

A study of bleximenib in combination with acute myeloid leukemia-directed therapies

Submission date 07/06/2023	Recruitment status Recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 17/07/2023	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 05/02/2025	Condition category Cancer	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

Leukaemia (cancer of the white blood cells) is diagnosed as acute when it progresses quickly and aggressively and usually requires immediate treatment. Acute myeloid leukaemia (AML) affects the myeloid cells that fight bacterial infections and other conditions. KMT2A or NPM1 gene alterations can be associated with AML. Treatment options for AML are limited, survival rates are poor, and many patients are ineligible for standard chemotherapy treatments due to toxicity. The study purpose is to determine the recommended phase II study dose(s) of bleximenib in combination with AML-directed therapies and further to evaluate the safety and tolerability of bleximenib in combination with AML-directed therapies at these dose(s).

Who can participate?

Male and female adult participants with AML, relapsed/refractory or newly diagnosed, with either KMT2A or NPM1 gene alterations.

What does the study involve?

AML patients will be enrolled into 1 of 3 study arms. Initially, patients with relapsed/refractory AML will be enrolled (Arm A). Once it has been determined that the combination treatment is safe in these patients, patients with newly diagnosed AML will be enrolled based on eligibility for intensive chemotherapy: ineligible (Arm B) or eligible (Arm C). Bleximenib will be given once or twice daily on a 28-day cycle, with cohort-specific AML-directed therapies.

The study has a screening (up to 28 days), treatment, and follow-up phase. The treatment phase will continue for as long as participants receive benefits from the combination treatment and/or until their participation is ended for any reason. While taking study treatment and during follow-up, participants will come to the clinic for health exams and tests.

The follow-up period will depend on the response to the study treatment and can last up to 1 year.

What are the possible benefits and risks of participating?

Taking bleximenib in combination with AML-directed therapies may improve AML. However, this cannot be guaranteed because bleximenib is still under investigation as a treatment and it is not

known whether the combination study treatment will work. It is also possible that known effects from the individual medications may worsen when given in combination.

Participants may experience some benefit from participation in the study that is not due to receiving study treatment but due to regular visits and assessments monitoring overall health.

Participation may help other people with myeloid in the future.

The expected risks for blaximenib are based on how the drug works and the results from laboratory studies and people who have received blaximenib as a single agent. These may include:

1. Blood cell count effects
2. Changes to heart rhythm
3. Impact on male fertility
4. Tumour Lysis Syndrome (when large numbers of leukaemia cells die in a short period of time)
5. Differentiation Syndrome (DS involves a large, rapid release of cytokines (immune substances) from leukemia cells after treatment with anticancer drugs)
6. Infections
7. Allergic reactions

There may also be other potential risks associated with blaximenib in combination with AML directed therapies. Side effects from the drugs or procedures used in this study may be mild to severe and even life-threatening, and they can vary from person to person. All possible discomforts, side effects, and risks related to the study treatment and procedures will be explained in full in the participant information sheet and discussed during the informed consent process. To minimise the risk associated with taking part in the study, participants are frequently evaluated for any side effects. Participants are educated to report any such events to the study doctor who will provide appropriate medical care. Any serious side effects that are reported to the sponsor are thoroughly reviewed by the global study team. The study doctor will tell participants as soon as possible about any new information that might make them change their mind about being in the study, such as new risks. There are no costs to participants to be in the study. The sponsor will pay for the study treatment and tests that are part of the study. The participant will receive reasonable reimbursement for study-related costs (e.g., travel/parking fees/occasional meals).

Where is the study run from?

Multiple healthcare locations around the world

When is the study starting and how long is it expected to run for?

February 2022 to February 2026

Who is funding the study?

Janssen Research & Development, LLC (UK)

Who is the main contact?

EMarwood@ITS.JNJ.com

Contact information

Type(s)

Principal Investigator

Contact name

Dr Emma Searle

Contact details

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Additional identifiers**EudraCT/CTIS number**

2021-003999-14

IRAS number

1005413

ClinicalTrials.gov number

NCT05453903

Secondary identifying numbers

75276617ALE1002, IRAS 1005413, CPMS 52246

Study information

Scientific Title

A phase Ib study of bleximenib in combination with AML-directed therapies for participants with acute myeloid leukemia harboring KMT2A or NPM1 alterations

Study objectives

The primary objectives of this study are to determine the recommended Phase II dose(s) (RP2Ds) of bleximenib in combination with AML-directed therapies, as well as the safety and tolerability of bleximenib in combination at the RP2D(s). The secondary objectives of this study are to assess the pharmacokinetics (PK) and pharmacodynamics (PD) of bleximenib in combination with AML-directed therapies and to assess the preliminary clinical activity of bleximenib when given in combination with AML-directed therapies.

Ethics approval required

Ethics approval required

Ethics approval(s)

Approved 01/08/2022, North West - Greater Manchester (GM) Central Research Ethics Committee (3rd Floor, Barlow House, 4 Minshull Street, Manchester, M1 3DZ, United Kingdom; +44 (0)2071048328, (0)2071048131; gmcentral.rec@hra.nhs.uk), ref: 22/NW/0176

Study design

Multicohort open-label non-randomized multicenter phase Ib study

Primary study design

Interventional

Secondary study design

Non randomised study

Study setting(s)

Hospital

Study type(s)

Treatment, Safety

Participant information sheet

No participant information sheet available

Health condition(s) or problem(s) studied

Acute myeloid leukemia

Interventions

AML patients will be enrolled into 1 of 3 study arms. Initially, patients with relapsed/refractory AML will be enrolled (Arm A). Once it has been determined that the combination treatment is safe in these patients, patients with newly diagnosed AML will be enrolled based on eligibility for intensive chemotherapy: ineligible (Arm B) or eligible (Arm C). Bleximenib will be given orally once or twice daily on a 28-day cycle, with cohort-specific AML-directed therapies. The dose and frequency of the dose are variable. The study has a screening (up to 28 days), treatment, and follow-up phase. The treatment phase will continue for as long as participants receive benefits from the combination treatment and/or until their participation is ended for any reason. While taking study treatment and during follow-up, participants will come to the clinic for health exams and tests. The follow-up period will depend on the response to the study treatment and can last up to 1 year. Duration is until completion of End of Trial (EOT) visit, or sooner if meets discontinuation criteria.

Intervention Type

Drug

Pharmaceutical study type(s)

Pharmacokinetic, Pharmacodynamic, Dose response

Phase

Phase I

Drug/device/biological/vaccine name(s)

Bleximenib, venetoclax, azacitidine, idarubicin, daunorubicin, cytarabine

Primary outcome measure

The following primary outcome measures will be measured by clinical assessment of adverse events (including dose-limiting toxicities) by the clinical Investigator:

1. Number of Participants with Adverse Events (AEs) up to 2 Years
2. Number of Participants with Adverse Events (AEs) by Severity up to 2 Years
3. Number of Participants with Dose-limiting Toxicity (DLT) up to the end of Cycle 1 (28 days)

Secondary outcome measures

1. Plasma Concentration of bleximenib measured using a pharmacological chemical assay up to 2 Years
2. Number of Participants with Depletion of Leukemic Blasts up to 2 Years
3. Number of Participants with Differentiation of Leukemic Blasts up to 2 Years
4. Changes in Expression of Menin-histone-lysine N-methyltransferase 2A (KMT2A) Target Genes measured using RNA nanostring technology up to 2 Years
5. Percentage of Participants who Achieve Complete Remission (CR) up to 2 Years
6. Percentage of Participants who Achieve Complete Remission with Partial Hematologic Recovery (CRh) up to 2 Years
7. Percentage of Participants who Achieve Complete Remission with Incomplete Hematologic Recovery (CRi) up to 2 Years
8. Percentage of Participants who Achieved Overall Response up to 2 Years
9. Duration of response up to 2 Years
10. Time to Response up to 2 Years

Overall study start date

03/02/2022

Completion date

02/02/2026

Eligibility

Key inclusion criteria

1. Diagnosis of AML according to World Health Organization (WHO) 2016 criteria:
 - 1.1. De novo or secondary AML
 - 1.2. Relapsed /refractory (Arm A)
 - 1.3. Harboring NPM1 / KMT2A alterations
2. Pretreatment clinical laboratory values meeting the following criteria -listed below: White blood cell (WBC) count: less than or equal to $\leq 25 \times 10^9$ per liter (/L), adequate liver and renal function
3. ECOG performance status grade of 0, 1 or 2
4. A woman of childbearing potential must have a negative highly sensitive serum beta-human chorionic gonadotropin at screening and within 48 hours prior to the first dose of study treatment
5. Must sign an informed consent form (ICF) indicating participant understands the purpose of the study and procedures required for the study and is willing to participate in the study.
6. Willing and able to adhere to the prohibitions and restrictions specified in this protocol

Participant type(s)

Patient

Age group

Mixed

Lower age limit

18 Years

Upper age limit

100 Years

Sex

Both

Target number of participants

150

Key exclusion criteria

1. Acute promyelocytic leukemia according to WHO 2016 criteria
2. Leukemic involvement of the central nervous system
3. Recipient of solid organ transplant
4. Cardiovascular disease that is uncontrolled, increases the risk for Torsades de Pointes or that was diagnosed within 6 months prior to the first dose of study treatment including, but not limited to:
 - 4.1. Myocardial infarction
 - 4.2. Severe or unstable angina
 - 4.3. Clinically significant cardiac arrhythmias, including bradycardia (less than $<$ 50 beats per minute)

- 4.4. Uncontrolled (persistent) hypertension: (example, blood pressure greater than [$>$] 140/90 millimeters of mercury [mm Hg])
- 4.5. Acute neurologic events such as stroke or transient ischemic attack, intracranial or subarachnoid hemorrhage, intracranial trauma
- 4.6. Venous thromboembolic events (for example, pulmonary embolism) within 1 month prior to the first dose of study treatment (uncomplicated Grade less than or equal to [\leq] 2 deep vein thrombosis is not considered exclusionary)
- 4.7. Congestive heart failure (NYHA class III to IV); (h) Pericarditis or clinically significant pericardial effusion
- 4.8. Myocarditis
- 4.9. Endocarditis
- 4.10. Clinically significant hypokalemia, hypomagnesemia, hypocalcemia (corrected for hypoalbuminemia)
- 5. Any toxicity (except for alopecia, stable peripheral neuropathy, thrombocytopenia, neutropenia, anemia) from previous anticancer therapy that has not resolved to baseline or to grade 1 or less
- 6. Pulmonary compromise that requires the need for supplemental oxygen use to maintain adequate oxygenation

Date of first enrolment

04/10/2022

Date of final enrolment

25/11/2025

Locations

Countries of recruitment

Australia

England

France

Germany

Italy

Spain

United Kingdom

United States of America

Study participating centre

The Christie NHS Foundation Trust

550 Wilmslow Road

Withington

Manchester

United Kingdom
M20 4BX

Study participating centre

University College London Hospitals NHS Foundation Trust
250 Euston Road
London
United Kingdom
NW1 2PG

Study participating centre

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Policlinico S. Orsola-Malpighi, Unità Operativa di Ematologia – Pad. 8, Via Giuseppe Massarenti, 9
Bologna
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40138

Study participating centre

Universitätsklinikum Dresden
Fetscherstr. 74
Dresden
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01307

Study participating centre

Institut Universitaire du Cancer de Toulouse-Oncopole (IUCT-O)
1 avenue Irène Joliot-Curie
Toulouse
France
31059

Study participating centre

Clinica Universidad de Navarra
Avda. Pio XII, 36
Pamplona
Spain
31008

Study participating centre

Monash Medical Centre

246 Clayton Road
Melbourne
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3168

Study participating centre**Novant Health Forsyth Medical Center**

3333 Silas Creek Parkway
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United States of America
27103

Study participating centre**Oxford University Hospitals NHS Foundation Trust**

Churchill Hospital
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Sponsor information

Organisation

Janssen Pharmaceutica NV

Sponsor details

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Sponsor type

Industry

Funder(s)

Funder type

Industry

Funder Name

Janssen Research and Development

Alternative Name(s)

Janssen R&D, Janssen Research & Development, Janssen Research & Development, LLC, Janssen Research & Development LLC, Janssen Pharmaceutical Companies of Johnson & Johnson, Research & Development at Janssen, JRD, J&J PRD

Funding Body Type

Private sector organisation

Funding Body Subtype

For-profit companies (industry)

Location

United States of America

Results and Publications

Publication and dissemination plan

Planned publication in a high-impact peer-reviewed journal

Intention to publish date

28/02/2027

Individual participant data (IPD) sharing plan

The data sharing policy of the Janssen Pharmaceutical Companies of Johnson & Johnson is available at www.janssen.com/clinical-trials/transparency. As noted on this site, requests for access to the study data can be submitted through Yale Open Data Access (YODA) Project site at yoda.yale.edu

IPD sharing plan summary

Available on request