Pharmacokinetics of- and interaction between aprepitant and dexamethasone

Gepubliceerd: 30-09-2020 Laatst bijgewerkt: 15-05-2024

Interaction between oral dexamethasone and aprepitant is different than the interaction between iv dexamethasone and aprepitant.

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON20649

Bron
Nationaal Trial Register

Verkorte titel
TBA

Aandoening

Oncology

Ondersteuning

Primaire sponsor: Princess Maxima Center for pediatric oncology
Overige ondersteuning: NA

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale:
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.

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 population:
All patients treated in the NKI who will receive intravenously administered chemotherapy and dexamethasone with or without aprepitant as standard of care antiemetic agents.
Two different patient groups will be enrolled in the study: 1) Stratum A: dexamethasone only (n=10); 2) Stratum B: dexamethasone and aprepitant (n=10). In both strata, we include 10 patients. These patients will be sampled twice: one course where dexamethasone is given orally and another course where dexamethasone is given intravenously.

Main study parameters/ endpoints:
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.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:
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.

We will measure 6 blood samples of 4 ml each per patient on the first treatment day allowing population pharmacokinetic modelling. Drug-levels of aprepitant and dexamethasone will be measured in each sample using a validated LC-MS/MS method.

Sample times:
Sample 1 (4 ml): t = 0.5 hour after first administration of dexamethasone and aprepitant
Sample 2 (4 ml): t = 1-2 hours after first administration of dexamethasone and aprepitant
Sample 3 (4 ml): t = 4 hours after first administration of dexamethasone and aprepitant
Sample 4 (4 ml): t = 6 hours after first administration of dexamethasone and aprepitant
Sample 5 (4 ml): t = 12 hours after first administration of dexamethasone and aprepitant
Sample 6 (4 ml): t = 24 hours, just before the second administration of dexamethasone and aprepitant

Doel van het onderzoek

Interaction between oral dexamethasone and aprepitant is different than the interaction between iv dexamethasone and aprepitant.

Onderzoeksopzet

Start date
2020-Nov-01

Stop date
2021-Apr-01

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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;

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

See inclusion criteria

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Cross-over
Toewijzing:	Niet-gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-11-2020
Aantal proefpersonen:	20
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	30-09-2020
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 52052
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL8981
CCMO	NL75380.031.20
OMON	NL-OMON52052

Resultaten