Pharmacokinetic and pharmacodynamic target attainment of cefuroxime in adult patients on general wards with different degrees of renal function: a prospective observational cohort study

Published: 19-11-2021
Last updated: 17-01-2025

To investigate whether the PK-PD target of cefuroxime (50%T>MIC) is attained in the first 24 hours of treatment in adult patients on general wards with adequate and impaired renal function receiving regular and reduced doses of cefuroxime.

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

Summary

ID

NL-OMON52078

Source
ToetsingOnline

Brief title
Target attainment of cefuroxime

Condition

- Bacterial infectious disorders
- Renal disorders (excl nephropathies)

Synonym
Infections, Renal impairment

Research involving
Human

Sponsors and support

Primary sponsor: Noordwest Ziekenhuisgroep
Source(s) of monetary or material Support: Interne subsidie wetenschapsbureau Noordwest Ziekenhuisgroep.

Intervention

Keyword: Cefuroxime, General ward, Renal impairment, Target attainment

Outcome measures

Primary outcome

Percentage of patients attaining the cefuroxime PK-PD target of 50%T>MIC. This will be investigated for patients with adequate renal function receiving a regular cefuroxime dose and impaired renal function receiving a guideline recommended reduced dose.

Secondary outcome

To investigate whether the current dosing regimen of cefuroxime, recommended by the SWAB guideline and applied at Noordwest Ziekenhuisgroep for adult patients with various degrees of renal function on general wards, results in PK-PD target attainment of 50%T>MIC after 24-48 hours of therapy.

To investigate whether the current dosing regimen of cefuroxime, recommended by the SWAB guideline and applied at Noordwest Ziekenhuisgroep for adult patients with various degrees of renal function on general wards, results in PK-PD target attainment of 100%T>MIC during the first 24 hours of therapy.

To compare cefuroxime exposure at 24 hours and 24-48 hours after start of treatment between two different renal function groups in terms of AUC and Cmin.

(Group A: eGFR >=30ml/min/1.73m2 treated with standard doses of cefuroxime,

Group B: eGFR 29-10 ml/min/1.73m2 treated with reduced doses of cefuroxime).

If a large proportion, defined as a percentage of 25% or a minimum of 10

patients, does not attain the primary objective (50%T>MIC), we will explore

whether or not attaining this target is associated with patients* clinical

outcome, in terms of:

length of hospital stay (LOS), since start of cefuroxime treatment, admission

to and duration of ICU stay after start of cefuroxime treatment, 30 days

mortality after start of cefuroxime treatment, antibiotic switch to carbapenems

(meropenem, imipenem or ertapenem) within 30 days after start of treatment with

cefuroxime and days of fever after start of treatment with cefuroxime

Study description

Background summary

The pharmacodynamic target can therefore be best described as the percentage of the dosing interval that the serum concentration remains above the minimum inhibitory concentration (MIC) of the bacteria (T>MIC). Attaining the pharmacokinetic-pharmacodynamic (PK-PD) target of 50%TMIC is associated with antimicrobial therapeutic efficacy of cefuroxime.
Because cefuroxime is almost exclusively excreted through the kidneys, dose reduction of cefuroxime for patients with renal impairment (eGFR<30ml/min/1.73m2) is standard of care. No prospective evidence exists that currently guideline-recommended cefuroxime dosing regimens result in at least 50%T>MIC in adult patients on general wards, especially not in patients with renal impairment receiving a reduced dose of cefuroxime.

Study objective

To investigate whether the PK-PD target of cefuroxime (50%T>MIC) is attained in the first 24 hours of treatment in adult patients on general wards with

adequate and impaired renal function receiving regular and reduced doses of cefuroxime.

Study design

Observational, prospective single center cohort study

Study burden and risks

Risks imposed by participation are considered negligible. Three venapunctures, obtaining a maximum of 18 ml venous blood are not expected to cause AEs or SAEs. Participation itself does not bring any benefit as cefuroxime treatment is part of standard care, but the group related benefit could be significant. With the results of this study, current recommended cefuroxime dosing regimens are prospectively validated or an advice to reconsider current guidelines will be obtained.

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

Receiving cefuroxime therapy intravenous (iv) as part of standard care
Age >= 18 years
Admitted to a general ward of Noordwest Ziekenhuisgroep location Alkmaar
Informed consent is obtained

Exclusion criteria

Mentally incapacitated patients , i.e. a minor or legally incompetent adult
Renal replacement therapy during treatment with cefuroxime
Patients admitted to the intensive care unit (ICU)
Severely burned patients, defined as a burned surface >= 10%
Patients with cystic fibrosis
Informed consent is not obtained

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	12-01-2022
Enrollment:	45
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ceftin
Generic name:	Cefuroxime
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	19-11-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-01-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-02-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2021-006860-26-NL
CCMO	NL78342.029.21