Een farmacokinetiek studie van vincristine bij het gelijktijdig gebruik van anti-schimmelmedicijnen bij kinderen die behandeld worden voor acute lymfatische leukemie (ALL).

Gepubliceerd: 02-05-2011 Laatst bijgewerkt: 13-12-2022

The aim of this study is to provide evidence based dosing guidelines for vincristine in combination with azoles. Therefore we will study the pharmacokinetics of vincristine with and without concomitant azole therapy in pediatric patients with acute…

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

Samenvatting

ID

NL-OMON21303

Bron
NTR

Verkorte titel
VCR-Azolen trial

Aandoening

ALL, children, vincristine, azole therapy, pharmacokinetics

Ondersteuning

Primaire sponsor: AMC Medical Centre Amsterdam
Overige ondersteuning: Stichting Go4Children

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Pharmacokinetic data of vincristine and the active metabolite M1 in peripheral blood.

Toelichting onderzoek

Achtergrond van het onderzoek

Vincristine (VCR) is an important component in the treatment of acute lymphoblastic leukemia (ALL) in children. Proper dosing of vincristine is required to maximize disease control while avoiding toxicity. Peripheral and autonomic neuropathies are the most common side effects which can be life-threatening. Vincristine pharmacokinetics are time- and dose-dependent and considerable intra- and interpatient variation have previously been reported. Vincristine is predominantly metabolized in the liver by the cytochrome P450 (CYP) 3A family of enzymes and eliminated by an efflux pump, P-glycoprotein (P-gp). Inhibition of CYP3A4 by several drugs, such as azole antifungals, could increase vincristine exposure and potentiate the side effects caused by vincristine. Since in paediatric oncology patients azoles are increasingly being used for prophylaxis and treatment of fungal infections, guidelines for the co-administration of vincristine and azole therapy are necessary. The azoles used for antifungal prophylaxis are itraconazole, voriconazole and fluconazole. Several case reports suggest that co-administration of azoles and vincristine lead to increased toxicity, but this has not been studied specifically. It is not known whether these side-effects are related to a higher exposure of vincristine, and to what extent this exposure is increased. Information of the increase in plasma levels of vincristine during concomitant azole therapy may lead to evidence-based dosing guidelines for the effective and safe co-administration of these drugs, assuming that lower dose-levels of vincristine are needed.

Doel van het onderzoek

The aim of this study is to provide evidence based dosing guidelines for vincristine in combination with azoles. Therefore we will study the pharmacokinetics of vincristine with and without concomitant azole therapy in pediatric patients with acute lymphoblastic leukemia.

Onderzoeksopzet

Sampling will be performed around 2 VCR administrations during induction and intensification phase of the standard treatment of ALL (DCOG-ALL-10 protocol).

Toxicity will be assessed during 4 weeks following the last sampling.

Onderzoeksproduct en/of interventie

No intervention, observation of blood levels of vincristine.

Contactpersonen

Publiek

Meibergdreef 9, F8-207
N.K.A. Eijkelenburg, van
Amsterdam 1105 AZ
The Netherlands
+31 (0)20 5663050

Wetenschappelijk

Meibergdreef 9, F8-207
N.K.A. Eijkelenburg, van
Amsterdam 1105 AZ
The Netherlands
+31 (0)20 5663050

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Diagnosed with acute lymphoblastic leukemia;

2. Treatment according to DCOG ALL-10-protocol, induction phase and intensification phase for Medium Risk Group patients;

3. Vincristine 1.5 mg/m2 or 2 mg/m2 as iv bolus;

4. Age 1 - < 18 years;

5. Azole group: Azole therapy started at least 5 days before planned VCR treatment (7 days for fluconazole);

6. Written informed consent from patients or from parents or legal guardians for minor patients, according to local law and regulations.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Blood sampling not possible;

2. Patient refusal or parent refusal;

3. Not able to comply with scheduled follow-up;

4. Patients with underlying neurological disease such as Charcot-Marie-Tooth disease or Guillain-Barre syndrome;

5. Patients with underlying Down syndrome.

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Parallel
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-07-2011
Aantal proefpersonen:	40
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	02-05-2011
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL2739
NTR-old	NTR2877
Ander register	ABR : 36660
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A