International Study for Treatment of High Risk Childhood Relapsed ALL 2010 - A randomized Phase II Study Conducted by the Resistant Disease Committee of the International BFM Study Group.

Published: 06-01-2020
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This study has been transitioned to CTIS with ID 2024-513070-21-00 check the CTIS register for the current data. Primary objectives: Improvement of CR2 rates after induction with ALL R3 with bortezomib versus withoutbortezomib in HR relapsed ALL...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON49335

Source
ToetsingOnline

Brief title
IntReALL HR 2010

Condition

- Leukaemias

Synonym
Acute lymphoblastic leukemia; blood cancer

Research involving
Human

Sponsors and support

Primary sponsor: Charité University Medicine Berlin
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: chemotherapy, childhood, Leukemia, relapse

Outcome measures

Primary outcome

Randomized induction trial:

*Rates of CR2 with standard chemotherapy + Bortezomib (Arm B) compared with

standard chemotherapy (Arm A), quantified by cytology

Secondary outcome

*Three years EFS and OS

*Rate of patients reaching HSCT

*MRD rates post-induction and pre-HSCT

*Prognostic relevance of MRD pre HSCT, CR2 and MRD rates during consolidation

*Toxicity of randomized arms

Study description

Background summary

Although 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. Risk has been defined by the International BFM Study Group (I-BFM-SG) based on duration of first remission, immunophenotype of malignant clone, and site of relapse. Patients classified as high risk (HR) by these criteria have poor response rates to standard induction therapy, high rates of subsequent relapse and require an allogeneic hematopoetic stem cell transplantation (allo-HSCT) for consolidation of 2nd remission. Over the last decade members of the I-BFM-SG have investigated the

use of different combinations of conventional cytotoxic agents. Even with allo-HSCT, none of these approaches have improved outcome above 40%. Therefore, for HR patients there is a need to investigate the curative potential of new agents combined with systemic therapy. The proteasome inhibitor bortezomib has shown synergistic activity with acceptable toxicity when combined with corticosteroids, anthracyclines and alkylating agents in adult patients with cancer as well as with dexamethasone, doxorubicin, vincristine and PEG-asparaginase in children with refractory or relapsed ALL. In the I-BFM-SG IntReALL HR 2010 study, the potential of Bortezomib combined with a modified ALL R3 backbone as induction regimen for HR patients to improve CR2 rates will be investigated in a randomized phase II design. Induction is followed by conventional intensive consolidation.

Study objective

This study has been transitioned to CTIS with ID 2024-513070-21-00 check the CTIS register for the current data.

Primary objectives:
Improvement of CR2 rates after induction with ALL R3 with bortezomib versus without
bortezomib in HR relapsed ALL patients

Secondary objectives:
Improvement of Event Free Survival (EFS) and overall survival (OS) rates
Improvement of minimal residual disease (MRD) reduction after induction with versus without bortezomib
Improvement of MRD load prior to SCT
Increasing the proportion of HR patients reaching SCT
Prognostic relevance of MRD pre SCT
Improvement of CR2 and/or MRD rates during consolidation
Toxicity of induction with versus without bortezomib

Study design

The IntReALL HR 2010 trial is an inter-group, international multi-centre, treatment optimization trial. It contains the following treatment arms:
- induction: prospective, randomized, adaptive, open label phase II trial comparing arm A (modified ALL R3) versus arm B (modified ALL R3 + Bortezomib)
- post-induction single arm observational trial with intensive multidrug chemotherapy courses HC1 (modified AIEOP-BFM ALL 2009 HR1), HC2 (modified HR3). This is the current treatment in The Netherlands
- a third post-induction chemotherapy block HC3 (modified AIEOP-BFM ALL HR2) may optionally be given within the IntReALL HR 2010 trial or used as standard comparator for an investigational window trial.
- all patients in morphological CR2 will be subjected to allogeneic HSCT

- termination of the trial after completion of the 2nd or 3rd consolidation block before investigational window trial and/or allogeneic HSCT. Follow-up will be done until reaching secondary EFS / OS endpoints.
- patients with insufficient treatment response (MRD >= 10-3 after induction) may be allocated to individualized consolidation therapy based on individual biologic features of the leukemia, if such approaches are available

Intervention

Randomization during remission induction treatment between standard remission induction treatment (ALL-R3) with or without Bortezomib

Study burden and risks

Participation in the trial does not result in additional investigations as compared to the standard treatment of children with relapsed ALL.
The risk of increased toxicity by adding Bortezomib to the standard ALL-R3 remission induction is considered to be low and will be closesly monitored by the pharmacovigilance system established within the IntReALL group. Strict stopping rules apply. The induction randomization implies realistic potential to improve remission, EFS and at the end cure rates in this unfavourable patient group with an acceptable and closely monitored risk for increased toxicity.

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

Relapsed precursor B-cell or T-cell ALL
Children less than 18 years
High-risk relapse (in study-protocol defined criteria)
Written informed consent

Exclusion criteria

BCR/ABL positive ALL
Pregnancy/breast feeding
Relapse post stemcell transplant
No consent

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:	Recruiting
Start date (anticipated):	19-10-2020
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Velcade
Generic name:	Bortezomib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	06-01-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	10-04-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	22-12-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-02-2021
Application type:	Amendment
Review commission:	METC NedMec

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: 26156
Source: NTR
Title:

In other registers

Register	ID
EU-CTR	CTIS2024-513070-21-00
EudraCT	EUCTR2012-000810-12-NL
ClinicalTrials.gov	NCT03590171
CCMO	NL67089.041.19