematology)

Study burden and risks

The safety of micafungin has been well established for repeated dosages (up to 896mg) and was well tolerated. In addition we expect a lower exposure in obese patient due to a (possible) increased volume of distribution and an increased clearance. With the combination of a single dose and an decreased exposure we don*t expect to find significant adverse events.

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 > 40 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 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 exclusion criteria apply:;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 4 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;;6. Subject has a normal blood pressure and pulse rate, determined by the investigator;;7. Subject does not smoke more than 10 cigarettes, 2 cigars, or 2 pipes per day for at least 3 months prior to study drug administration.

Exclusion criteria

1. Documented history of sensitivity to medicinal products or excipients similar to those found in the micafungin preparation;;2. History of, or known abuse of drugs, alcohol or solvents (up until a maximum of three months before study drug administration);;3. Inability to understand the nature of the trial and the procedures required;;4. Use of medication that has known interaction with study drug as determined by the investigator up to 4 weeks prior to study drug administration.;For the non-obese subjects the following additional exclusion criteria apply:;5. Evidence of organ dysfunction or any clinically significant deviation from normal in physical examination, vital signs or clinical laboratory determinations;;6. Clinical relevant liver enzymes (alkaline phosphatase, ALT, AST) abnormalities at screening;;7. 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;;8. Blood transfusion within 8 weeks prior to study drug administration;;9. Inability to be venipunctured and/or tolerate venous access;;10. Relevant history or presence of pulmonary disorders (especially COPD), cardiovascular disorders, neurological disorders (especially seizures and migraine), psychiatric disorders, gastro-intestinal disorders, renal disorders, hepatic disorders (Child-Pugh B or C), hormonal disorders (especially diabetes mellitus), coagulation disorders;;11. 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:	Recruitment stopped
Start date (anticipated):	30-01-2017

Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Mycamine
Generic name:	Micafungin
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	25-04-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-11-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2016-000611-32-NL

Register	ID
CCMO	NL56834.091.16