Pharmacokinetics and pharmacodynamics of corticosteroids in paediatric patients with autoimmune and autoinflammatory diseases

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To assess the PK/PD relationship of prednisolone regarding toxicity as clinical outcome in paediatric patients with autoimmune or autoinflammatory diseases.

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

Summary

ID

NL-OMON51250

Source
ToetsingOnline

Brief title
CARPE DIEM-study

Condition

- Autoimmune disorders

Synonym
Autoimmune disease, Immune system disorders

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W,NVLE fonds

Intervention

Keyword: Autoimmune diseases, Pharmacodynamics, Pharmacokinetics, Population PK/PD

Outcome measures

Primary outcome

The primary objective of this study is to assess the association between exposure (PK) and prednisolone toxicity (PD) in paediatric patients with autoimmune or autoinflammatory diseases.

Secondary outcome

The secondary objectives of this study are:

- To assess information about occurrence and grade of toxicity in paediatric patients with autoimmune or autoinflammatory diseases

- To identify determinants and its associated variability for development of a population PK model

Study description

Background summary

The prevalence and incidence of autoimmune and autoinflammatory diseases have been increasing in the past few years. One of the biggest concerns in paediatric patients with systemic autoimmune and autoinflammatory diseases remains the high prevalence of toxicity due to the long-term treatment with systemic corticosteroids. The standard-of-care treatment of the majority of onset autoimmune disorders in paediatric patients is high dose systemic corticosteroids, like prednisolone. While systemic prednisolone have shown to be highly effective in the treatment of autoimmune and autoinflammatory diseases, the occurrence and severity of adverse events (AE) in patients treated with prednisolone is substantial. Toxicity is often severe but highly variable between patients and includes psychiatric and metabolic AE i.e., depression, personality and behavioural changes, sleep disturbances, excessive weight gain, hypertension, diabetes mellitus, growth retardation and cushingoid features. The association of pharmacokinetics (PK) of prednisolone and (level

of) toxicity has not yet been investigated in children. University Medical Center (UMC) Utrecht has the unique facility of Liquid Chromatog-raphy-Mass Spectrometry (LC-MS) which enables to measure PK in an extremely precise manner. We hypothesize that precise dosing of prednisolone, with optimal exposure in every individual patient, will decrease the incidence of AE in paediatric patients with autoimmune and autoinflammatory diseases. Therefore, we aim to investigate the PK in relation to toxicity (pharmacodynamics (PD)) of prednisolone in children with autoimmune and autoinflammatory diseases.

Study objective

To assess the PK/PD relationship of prednisolone regarding toxicity as clinical outcome in paediatric patients with autoimmune or autoinflammatory diseases.

Study design

This is a prospective observational study.

Study burden and risks

Patients will not have direct benefit from participating in this study. The data obtained in this study will be used to assess the population PK and PD of prednisolone in children with onset autoimmune and autoinflammatory diseases. Burden will be minimal since for PK 4 (additional to standard of care) blood samples of 2 ml will be drawn (limited sampling strategy). The volume of blood that is drawn for the study does not exceed the recommended maximum. The applied sampling strategy is minimally invasive, since all the patients that are included are present during a routine outpatient clinic visit and will get a peripheral cannula for the purpose of routine sampling and PK-sampling, therefore there will be no extra blood punctures. Patients will be asked to stay 4-5 hours for the PK-sampling and to fill in a questionnaire about experiencing mental health AE. Patients will be asked to fill in 3 questionnaires in total.

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. Patients treated by the WKZ with an autoimmune disease or autoinflammatory disease including IBD;
2. Patients both newly diagnosed and with refractory or relapsed disease with an indication for systemic prednisolon;
3. Planned to receive systemic prednisolone until at least one scheduled follow-up visit between the 2nd and 6th week;
4. Informed consent form (ICF) signed prior to participation in the study.

Exclusion criteria

None in advance. However, according to expert opninion of the principal investigator, any disease/circumstance that may influence the participation of the potential subject in a negative way, will be excluded from participation in this study.

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):	24-03-2022
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO Date:	02-12-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	02-04-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 24592
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
Other	https://onderzoekmetmensen.nl/nl/trial/51250
CCMO	NL76235.041.21