Bortezomib for children with acute lymphoblastic leukemia (ALL) without other treatment options.

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This is a phase II study of bortEzomib in combination with other chemotherapy as re-induction therapy for childhood relapsed/refractory ALL.

Ethische beoordeling	Positief advies
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON23341

Bron
NTR

Verkorte titel
Bortezomib in relapsed ALL

Aandoening

acute lymphoblastic leukemia
relapse
refractory
children

Ondersteuning

Primaire sponsor: Erasmus MC, Rotterdam, Netherlands
Overige ondersteuning: Stcichting Kinderen Kankervrij and Janssen Pharmaceutica NV

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Determine the antileukemic activity of combination chemotherapy including bortezomib as reinduction therapy in childhood relapsed/refractory ALL.

Toelichting onderzoek

Achtergrond van het onderzoek

Multicenter, multinational, open label, comparative and randomised phase II study on the antileukemic activity of bortezomib with conventional combination chemotherapy in relapsed/refractory ALL in children and adolescents. The study will include one cohort of patients with relapsed/refractory ALL, with treatment guidelines for all patients for 3 weeks. Thereafter, bortezomib may be repeated in combination with the same conventional chemotherapy for patients with a good initial response to reinduction therapy, while treatment of all other patients will be left at the discretion of the patient, parents and the responsible clinician. Standard reinduction chemotherapy will consist of 2 weeks of dexamethasone plus vincristine given twice, plus intrathecal administration of methotrexate. In addition, all patients will be treated with one cycle of bortezomib, consisting of 4 doses in 2 weeks. However, they will be randomised 1:1 in 2 arms, group A getting 'early' bortezomib, starting at day 1 of therapy, and group B getting 'late' bortezomib, starting at day 8. Randomisation will be stratified for the number of circulating leukemic blasts at diagnosis. This design allows demonstrating an additional antileukemic effect of bortezomib when added to dexamethasone, after 1 week of therapy, measured by a reduction in ALL cells in peripheral blood and bone marrow. In addition, this design allows comparing the toxicity of limited (group A) and more extended (group B) overlap of administrations of bortezomib and vincristine. A total of 24 patients must be randomised and be fully evaluable in order to prove additional antileukemic effect of bortezomib when added to dexamethasone. Bortezomib will be available for further use in case of patients with a favourable early treatment response, i.e. bone marrow M1 or M2 (¡Ü15% blasts) 3 weeks after start of reinduction therapy, in combination with the same combination chemotherapy.

Doel van het onderzoek

This is a phase II study of bortEzomib in combination with other chemotherapy as re-induction therapy for childhood relapsed/refractory ALL.

Onderzoeksopzet

The major time point is the steroid response at day 8 and the response rate at day 22.

Onderzoeksproduct en/of interventie

The patients will be treated with bortezomib (1.3 mg/m2/dose twice weekly (days 1 and 4 of each week) for a total of 2 weeks. Group A will get bortezomib on days 1, 4, 8 and 11, while group B will get it on days 8, 11, 15 and 18. Bortezomib will be administered as i.v. push. In addition, patients will get standard reinduction chemotherapy consisting of dexamethasone and vincristine. Dexamethasone will be given from day 1 onwards for 2 weeks at 10 mg/m2/day in 3 doses, orally. In addition, patients will receive vincristine on days 8 and 15, at 1.5 mg/m2/dose, in a 60 minutes i.v. infusion.
Finally, intrathecal methotrexate will be given on days 1 and 22 with age-adjusted dosing.

Further therapy for good responders (bone marrow (BM) M1 or M2 on day 22) may consist of an additional cycle of bortezomib, but this decision is left to the discretion of the treating physician. A next cycle should start 11 days after the previous administration of bortezomib. Then, bortezomib must again be combined with 2 weeks of dexamethasone (same dose and schedule) and vincristine twice (same dose and schedule). Such cycles may be repeated if justified by efficacy and (lack of) toxicity, which again is left to the discretion of the treating physician.

Patients with a BM M3 on day 22 and/or those with progressive disease will go off study.

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Age between 6 months and 19 years;

2. Patients with a second or subsequent relapsed ALL;

3. Patients with first relapsed ALL after prior allogeneic stem cell transplantation in first complete remission;

4. Patients with refractory first relapse of ALL, as defined by the ALL relapse protocol these patients were enrolled in;

5. Circulating leukemic blasts of at least 100/ul peripheral blood (i.e. at least 0.1x109/l);

6. Patients must take adequate contraceptives when of childbearing potential;

7. Written informed consent.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Relapse not involving bone marrow;

2. Symptomatic CNS leukemia;

3. Active uncontrolled infection;

4. Performance status (Lansky or Karnofsky score) of 60% or less;

5. Life expectancy of less than 6 weeks;

6. Existing peripheral neuropathy NCI grade 2 or higher;

7. Presence of acute diffuse infiltrative and/or pericardial disease;

8. Existing clinical signs of cardiotoxicity;

9. Previous allogeneic stem cell transplantation within 100 days;

10. Pregnant or breastfeeding;

11. Other contra-indications for chemotherapy, including no recovery from previous treatment;

12. Previous exposure to bortezomib;

13. Other experimental or conventional antileukemic treatment within 7 days from start of bortezomib;

14. Allergy to boron and its metabolites;

15. Concomitant anti-leukemic therapy other than according to this protocol.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-09-2009
Aantal proefpersonen:	24
Type:	Werkelijke startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	25-06-2009
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	NL1771
NTR-old	NTR1881
Ander register	Innovative Therapies for Children with cancer : Study ITCC 021
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A