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Bleximenib absorption, metabolism, and excretion in participants with acute leukemia

Submission date
07/08/2025

Recruitment status
Recruiting

Registration date
10/11/2025

Overall study status
Ongoing

Last Edited
04/12/2025

Condition category
Cancer

[X] 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
Acute leukemias are highly aggressive blood cancers characterized by uncontrolled proliferation of immature white blood cells in the bone marrow, peripheral blood and/or other sites in the body. Although treatment options are available, some participants either do not respond or may not be able to tolerate them because of their side effects. Hence, there is a need for better treatments. Bleximenib is a medicine that specifically targets and blocks the interaction between the proteins histone-lysine N-methyltransferase 2A (KMT2A) and menin, which has been shown to be responsible for the worsening of acute leukemias with KMT2A, nucleophosmin 1 (NPM1, NUP 98 or NUP214 gene alterations. Blocking this interaction kills cancer cells and stops the disease from worsening. In this study, researchers want to determine how radiolabeled (14-C) bleximenib is absorbed, broken down and removed from the body.

Who can participate?
Participants will be aged 18 years or older with relapsed or refractory acute leukemia with KMT2A, NPM1, NUP98, or NUP214 gene alterations.

What does the study involve?
The study consists of:
1. Screening phase (up to 30 days)
2. Open-label treatment phase (up to 28 days): Participants will receive a single oral dose of 14C-bleximenib on Day 1. On Day 2, participants will receive non-radiolabeled bleximenib at a safe and effective dose (recommended phase 2 dose [RP2D]) twice daily until Day 28.
Eligible participants may have the option to join the 75276617ALE1001 (NCT04811560) study for continued treatment with non-radiolabeled bleximenib.
3. Safety follow-up phase (up to 30 days after last dose of non-radiolabeled bleximenib until transition to 75276617ALE1001 study [as applicable] or until start of subsequent anticancer therapy, whichever occurs first). Safety assessments will include monitoring adverse events, physical examinations, clinical laboratory tests and Eastern Cooperative Oncology Group performance status (measures how well participants live). Overall duration of the study will be ~28-58 days.

What are the possible benefits and risks of participating?
Participants may not receive any benefit from taking part in this study, but the information that is learned from the study may help people with acute leukemia in the future. The potential risks for bleximenib, based on how the drug works, are listed below:
- reduced production of blood cells in bone marrow (myelosuppression)
- cancer treatment causing rapid changes in cancer cells, resulting inan inflammatory response (differentiation syndrome)
- cancer cells breaking down and releasing their contents into the bloodstream (tumor lysis syndrome)
- infections
- extended interval on an electrocardiogram indicating heart problems (ECG, QT prolongation)
- impact on ability to reproduce (fertility effects).

The participant information sheet and informed consent form, which will be signed by every participant agreeing to take part in the study, include a detailed section outlining the potential risks of participating in the study. Participants may have none, some, or all of the possible side effects listed, and they may be mild, moderate, or severe.

To minimise the risks associated with taking part in this study, participants are frequently evaluated for any side effects or other medical events. If there are any side effects or if participants are worried about potential side effects, or if any new or unusual symptoms appear, participants are encouraged to talk with their study doctor/team. The study doctor and study team will also be looking out for side effects and will provide appropriate medical care as necessary.

There may also be side effects that the researchers do not expect or do not know about and that may be serious. Many side effects go away shortly after the intervention ends. However, sometimes side effects can be serious, long-lasting, or permanent. If a severe side effect or reaction occurs, the study doctor may need to stop the study drug. The study doctor will discuss the best way of managing any side effects with participants. There is always a chance that an unexpected or serious side effect may happen. This can happen to people who take this or any other drug.

Where is the study run from?
The Christie NHS Foundation Trust, UK.

When is the study starting and how long is it expected to run for?
August 2025 to July 2026

Who is funding the study?
Janssen Research & Development, USA.

Who is the main contact?
medinfo@its.jnj.com

Contact information

Type(s)
Public

Contact name

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Scientific

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Additional identifiers

Central Portfolio Management System (CPMS)
67844

Integrated Research Application System (IRAS)
1012471

Protocol serial number
75276617ALE1006

Study information

Scientific Title
An open-label study to investigate the absorption, metabolism, and excretion (AME) of 14C-bleximenib (JNJ-75276617) in participants with acute leukemia

Study objectives
To identify how the body absorbs, breaks down , and removes bleximenib after a single oral dose of radiolabeled bleximenib (a medicine that has been chemically attached to a radioactive material which emits radiation making it easier to track in the body).

To assess how safe bleximenib is and how well participants can tolerate it.

Ethics approval required

Ethics approval required

Ethics approval(s)
approved 07/10/2025, Wales Research Ethics Committee 1, Cardiff (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 02922940912; Wales.REC1@wales.nhs.uk), ref: 25/WA/0248

Study design
Open-label study

Primary study design
Interventional

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Medical condition: Acute leukaemia
Medical condition in lay language: Blood cancer
Therapeutic areas: Diseases [C] - Cancer [C04]

Interventions
The study consists of:
1. Screening phase (up to 30 days)
2. Open-label treatment phase (up to 28 days): Participants will receive a single oral dose of 14C-bleximenib on Day 1. On Day 2, participants will receive non-radiolabeled bleximenib at a safe and effective dose (recommended phase 2 dose [RP2D]) twice daily until Day 28.
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Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
14C-bleximenib [14c-bleximenib] , bleximenib [bleximenib]

Primary outcome(s)
1. Percentage of Dose Excreted in Urine (feu) - Total amount excreted into the urine, expressed as a percentage of the administered dose, will be reported up to day 28
2. Percentage of Dose Excreted in Feces (fef) - Total amount excreted into the feces expressed as a percentage of the administered dose, will be reported up to day 28
3. Amount Excreted in Urine (Aeu) - Aeu defined as the total amount of bleximenib and

radioactivity excreted into the urine, and will be reported up to day 28
4. Amount Excreted in Feces (Aef) - Aef defined as the total amount of bleximenib and radioactivity excreted into the feces, and will be reported up to day 28
5. Area Under the Concentration-Time Curve from Time 0 to the Last Measurable Concentration (AUC0-t) - AUC0-t in whole blood and plasma will be reported on Cycle 1 Day 1, and Cycle 1 Day 2 (Cycle duration=28 days)
6. Maximum Observed Concentration (Cmax) - Maximum observed concentration in whole blood and plasma will be determined on Cycle 1 Day 1, and Cycle 1 Day 2 (Cycle duration=28 days)

Key secondary outcome(s))
Number of Participants with Adverse Events (AEs) and Serious Adverse Events (SAEs) measured using electronic Case Report Forms (eCRF) up to 58 days

Completion date
13/07/2026

Eligibility

Key inclusion criteria
1. ≥18 years of age and with a body weight of ≥ 40 kg.
2. R/R acute leukaemia harbouring KMT2Ar (eg, gene rearrangement/translocation), NPM1m(eg, Exon 12 frameshift), or nucleoporin (NUP98 or NUP214, eg, gene rearrangement/translocation) alterations and has exhausted, or is ineligible for available therapeutic options.
3. Pretreatment clinical laboratory values meeting the following criteria: White blood cell (WBC) count ≤20 x 109/L; Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤2.5 × upper limit of normal (ULN); Total bilirubin ≤1.5 × ULN; Renal function Estimated or measured glomerular filtration rate ≥60 mL/min per four variable MDRD equation
4. ECOG performance status grade of 0 or 1 (Oken 1982)
5. Regular bowel movements (i.e., average production of at least one stool every 2 days).
6. A woman of childbearing potential must have a negative highly sensitive serum β-human chorionic gonadotropin at screening and within 48 hours prior to the first dose of study treatment.
7. A woman of childbearing potential must agree to all the following during the study and for 6 months after the last dose of study treatment:
7.1. Use a barrier method of contraception
7.2. Use a highly effective, preferably user-independent method of contraception
7.3. Not to donate eggs (ova, oocytes) or freeze for future use for the purposes of assisted reproduction
7.4. Not planning to become pregnant
7.5. Not to breast-feed
8. A male must agree to all the following during the study and for 90 days after the last dose of study treatment:
8.1. Wear a condom when engaging in any activity that allows for the passage of ejaculate to another person.
8.2. Not to donate sperm or freeze for future use for the purpose of reproduction.
8.3. In addition, the participant should be advised of the benefit for a female partner to use a highly effective method of contraception, as a condom may break or leak.
9. Must sign an informed consent form (ICF) indicating participant (or their LAR) understands the purpose of the study and procedures required for the study and is willing to participate in the

study. Consent is to be obtained prior to the initiation of any study-related tests or procedures that are not part of the standard of care for the participant's disease.
10. Willing and able to adhere to the prohibitions and restrictions specified in this protocol.

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. Acute promyelocytic leukemia or diagnosis of Down syndrome associated leukemia, according to WHO 2016 criteria (Arber 2016).
2. Active CNS disease.
3. Recipient of solid organ transplant.
4. Cardiovascular disease that is uncontrolled, increases risk for Torsades de Pointes, or that was diagnosed within 6 months prior to Day1.
5. QTc according to Fridericia's formula (QTcF) for males ≥450 msec or for females ≥470 msec. Participants with a family history of Long QT syndrome are excluded.
6. 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.
7. Pulmonary compromise that requires the need for supplemental oxygen use to maintain adequate oxygenation.
8. Reported temperature >100.4°F/38°C within 48 hours prior to study Day 1.
9. Known allergies, hypersensitivity, or intolerance to bleximenib or its excipients (refer to IB).
10. Exclusion criteria related to stem cell transplant: prior treatment with allogenic bone marrow or stem cell transplant ≤3 months before first dose of study treatment; evidence of graft versus host disease; received donor lymphocyte infusion ≤1 month before first dose of study treatment; requires immunosuppressant therapy (exception: daily doses ≤10 mg prednisone or equivalent are allowed for adrenal replacement).
11. Any prior treatment with a menin-KMT2A inhibitor. (Participants with R/R acute leukemia and prior menin-KMT2Ainhibitor exposure, without prior evidence of DS, may be considered with Sponsor approval with proper washout.)
12. Prior cancer immunotherapy (ie, CAR-T, inotuzumab, gemtuzumab ozogamicin) within 4 weeks prior to enrollment or blinatumomab within 2 weeks prior to enrollment. Additional prior

cancer therapies must not be given within 2 weeks prior to enrollment or 5 half-lives of the agent (whichever is shorter).
13. Administration of: live-attenuated vaccine within 4 weeks before the first dose of study treatment or planned during study treatment; or investigational vaccine within 2 weeks before the first dose of study treatment.
14. Received investigational treatment or used an invasive investigational medical device within 2 weeks before planned first dose of study treatment or is currently receiving active treatment on an investigational study.
15. Major surgery (eg, requiring general anesthesia) within 2 weeks prior to first dose of study treatment or has not recovered from surgery. Must not have major surgery planned during the time the participant is receiving study treatment.
16. Requires prohibited medication that cannot be discontinued or substituted or temporally interrupted during the study.
17. Known to be positive or tests positive at screening for human immunodeficiency virus (HIV), unless viral load is undetectable and CD4 count is above 200 in stable highly active antiretroviral therapy (see Section 6.9.2 for prohibited and restricted medications)
18. Active or chronic hepatitis B virus (HBV) or hepatitis C virus (HCV) infection (as defined below) or clinically active infectious liver disease:
18.1. Positive hepatitis B surface antigen (HBsAg). NOTE: Participants with a prior history of hepatitis B virus (HBV) demonstrated by positive hepatitis B core antibody are eligible if they have at screening 1) a negative HbsAg and 2) a HBV DNA (viral load) below the lower limit of quantification, per local testing. Participants with a positive HBsAg due to recent vaccination are eligible if HBV DNA (viral load) is below the lower limit of quantification, per local testing.
18.2. Positive hepatitis C antibody (anti-hepatitis C virus [HCV]). NOTE: Participants with a prior history of HCV, who have completed antiviral
treatment and have subsequently documented HCV RNA below the lower limit of quantification per local testing are eligible.
19. Any serious underlying medical or psychiatric conditions, such as seizure disorder or psychiatric conditions (e.g., alcohol or drug abuse), dementia, or altered mental status.
20. Active infection that is uncontrolled prior to first dose of study treatment and may interfere with the study objectives or expose the participant to undue risk by participating in the trial; an infection controlled with therapy is allowed.
21. Inability to take an orally administered drug, or medical disorder or prior surgical resection that may affect the absorption of the oral study treatment.
22. Any condition for which, in the opinion of the investigator, participation would not be in the best interest of the participant.
23. Active malignancies (those progressing or requiring treatment change in the last 24 months) other than the disease being treated under study.
24. Diagnosis of Fanconi anemia, Kostmann syndrome, Shwachman Diamond syndrome, or any other known bone marrow failure syndrome.
25. Previous participation in an AME study within 3 months before screening.

Date of first enrolment
10/11/2025

Date of final enrolment
15/06/2026

Locations

Countries of recruitment

United Kingdom

England

Study participating centre
The Christie NHS Foundation Trust
550 Wilmslow Road
Withington
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Sponsor information

Organisation
Janssen-Cilag International 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

IPD sharing plan summary
Not expected to be made available