International Study for Treatment of Standard Risk Childhood Relapsed ALL

Published: 05-08-2014
Last updated: 15-05-2024

Primary objectives: - Overall: Improvement of event-free survival (EFS) probabilities in childhood relapsed ALL - Randomization 1: EFS of Arm A (ALL-REZ BFM 2002) versus B (ALLR3) in SR patients - Randomization 2: Influence of...

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

Summary

ID

NL-OMON27511

Source
NTR

Brief title
IntReALL SR 2010

Condition

- Leukaemias

Health condition

IntReALL, Relapsed ALL 2010

Research involving
Human

Sponsors and support

Primary sponsor: Charité Unversity Medizin Berlin
Source(s) of monetary or material Support: EU Project FP7
European Union

Intervention

Explanation

Outcome measures

Primary outcome

Primary parameters:

- Overall: Improvement of event-free survival (EFS) probabilities in childhood relapsed ALL

- Randomization 1: EFS of Arm A (ALL-REZ BFM 2002) versus B (ALLR3) in SR patients

- Randomization 2: Influence of epratuzumab on EFS in consolidation of SR patients

Secondary outcome

Secondary parameters:

- OS of Arm A (ALL-REZ BFM 2002) versus B (ALLR3) in SR patients

- Influence of epratuzumab on OS in consolidation of SR patients

- Rate of second complete remission (CR2) of Arm A versus Arm B

- Rate of SCT performed in Arm A versus Arm B

- Toxicity of randomized SR arms A versus B

- Toxicity of consolidation with versus without epratuzumab

- Improvement of MRD reduction during consolidation with versus without epratuzumab

- Rate of MRD negativity prior to SCT with Arm A vs. Arm B

- Rate of MRD negativity prior to SCT after consolidation with versus without epratuzumab

- Pharmacokinetic of epratuzumab in context with arm A and arm B

Study description

Background summary

Though survival of children with acute lymphoblastic leukemia (ALL) has considerably improved over the past few decades, relapsed ALL remains a leading cause of mortality in children with cancer. Given the rarity of the disease, prospective clinical trials need to be coordinated within an international cooperative group such as the International BFM Study Group (I-BFM-SG).

Within the group, over the last few years two different treatment protocols, ALL-REZ BFM 2002 and ALL R3 have been used by most study groups for treatment of relapsed ALL. Both trials have produced comparable results. The trials risk stratified patients based on duration of first

remission, immunophenotype, site of relapse and post induction minimal residual disease (MRD) levels to identify patients who should be transplanted. For non-HR or standard risk (SR) patients both ALL-REZ BFM 2002 and ALL R3 have achieved better results than previous trials.

Both protocols have however been primarily used in patients relapsing off different frontline protocols. Thus there is need for a prospective randomized controlled comparison across the study groups (randomization 1), before a uniform backbone for further trials can be developed.

[The 2nd randomisation with/without Epratuzumab closed 01-02-2019]

In SR patients, survival may be improved by modifying the consolidation therapy using targeted non-myelotoxic drugs. As ideal candidate, epratuzumab (humanised chimeric anti CD22 antibody) will be randomly tested in combination with conventional chemotherapy (randomization 2). CD22 is well expressed in all B-cell precursor ALL cells. Epratuzumab has been developed in combination phase I and II trials in childhood relapsed ALL and has shown a favourable toxicity profile and moderate antileukemic activity.

Study objective
Primary objectives:

- Overall: Improvement of event-free survival (EFS) probabilities in childhood relapsed ALL

- Randomization 1: EFS of Arm A (ALL-REZ BFM 2002) versus B (ALLR3) in SR patients

- Randomization 2: Influence of epratuzumab on EFS in consolidation of SR patients

Secondary objectives:

- OS of Arm A (ALL-REZ BFM 2002) versus B (ALLR3) in SR patients

- Influence of epratuzumab on OS in consolidation of SR patients

- Rate of second complete remission (CR2) of Arm A versus Arm B

- Rate of SCT performed in Arm A versus Arm B

- Toxicity of randomized SR arms A versus B

- Toxicity of consolidation with versus without epratuzumab

- Improvement of MRD reduction during consolidation with versus without epratuzumab

- Rate of MRD negativity prior to SCT with Arm A vs. Arm B

- Rate of MRD negativity prior to SCT after consolidation with versus without epratuzumab

- Pharmacokinetic of epratuzumab in context with arm A and arm B

Study design
The IntReALL SR 2010 trial is an inter-group, international multi-centre, treatment optimization trial. It contains the followings branches:

- SR induction/consolidation arm A (ALL-REZ BFM 2002, arm protocol II-IDA) versus B (UKALL-R3, arm MITOX): prospective, randomized, open label, phase III trial

[The 2nd randomisation with/without Epratuzumab closed 01-02-2019]

- SR consolidation +/- epratuzumab: prospective, randomized, open label, phase III trial

Intervention
Epratuzumab

Study burden and risks
None, other than the usual risk of the intensive, standard-chemotherapy that is needed in the treatment of children with relapsed ALL.

Contacts

Public
Prinses Máxima Centrum

Prof. dr. P.M. Hoogerbrugge
Heidelberglaan 25

3584 CS
Utrecht
Nederland

088 972 72 72
Scientific
Prinses Máxima Centrum

Prof. Dr. P.M. Hoogerbrugge
Heidelberglaan 25
3584 CS
Utrecht
Nederland

088 972 72 72

Eligibility criteria

Age
Babies and toddlers (28 days-23 months)
Babies and toddlers (28 days-23 months)
Children (2-11 years)
Children (2-11 years)
Adolescents (12-15 years)
Adolescents (12-15 years)
Adolescents (16-17 years)
Adolescents (16-17 years)

Inclusion criteria

• Morphologically confirmed diagnosis of 1st relapsed precursor B-cell or T-cell ALL

• Children less than 18 years of age at inclusion

• Meeting SR criteria: late isolated or late/early combined BCP BM relapse, any late/early isolated extramedullary relapse

• Patient enrolled in a participating centre

• Written informed consent

• Start of treatment falling into the study period

• No participation in other clinical trials 30 days prior to study enrolment that interfere with this protocol, except trials for primary ALL Inclusion criteria specific for the epratuzumab randomization

• Precursor B-cell immunophenotype. A specific CD22 expression level is not required

• M1 or M2 status of the bone marrow after induction

Exclusion criteria

• BCR-ABL / t(9;22) positive ALL

• Pregnancy or positive pregnancy test (urine sample positive for β-HCG > 10 U/l)

• Sexually active adolescents not willing to use highly effective contraceptive method (pearl index <1) until 2 years after end of antileukemic therapy

• Breast feeding

• Relapse post allogeneic stem-cell transplantation

• The whole protocol or essential parts are declined either by patient himself/herself or the respective legal guardian

• No consent is given for saving and propagation of pseudonymized medical data for study reasons

• Severe concomitant disease that does not allow treatment according to the protocol at the investigator’s discretion (e.g. malformation syndromes, cardiac malformations, metabolic disorders)

• Karnovsky / Lansky score < 50%

• Subjects unwilling or unable to comply with the study procedures

• Subjects who are legally detained in an official institute

Study design

Design

Study phase: 2

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-04-2017
Enrollment:	25
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Approved WMO

Date:	26-04-2016
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

ID: 50278
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL4579
NTR-old	NTR4720
EudraCT	2012-000793-30
CCMO	NL42228.078.14
OMON	NL-OMON50278

Study results