**Trial Description**

**Title**

International Study for Treatment of Standard Risk Childhood Relapsed ALL 2010 A Randomized Phase III Study Conducted by the Resistant Disease Committee of the International BFM Study Group

**Trial Acronym**

[--*-]

**URL of the trial**

[--*-]

**Brief Summary in Lay Language**

The main goal of this study is to improve the outcome of children and adolescents with standard risk first relapsed acute lymphoblastic leukemia. Furthermore, goal is to set up a large international study group platform allowing for optimization of standard treatment strategies and integration of new agents.

**Brief Summary in Scientific Language**

ALL is the most frequent malignancy in childhood and has favourable event-free and overall survival rates. About 15% of patients suffer relapse. At relapse prognosis is much inferior (about 50% survival) leukemic clones exhibit much more resistance to conventional chemotherapy. Patients with relapse require treatment intensification and different therapeutic strategies. At relapse, new targeted agents can provide the chance for better cure rates and need to be investigated in prospective controlled trials before they may be even eligible for frontline treatment strategies.

The IntReALL SR 2010 trial is designed to achieve 2 major aims: Establishment of the best available standard chemotherapy treatment. This is addressed with the randomization of the 2 best developed strategies for treatment of childhood relapsed ALL, the
German ALL-REZ BFM
2002 Protocol with the Protocol II IDA arm, and the British ALL-R3 protocol with the mitoxantrone arm. This randomization allows confirming the feasibility of both protocols in a large variety of different countries and study groups with different frontline therapy strategies. As result from this trial a common standard chemotherapy for childhood relapsed ALL will be developed which can serve as backbone for investigation of the most attractive targeted new agents.

The 2nd aim is the investigation of the efficacy and tolerability of the humanized CD22 directed monoclonal antibody Epratuzumab, manufactured and provided by the company Immunomedics, US. The drug will be randomly added to the respective consolidation chemotherapy, using EFS as primary endpoint. Epratuzumab has been developed in adult rheumatology indications and in B-cell malignancies. A phase I and early phase II combination trial in childhood relapse ALL has been conducted and published by the Children’s Oncology Group (COG), and results of an extended phase II trial have been recently presented at the ASH meeting (12/2011). The drug showed a very favourable safety profile as single drug and in combination with multidrug chemotherapy. Activity was moderate, the recent trial showed a significantly better elimination of minimal residual disease (MRD) in patients achieving a 2nd complete remission. This finding supports the strategy to use Epratuzumab in combination with consolidation chemotherapy after induction in patients having reduced the leukemia burden in the bone marrow to at least below 25%, most of them will be in 2nd complete remission. Epratuzumab will be given weekly at the established dose. Pharmacokinetics will be investigated in a reduced number of patients. The further treatment will be conventional intensive chemotherapy and maintenance therapy in patients with good MRD response after induction, or with allogeneic stem-cell transplantation (SCT) in those with insufficient MRD response. SCT will be considered as standard treatment element and will not lead to censoring of the patients of considered as endpoint. Epratuzumab is not licensed so far and the trial may add to the approval process in case.

Scientific advice for the trial has been requested at the FDA and the EMA. Both
institutions
  have responded supportively. Concerns and recommendations of FDA and EMA
have been addressed
  in the protocol and the corresponding statistical analysis plan.

  The IntReALL SR 2010 trial will be financed within the FP7 project IntReALL
2010 supported
by the European Commission. Within the project next to the SR trial a strategy
for HR
  patients will be addressed, the establishment of harmonized diagnostic
procedures, an
  international tumour bank and a comprehensive biologic/scientific programme
will be set up,
  a web-based GCP conform database will be established, a comprehensive
statistical strategy
  for both trials are established, and drug development in this indication will be
promoted
  and organized from side of the disease experts in cooperation with the
established academic
  structures ITCC (Innovative Therapies for Children with Cancer), the ENCCA
project (European
  Network for Cancer in Children and Adolescents) and SIOPe (International
Society for
  Pediatric Oncology Europe), the central authorities (EMA, FDA) and Industry.
Parent
organisation and former patients are integrated into and accompany the
process.

  Main aims of the IntReALL FP7 project are to establish a therapeutic platform
for children
  with relapsed ALL in Europe and beyond and to give them access to the most
promising new
  agents under academic control and free from commercial interests.

  Randomized evidence for efficacy and tolerability of new drugs are demanded
by competent
  authorities. These trials are conducted beyond the mostly palliative patient
group eligible
  for phase I/II trials in curative indications. Treatment protocols for with
curative
  indications need to be conducted in the best interests of the patients, ideally
with an
  academic sponsor. The design should be driven by medical and scientific
evidence and not by
  commercial interests as is the case in industry sponsored trials. This concept
was
  acknowledged by the European Commission selecting the project for funding
from many other
  powerful applications.

Do you plan to share individual participant data with other researchers?

[---]*

Description IPD sharing plan
Organizational Data

- DRKS-ID: DRKS00003910
- Date of Registration in DRKS: 2014/04/25
- Date of Registration in Partner Registry or other Primary Registry: 2013/02/18
- Investigator Sponsored/Initiated Trial (IST/IIT): yes
- Ethics Approval/Approval of the Ethics Committee: [---]*
- (leading) Ethics Committee Nr.: [---]*

Secondary IDs

- Primary Registry-ID: NCT01802814 (ClinicalTrials.gov)
- Sponsor-ID: IntReALL SR 2010 (University Hospital of Berlin)

Health condition or Problem studied

- Free text: Acute Lymphoblastic Leukemia (ALL)
- ICD10: C91.0 - Acute lymphoblastic leukaemia

Interventions/Observational Groups

- Arm 1: Drug: SR-A + Epratuzumab
- Arm 2: Drug: SR-B + Epratuzumab

Characteristics

- Study Type: Interventional
- Study Type Non-Interventional: [---]*
- Allocation: Randomized controlled trial
- Blinding: [---]*
- Who is blinded: [---]*
- Control: Active control (effective treatment of control group), Control group receives no treatment
- Purpose: Treatment
- Assignment: Parallel
- Phase: III
Study Type: **Interventional**

Allocation: **Randomized controlled trial**

Control: **Active control (effective treatment of control group), Control group receives no treatment**

Purpose: **Treatment**

Assignment: **Parallel**

Phase: **III**

Primary Outcome

- SR induction/consolidation ALL-REZ BFM 2002 versus UK-ALL-R3 (randomisation 1); time frame: at 4 years of arm A; SR induction/consolidation ALL-REZ BFM 2002 versus UK-ALL-R3 (randomisation 1): 10% pEFS superiority of arm B above a 65% pEFS at 4 years of arm A
- SR consolidation +/- epratuzumab (randomisation 2); time frame: at 4 years of standard arm; SR consolidation +/- epratuzumab (randomisation 2): 10% pEFS superiority of the arm with epratuzumab above an expected 74% pEFS at 4 years of the standard arm

Secondary Outcome

- SR induction/consolidation; time frame: year 7; SR induction/consolidation: comparison of OS, toxicity, rate of CR2, and rate of MRD between treatment groups
- SR consolidation +/- epratuzumab; time frame: year 7; SR consolidation +/- epratuzumab: comparison of OS, toxicity, MRD levels, rate of MRD and evaluation of pharmacokinetic parameters of Epratuzumab

Countries of recruitment

- AU Australia
- AT Austria
- BE Belgium
- CZ Czech Republic
- DK Denmark
- FI Finland
Locations of Recruitment

- Charité - Universitätsmedizin Berlin, Berlin

Recruitment

- Planned/Actual: [---]*
- (Anticipated or Actual) Date of First Enrollment: 2013/06/30
- Target Sample Size: 1242
- Monocenter/Multicenter trial: Multicenter trial
- National/International: International

Inclusion Criteria

- Gender: Both, male and female
- Minimum Age: no minimum age
- Maximum Age: 17 Years

Additional 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
  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
Addresses

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Sources of Monetary or Material Support

Status

■ Recruitment Status: Recruiting planned
■ Study Closing (LPLV): [---]*

Trial Publications, Results and other documents

■ Further trial documents Public Website of the FP7 Collaborative Project "IntReALL"
The parameters in ClinicalTrials.gov and DRKS are not identical. Therefore the data import from ClinicalTrials.gov required adjustments. For full details please see the DRKS FAQs.
- Translation on version: 361
- Last processed date by ClinicalTrials.gov: 2013/10/30
Please note:
There are additional attributes available concerning this trial. To open an extended view please click here.