

# 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.

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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...

<b>Ethical review</b>	Approved WMO
<b>Status</b>	Recruiting
<b>Health condition type</b>	Leukaemias
<b>Study type</b>	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 hematopoietic 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  $\geq 10^{-3}$  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 closely 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: Nationaal Trial Register  
Title:

**In other registers**

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