Management of the combination of tacrolimus with azoles: effect of tacrolimus formulation on drug-drug interaction magnitude

Published: 15-04-2021
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To assess whether IR-Tac and ER-Tac exhibit a different magnitude of drug-drug interaction after co-administration with voriconazole

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Fungal infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON54925

Source
ToetsingOnline

Brief title
TAFI study

Condition

- Fungal infectious disorders

Synonym
Mycoses due to opportunistic pathogens; fungal infection in patients with immune deficiencies who would otherwise not be infected

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: Chiesi Farmaceutici

Intervention

Keyword: drug-drug interaction, fluconazole, tacrolimus, voriconazole

Outcome measures

Primary outcome

To assess whether IR-Tac and ER-Tac exhibit a different magnitude of drug-drug interaction after co-administration of voriconazole in lung, kidney, pancreas or heart transplant recipients.

Secondary outcome

- To describe all relevant PK parameters for IR-Tac and ER-Tac, their fold-change after azole initiation and the relevant azole PK parameters (which are: Cmax, dose-adjusted Cmax, Cmin, dose-adjusted Cmin, Tmax, t1/2).
- To describe whether pharmacogenetic genotype and inflammatory markers have an additional influence on tacrolimus and azole pharmacokinetics
- To investigate whether and with what extend the interaction diminishes over time after discontinuation of the interacting drug, as measured with Cmin/dose ratio
- To evaluate how tacrolimus dose should be adjusted at start and discontinuation of the voriconazole, and how many dose adjustments are needed for both formulations

Study description

Background summary

Tacrolimus treatment is delicate and increases risk of (invasive) fungal infections, which need azole treatment. Tacrolimus and azoles exhibit drug-drug interactions through CYP3A4/5 enzymes in gut and liver, increasing tacrolimus exposure. The choice of tacrolimus formulation for immediate release tacrolimus (IR-Tac) or extended release tacrolimus (ER-Tac) may influence the magnitude of the interaction with voriconazole, as shown in healthy volunteers.

Study objective

To assess whether IR-Tac and ER-Tac exhibit a different magnitude of drug-drug interaction after co-administration with voriconazole

Study design

Single center, observational open-label pharmacokinetic study with 4 parallel arms.

Study burden and risks

The burden exists of extra time and extra blood sampling. There are no changes in regular care. Because of the logistics, the start of the study may delay the azole initiation with one day. This may not lead to addional risk of the patient.
Benefits are increased therapeutic drug monitoring of the tacrolimus.

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

- Lung, kidney, pancreas or heart transplant recipient
- Age >18 years
- Stable use of tacrolimus formulations Prograf/generic tacrolimus/Envarsus
- Indication for antifungal therapy with voriconazole
- Written informed consent

Exclusion criteria

- Administration of mTOR inhibitors, cyclosporine or quadruple immunosuppression
- Concomitant use of drugs that have a pharmacokinetic interaction with tacrolimus
- Acute liver- or intestinal function impairment
- Pregnancy

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting

Start date (anticipated):	01-06-2021
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO Date:	15-04-2021
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-09-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-04-2024
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
CCMO	NL75111.042.20
Other	NTR: NL9080