Phase 3 Randomized, Controlled Study of Blinatumomab Alternating With Low-intensity Chemotherapy Versus Standard of Care for Older Adults With Newly Diagnosed Philadelphia-negative B-cell Precursor Acute Lymphoblastic Leukemia With Safety Run-in (Golden Gate Study)

Published: 16-02-2023
Last updated: 14-09-2024

This study has been transitioned to CTIS with ID 2023-503640-14-00 check the CTIS register for the current data. Primary:• To compare event-free survival (EFS) of subjects receiving blinatumomab alternating with low-intensity chemotherapy to EFS of...

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON53323

Source
ToetsingOnline

Brief title
20190360 - Golden Gate Study

Condition

- Other condition
- Leukaemias

Synonym

Leukemia / Philadelphia negative (Ph[-]) B-cell precursor acute lymphoblastic leukaemia (ALL)

Health condition

recentelijk gediagnosticeerde Philadelphia-negatieve precursor B-cel acute lymfoblastische leukemie

Research involving
Human

Sponsors and support

Primary sponsor: Amgen
Source(s) of monetary or material Support: Amgen

Intervention

Keyword: Blinatumomab, Low-intensity chemotherapy, Newly diagnosed, Standard of care chemotherapy

Outcome measures

Primary outcome

• EFS: time from randomization until treatment failure, relapse, or death from

any cause, whichever is earlier. Subjects without an event will be censored at

their last evaluable disease assessment date.

• OS: time from randomization until death due to any cause. Subjects alive will

be censored at the date last known to be alive.

Secondary outcome

Key Secondary

• change from baseline to end of the initial disease assessment period in

fatigue score measured by Patient-Reported Outcomes Measurement Information

System (PROMIS) Fatigue - Short Form 7a

• change from baseline to end of the initial disease assessment period in pain

score measured by Brief Pain Inventory - Short Form (BPI-SF); Item 3: pain at

its worst in the last 24 hours

• change from baseline to end of the initial disease assessment period in global health status measured by the QLQ-C30 global health status quality of life scale

• change from baseline to end of the initial disease assessment period in physical function measured by the QLQ-C30 functional scale

• change from baseline to end of the initial disease assessment period in nausea/vomiting measured by the QLQ-C30 symptom scale

Secondary

• CR by the end of the initial disease assessment period

• MRD response < 10-4 by the end of the initial disease assessment period

• RFS: in subjects who achieve CR, the time from first achievement of this response until date of the first relapse including hematologic relapse, extramedullary relapse, or death due to any cause, whichever occurs first. Subjects without an event will be censored at their last evaluable disease assessment date.

• MRD RFS in subjects who achieve CR with MRD response, the time from first achievement of this response until date of the first relapse including molecular relapse, hematologic relapse, and/or extramedullary relapse, or death due to any cause, whichever occurs first. Molecular relapse will be defined 2 ways: MRD >= 10-3 and MRD >= 10-4. Subjects without an event will be censored at their last evaluable disease assessment date.

• MRD level over time

• treatment-emergent adverse events (TEAEs), serious TEAEs, treatment related adverse events, and adverse events of interest

• CD19 positive relapse and CD19 negative relapse identified by flow cytometry or immunocytochemistry for bone marrow (mandatory)

• CD19 positive relapse and CD19 negative relapse identified by flow cytometry or immunohistochemistry for cerebrospinal fluid (mandatory)

• CD19 positive relapse and CD19 negative relapse for extramedullary sites other than cerebrospinal fluid (optional - if data is available)

• lineage switch to acute myeloid leukemia (AML)

• localization of relapse by clinical assessment

• Mortality in CR

• autologous and allogeneic HSCT in continuous first CR*

• mortality in CR after autologous and allogeneic HSCT*

• mortality in CR after autologous and allogeneic HSCT*

• time to deterioration and time to improvements for fatigue score measured by PROMIS Fatigue - Short Form 7a

• time to deterioration and time to improvements for pain score measured by BPI-SF, Item 3: pain at its worst in the last 24 hours

• change from baseline in all other subscales of QLQ-C30

• time to deterioration and time to improvements for global health status, physical function, nausea/vomiting

* this does not refer to CR after a patient has received both allogeneic and

autologous HSCT

Study description

Background summary

This study is trying to establish an improved treatment for older adults with newly diagnosed Philadelphia negative Bcell Precursor Acute Lymphoblastic Leukaemia (bone marrow cell cancer). This study will determine if the experimental arm (the new therapy being tested) consisting of blinatumomab (a molecule that binds to leukaemia cells and cells of the immune system and thereby helps the immune system to destroy the leukaemia cells) combined with less intensive chemotherapy, compared with standard of care (SOC) - (GMALL Regimen and HyperCVAD Regimen), will prolong survival, duration of remission (when no leukaemia cells are present) while also decreasing toxicities that can occur with chemotherapy presently used in the SOC arm. Patients on the SOC arm will also be eligible to receive blinatumomab to treat their leukaemia if, during their treatment phase, the week 14 disease assessment shows any leukaemia cells. All patients in this study are randomised into 1 of 2 groups (the experimental therapy-blinatumomab with low intensity chemotherapy or SOC arm). Randomised means that patients are put into a group by chance. It is like flipping a coin. They will have a 50% chance of receiving blinatumomab with low intensity chemotherapy or the SOC - (GMALL Regimen or HyperCVAD). The treatment length is approximately 2.5 years. After treatment patients will continue to be monitored for evidence of leukaemia under this study for up to approximately 5 years.

Study objective

This study has been transitioned to CTIS with ID 2023-503640-14-00 check the CTIS register for the current data.

Primary:
• To compare event-free survival (EFS) of subjects receiving blinatumomab alternating with low-intensity chemotherapy to EFS of subjects receiving standard of care (SOC) chemotherapy
• To compare overall survival (OS) of blinatumomab alternating with low-intensity chemotherapy to SOC chemotherapy

Key Secondary
• To compare patient-reported fatigues with blinatumomab alternating with low-intensity chemotherapy to SOC chemotherapy
• To compare patient-reported pain with blinatumomab alternating with low-intensity chemotherapy to SOC chemotherapy

• To compare patient-reported outcomes (PROs) and global health status as measured by the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQC30)

Secondary
• To compare other efficacy endpoints of blinatumomab alternating with low-intensity chemotherapy to SOC chemotherapy
• To compare the safety of blinatumomab alternating with low-intensity chemotherapy to SOC chemotherapy
• To characterize relapses by cluster of differentiation (CD)19 expression, lineage switch and relapse localization in both treatment arms.
• To evaluate non-relapse mortality in both treatment arms
• To evaluate the proportion of allogeneic and autologous HSCT in continuous first CR after receiving blinatumomab alternating with low-intensity chemotherapy compared to SOC chemotherapy
• To evaluate non-relapse mortality following autologous and allogeneic HSCT in both treatment arms
• To evaluate relapse rate following autologous and allogeneic HSCT in both treatment arms
• To compare patient-reported fatigues with blinatumomab alternating with low-intensity chemotherapy to SOC chemotherapy
• To compare patient-reported pain with blinatumomab alternating with low-intensity chemotherapy to SOC chemotherapy
• To compare additional PROs and global health status as measured by the EORTC QLQ-C30

Study design

This is a phase 3, multicenter, randomised, controlled, open-label clinical study. Enrolled patients will be in this study for about 5 years. This includes: - An up to a 21-day screening period where subjects are also likely to receive pre-phase chemotherapy before enrolment into the study to decrease the amount of leukaemia cells present before starting the study. - A treatment period of about 2 years during which patients will be randomised to receive either blinatumomab with low intensity chemotherapy or standard of care (SOC) - GMALL Regimen or HyperCVAD.

Experimental arm: This will consist of a treatment period of two induction, consolidation and maintenance cycles. The induction cycles consist of 4 or 5 weeks of treatment depending on how fast the leukaemia responds to the therapy. Patients will be treated for a minimum of 2 and up to 21 cycles during this study and will be an inpatient for the first 9 days of their first induction cycle and either 9 or 3 days at the start of cycle 2. The remainder of the treatment will require hospitalization for 2 to 3 days when blinatumomab is initiated and other hospitalization requirements are per local standard of care (SOC) policies. For all patients receiving blinatumomab, he/she will be administered dexamethasone prior to initiation of treatment and each dose

escalation for the prevention of cytokine release syndrome resulting from blinatumomab treatment.

SOC Arm: The SOC- GMALL Regimen arm will consist of the following treatment period* two induction cycles, consolidation cycles, re-induction cycles, maintenance cycles up to 2.5 years of total therapy from enrollment. There will be approximately 2 times per cycle and the patient may receive blinatumomab on the SOC arm if there bone marrow after consolidation cycle 1 shows evidence of leukaemic cells. Each blinatumomab cycle will include 28 days of blinatumomab continuous intravenous infusion followed by a 7 day treatment free interval. The patient will be required to stay in hospital for the first 3 days at the start of the first cycle and for all subsequent cycles the patient will require a hospital stay for the first 2 days of the cycle.

SOC Arm: The SOC - HyperCVAD Regimen arm will consist of the following treatment period; two induction cycles, consolidation cycles, no re-induction cycles, maintenance cycles up to 30 months of total therapy from enrollment. There will be approximately 2 times per cycle and the patient may receive blinatumomab on the SOC arm if there bone marrow after consolidation cycle 1 shows evidence of leukaemic cells. Each blinatumomab cycle will include 28 days of blinatumomab continuous intravenous infusion followed by a 7 day treatment free interval. The patient will be required to stay in hospital for the first 3 days at the start of the first cycle and for all subsequent cycles the patient will require a hospital stay for the first 2 days of the cycle.

A safety follow up visit about 30 days after the last dose on treatment.

Long term follow up visits occurring every 3 months for up to 5 years from enrollment. This may be by telephone or by clinical visit to the hospital site. Along with study related activity procedures invasive and non-invasive.

Intervention

In the phase 3 portion of the study, after completing the screening period, eligible subjects will be randomized 1:1 between the experimental arm consisting of blinatumomab alternating with low-intensity chemotherapy versus SOC chemotherapy (GMALL regimen or hyperCVAD regimen).

Study burden and risks

There are no additional adverse effects, risks or hazards etc. associated with this study and its procedures that the researchers would not encounter during their day-to-day standard of care activities (see above for risk/ mitigation). Participants on active product may get better or see an improvement to their condition/ disease. However, there is no guarantee that participants will benefit from taking part in this study. If they do not personally benefit, the

knowledge gained from their participation in this study may provide useful information that will help individuals suffering from newly diagnosed Philadelphia negative B-cell Precursor Acute Lymphoblastic Leukemia.

Please refer to E2, E3, E6 en E9 of this ABR-form.

Contacts

Public
Amgen

Minervum 7061
Breda 4817 ZK
NL
Scientific
Amgen

Minervum 7061
Breda 4817 ZK
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• 101 Subject has provided informed consent prior to initiation of any study specific activities/procedures.
OR
Where permitted by local law, subject*s legally acceptable representative has provided informed consent prior to any study-specific

activities/procedures being initiated when the subject has any kind of condition that, in the opinion of the investigator, may compromise the ability of the subject to give written informed consent.

• 102 Age >= 55 years at the time of informed consent.
OR
Age 40 to < 55 years of age if at least 1 of the following comorbidities at the time of informed consent:
o history of grades 3 and 4 pancreatitis
o diabetes mellitus with end-organ damage
o severe liver disease such as cirrhosis stage 2 with portal hypertension or history of esophageal variceal bleeding and AST/ALT > 10 x ULN (liver cirrhosis must be confirmed by biopsy)
o body mass index (BMI) >= 40 combined with relevant comorbidities such as metabolic syndrome
o Any further combination of documented severe comorbidities that the investigator judges to be incompatible with administering an intensive pediatric-based, adult adapted standard chemotherapy regimen but still compatible with the suggested protocol for older subjects in both the experimental and the SOC arm. The subject history will be reviewed by the medical monitor during screening to determine enrollment acceptability based on a standard list with types of comorbidities allowed.

• 103 Subjects with newly diagnosed Philadelphia (Ph)-negative B-cell precursor acute lymphoblastic leukemia (ALL)

• 104 Eastern Cooperative Oncology Group (ECOG) performance status <= 2, higher ECOG score allowed if due to underlying leukemia.

• 105 All subjects must have adequate organ function as defined below:
o renal: estimated glomerular filtration rate based on MDRD calculation >= 50 mL/min/1.73 m2
o liver function: total bilirubin <= 2x upper limit of normal (ULN; unless Gilbert*s Disease or if liver involvement with leukemia); exception for subjects 40 to < 55 years of age if comorbidity is per inclusion 102: severe liver disease such as cirrhosis stage 2 with portal hypertension or history of esophageal variceal bleeding and AST/ALT > 10 x ULN (liver cirrhosis must be confirmed by biopsy)
o cardiac: left ventricular ejection fraction (LVEF) >= 50%

Exclusion criteria

Disease Related
• 201 Active CNS leukemia not resolved with IT chemotherapy during screening.

Other Medical Conditions
• 202 History of other malignancy within the past 3 years, with the following exceptions:
o Malignancy treated with curative intent and with no known active disease present for >= 3 years before enrollment and felt to be at low risk for recurrence by the treating physician.
o Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease.
o Adequately treated cervical carcinoma in situ without evidence of disease.
o Adequately treated breast ductal carcinoma in situ without evidence of disease.
o Prostatic intraepithelial neoplasia without evidence of prostate cancer.
o Adequately treated urothelial papillary noninvasive carcinoma or carcinoma in situ.
• 203 Clinically relevant CNS pathology requiring treatment (eg, unstable epilepsy).
• 204 Current autoimmune disease or history of autoimmune disease with potential CNS involvement
• 219 Known infection with human immunodeficiency virus (HIV)
• 220 Known infection with chronic or active hepatitis B (eg, hepatitis b surface [HBs] antigen reactive or quantifiable hepatitis b virus [HBV] viral load) or hepatitis C virus (HCV) (eg, HCV RNA [qualitative] is detected). Active hepatitis B and C based on the following results:
o Positive for hepatitis B surface antigen (HepBsAg) (indicative of chronic hepatitis B or recent acute hepatitis B)
o Negative HepBsAg and positive for hepatitis B core antibody: negative HBV DNA by PCR result is necessary to enroll.
o Positive Hepatitis C virus antibody (HepCAb): negative hepatitis C virus RNA by PCR result is necessary to enroll.
• 221 Subject with symptoms and/or clinical signs and/or radiographic and/or sonographic signs that indicate an acute or uncontrolled chronic infection.

Prior/Concomitant Therapy
• 207 Cancer chemotherapy for this newly diagnosed B cell ALL before the start of protocol-required therapy with the exception of IT chemotherapy or pre-phase chemotherapy. Radiation to a spot lesion such as chloroma or lytic lesion of bone or vertebrae for pain or vertebral stabilization is allowed.

Prior/Concurrent Clinical Study Experience
• 208 Currently receiving treatment in another investigational device or drug study, or less than 30 days since ending treatment on another investigational device or drug study(ies). Other investigational procedures while participating in this study are excluded.

Other Exclusions

• 209 Female subjects of childbearing potential unwilling to use protocol specified method of contraception (see Section 11.5) during treatment and for an additional 12 months after the last dose of protocol-required therapy.
• 210 Female subjects who are breastfeeding or who plan to breastfeed while on study through 12 months after the last dose of protocol-required therapy.
• 211 Female subjects planning to become pregnant while on study through 12 months after the last dose of protocol-required therapy.
• 212 Female subjects of childbearing potential with a positive pregnancy test assessed at screening and/or assessed within 3 days prior to starting study chemotherapy treatment on day 1 by a highly sensitive urine or serum pregnancy test.
• 223 Male subjects with a female partner of childbearing potential who are unwilling to practice sexual abstinence (refrain from heterosexual intercourse) or use contraception during treatment and for an additional 6 months after the last dose of protocol-required therapy. Refer to Section 11.5 for additional contraceptive information.
• 224 Male subjects with a pregnant partner who are unwilling to practice abstinence or use a condom during treatment and for an additional 6 months after the last dose of protocol-required therapy.
• 225 Male subjects unwilling to abstain from donating sperm during treatment and for an additional 6 months after the last dose of protocol-required therapy.
• 216 Subject has known sensitivity to any of the products or components to be administered during dosing.
• 222 Subject likely to not be available to complete all protocol-required study visits or procedures, and/or to comply with all required study procedures (eg, Clinical Outcome Assessments) to the best of the subject and investigator*s knowledge; exception - availability of a patient-reported outcome (PRO) in the subject*s preferred/native language is not prohibitive to enrollment for eligible subjects.
• 218 History or evidence of any other clinically significant disorder, condition or disease (with the exception of those outlined above) that, in the opinion of the investigator or Amgen physician, if consulted, would pose a risk to subject safety or interfere with the study evaluation, procedures or completion.

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:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	02-10-2023
Enrollment:	2
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	6-mercaptopurine
Generic name:	6-mercaptopurine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Blincyto
Generic name:	Blinatumomab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Dexamethasone
Generic name:	Dexamethasone
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Methotrexate
Generic name:	Methotrexate
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Truxima
Generic name:	Rituximab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	16-02-2023
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-05-2023
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-07-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-08-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-09-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-10-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	CTIS2023-503640-14-00
EudraCT	EUCTR2020-004498-29-NL
ClinicalTrials.gov	NCT04994717
CCMO	NL83607.056.23