Efficacy and safety of recombinant asparaginase in infants (< 1 year) with previously untreated acute lymphoblastic leukemia, a phase II clinical trial

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON33689

Source
ToetsingOnline

Brief title
Efficacy and safety of r-asp in infants with previously untreated ALL

Condition

- Leukaemias

Synonym
acute lymphoblastic leukemia in infants

Research involving
Human

Sponsors and support

Primary sponsor: Medac

Source(s) of monetary or material Support: door de sponsor Medac

Intervention

Keyword: acute lymphoblastic leukemia, infants, recombinant asparaginase

Outcome measures

Primary outcome

To determine the number of patients with hypersensitivity reactions to rASNase.

Secondary outcome

- ASNase activity in serum just before rASNase infusions 1, 2, 4, and 6 during induction treatment,

- Concentrations of the amino acids asparagine (ASN), aspartic acid (ASP), glutamine (GLN), and glutamic acid (GLU) in serum at defined time points during induction treatment,

- Anti-ASNase antibodies in serum during repeated administration of rASNase,

- CR rate and MRD status after induction treatment phase A,

- Relapse rate, relapse-free survival and event-free survival at end of study,

- Number of patients who could complete their full course of rASNase treatment,

- Incidence and severity of adverse events.

Study description

Background summary

Acute Lymphoblastic Leukemia (ALL) is a clonal disease resulting from genetic mutations and transformations of a single early progenitor lymphoid cell. Uncontrolled expansion of leukemic blasts in the bone marrow leads to suppression of normal haematopoieses as well as disseminated infiltration of organs and release of blasts into the peripheral blood.

ALL is the most common malignancy in childhood accounting for 30% of all cancers and 80% of all leukemias in this age group. Four % of the patients are diagnosed int the first year of their life.

The treatment of of ALL depends on the use of intensive multiagent chemotherapy given for 2 years. In selected patients stem cell transplantation is used. Patients with ALL are usually treated within a study protocol. In the Netherlands, infants with newly diagnosed ALL are treated according to the international Interfant-06 protocol.

ASNase is an essential component of treatment of children with newly diagnosed ALL. Several recently published data have clearly demonstrated that this drug contributes to the total treatment outcome of children with ALL by at least 10-20%. It is not known if this percentage is the same in infants. But, allergy against asparaginase is an important clinical problem, as this may lead to early interruption of asparaginase therapy, resulting in lower cumulative asparaginase dose which worsens prognosis.

Recombinant Asparaginase (rASNase) has similar enzymatic , pharmacokinetic and pharmacodynamic properties as E-coli ASNase but is a much purer preparation. This new ASNase may therefore cause less hypersensitivity reactions than the currently approved drugs. In a recent pilot study at ErasmusMC Sophia it was shown that this drug has similar safety profile as regular native E-coli derived ASNase, and leads to similar asparagine depletion. Currently a larger national study is conducted to compare the efficacy and safety of rASNase and E-coli ASNase in a larger number of children (1-18 yr) with newly diagnosed ALL. The current study aims the efficacy and safety of recombinant ASNase in infants (children < 1 yr) with newly diagnosed ALL.

Study objective

This non-controlled multicentric phase II study is designed to assess the safety and to describe (in relation to children of higher age) the pharmacodynamics of recombinant ASNase for first-line treatment of infants (< 1 year of age at diagnosis) with de novo ALL treated according to the Interfant-06 protocol.

Study design

a non-controlled, multicentric phase II clinical trial to evaluate the efficacy and safety of repeated infusions with recombinant ASNase during induction treatment of infants with ALL.

Intervention

Treatment consists of recombinant asparaignase (6 doses) in induction therapy.

Study burden and risks

The risk and burden of participation are similar to a standard infant ALL therapy. A potential benefit may arise if we can prove that patients with recombinant asparaginase indeed have fewer allergic reactions to asparaginase, which may increase the cumulative asparaginase dose and leads to a better prognosis for these children. Potential risk factors are associated with the blood sampling - although this is always combined with regular blood sampling time points according to the Interfant-06 protocol. All patients will have a central venous line. New side-effects may occur, although based on chemical, PK and PD properties of the drug this will be unlikely.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

- Previously untreated T-lineage or precursor B-lineage ALL or biphenotypic leukaemia according to EGIL criteria
- Morphological verification of the diagnosis, confirmed with cytochemistry and immunophenotyping. In case a bone marrow aspiration results in a *dry tap*, a trephine biopsy is advised unless it is possible to confirm the diagnosis by peripheral blood examination.
- Age < 1 year at diagnosis
- Written informed consent of the parents or other legally authorised guardians of the patient
- Treatment according to protocol INTERFANT 06 (EudraCT Number 2005-004599-19)

Exclusion criteria

- Mature B-lineage ALL
-The presence of the t(9;22)(q34;q11) or bcr-abl fusion in the leukaemic cells (if these data are not known, the patient is eligible)
- Systemic use of corticosteroids less than 4 weeks before diagnosis. Patients who received corticosteroids by aerosol are eligible.
- Known allergy to any ASNase preparation
- Pre-existing known coagulopathy (e.g. haemophilia)
- Pre-existing pancreatitis
- Liver insufficiency (bilirubin > 50 µmol/L; SGOT/SGPT > 10 x the upper limit of normal).

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-10-2009

Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	rASNase
Generic name:	recombinant asparaginase

Ethics review

Approved WMO Date:	17-03-2009
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-08-2009
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
EudraCT	EUCTR2008-006300-27-NL

Register	ID
CCMO	NL25228.078.09