Blinatumomab added to prephase and consolidation therapy in precursor B-acute lymphoblastic leukemia in adults. A phase II trial.

Published: 14-12-2017
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This study has been transitioned to CTIS with ID 2024-511050-44-00 check the CTIS register for the current data. Primary objective:-To assess the proportion of patients that achieve MRD negative response (by PCR/FCM) after the first consolidation...

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

Summary

ID

NL-OMON50553

Source
ToetsingOnline

Brief title
HOVON 146 ALL

Condition

- Leukaemias

Synonym
acute lymphoblastic leukemia, precursor B-acute lymphoblastic leukemia

Research involving
Human

Sponsors and support

Primary sponsor: HOVON

Source(s) of monetary or material Support: Amgen,Er is KWF subsidie aangevraagd,Shire

Intervention

Keyword: Acute lymphoblastic leukemia, Blinatumomab, Consolidation therapy, Prephase

Outcome measures

Primary outcome

Proportion of MRD negative response by PCR/FCM after the first blinatumomab consolidation course. MRD negative response is defined as MRD <10^-4.

Secondary outcome

-MRD level following induction chemotherapy

-MRD level after second blinatumomab consolidation

-Hematological response after induction, blinatumomab consolidation I and blinatumomab consolidation II

-Event free survival, i.e. time from registration until no CR on protocol (i.e. after prephase, induction, consolidation I, or blinatumomab after consolidation I), relapse or death from any cause, whichever comes first. EFS for patients without a CR on protocol will be set at 1 day; this also includes patients with a first CR only after start intensification 1. Patients still in first CR and alive are censored at the last day they were last known to be alive.

-Relapse free survival (hematologically; i.e. time from CR on protocol until relapse or death from any cause, whichever comes first)).. Patients still in first CR and alive are censored at the last day they were last known to be alive.

-Overall survival, measured from the time of registration until death from any

cause. Patients still alive or lost to follow up are censored at the date they

were last known to be alive.

-Adverse events

-RFS and OS from start allogeneic transplantation and from start maintenance

RFS, whichever is applicable

-T-cell and B-cell kinetics and assessment of predictive value

-Comparison of the results of molecular and flowcytometric MRD measurements at

the same timepoints (sidestudy)

Study description

Background summary

Blinatumomab is a new active bispecific monoclonal antibody for treatment of lymphoid malignancies, including ALL whose activity for remission induction needs to be explored in combination with standardized treatment in order to improve outcome of this disease which is still lethal in most adult patients. Ultimate proof of efficacy resides in an increase of reaching MRD negativity, prolongation of that response, and long-term survival. Since hematological response rate in adult ALL is high already and defining long-term survival in a large clinical trial takes many years, this trial aims to improve the strength of the MRD response as defined by achieving complete MRD negative response (ie, < 10^-4) after the first consolidation phase including blinatumomab. This MRD response will be assessed by RQ-PCR analysis of patient-specific Ig/TCR gene rearrangements. When MRD data are missing, MRD positivity will be assumed. Although younger (up to 40 years of age) patients are treated more intensively than older patients (older than 40 years of age), the investigational questions concerning blinatumomab can be examined in both subgroups as both younger and older patients receive the same type of chemotherapy courses with dose adjustments for chemotherapeutic agents only for patients above 60 years of age.

Study objective

This study has been transitioned to CTIS with ID 2024-511050-44-00 check the CTIS register

for the current data.

Primary objective:
-To assess the proportion of patients that achieve MRD negative response (by PCR/FCM) after the first consolidation phase including blinatumomab.

Secondary objectives:
-To assess the MRD level following induction chemotherapy
-To assess the MRD level after second blinatumomab consolidation
-To assess the hematological response after induction, blinatumomab consolidation I and blinatumomab consolidation II
-To evaluate event-free survival (EFS)
-To evaluate relapse-free survival (RFS)
-To evaluate overall survival (OS)
-To document safety and toxicity of blinatumomab
-To assess clinical outcome of patients receiving maintenance or allogeneic SCT
-To assess kinetics of T-cells and B-cells and their various subsets during treatment and assess their predictive value as regard to molecular response
-To compare the results of molecular and flowcytometric MRD measurements at the same timepoints.

Study design

A prospective, single arm, phase II study in which i.v. blinatumomab is added to standard prephase and subsequent therapy.

Intervention

After a 5-day steroid prephase patients will receive two weeks continuous infusion of blinatumomab. Then the first remission-induction course will be given after one week interruption. Subsequent therapy with 4 cycles of chemotherapy and two 4-week courses of blinatumomab will follow, and subsequently depending on risk group, eligibility and a suitable donor either allogeneic stem cell transplantation or 2 year maintenance treatment.

Study burden and risks

Longer period of treatment and a potential cytokine release syndrome (<5%) and neurological complications which are mostly completely reversible.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Primary CD19 positive precursor B-ALL (excluding mature B-cell ALL and B-lymphoblastic lymphoma, but including Philadelphia positive/BCR-ABL positive ALL) and CD19 positive mixed phenotype acute lymphoblastic leukemia (MPAL);
- Patients aged 18 to 70 years inclusive;
- WHO performance status 0-2;
- Negative pregnancy test at inclusion, if applicable;
- Written informed consent;
- Patient is capable of giving informed consent.

Exclusion criteria

- Mature B-cell leukemia/lymphoma, B-lymphoblastic lymphoma, isolated extramedullary disease;
- CML in blast crisis;
- Acute undifferentiated leukemia;
- Previous treatment with chemotherapy for precursor B-ALL (maximum 5 days of steroid treatment is allowed);

- Persistent liver enzyme disorders (ASAT/ALAT) >5xULN despite steroid pre-treatment;
- Severe cardiovascular disease (arrhythmias requiring chronic treatment, congestive heart failure or symptomatic ischemic heart disease);
- Severe pulmonary dysfunction (CTCAE grade III-IV);
- Severe neurological or psychiatric disease;
- Active, uncontrolled infection;
- Clinically overt central nervous system disease;
- Patients with a currently active second malignancy. Patients are not considered to have a currently active malignancy if they have completed therapy and are considered by their physician to be at < 30% risk of relapse within one year. However, patients with the following history/concurrent conditions are allowed:
o Basal or squamous cell carcinoma of the skin
o Carcinoma in situ of the cervix
o Carcinoma in situ of the breast
o Incidental histologic finding of prostate carcinoma

- Patient known to be HIV-positive;
- Pregnant or breast-feeding female patients;
- Unwilling or not capable to use effective means of birth control (all men, all premenopausal women under the age of 50 need contraception for two years after the last period, and women older than 50 years for at least one year);
- Current participation in another clinical trial;
- Any psychological, familial, sociological and geographical condition potentially hampering compliance with the study protocol and follow-up schedule.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Recruiting

Start date (anticipated):	04-06-2018
Enrollment:	65
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Blincyto
Generic name:	Blinatumomab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	14-12-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-03-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-09-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-10-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-08-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	20-10-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-07-2021
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

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2024-511050-44-00
EudraCT	EUCTR2017-000766-30-NL
ClinicalTrials.gov	NCT03541083
CCMO	NL61022.078.17