Influence of flucloxacillin treatment on plasma concentration of CYP - and UGT-substrate drugs.

Published: 26-07-2024
Last updated: 08-02-2025

To investigate the influence of flucloxacillin treatment on CYP - and UGT substrate plasma concentration, to gain further understanding of potential clinically relevant drug-drug interactions with flucloxacillin.

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

Summary

ID

NL-OMON56926

Source
ToetsingOnline

Brief title
Flucloxacillin interaction study

Condition

- Bacterial infectious disorders

Synonym
infection, Staphylococcus Aureus infection

Research involving
Human

Sponsors and support

Primary sponsor: HagaZiekenhuis
Source(s) of monetary or material Support: Haga Ziekenhuis;Apotheek Haagse Ziekenhuizen;eventuele andere subsidieverstrekkers

Intervention

Keyword: CYP, Flucloxacillin, Interaction, UGT

Outcome measures

Primary outcome

Endpoint:

The main study endpoint is the difference in AUC of each substrate drug (diclofenac, metoprolol, oxycodone, pantoprazole and paracetamol) between day 1/2 and day 10 (+/- 3 days) of flucloxacillin treatment.

Parameter:

Total substrate drug plasma concentration at specific time points (see section 7.3: study procedures).

Secondary outcome

Endpoints:

- Difference in trough concentration of the substrate drugs between day 1/2 and day 10 (+/- 3 days) of flucloxacillin treatment.
- Difference in trough concentration of substrate drug metabolites (4-OH diclofenac, alfa-OH-metoprolol, oxymorfon, noroxycodone, pantoprazole-sulfone, paracetamol-glucuronide) between day 1 and day 10 of flucloxacillin treatment.
- Difference in AUC of substrate drug metabolites between day 1/2 and day 10 (+/- 3 days) of flucloxacillin treatment.
- Difference in the ratio of the AUC of the substrate drugs and their metabolites between day 1/2 and day 10 (+/- 3 days) of flucloxacillin treatment.

- Difference in the ratio of the trough concentration of the substrate drugs and their metabolites between day 1/2 and day 10 (+/- 3 days) of flucloxacillin treatment.
- Difference in substrate drug dose between day 1/2 and day 10 (+/- 3 days) of flucloxacillin treatment.

- Subgroup analysis of the above mentioned primary and secondary endpoints in groups of patients with specific CYP2C9 -, CYP2D6 -, CYP2C19 -, UGT1A1 - and UGT1A9 phenotypes (see supplementary material S2, table S2 for detailed information about the genotypes and corresponding phenotypes).

Parameters

CYP2C9 -, CYP2D6 -, CYP2C19 -, UGT1A1 - and UGT1A9 genotypes

Gender

Height

Indication flucloxacillin treatment

Substrate drug metabolite concentration in samples 1-3 at day 1/2 and day 10 (+/- 3 days) of flucloxacillin treatment (see section 7.3 *study procedures*).

Age

Weight

Co-morbidities

Co-medication (incl. dose)

Flucloxacillin dose

Substrate drug dose

Total and unbound serum flucloxacillin concentration

Unbound serum diclofenac and pantoprazole concentration

Plasma creatinine

Plasma ureum

eGFR (CKD-EPI)

Plasma CRP

Plasma albumin

Optional: plasma alpha-1-acid glycoprotein5

Plasma AST

Plasma ALT

Plasma ALP

Plasma GGT

Plasma Bilirubin

Plasma LD

Plasma triglyceride

Study description

Background summary

Several studies have reported altered pharmacokinetics - and pharmacodynamics of multiple drugs in patients that are concomitantly treated with flucloxacillin. As a result, these patients may suffer from suboptimal plasma concentrations. To date, the degree and mechanism of these potential drug-drug interactions with flucloxacillin are unknown. To better understand the clinical relevance of flucloxacillin*s inducing potential, a prospective drug-drug interaction (DDI) study is needed where the change in plasma concentration of common-used drugs that are CYP- UGT substrate drugs is investigated.

Study objective

To investigate the influence of flucloxacillin treatment on CYP - and UGT substrate plasma concentration, to gain further understanding of potential clinically relevant drug-drug interactions with flucloxacillin.

Study design

Prospective pharmacokinetics study

Study burden and risks

The risks of this study are limited to the risk of blood sampling. Besides knowledge about at least one CYP - and/or UGT genotype, patients will obtain no benefit from this study as blood samples will be collected and analysed at a later moment.

Contacts

Public
HagaZiekenhuis

Els Borst-Eilersplein 275
Den Haag 2545 AA
NL
Scientific
HagaZiekenhuis

Els Borst-Eilersplein 275
Den Haag 2545 AA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

- Aged >=18 years
- Treated with >=6 grams/24h flucloxacillin iv (or equivalent dose in case of renal impairment) for an intended duration of at least 10 days.
- Concomitant treatment with at least one of the following substrate drugs at the moment of patient selection: diclofenac, metoprolol, oxycodone extended release tablet, pantoprazole or paracetamol.
- Written informed consent.

Exclusion criteria

- Concomitant use of specific CYP-, UGT- and P-gp inducers and inhibitors (see table S1 in the supplementary material of the study protocol).
- Pregnancy
- Dialysis patients
- Dementia
- IC-admission

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):	20-11-2024
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	26-07-2024
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	27-01-2025
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL86382.058.24