PHARMACOKINETICS OF APREPITANT, DEXAMETHASONE AND THEIR INTERACTION IN PATIENTS WITH CHEMOTHERAPY INDUCED NAUSEA AND VOMITING

Published: 21-01-2021
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Primary objective:The primary objective of this study is to define the differences in the interaction between oral dexamethasone and aprepitant and the interaction between iv dexamethasone and aprepitant.Secondary objective:The secondary objective...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Gastrointestinal signs and symptoms
Study type	Observational invasive

Summary

ID

NL-OMON52052

Source
ToetsingOnline

Brief title
PHARMACOKINETICS OF APREPITANT, DEXAMETHASONE AND THEIR INTERACTION

Condition

- Gastrointestinal signs and symptoms
- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Chemotherapy induced vomiting and nausea

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: Kika

Intervention

Keyword: Aprepitant, Dexamethasone, Pharmacokinetics

Outcome measures

Primary outcome

Pharmacokinetic parameters (i.e. clearance and volume of distribution) will be assessed using non-linear mixed effects modelling (NONMEM). Influence of relevant co-variates will be assessed by standard model building methods.

Secondary outcome

NA

Study description

Background summary

Prophylaxis on chemotherapy induced nausea and vomiting (CINV) is still a major problem in patients receiving highly emetogenic therapy, which has important consequences for quality of life during chemotherapy administration. Despite standardized prophylaxis patients receiving highly emetogenic therapy achieve a variable complete response rate (no vomiting and no rescue treatment) of 70-90%.6-8 One of the possible explanations could be that the interaction between oral dexamethasone and aprepitant is different from the interaction between iv dexamethasone and aprepitant. Aprepitant and dexamethasone show a mutual drug-drug interaction, which has been studied in adults. As a rule of thumb a 50% dose-reduction of dexamethasone is applied with treatment is combined with aprepitant. However, the difference in interaction between these dosage forms has not been studied yet. From pharmacological perspective, it can be expected that the interaction is stronger for orally given dexamethasone, since aprepitant can inhibit CYP3A4-enzymes in the GI-tract as well, which can alter the absorption of dexamethasone. With the results of this proposed study the differences in the interaction between oral dexamethasone and aprepitant

and the interaction between iv dexamethasone and aprepitant will be studied.

Study objective

Primary objective:
The primary objective of this study is to define the differences in the interaction between oral dexamethasone and aprepitant and the interaction between iv dexamethasone and aprepitant.

Secondary objective:
The secondary objective of this study is to describe the PK of aprepitant and dexamethasone together with the results of an ongoing study in pediatric patients (in the Princess Maxima Center for pediatric oncology), to describe the age dependent differences in PK of dexamethasone and aprepitant.

Study design

Prospective observational study

Study burden and risks

The patient has no direct benefit from participating in this study. The data obtained in this
study will be used to assess the population PK of aprepitant and dexamethasone, and their interaction in patients with cancer. Insight in the PK of these antiemetic drugs may result in improved dosing guidelines and/or individualized dosing regimens based on therapeutic drug monitoring, ultimately resulting better anti-emetic control. The only consequence of study participation is that additional blood samples will be withdrawn. The here applied sampling strategy is minimally invasive. The volume of blood that is withdrawn for the study does not exceed the recommended maximum; see 6.3.3 Blood sampling for pharmacokinetics. Sampling, using a flexible time scheme, will only be requested during regular hospital visits.

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

1. Planned to receive chemotherapy intravenously as regular treatment (standard of care);
2. Receiving dexamethasone with or without aprepitant as standard of care
3. Receiving the chemotherapy and anti-emetics during hospitalized treatment.
4. Age >=18;
5. Signed Informed consent form (ICF) prior to participation in the study;
6. Able and willing to undergo blood draw for the study (two different days, 6 times per day) and does not have any condition that makes participation disadvantageous.
7. For women: not pregnant
8. No use of strong CYP3A4 substrates or inhibitors within 7 days or CYP3A4 inducers within 30 days of treatment (appendix 2);

Exclusion criteria

See inclusion criteria

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):	23-06-2021
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	21-01-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	16-07-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-12-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-02-2025
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: 20649
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL75380.031.20