Blinatumomab in Adult Patients With Minimal Residual Disease (MRD) of B-precursor Acute Lymphoblastic Leukemia

This study is currently recruiting participants. (see Contacts and Locations)

Verified April 2017 by Johann Wolfgang Goethe University Hospital

Sponsor:
Johann Wolfgang Goethe University Hospital

Information provided by (Responsible Party):
Nicola Goekbuget, Johann Wolfgang Goethe University Hospital

ClinicalTrials.gov Identifier:
NCT03109093

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History of Changes

Purpose

This study is designed to confirm the efficacy, safety, and tolerability of blinatumomab in patients with MRD of B- precursor ALL in complete hematological remission including patients with relapse after SCT. The study aims to expand experience generated in previous trials in patients with MRD positive ALL with a focus on additional specific questions.

Condition	Intervention	Phase
ALL, Recurrent, Adult	Drug: Blinatumomab	Phase 2

Study Type: Interventional
Study Design: Intervention Model: Single Group Assignment
Masking: No masking
Primary Purpose: Treatment

Official Title: A Multicenter, Single-arm Study to Assess the Efficacy, Safety, and Tolerability of the BiTE® Antibody Blinatumomab in Adult Patients With Minimal Residual Disease (MRD) of B-precursor Acute Lymphoblastic Leukemia (Blast Successor Trial)

Resource links provided by NLM:

MedlinePlus related topics: Chronic Lymphocytic Leukemia Leukemia

Drug Information available for: Blinatumomab

Genetic and Rare Diseases Information Center resources: Acute Lymphoblastic Leukemia Lymphosarcoma

U.S. FDA Resources

Further study details as provided by Johann Wolfgang Goethe University Hospital:

Primary Outcome Measures:

- MRD response after one cycle [Time Frame: after one cycle of treatment (up to 43 days)]

  Proportion of patients who achieve complete MRD response after one cycle of treatment with blinatumomab in patients with and without prior SCT

Secondary Outcome Measures:

- Continuous complete remission [Time Frame: 18 months following initiation of blinatumomab]

  Probability of continuous complete remission (remission duration) at 18 months following initiation of blinatumomab

- Hematological relapse-free survival [Time Frame: 18 months following initiation of blinatumomab]

  Probability of hematological relapse-free survival rate at 18 months following initiation of blinatumomab

- Overall survival [Time Frame: 18 months following initiation of blinatumomab]

  Probability of overall survival at 18 months following initiation of blinatumomab

- Relapse localisations [Time Frame: In Case of Relapse, continuously until End of Follow-Up (up to 18 Months)]

  Frequency of different relapse localisations in proportion to total hematological relapses

- Biological evaluation of hematological and extramedullary relapse [Time Frame: In Case of Relapse, continuously until End of Follow-Up (up to 18 Months)]

  Biological evaluation of hematological and extramedullary relapses including CD19 expression

- Serious Adverse Event (SAE) incidence [Time Frame: continuously until End of Safety-Follow-Up (up to 26 weeks)]

  Overall incidence and severity of adverse events in patients with and without prior SCT (CTCAE 4.0)

- MRD response after two cycles [Time Frame: after two cycles of treatment (up to 85 days)]

  Proportion of patients who achieve complete MRD response after two cycles of treatment with blinatumomab in patients with and without prior SCT

- duration of MRD response [Time Frame: 18 months following initiation of blinatumomab]

  Probability of continuous MRD response and complete MRD response and duration of MRD response at 18 months following initiation of blinatumomab

- Time to MRD response [Time Frame: MRD determination after each cycle of treatment (up to 24 weeks)]

  Time to MRD response measured by time-point of first achievement

- GvHD [Time Frame: until End of Safety-Follow-Up (up to 26 weeks)]

  Evaluation of GvHD as part of AE documentation and according to Glucksberg Criteria, grade and localisation.

- treatment related mortality after subsequent SCT [Time Frame: after subsequent SCT (at day 100 and later)]

  • Evaluation of overall survival, remission duration, relapse-free survival and treatment related mortality (at day 100 and later) in patients with SCT in complete remission after blinatumomab

- treatment related mortality [Time Frame: continuously until End of Follow-Up (up to 18 Months)]

  Evaluation of overall survival, remission duration, relapse-free survival and treatment related mortality in patients without SCT in complete remission after blinatumomab

- Quality of Life [Time Frame: until End of Follow-Up (up to 18 Months)]

  Measurement of Quality of Life with EORTC instruments (EORTC QLQ C30 and EQ-5D) at different time-points during treatment

Other Outcome Measures:

- Treatment deviation1 [Time Frame: until end of treatment (up to 22 weeks)]

  Incidence of dose reductions

- Treatment deviation2 [Time Frame: until end of treatment (up to 22 weeks)]

  incidence of treatment interruptions

- Treatment deviation3 [Time Frame: until end of treatment (up to 22 weeks)]

  days of interruption

- Treatment deviation4 [Time Frame: until end of treatment (up to 22 weeks)]

  withdrawals

- Treatment deviation5 [Time Frame: until end of treatment (up to 22 weeks)]

  total delivered dose

- Treatment deviation6 [Time Frame: until end of treatment (up to 22 weeks)]

total days of treatment

- Treatment deviation7 [Time Frame: until end of treatment (up to 22 weeks)]

  realisation rate calculated as scheduled total dose/delivered total dose

- Hospitalisation days [Time Frame: until end of treatment (up to 22 weeks)]

  Number of hospitalisation days

Estimated Enrollment:	30
Actual Study Start Date:	March 15, 2017
Estimated Study Completion Date:	January 2020
Estimated Primary Completion Date:	July 2018 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Blinatumomab Patients will receive four cycles of treatment, unless criteria for treatment discontinuation apply. The duration of one cycle is 6 weeks, including a four week continuous intravenous infusion and a two week infusion free interval, which may be extended by a maximum of 7 days. Transfer of patients to alloHSCT after one cycle or after subsequent cycles is considered as per protocol discontinuation and as premature treatment discontinuation In case of hematological or extramedullary relapse, the study treatment will be permanently discontinued.	Drug: Blinatumomab Patients will receive blinatumomab at a dose of 28 µg/day as continuous intravenous infusion at constant flow rate for four weeks, followed by a two-week infusion free interval, defined as one treatment cycle. Up to of four cycles will be performed. In case of defined toxicities, the dose of blinatumomab may be reduced to 9µg/day. Patients with an MRD relapse may qualify to receive additional treatment with blinatumomab. Other Name: blincyto

Detailed Description:

Transfer of patients to alloHSCT after one cycle or after subsequent cycles is considered as per protocol discontinuation and as premature treatment discontinuation In case of hematological or extramedullary relapse, the study treatment will be permanently discontinued.

There will be a safety follow-up visit at 30 days after end of the last infusion. There will be efficacy follow-up until 18 months after treatment start. In patients scheduled for SCT the 30-day safety-visit may be performed at the latest time point possible before initiation of subsequent treatment.

Eligibility

Ages Eligible for Study:	18 Years and older (Adult, Senior)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

1. Patients with CD19 positive B-precursor ALL in complete hematological remission defined as less than 5% blasts in bone marrow after at least three intense chemotherapy blocks (e.g., GMALL induction I-II/consolidation I).
2. Presence of minimal residual disease (MRD) at a level of ≥10-4 (molecular failure or molecular relapse) in an assay with a minimum sensitivity of 10-4 documented after an interval of at least 2 weeks from last systemic chemotherapy
3. For evaluation of MRD patients must have at least one molecular marker based on individual rearrangements of immunoglobulin, TCR-genes or other suitable genes evaluated by the reference laboratory of the trial
4. Bone marrow function as defined below:
   - ANC (Neutrophils) >= 1,000/µL
   - Platelets >= 50,000/µL (transfusion permitted)
   - HB level >= 9g/dl (transfusion permitted)
5. Renal and hepatic function as defined below:
   - AST (GOT), ALT (GPT), and AP < 5 x upper limit of normal (ULN)
   - Total bilirubin < 1.5 x ULN (unless related to Gilbert's Meulengracht disease)
   - Creatinine < 1.5x ULN
   - Creatinine clearance >= 60 mL/min (e.g. calculated according Cockroft&Gault)
6. Negative HIV test, negative hepatitis B (HbsAg) and hepatitis C virus (anti-HCV) test
7. Negative pregnancy test in women of childbearing potential
8. ECOG Performance Status 0 or 1
9. Age >=18 years
10. Ability to understand and willingness to sign a written informed consent

11. Signed and dated written informed consent is available
12. Participation in the registry of the German Multicenter Study Group for Adult ALL (GMALL)

Exclusion Criteria:

1. Ph/BCR-ABL positive ALL
2. Presence of circulating blasts or current extramedullary involvement by ALL
3. History or presence of clinically relevant CNS pathology (e.g. seizure, paresis, aphasia, cerebrovascular ischemia/hemorrhage, severe brain injuries, dementia, Parkinson's disease, cerebellar disease, organic brain syndrome or psychosis)
4. Current detection of ALL blast cells in cerebro-spinal fluid
5. History of or active relevant autoimmune disease
6. Systemic cancer chemotherapy within 2 weeks prior to study treatment (except for intrathecal prophylaxis)
7. Radiotherapy within 4 weeks prior to study treatment
8. Live vaccination within 2 weeks before the start of study treatment
9. Autologous hematopoietic stem cell transplantation (SCT) within six weeks prior to study treatment
10. Allogeneic SCT within 12 weeks before the start of study treatment
11. Any active acute Graft-versus-Host Disease (GvHD), grade 2-4 according to the Glucksberg criteria or active chronic GvHD requiring systemic treatment
12. Any systemic therapy against GvHD within 2 weeks before start of study treatment
13. Therapy with monoclonal antibodies (rituximab, alemtuzumab) within 4 weeks prior to study treatment
14. Treatment with any investigational product within four weeks prior to study treatment
15. Previous treatment with blinatumomab or other anti-CD19-therapy
16. Known hypersensitivity to immunoglobulins or to any other component of the study drug formulation
17. History of malignancy other than ALL diagnosed within 5 years prior to start of protocol-specified therapy with the exception of:
    - Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease
    - Adequately treated cervical carcinoma in situ without evidence of disease
    - Adequately treated breast ductal carcinoma in situ without evidence of disease
    - Prostatic intraepithelial neoplasia without evidence of prostate cancer
18. Active infection, any other concurrent disease or medical condition that are deemed to interfere with the conduct of the study as judged by the investigator
19. Nursing women
20. Woman of childbearing potential and is not willing to use 2 highly effective methods of contraception while receiving study treatment and for an additional 3 months after the last dose of study treatment.
21. Male who has a female partner of childbearing potential, and is not willing to use 2 highly effective forms of contraception while receiving study treatment and for at least an additional 3 months after the last dose of study treatment

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT03109093

Contacts

Contact: GMALL Study Center +49 (0)69 - 6301 ext 6366 gmall@em.uni-frankfurt.de

Locations

Germany

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Sponsors and Collaborators

Johann Wolfgang Goethe University Hospital

Investigators

Principal Investigator: Nicola Goekbuget, MD GMALL-Study-Group

More Information

Additional Information:

Trial Register of the Kompetenznetz Leukämien, additional trial information

Trial register of University Cancer Center Frankfurt, additional trial information

Responsible Party:	Nicola Goekbuget, Principal Investigator, Johann Wolfgang Goethe University Hospital
ClinicalTrials.gov Identifier:	NCT03109093 History of Changes
Other Study ID Numbers:	GMALL-**MOLACT1**-BLINA 2015-000733-76 (EudraCT Number)
Study First Received:	March 13, 2017
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Individual Participant Data Plan to Share IPD:	Undecided

Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No
Product Manufactured in and Exported from the U.S.:	No

Keywords provided by Johann Wolfgang Goethe University Hospital:
ALL
acute lymphoblastic leukemia
MRD positive
minimal residual disease
blinatumomab

Additional relevant MeSH terms:

Leukemia
Precursor Cell Lymphoblastic Leukemia-Lymphoma
Leukemia, Lymphoid
Neoplasm, Residual
Neoplasms by Histologic Type
Neoplasms
Lymphoproliferative Disorders
Lymphatic Diseases
Immunoproliferative Disorders
Immune System Diseases
Neoplastic Processes
Pathologic Processes
Blinatumomab
Antibodies, Bispecific
Antineoplastic Agents
Immunologic Factors
Physiological Effects of Drugs

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