ISRCTN52962455 https://doi.org/10.1186/ISRCTN52962455

A study investigating the use of blinatumomab to treat acute myeloid leukaemia with low level residual disease

Submission date
25/05/2021

Recruitment status
No longer recruiting

Registration date
27/05/2021

Overall study status
Completed

Last Edited
19/12/2025

Condition category
Cancer

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-of-blinatumomab-for-acute-myeloid-leukaemia-blinaml

Background and study aims
This study will evaluate the safety and effectiveness of an antibody treatment (blinatumomab) in patients who have received treatment for a particular type of acute myeloid leukaemia (AML), but in whom molecular testing shows that the disease has not completely gone away or is starting to come back. The standard treatment for these patients is intensive chemotherapy which has severe side effects. We wish to investigate whether the antibody treatment can achieve the same results with less toxicity. Blinatumomab is very effective in this situation in a different type of leukaemia (B-cell acute lymphoblastic leukaemia, B-ALL) and is now standard treatment in the NHS and worldwide. This is the first time that blinatumomab has been tested in AML.

Who can participate?
Patients with a sub-type of AML where there is a specific genetic change in the leukaemia cell. This is known as translocation 8;21 or t(8;21). Patients must have previously received chemotherapy and be in remission on a bone marrow biopsy (no leukaemia cells seen under the microscope), but have very low levels of leukaemia detectable with specialised molecular tests.

What does the study involve?
The first step is a consultation with the study team to determine if you are eligible for the study. This will include a number of blood tests and a bone marrow biopsy. If you decided to take part, you will receive 1 to 4 cycles of blinatumomab therapy. Each treatment cycle is 6 weeks.

You would be admitted to hospital for the first 3 days of cycle 1 and the first 2 days of subsequent cycles. This is to monitor closely for any side effects associated with starting the treatment. Some patients may require longer hospital stays. Blinatumomab is giving into a vein

(intravenously) as a continuous infusion for 28 days. This will require a central venous catheter (CVC) to ensure reliable access to a vein. Prior to the start of the blinatumomab you will receive intravenous dexamethasone, a corticosteroid designed to reduce treatment side effects.

If you do not experience significant side effects from the treatment, you will be discharged home for the remainder of the cycle. The blinatumomab will remain connected to your CVC to allow for a continuous infusion. The medication will be loaded into a Continuous Ambulatory Delivery Device (CADD) pump.

What are the possible benefits and risks of participating?
There is no guaranteed benefit to taking part in this study because we do not yet how effective blinatumomab is in this situation. The careful monitoring you will receive if you take part in this study is a safeguard against this risk. If the therapy is not working, you will be able to quickly change to standard chemotherapy. As blinatumomab is likely to be less toxic than standard chemotherapy, it is possible that patients receiving this treatment may experience fewer side effects. The information gained from this study will help improve treatment for other people with AML in the future.

The risks of the study include that blinatumomab may not be effective in this type of leukaemia. You will be closely monitored to see if this is the case, and switched back to standard chemotherapy. Blinatumomab is not chemotherapy and has a unique set of side effects. In the majority of cases these are manageable with medications and temporary interruption or dose reduction of the infusion. If side effects are very severe, it is possible the treatment will need to be permanently stopped. These unique side effects include a syndrome known as cytokine release syndrome, which causes fevers, blood pressure changes and other abnormalities; as well as reversible neurological (brain and nervous system) side effects. As these tend to occur early in each treatment cycle, you will be admitted to hospital for 2-3 days in each cycle to monitor for the side effects.

The study medication may cause harm to an unborn child if administered during pregnancy. As such all participants must agree to use at least one form of highly effective contraception during the study without interruption.

Where is the study run from?
Guy’s and St Thomas’ NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
January 2020 to December 2025

Who is funding the study?
Amgen Inc (USA)

Who is the main contact?
Dr Richard Dillon, richard.dillon@kcl.ac.uk

Contact information

Type(s)
Scientific

Contact name

Dr Richard Dillon

Contact details
Department of Haematology
4th Floor Southwark Wing
Guy's Hospital
London
United Kingdom
SE1 9RT
+44 (0)20 7188 2579
richard.dillon@kcl.ac.uk

Type(s)
Scientific

Contact name
Prof Nigel Russell

Contact details
Department of Haematology
4th Floor Southwark Wing
Guy's Hospital
London
United Kingdom
SE1 9RT
+44 (0)20 7188 2724
nigel.russell@nottingham.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2020-002019-23

Integrated Research Application System (IRAS)
1003598

Central Portfolio Management System (CPMS)
48293

Protocol serial number
Grant Codes: 311481

Study information

Scientific Title
Blinatumomab in molecular relapse of AML with a t(8;21) translocation

Acronym
BlinAML

Study objectives
This is a single-arm, single centre phase 4 study of the anti-CD19 bispecific T-cell engager (BITE) blinatumomab for the treatment of patients with acute myeloid leukaemia (AML) with a t(8;21) chromosome translocation who experience molecular relapse.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 09/09/2021, Wales REC 2 (Health and Care Research Wales, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, UK; no telephone number provided; Wales. REC2@wales.nhs.uk), ref: 21/WA/0243

Primary study design
Interventional

Study design
Interventional non-randomized

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Acute myeloid leukaemia (AML)

Interventions
All patients will receive blinatumomab by continuous intravenous infusion in 28 day cycles, with 14 days between cycles. The first 2-3 days of each cycle is administered as an inpatient, with the remainder being infused at home using a continuous infusion device. Patients will present to the treatment unit twice a week for infusion bag changes, and at least weekly for clinical review. A minimum of 1, and up to 4 cycles, will be administered, depending on clinical response and the requirement/availability of stem cell transplant. The total duration of treatment is up to 24 weeks, with 2 years follow-up after the completion of therapy.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Blinatumomab

Primary outcome(s)
Detection RUNX1-RUNX1T1 fusion transcripts on a bone marrow biopsy after one cycle of treatment with blinatumomab

Key secondary outcome(s)
Measured using patient records:
1. Incidence of patients experiencing a grade 3 or greater non-haematological toxicity during the

first cycle of treatment.
2. Incidence of molecular complete remission on bone marrow biopsy at any time from trial entry (evaluated at end of trial)
3. Molecular relapse-free survival time (evaluated at end of trial)
4. Overall survival time (evaluated at end of trial)
5. Number of days of hospital admission at 1, 3 and 6 months from entry
6. Number of days on intravenous antibiotics or antifungals at 1, 3 and 6 months
7. Number of blood components infused at 1, 3 and 6 months

Completion date
31/12/2025

Eligibility

Key inclusion criteria
1. Patients with AML with a t(8:21) translocation in complete haematological remission (defined as less than 5% blasts in bone marrow) with a confirmed first or subsequent molecular relapse or molecular persistence of disease (defined according to European Leukaemia Net criteria) following remission induction therapy comprising 2 courses of an anthracycline based regimen or one course of an anthracycline based regimen plus a second course of high dose cytarabine (HDAC).
2. Bone marrow or peripheral blood specimen from primary AML sample taken at diagnosis documented as showing expression of CD19.
3. Bone marrow function as defined below:
3.1. Neutrophils >1x10^9/L - Platelets >20 x 10^12/L (transfusion permitted)
3.2. Haemoglobin level >9g/dl (transfusion permitted)
4. Renal and hepatic function as defined below:
4.1. AST, ALT, and ALP <2 x upper limit of normal (ULN) - Total bilirubin <1.5 x ULN
4.2. Creatinine clearance >50 mL/min (calculated according Cockroft & Gault)
5. Negative HIV test,negative hepatitis B (HbsAg) and hepatitis C virus (anti-HCV) test with the exception of well controlled chronic infections with at least two documented negative PCR tests for viral load.
6. Negative pregnancy test in women of childbearing potential, (as defined in CTFG guidelines)
7. ECOG Performance Status 0 – 2
8. Age 18 years or older
9. Ability to understand and willingness to provide written informed consent.
10. Signed and dated written informed consent is available

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit

99 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. 5% or more blasts in the bone marrow or the presence of circulating blasts or current extramedullary involvement by AML.
2. History of relevant CNS pathology or current relevant CNS pathology (e.g. seizure,paresis, aphasia,cerebrovascular ischemia/haemorrhage,severe brain injuries,dementia,Parkinson’s disease,cerebellar disease,organic brain syndrome,psychosis,coordination or movement disorder).
3. Current infiltration of cerebrospinal fluid by AML.
4. History of or active relevant autoimmune disease.
5. Prior allogeneic HSCT within the last 3 months prior to study treatment.
6. Systemic cancer chemotherapy within 2 weeks prior to study treatment.
7. Radiotherapy within 4 weeks prior to study treatment.
8. Treatment with any investigational product within four weeks prior to study treatment.
9. Previous treatment with blinatumomab.
10. Known hypersensitivity to immunoglobulins or to any other component of the study drug formulation.
11. History of malignancy other than AML within five years prior to treatment start with blinatumomab,with the exception of basal cell or squamous cell carcinoma of the skin,or carcinoma "in situ" of the cervix.
12. 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.
13. Nursing women or those with a positive pregnancy test
14. Women of childbearing potential (as defined in CTFG guidelines,see appendix) not willing to use a highly effective form of contraception (as defined in CTFG guidelines) during participation in the study and for at least 3 months thereafter,or male patients not willing to ensure use of highly effective contraception during participation in the study and for at least three months thereafter.
15. Patients with insufficient understanding of the trial to provide informed consent.

Date of first enrolment
22/11/2021

Date of final enrolment
30/06/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Guy’s Hospital
Guy’s & St Thomas’ NHS Foundation Trust
Great Maze Pond
London
England
SE1 9RT

Sponsor information

Organisation
Guy's and St Thomas' NHS Foundation Trust

ROR
https://ror.org/00j161312

Funder(s)

Funder type
Industry

Funder Name
Amgen

Alternative Name(s)
Amgen Inc., Applied Molecular Genetics Inc.

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Richard Dillon (Richard.dillon@kcl.ac.uk). Fully anonymised patient level data

will be shared provided that a research proposal and statistical analysis plan are provided by a suitably qualified researcher.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	version v1.0	09/05/2021	27/05/2021	No	Yes
Protocol file	version 0.7	03/03/2021	19/12/2025	No	No