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A study of JNJ-89853413 for relapsed or refractory acute myeloid leukemia or myelodysplastic neoplasms

Submission date 11/10/2024	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 04/12/2024	**Overall study status** Ongoing	
Last Edited 11/02/2025	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
Acute leukemias are characterized by uncontrolled proliferation of immature white blood cells (WBCs) in bone marrow (soft, fatty tissue inside of bone cavities), peripheral blood and/or other sites in the body. Acute myeloid leukemia (AML) and myelodysplastic neoplasms (MDS) are cancers in which abnormal myeloid cells, called blasts, grow uncontrollably, instead of developing into cells that fight infections and help to heal. JNJ-89853413 (CD33xVδ2) is a bispecific antibody, a type of protein that binds to other proteins and fights off an infection, that binds CD33 protein on AML and MDS blast cells and the Vδ2 chain on Vγ9Vδ2 T-cells. The goal of binding these two cells together is that the T-cells will selectively kill cancer cells. In this study, researchers want to determine the safety and tolerability of JNJ-89853413 and to identify safe doses in participants with relapsed or refractory (R/R) AML or R/R higher-risk types of MDS.

Who can participate?
Participants aged 18 years or older or those who are at least the age of majority diagnosed with R/R AML or R/R higher-risk types of MDS.

What does the study involve?
The study will be conducted in 2 parts:
Part 1 (Dose Escalation): In part 1, participants will get JNJ-89853413 with increasing doses. The goal of increasing the dose is to study the safety of each dose and to establish a safe dose for further evaluation in part 2.
Part 2 (Cohort Expansion): Participants will get treatment at the recommended dose and schedule of JNJ-89853413 established in Part 1.
The study will consist of a screening period followed by a treatment period. During the treatment period, participants will be treated with JNJ-89853413 until the worsening of AML /MDS, serious side effects, or withdrawal from the study. After discontinuation of treatment, participants will be followed to monitor their health.

Safety assessments include blood tests, vital sign measurements, and physical exams. Blood samples will be taken at multiple timepoints to understand how the body responds to treatment.

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 AML or MDS in the future.

This is a first-in-human study which means that JNJ-89853413 has not been given to people before. The expected risks for JNJ-89853413, based on how the drug works and results from laboratory studies are unknown.

Possible risks are predicted based on data from other bispecific antibodies and include cytokine release syndrome (CRS), neurologic problems (immune effector cell-associated neurotoxicity syndrome [ICANS]), tumour lysis syndrome (metabolic abnormalities that can occur as a complication from the treatment of cancer), infusion-related reactions (IRRs), allergic reactions, infections, decreases in neutrophil counts, and liver injury. It is unknown whether these side effects will be seen with JNJ-89853413.

The participant information sheet and informed consent form, which will be signed by every participant agreeing to take part in the study, includes a detailed section outlining the 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 risk associated with taking part, participants are frequently reviewed for any side effects and other medical events. If they have any side effects, are worried about them, or have any new or unusual symptoms, participants will be encouraged to talk with their study doctor. The study doctor will also be looking out for side effects and will provide appropriate medical care. 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 procedure. 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?
Janssen-Cilag International

When is the study starting and how long is it expected to run for?
October 2024 to July 2027

Who is funding the study?
Janssen Research and Development

Who is the main contact?
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Contact information

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Public

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ClinicalTrials.gov (NCT)
NCT06618001

Clinical Trials Information System (CTIS)
2024-513199-16

Integrated Research Application System (IRAS)
1010815

Central Portfolio Management System (CPMS)
64352

Protocol serial number
89853413AML1001

Study information

Scientific Title
A phase I, first-in-human, dose escalation study of JNJ-89853413 for relapsed or refractory acute myeloid leukemia or myelodysplastic neoplasms

Study objectives
Main objectives
- Part 1 (Dose Escalation) & Part 2 (Cohort Expansion): To determine the safety across tested dose regimens and the safer effective dose (recommended phase 2 dose [RP2D]) of JNJ-89853413.

Secondary objectives
- To assess the Pharmacokinetic (PK) (what the body does to the drug) and immunogenicity (immune response against the drug) of JNJ-89853413.
- To evaluate the preliminary clinical activity of JNJ-89853413 in participants with relapsed /refractory* (R/R) acute myeloid leukemia (AML) or relapsed/refractory higher-risk types of myelodysplastic neoplasms (MDS).
*Cancer is called relapsed if it returns after treatment and is refractory if it does not respond to treatment.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 29/12/2024, South Central - Oxford C Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 1048144, 207 104 8089, 2071048063; oxfordc.rec@hra.nhs.uk), ref: 24/SC/0351

Study design
Phase I first-in-human dose-escalation study

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Medical condition: Relapsed or Refractory Acute Myeloid Leukemia or Relapsed or Refractory Higher-risk Types of Myelodysplastic Neoplasms
Medical condition in lay language: Acute myeloid leukemia (AML) & Myelodysplastic neoplasms (MDS) are cancers in which abnormal myeloid cells, called blasts, grow uncontrollably, instead of developing into cells that fight infections and help to heal.

Interventions

Participants will receive JNJ-89853413 in Part 1 (Dose escalation) of the study and the dose levels will be escalated sequentially based on the decisions of the Study Evaluation Team (SET) until the recommended Phase 2 Dose (RP2D) has been identified.

Participants in Part 2 (Dose expansion) will receive JNJ-89853413 at the RP2D determined in Part 1.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
JNJ-89853413 [JNJ-89853413]

Primary outcome(s)
1. The number of adverse events by severity measured using data recorded in case report forms from screening until 30 days after the last dose of the study drug (that is approximately 2.5 years)
2. In Part 1 of the study: the number of participants with Dose-Limiting Toxicity (DLTs) measured using data recorded in case report forms within 14 days

Key secondary outcome(s))
The following secondary outcome measures are measured over approximately 2.5 years:
1. Serum concentration of JNJ-89853413 measured using an immunoassay method
2. Area under the plasma concentration-time (AUC[t]) curve of JNJ-89853413 measured using pharmacokinetic methods
3. Maximum serum concentration (Cmax) of JNJ-89853413 measured using pharmacokinetic methods
4. The trough observed serum concentration (Ctrough) of JNJ-89853413 measured using pharmacokinetic methods
5. The number of participants with the presence of anti-drug antibodies of JNJ-89853413 measured using a bridging electrochemiluminescence (ECL) enzyme-linked immune assay
6. Complete response (CR) in acute myeloid leukaemia (AML) CR is achieved when a participant has a best response of CR (complete response with partial hematologic recovery [CRh] or complete response with incomplete hematologic recovery [CRi]), measured according to the European Leukaemia Network (ENL) 2022 criteria
7. The number of trial participants with overall response (OR) in Myelodysplastic Neoplasms (MDS). OR is achieved when a participant with MDS has a CR (any type, that is CRh or complete response with limited count recovery [CRL]), partial response (PR), or hematologic improvement (HI), measured according to the International Working Group (IWG) 2023 criteria
8. The number of trial participants with complete response (CR) in MDS. CR is achieved when a participant has a best response of CR (including CRh/CRL), measured according to the IWG 2023 criteria
9. The duration of response (DOR) for trial participants. DOR is defined for responders only, as time from the date of initial documentation of a response to the first documented evidence of no response, disease progression, relapse, initiation of a new systemic anti-cancer therapy (besides hematopoietic stem cell transplant [HSCT]), or death, whichever comes first
10. The trial participants time to response (TTR). TTR is defined for responders only, as the time from the first dose of the study drug to the first qualifying response

11. The number of participants achieving transfusion independence. Transfusion independence is defined as the absence of red blood cell (RBC) and platelet transfusions for 8 weeks or longer after starting study treatment for participants with AML and 16 weeks or longer for participants with MDS

Completion date
15/07/2027

Eligibility

Key inclusion criteria
1. Have a diagnosis, per World Health Organization (WHO) 2022 criteria of:
1.1. Relapsed/refractory acute myeloid leukemia (AML)
1.2. Relapsed/refractory moderate-high, high, or very high-risk myelodysplastic neoplasms (MDS) per Molecular International Prognostic Scoring System (IPSS-M)
2. Body weight greater than or equals to (>=) 40 kilograms (kg)
3. Have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 - 2
4. Have adequate renal function defined as Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) Estimated Glomerular Filtration Rate (eGFR) >=40 milligrams per minute (mL/min)
5. Participants must have laboratory parameters in the required range

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Has a medical history of clinically significant pulmonary compromise, particularly the need for current supplemental oxygen use to maintain adequate oxygenation
2. Has evidence of an uncontrolled systemic viral, bacterial, or fungal infection
3. Has known allergies, hypersensitivity, or intolerance to the excipients of JNJ-89853413
4. Had major surgery or had significant traumatic injury within 14 days of the planned first dose of JNJ-89853413
5. Has known active central nervous system involvement

Date of first enrolment
02/01/2025

Date of final enrolment
28/08/2026

Locations

Countries of recruitment
United Kingdom

England

Canada

Spain

Study participating centre
University College London Hospital
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Study participating centre
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Study participating centre
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Sponsor information

Organisation
Janssen (Netherlands)

ROR
https://ror.org/04cxegr21

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 datasets generated during and/or analysed during the current study are/will be available upon request. 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 the Yale Open Data Access (YODA) Project site at yoda.yale.edu.

IPD sharing plan summary
Available on request