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A study of bleximenib, venetoclax and azacitidine for treatment of participants with newly diagnosed acute myeloid leukemia (cAMeLot-2)

Submission date 20/03/2025	**Recruitment status** Recruiting	[ ] Prospectively registered [ ] Protocol
Registration date 19/08/2025	**Overall study status** Ongoing	[ ] Statistical analysis plan [ ] Results
Last Edited 01/09/2025	**Condition category** Cancer	[ ] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
Acute myeloid leukemia (AML) is a highly aggressive blood cancer typically characterized by large numbers of immature white blood cells in the bone marrow, and it affects blood cells that fight bacterial infections. Treatment options for AML are limited, survival rates are poor, and many patients are ineligible for standard chemotherapy treatments due to toxicity.
The study drug, bleximenib, specifically targets and blocks the interaction between the proteins histone-lysine N-methyltransferase 2A (KMT2A) and menin. In AML with KMT2A gene rearrangements (KMT2Ar) or NPM1 mutations (NPM1m), blocking this protein-protein interaction kills leukemia cells and helps stop the disease from worsening.
The purpose of this study is to find out how well bleximenib and Venetoclax (VEN)+ Azacitidine (AZA) works as compared to placebo and VEN+AZA for the treatment of participants with KMT2Ar or NPM1m AML.

Who can participate?
Participants with newly diagnosed AML with KMT2A rearrangements or NPM1 mutations who are ineligible for intensive chemotherapy.

What does the study involve?
Study will be conducted in 3 phases:
1. Screening (Up to 28 days): Confirm if the participants can take part in the study.
2. Treatment Phase: Participants will be randomly (by chance) assigned in the following arms:
• Arm A: Bleximenib and Venetoclax (VEN) + Azacitidine (AZA)
• Arm B Placebo and VEN + AZA
Participants will receive treatment until disease progression, unacceptable toxicity, or if any of the discontinuation criteria defined in the protocol are met.
3. Follow-up Phase: Participants will be followed-up for their overall health throughout the study until death, withdrawal of consent, loss to follow-up, or end of the study, whichever occurs first.
During the study, some tests such as blood & urine tests and physical examination will be

performed. Information on side effects will be collected while participants are receiving study treatment and for a period of time after study treatment is discontinued. The overall duration of the study will be approximately 4.5 years.

What are the possible benefits and risks of participating?
There is no established benefit to participants of this study. Based on scientific theory adding bleximenib to VEN+AZA may improve acute myeloid leukaemia outcomes. However, this cannot be guaranteed because bleximenib is still under investigation as a treatment, and it is not known whether the study treatment will work.
If participants are assigned to the placebo treatment group, they will receive VEN+AZA along with placebo during this study.
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 acute myeloid leukaemia in the future.
Participants may have side effects from the drugs or procedures used in this study that may be mild to severe and even life-threatening, and they can vary from person to person.
The potential risks for bleximenib are based on how the drug works, results from laboratory studies, people who have received bleximenib, or general risks for new medicines. These may include:
• Differentiation Syndrome (when there is a large, rapid release of immune substances known as cytokines from leukemia cells after treatment with anticancer drugs)
• Tumour Lysis Syndrome (when large numbers of leukaemia cells die in a short period of time)
• Cytopenias (reduction in blood cells)
• Infections
• Changes to heart rhythm
• Fertility effects
There may also be other potential risks associated with bleximenib.

The participant information sheet and informed consent form, which will be signed by every participant agreeing to participate in the study, includes a detailed section outlining the known risks to participating in the study. Not all possible side effects and risks related to bleximenib are known at this moment. During the study, the sponsor may learn new information about bleximenib. 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. To minimise the risk associated with taking part in the study, participants are frequently reviewed for any side effects and other medical events. Participants are educated to report any such events to their study doctor who will provide appropriate medical care. Any serious side effects that are reported to the sponsor are thoroughly reviewed by a specialist drug safety team. 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 costs).

Where is the study run from?
Janssen-Cilag International NV (Netherlands)

When is the study starting and how long is it expected to run for?
March 2025 to August 2029

Who is funding the study?
Janssen Research and Development, LLC (Netherlands)

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

Contact information

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Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1011871

ClinicalTrials.gov (NCT)
NCT06852222

Protocol serial number
75276617AML3001, CPMS 66634

Study information

Scientific Title
A phase 3 randomized, double-blind, placebo-controlled, study of bleximenib, venetoclax and azacitidine for the treatment of participants with newly diagnosed acute myeloid leukemia harboring KMT2A rearrangements or NPM1 mutations who are ineligible for intensive chemotherapy

Acronym
cAMeLot-2

Study objectives
Primary objective:
To compare the efficacy of bleximenib and Venetoclax (VEN)+ Azacitidine (AZA) as compared to placebo and VEN+AZA treatment.

Secondary objectives:
1. To compare additional measures of the efficacy of bleximenib and VEN+AZA compared to placebo and VEN+AZA.
2. To assess the safety profile.
3. To assess symptoms, functioning, and health-related quality of life.
4. To characterize bleximenib drug levels in the blood.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 14/05/2025, London - Brighton & Sussex Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8140; brightonandsussex.rec@hra.nhs.uk), ref: 25/LO/0274

Study design
Interventional double blind randomized parallel group placebo controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied

Acute myeloid leukemia

Interventions
Experimental: Arm A: Bleximenib (administered orally) and Venetoclax (administered orally) + Azacitidine (administered intravenously or subcutaneously). Participants with acute myeloid leukemia (AML) will receive bleximenib in combination with venetoclax (VEN) and azacitidine (AZA) for 28-days treatment cycle and treatment will continue until progression or unacceptable toxicity.

Placebo Comparator: Arm B: Placebo (administered orally) and Venetoclax (administered orally) + Azacitidine (administered intravenously or subcutaneously). Participants with AML will receive placebo in combination with VEN and AZA for 28-days treatment cycle, and treatment will continue until progression or unacceptable toxicity.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
JNJ-75276617 [bleximenib]

Primary outcome(s)
1. Percentage of Participants who Achieve Complete Remission (CR)
CR is defined as Bone marrow blasts less than (<) 5 percent (%); Absence of circulating blasts; Absence of extramedullary disease; Absolute neutrophil count (ANC) greater than or equal to (>=) 1.0 * 10^9/Liter (1,000/microliter [mcL]); Platelet count >= 100 * 10^9/L (100,000/mcL). [Time Frame: Up to 4 years and 1 month]
2. Overall Survival (OS)
Overall survival time is defined as the time duration from the date of randomization to death due to any cause. [Time Frame: Up to 4 years and 1 month]

Key secondary outcome(s))
1. Event-free survival (EFS). EFS is defined as the time from randomization to treatment failure, relapse, or death due to any cause, whichever occurs first. [Time Frame: Up to 4 years and 1 month]
2. Duration of CR. Duration of CR will be estimated among responders from the date of initial documentation of CR, to the date of first documented evidence of relapse, or death due to any cause, whichever occurs first, respectively. [Time Frame: Up to 4 years and 1 month]
3. Time to CR. Time to CR is defined as time from randomization to first documented response. [Time Frame: Up to 4 years and 1 month]
4. Rate of CR-Measurable Residual Disease (MRD). Rate of CR-MRD is defined as percentage of participants who have achieved CR-MRD. [Time Frame: Up to 4 years and 1 month]
5. Percentage of Participants who Achieved Transfusion Independence. Transfusion independence is defined as lack of requirement for red blood cell (RBC) and platelet transfusions during any 56-day period. [Time Frame: Up to 4 years and 1 month]
6. Percentage of Participants with Allogeneic Hematopoietic Stem Cell Transplant (Allo-HSCT). Allo-HSCT is defined as the percentage of participants who have undergone allo-HSCT after randomization. [Time Frame: Up to 4 years and 1 month]
7. Number of Participants with Adverse Events (AEs). An AE is any untoward medical occurrence

in a participant participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/biological agent under study. Severity will be graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 5.0. Severity scale ranges from Grade 1 (Mild) to Grade 5 (Death). Grade 1= Mild, Grade 2= Moderate, Grade 3= Severe, Grade 4=Life-threatening and Grade 5= Death related to adverse event. [Time Frame: Up to 4 years and 1 month]
8. Number of Participants with Abnormalities in Clinical Laboratory Parameters. Participants with abnormalities in clinical laboratory parameters will be reported. [Time Frame: Up to 4 years and 1 month]
9. Serum Concentration of Bleximenib. Serum samples will be analyzed to determine concentrations of bleximenib. [Time Frame: Up to 4 years and 1 month]

Completion date
27/08/2029

Eligibility

Key inclusion criteria
1. Be 18 years of age or older at the time of informed consent.
2. Previously untreated lysine N-methyltransferase 2A gene rearranged (KMT2Ar) or nucleophosmin 1 gene mutated (NPM1m) acute myeloid leukemia (AML) with greater than or equal to (≥) 10% bone marrow blasts per 2022 international Consensus Classification criteria.
3. Ineligible for intensive chemotherapy based on the criteria defined in the protocol.
4. Participants must have adequate hepatic and renal function.
5. A female participant must agree not to be pregnant, breast-feed, plan to become pregnant and use protocol-specified contraception while enrolled in this study and for 6 months after the last dose of study treatment.
6. A male participant must agree to use protocol-specified contraception while enrolled in this study and for 6 months after the last dose of study treatment.
7. Must sign an informed consent form indicating that the participant understands the purpose of, and procedures required for, the study and is willing to participate in the study.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Diagnosis of acute promyelocytic leukemia (APL).
2. Known active leukemic involvement of the central nervous system (CNS).

3. Recipient of solid organ transplant.
4. Any cardiac disorders such as:
4.1. Heart attack.
4.2. Uncontrolled/unstable chest pain.
4.3. Congestive heart failure.
4.4. Uncontrolled or symptomatic irregular heartbeat.
4.5. Blockage of a blood vessel to the brain.
4.6. Transient ischemic (decreased oxygen in tissue) attack within 6 months of randomization.
5. Active infectious hepatitis.
6. Live, attenuated vaccine within 4 weeks of randomization.
7. Known allergies, hypersensitivity, or intolerance of bleximenib excipients.

Date of first enrolment
14/04/2025

Date of final enrolment
19/09/2027

Locations

Countries of recruitment
United Kingdom

England

Scotland

Australia

Austria

Belgium

Brazil

Canada

China

Denmark

France

Germany

Greece

Hungary

Israel

Italy

Japan

Mexico

Poland

Portugal

Spain

Taiwan

Study participating centre
Western General Hospital
Crewe Road South
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Study participating centre
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CT1 3NG

Study participating centre
Royal Sussex County Hospital
Eastern Road
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BN2 5BE

Study participating centre
Colchester
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Turner Road
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65 Pembroke PLACE
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Sponsor information

Organisation
Janssen-Cilag International NV

Funder(s)

Funder type
Industry

Funder Name
Janssen Research and Development, LLC

Results and Publications

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Data sharing statement to be made available at a later date