Pharmacokinetics of anidulafungin (Ecalta ®) given intravenously as antifungal prophylaxis to recipients of an allogeneic haematopoietic stem cell transplant following myeloablative chemotherapy or patients receiving intensive chemotherapy for AML-MDS who are at high risk for developing invasive fungal disease

Published: 03-09-2010
Last updated: 04-05-2024

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

Summary

ID

NL-OMON34306

Source
ToetsingOnline

Brief title
Ecalta PK in HSCT and AML-MDS patients

Condition

- Fungal infectious disorders

Synonym
fungal infection, hematology patients

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: anidulafungin, echinocandins, hematology, pharmacokinetics

Outcome measures

Primary outcome

To determine the pharmacokinetics of anidulafungin given once in every 2 days (q48h) or once in every 3 days (q72h) to patients undergoing an allogeneic haematopoietic stem cell transplant following myeloablative chemotherapy or receiving intensive chemotherapy for AML-MDS

Secondary outcome

To determine whether adequate exposure is attained by patients undergoing an allogeneic haematopoietic stem cell transplant following myeloablative chemotherapy or receiving in-tensive chemotherapy for AML-MDS when using a q48 hour or a q72 hour dosing regimen

To determine whether infusion time can be advanced to 2 mg/min (both regimens)

To determine the safety of anidulafungin in this patient population

Study description

Background summary

Alternate dosing strategies of echinocandin drugs might provide a better efficacy in the treatment of fungal infections as compared to the current label dosing strategy. Before conducting a controlled efficacy trial of echinocandines in haematology patients, the pharmacokinetics of these alternate dosing strategies need to be tested before bringing this idea to practice in a large randomised trial.
Therefore we want to conduct a pharmacokinetic study with anidulafungin given every 48 hours or every 72 hours. This research can be performed best in a group of patients at high risk for de-veloping invasive fungal infections. Recipients of an allogeneic haematopoietic stem cell transplant (HSCT) or patients receiving intensive chemotherapyfor acute myeloid leukaemia (AML) or myelodysplastic syndrome (MDS) are at a relatively high risk of developing invasive fungal infections and are therefore candidates for primary prophylaxis. However, the options are limited to fluconazole which affords no protection against mould infections. Amphotericin B is not considered useful because of its desoxycholate formulation has too many side effects and its lipid formulations are too expensive nor have the broad-spectrum triazoles itraconazole and voriconazole proved their value in this setting. Anidulafungin belongs to the class of echinocandins, attacking specifically the ß 1-3 - D-glucan synthase of the cell wall. It has relatively few side effects and appears safe and effective for treating Aspergillus and Candida infections. Since these two genera account for 90% of fungal infections in HSCT recipients the drug would seem an ideal candidate for prophylaxis.

Importantly, nothing is known about the pharmacokinetics of alternate dosing regimens of anidulafungin in this patient population. Therefore a pharmacokinetic study of a homogenous cohort of patients is necessary to test the assumption, that adequate exposure is obtained with alternate dosing and that it is safe.

Study objective

The primary objective of this trial is as follows:
• To determine the pharmacokinetics of anidulafungin given once in every 2 days (q48h) or once in every 3 days (q72h) to patients undergoing an allogeneic haematopoietic stem cell transplant following myeloablative chemotherapy or receiving intensive chemotherapy for AML-MDS

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• To determine whether adequate exposure is attained by patients undergoing an allogeneic haematopoietic stem cell transplant following myeloablative chemotherapy or receiving in-tensive chemotherapy for AML-MDS when using a q48 hour or a q72 hour dosing regimen
• To determine whether infusion time can be advanced to 2 mg/min (both regimens)
• To determine the safety of anidulafungin in this patient population*

Study design

This is an open-label, single-period, single-centre, phase-II, multiple-dose trial in 20 patients receiving an allogeneic haematopoietic stem cell transplant following myeloablative chemother-apy or receiving intensive chemotherapy. After meeting the inclusion criteria and passing the exclusion criteria, the 20 subjects will be divided into 2 groups of 10 subjects.

Intervention

During this study, patients will receive, depending on the group, 5 or 8 infusions of study medication.
20 participants will be divided into two groups of 10 patients each. After 5 or 8 infusions of study drugs, there will be a follow-up period of 9 days.

Study burden and risks

First and most important of all, there is a benefit for the patient who will receive antifungal prophylaxis, like recommended in the ECIL guidelines as recently published by Maertens et al.

Anidulafungin, like other echinocandins, is well tolerated with less side effects than fluconazole.
Administration is limited to either 5 or 8 administrations of anidulafungin, depending on the treatment group.
All patients will be managed with a central venous catheter. This will be according to regular practice in the very near future and is thus regarded as no additional burden.

For specific, drug related, side effects, we refer to the study protocol.

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 receives an allogeneic haematopoietic stem cell transplant following myeloablative chemotherapy or receives first remission induction treatmentintensive chemotherapy for AML-MDS
2. Subject is at least 18 and not older than 65 years of age on the day of the first dosing
3. Has no signs or symptoms of invasive fungal disease
4. If a woman, is neither pregnant nor able to become pregnant and is not nursing an infant
5. Has an ALAT, ALAT, alkaline phosphatase < 5 times the upper limit of normal and a bilirubin level < 3 times the upper limit of normal
6. Is not known to be hypersensitive to echinocandin antifungal agents
7. Is managed with a quadruple central venous catheter (Arrow-Howes* Quad- Lumen 8.5,5 French; Arrow International)
8. Subject is 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. Known of Positive HIV test or hepatitis B or C test in history
3. History of QT time prolongation
4. History of or current abuse of drugs, alcohol or solvents
5. Inability to understand the nature of the trial and the procedures required
6. Has not previously participated in this trial

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-12-2010
Enrollment:	20
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:	03-09-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO Date:	19-11-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-03-2011
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	31-07-2012
Application type:	Amendment
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	EUCTR2010-018752-27-NL
CCMO	NL33431.091.10