Anidulafungin pharmacokinetics given as a single intravenous dose to obese patients (ADOPT).

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The primary objective of this trial is as follows:• To determine the pharmacokinetics of anidulafungin administered to obese patients with a BMI >= 40 kg/m2. The secondary objective of this trial is as follows:• To simulate pharmacokinetics to...

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

Summary

ID

NL-OMON40398

Source
ToetsingOnline

Brief title
ADOPT

Condition

- Fungal infectious disorders

Synonym
Candidiasis / Fungal infections

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Pfizer,Pfizer inc.

Intervention

Keyword: Anidulafungin, Bariatric surgery, Obese

Outcome measures

Primary outcome

The primary outcome measurement will be the area under the plasma concentration-time curve (AUC) from time 0 to infinity (inf) post infusion (AUC0- inf) value of anidulafungin. This will be determined by use of the log-linear trapezoidal rule.

Peak plasma concentrations (Cmax) will be directly observed from the data.

The elimination rate constant will be determined by linear regression of the terminal points of the log-linear plasma concentration time curve. Clearance (CL) will be calculated as dose/AUC0- inf.

Secondary outcome

N/A

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.

Whilst anidulafungin has much to offer, little is known about its pharmacokinetic profile in the morbidly obese patient populations.

In a study of alternate dosing strategies of anidulafungin (200mg q48h) administered to 13 patients admitted to the hematology ward for an allogeneic haematopoietic stem cell transplant (HSCT) or intensive chemotherapy for acute

myeloid leukemia, we performed an interim simulation after the inclusion of 10 patients. Using the 2-compartement model with proportional error in Nonmem 7.2, we identified that weight as a covariate identifies 19% of the inter-individual variability in volume of distribution. Yet, in this cohort there were no morbidly obese patients and in the public domain, there are no specific data on patients in the upper weight bands (BMI >= 40).

Therefore it seems prudent to conduct a trial in a cohort of obese patients who receive anidulafungin and define the pharmacokinetics. These can then be compared to the pharmacokinetics in a normal-weight group. To build a valid pharmacokinetic model, obese patients with a BMI >= 40 undergoing bariatric surgery will receive a single dose of 100 mg anidulafungin (besides standard anti-bacterial prophylaxis). A 100 mg dose is chosen as the reference dose instead of the regular 200 mg loading dose. We assume a linear relation based on the results obtained in our previous experiments. Therefore a single dose of 100 mg will be sufficient to define the PK and make simulations for other dosing regimens. To minimize exposure to the study drug an initial trial with a single dose is preferred. At a later stage a multiple dose pharmacokinetic study may be performed to examine toxic effects of the drug.

Study objective

The primary objective of this trial is as follows:
• To determine the pharmacokinetics of anidulafungin administered to obese patients with a BMI >= 40 kg/m2.

The secondary objective of this trial is as follows:
• To simulate pharmacokinetics to provide a rationale for optimal dosing strategy in obese patients.

Study design

This is an open-label, non-randomised, single-centre, phase-IV, single-dose trial.

Day 1: A single dose of anidulafungin 100 mg administered according to SPC (pre-operative). Total body weight and body fat will be measured (using the Taninta, a body composition analyzer).

An attempt will be made to have a PK curve up until sampling point t=48 h, with an optional sample at t=72 hours. All infusion rates will be according to the SPC label information.

Patients are considered to have completed the study if at least the PK curve up until t=48 hours (with all samples resulting in an evaluable PK curve) has been completed.

Intervention

Inserting indwelling venous cannula/venflon for study.
A single dose of anidulafungin 100 mg administered according to SPC (pre-operative).
A PK curve will be determined after administration of a single, pre-operative dose of anidulafungin at t=0.5, 1, end of infusion, 2, 4, 6, 8, 10, 12, 24, and 48 and (if feasible) 72 hours post infusion (n=12 samples). Blood samples (4 mL) on PK days will be taken to obtain at least 2.0 mL of plasma.

Study burden and risks

This is a prospective non-randomized, phase IV clinical study, which will be performed in morbidly obese patients undergoing bariatric surgery. Due to surgery in the upper gastrointestinal region, this specific population is more prone to various kinds of infection including yeast infections. Thus, it seems justified to administer a prophylactic dose of anidulafungin against candida infections.
To determine the pharmacokinetics of anidulafungin in patients with very high body weight, this specific patient population is ideal for conducting this PK study. Because of the high frequency of endoscopic gastric bypass surgeries in our study center (300-500 per year), it is expected that enrollment in this study will be within a relative short period of time (expected time: 6 months) compared to other cohorts. Moreover, because only a single prophylactic dose of anidulafungin is administered, the attributable risk in this cohort of otherwise healthy persons seems relatively lower if compared to other patients possibly at risk of fungal infections (e.g. Intensive Care patients).

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. Patient has a BMI >=40 kg/m2 and is undergoing bariatric surgery.
2. Subject is at least 18 years of age on the day of screening.
3. If subject is female: neither pregnant, nor able to become pregnant and is not nursing an infant.
4. Subject or legal representatives are able and willing to sign the Informed Consent before screening evaluations.

Exclusion criteria

1. Documented history of sensitivity to medicinal products or excipients similar to those found in the anidulafungin preparation.
2. History of or current abuse of drugs, alcohol or solvents.
3. Inability to understand the nature of the trial and the procedures required.

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):	22-08-2014
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ecalta
Generic name:	Anidulafungin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	11-12-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-01-2014
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	EUCTR2013-004401-11-NL
CCMO	NL46907.091.13