International Study for Treatment of Standard Risk Childhood Relapsed ALL 2010

Published: 14-10-2014
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 epratuzumab on EFS in...

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

Summary

ID

NL-OMON50278

Source
ToetsingOnline

Brief title
IntReALL SR 2010

Condition

- Leukaemias

Synonym
relapse cancer from the bone marrow, Relapse leukemia

Research involving
Human

Sponsors and support

Primary sponsor: Charité Unversity Medizin Berlin
Source(s) of monetary or material Support: Ministerie van OC&W,Charité - Universitätsmedizin Berlin / Germany,Immunomedix

Intervention

Keyword: ALL, Relapse

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

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

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
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- 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

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

- SR arm A (ALL-REZ BFM 2002 arm Prot II-IDA): Induction: SIA (F1, F2); Post induction: SCA1 and SCA2 ± epratuzumab (8x360mg/m²/ 1 hrs IV weekly, week 5-12), 5 courses SCA3-7 (R1/2/1/2/1), 24 months maintenance (6MP, MTX) with 6 x TIT / 4 weeks. Cranial irradiation 18Gy for CNS relapse.

- SR arm B (UK-R3, arm mitoxantrone): Induction: SIB (phase I); Post induction: SCB1 and SCB2 (R3-consolidation and intensification) ± epratuzumab (8x360mg/m²/ 1hrs IV weekly, week 6-13), 2 courses SCB3-4 (R3-interim maintenance 1 and 2), 88 weeks maintenance (6MP,
MTX, 4-weekly VCR/DEX/IT reinduction pulses). Cranial irradiation 18 Gy for CNS disease.

- SCT indications: Any donor Arm A with MRD >10-3 after SIA, arm B with > 10-4 after SIB.
Matched donor any early combined, isolated extramedullary relapse or patients

without MRD results. SCT is scheduled at week 16

Study burden and risks

None, otherthan the usual risk of the intensive, standard-chemotherapy that is needed in the treatment of children with relapsed ALL.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 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: (Randomisation closed 01-02-2019)
• 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)
•
• Subjects unwilling or unable to comply with the study procedures
• Subjects who are legally detained in an official institute

Study design

Design

Study phase: 3

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-02-2017
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Epratuzumab 10 mg/mlhLL2IgG solution 17.5 ml/vial Intravenous Administration
Generic name:	Epratuzumab

Ethics review

Approved WMO

Date:	14-10-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	26-04-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	01-03-2017
Application type:	Amendment

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-05-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-01-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-03-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-09-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-10-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-12-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-01-2021
Application type:	Amendment
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

ID: 27511
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2012-000793-30-NL
CCMO	NL42228.078.14
OMON	NL-OMON27511