Pharmacokinetics of fluconazole given orally or intravenously as prophylaxis or therapy to children and adolescents with invasive fungal infections

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This study has been transitioned to CTIS with ID 2024-518305-17-01 check the CTIS register for the current data. Primary objective:• To establish an improved fluconazole dosing regimen for paediatric and adolescent patients aged 2-18 years....

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

Summary

ID

NL-OMON51517

Source
ToetsingOnline

Brief title
FOCUS

Condition

- Fungal infectious disorders

Synonym
fungal infection

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum

Source(s) of monetary or material Support: Intern budget hoofdonderzoeker

Intervention

Keyword: fluconazole, invasive fungal disease, pediatrics, pharmacokinetics

Outcome measures

Primary outcome

Primary study parameters/endpoints:

Since the primary objective of this study is to establish an improved fluconazole dosing regimen for paediatric and adolescent patients aged 2-18 years, we aim to describe fluconazole pharmacokinetics in this patient population by means of population pharmacokinetic (pop-PK) modelling. The pharmacokinetic parameters of the developed pop-PK model are among others, clearance (CL), volume of distribution (Vd) and exposure described by the area under the concentration-time curve (AUC). With the developed model, simulations will be performed to estimate the percentage of patients reaching the predefined PK target of AUC above 400 mg*h/L. We subsequently aim to establish an improved fluconazole dosing regimen for the studied population which will consist of a loading dose and a maintenance dose that will result in adequate fluconazole exposure in these patients.

Secondary outcome

Other study parameters are factors that might influence the primary study parameters, the covariates. Since this is an observational study, potential covariates will only be explored. Covariates of interest are renal clearance and body weight. Another study parameter that will be explored is the oral bioavailability (F) of fluconazole, which is the percentage of the drug that is

systemically available after oral administration compared to the exposure after

intravenous administration.

Study description

Background summary

Fluconazole has been available since 1990, however a limited number of studies addressed the pharmacokinetics of fluconazole in children and adolescent patients. Solid PK data are lacking, despite there being expected variation due to physiological differences with adults likely resulting in significant clinical impact. Especially in the paediatric population where fluconazole is extensively used, including in patients who have moderate to severe renal function disturbances, this information is needed. Therefore, it seems prudent to conduct a study in a cohort of paediatric patients who receive fluconazole as prophylaxis or treatment.

Study objective

This study has been transitioned to CTIS with ID 2024-518305-17-01 check the CTIS register for the current data.

Primary objective:
• To establish an improved fluconazole dosing regimen for paediatric and adolescent patients aged 2-18 years.

Exploratory objectives:
• To explore the role of renal function on the clearance of fluconazole.
• To explore the bioavailability of oral fluconazole versus intravenous fluconazole in paediatric patients.

Study design

Prospective, observational pharmacokinetic study

Study burden and risks

Patients are treated according to standard care. No changes to fluconazole therapy are made for the purpose of this study. Patients are treated to the discretion of the treating physician. Therefore, no additional risks are expected compared to the standard risks expected with the use of fluconazole.

The collection of a minimal amount of extra blood (maximal amount of 12 ml for

all patients, and maximal amount of 18 ml for patients with an extra PK-day due to switching from oral to iv therapy) from an already indwelling arterial line or CVC before the start of the study will result in a minimal risk for of clotting or infection in the line. This risk is reduced to a minimum.

Because the goal of the study is to describe the PK of fluconazole in children with the aim of establishing an improved dosing regimen, it is of importance to collect data from a population that resembles the real-life population. This real-life population consists for a large part of patients admitted to the IC, which sometimes are unconscious and therefore incapacitated.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

1. Subject is treated with fluconazole for prophylaxis or treatment of an invasive fungal infection;
2. Subject is 2 - 18 years of age on the day of the first fluconazole dosing;
3. Subject is managed with a central venous catheter or arterial line from which blood can be easily obtained.

Exclusion criteria

1. Subject is managed by means of an extracorporeal clearance technique;
2. Subject has previously participated in this study.

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2022
Enrollment:	15
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Diflucan
Generic name:	Fluconazole
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	22-06-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-08-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-02-2023
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
EU-CTR	CTIS2024-518305-17-01
EudraCT	EUCTR2021-006868-24-NL
ClinicalTrials.gov	NCT05130723
CCMO	NL80071.091.22