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

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON21303

Source
NTR

Brief title
VCR-Azolen trial

Health condition

ALL, children, vincristine, azole therapy, pharmacokinetics

Sponsors and support

Primary sponsor: AMC Medical Centre Amsterdam
Source(s) of monetary or material Support: Stichting Go4Children

Intervention

Outcome measures

Primary outcome

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

Secondary outcome

1. Serum levels of azoles;

2. Vincristine toxicity will be assessed.

Study description

Background summary

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.

Study objective

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.

Study design

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.

Intervention

No intervention, observation of blood levels of vincristine.

Contacts

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Eligibility criteria

Inclusion criteria

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.

Exclusion criteria

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.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-07-2011
Enrollment:	40
Type:	Anticipated

Ethics review

Positive opinion

Date:	02-05-2011
Application type:	First submission

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
NTR-new	NL2739
NTR-old	NTR2877
Other	ABR : 36660
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A