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

Submission date
07/06/2023

Recruitment status
Recruiting

Registration date
17/07/2023

Overall study status
Ongoing

Last Edited
25/11/2025

Condition category
Cancer

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] 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, NPM1, or NUP 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 participants with AML, relapsed/refractory or newly diagnosed, with KMT2A , NPM1, NUP98, or NUP214 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 18 months.

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 bleximenib are based on how the drug works and the results from laboratory studies and people who have received bleximenib as a single agent. These may include:
1. Blood cell count effects
2. Changes to heart rhythm
3. Fertility effects
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

There may also be other potential risks associated with bleximenib 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 March 2027

Who is funding the study?
Janssen Research & Development, LLC (UK)

Who is the main contact?
Ellice Marwood, RA-JanssenUKRegistry@ITS.JNJ.com

Contact information

Type(s)

Public

Contact name
Mrs Ellice Marwood

Contact details
Senior Local Trial Manager, ED&CP, Janssen UK
50-100 Holmers Farm Way
High Wycombe
United Kingdom
HP12 4DP
-
RA-JanssenUKRegistry@ITS.JNJ.com

Type(s)
Public

Contact name
Dr Sponsor Contact

Contact details
Medical Information and Product Information Enquiry
-
United Kingdom
-
+44 (0)800 731 8450; (0)1494 567444
medinfo@its.jnj.com

Additional identifiers

Clinical Trials Information System (CTIS)
2021-003999-14

Integrated Research Application System (IRAS)
1005413

ClinicalTrials.gov (NCT)
NCT05453903

Protocol serial number
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 2 dose(s) (RP2Ds) of bleximenib in combination with acute myeloid leukemia (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

Study type(s)
Safety, Treatment

Health condition(s) or problem(s) studied
Acute myeloid leukemia

Interventions
Current interventions as of 25/11/2025:
AML patients will be enrolled into 1 of 3 study arms. Participants with relapsed/refractory AML will be enrolled (Arm A). Participants with newly diagnosed AML will be enrolled in treatment arms based on eligibility for intensive chemotherapy: ineligible for intensive chemotherapy (Arm B) or eligible for intensive chemotherapy (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. 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 18 months.

Previous 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

Phase
Phase I

Drug/device/biological/vaccine name(s)
Bleximenib, venetoclax, azacitidine, idarubicin, daunorubicin, cytarabine

Primary outcome(s)
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)

Key secondary outcome(s))
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

Completion date
19/03/2027

Eligibility

Key inclusion criteria
Current inclusion criteria as of 25/11/2025:
1. Adolescent participants (defined as greater than or equal to [>=] 12 and less than [<] 18 years of age) are only eligible for the relapsed/refractory (R/R) cohort (Arm A, cohort A4)
2. Diagnosis of AML according to World Health Organization (WHO) 2016 criteria:

2.1. De novo or secondary AML
2.2. Relapsed /refractory (Arm A)
2.3. Harboring NPM1, KMT2Am NUP98 or NUP214 alterations
3. Pretreatment clinical laboratory values meeting the following criteria -listed below: White blood cell (WBC) count: less than or equal to <=25 x 10^9 per liter (/L), adequate liver and renal function
4. Eastern Cooperative Oncology Group (ECOG) performance status grade of 0, 1 or 2. Adolescent participants only: Performance status >70 by Lansky scale (for participants <16 years of age) or >70 Karnofsky scale (for participants >16 years of age)
5. A female 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
6. Must sign an informed consent form (ICF) indicating participant (or their legally authorised representative) understands the purpose of the study and procedures required for the study and is willing to participate in the study.
7. Willing and able to adhere to the prohibitions and restrictions specified in this protocol

Previous 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 <=25 x 10^9 per liter (/L), adequate liver and renal function
3. ECOG performance status grade of 0, 1 or 2
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Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
12 years

Upper age limit
100 years

Sex
All

Total final enrolment
0

Key exclusion criteria
Current exclusion criteria as of 25/11/2025:
1. Acute promyelocytic leukemia, diagnosis of Downs Syndrome associated lekaemia or diagnosis of Down syndrome associated 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 [≤]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
7. Participants with diagnosis of Fanconi anemia, Kostmann syndrome, Shwachman diamond syndrome, or any other known bone marrow failure syndrome

Previous 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
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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
14/08/2026

Locations

Countries of recruitment
United Kingdom

England

Australia

France

Germany

Italy

Spain

United States of America

Study participating centre
The Christie NHS Foundation Trust
550 Wilmslow Road
Withington
Manchester
England
M20 4BX

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
London
England
NW1 2PG

Study participating centre
Oxford University Hospitals NHS Foundation Trust
Churchill Hospital
Old Road
Headington
Oxford
England
OX3 7LE

Sponsor information

Organisation
Janssen Pharmaceutica NV

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

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes