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A study of JNJ-88549968 for the treatment of calreticulin (CALR)-mutated myeloproliferative neoplasms

Submission date
10/10/2023

Recruitment status
Recruiting

Registration date
15/12/2023

Overall study status
Ongoing

Last Edited
24/06/2025

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
Myeloproliferative neoplasms (MPNs) are rare blood cancers causing abnormal blood cell growth in bone marrow. Essential thrombocythemia (ET) is an MPN where excessive platelet production increases clotting and bleeding risk, as well as a risk of marrow fibrosis (injury /damage) and even leukaemia. Myelofibrosis (MF) involves bone marrow fibrosis (injury /damage), low blood counts and an enlarged spleen. MPNs may cause complications like blood clots and heart attacks due to blood cell overproduction as well as an increased risk of infection because the blood cells do not work properly. Both ET and MF may transform into a serious, uncontrolled condition called leukaemia. Drug JNJ-88549968 is a T-cell redirecting antibody* that targets CD3 antigen on T lymphocytes (immune cells) and mutant forms of calreticulin (CALRmut) found on MPN-associated cancer cells. The drug links cancer cells and T lymphocytes of the immune system, with the intention to clear the cancer cells from the body.*Antibody is a type of protein produced by the body's immune system that can recognize and bind to antigens (specific targets) in the body. The study aims to find the recommended phase II dose (RP2D) and dosing schedule for drug JNJ-88549968 in Part 1 and further test the safety of JNJ-88549968 at RP2D in Part 2.

Who can participate?
Patients with CALRmut MPN are diagnosed as either ET or MF

What does the study involve?
The study comprises 2 parts:
Part 1: Participants will receive JNJ-88549968 to find the optimal drug dose (RP2D) and schedule. This will be determined by assessing its safety, how the body processes it, how it affects the body and its initial effectiveness in different dosing regimens. Part 2: Participants will receive JNJ-88549968 at the RP2D regimen(s) determined in Part 1. Safety and effectiveness data will be regularly reviewed. Safety assessments will include physical examination, vital signs, clinical laboratory tests, ECOG performance status, electrocardiograms, AE monitoring and DLTs Total study duration will be up to approximately 2 years.

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 CALR-mutated MPN in the future.

This is a first-in-human study which means that JNJ-88549968 has not been given to people before.

The expected risks for JNJ-88549968, based on how the drug works and results from laboratory studies are listed as thrombocytopenia, infection, tumour lysis syndrome (TLS), cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), injection site reactions (ISR), systemic administration-related reactions (sARRs), immune-related adverse events (irAEs).

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 and 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?
Guy's Hospital (UK)

When is the study starting and how long is it expected to run for?
October 2023 to December 2026

Who is funding the study?
Janssen Research and Development (USA)

Who is the main contact?
Ms Florence Baluwa, Janssen Research and Development, JanssenUKRegistryQueries@its.jnj.com (UK)

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Public, Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1008190

ClinicalTrials.gov (NCT)
NCT06150157

Protocol serial number
88549968MPN1001, IRAS 1008190, CPMS 57124

Study information

Scientific Title
A first-in-human study of the safety, pharmacokinetics, and pharmacodynamics of JNJ-88549968, a T-cell redirecting bispecific antibody for CALR-mutated myeloproliferative neoplasms

Study objectives
• Part 1 (Dose Escalation): The study aims to find the safest and most effective dose (Recommended Phase 2 Dose [RP2D]) and dosing schedule for drug JNJ-88549968.
• Part 2 (Cohort Expansion): The study will further test the safety of drug JNJ-88549968 at most effective dose levels determined in Part 1.

• To examine how drug JNJ-88549968 is absorbed, used and eliminated by the body (pharmacokinetics).
• To examine the body's immune system response to the drug JNJ-88549968.
• To evaluate effectiveness of drug JNJ-88549968 in participants with diseases essential thrombocythemia (ET) in which the bone marrow produces too many platelets or myelofibrosis (MF) which is a type of bone marrow disorder that disrupts the normal production of blood cells.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 08/12/2023, East of England - Cambridgeshire and Hertfordshire Research Ethics Committee (2 Redman Place, Stratford, London, EC20 1JQ, United Kingdom; +44 (0)2071048096, (0)207 104 8061, (0)207 104 8269; cambsandherts.rec@hra.nhs.uk), ref: 23/EE/0239

Study design
Open-label first-in-human study

Primary study design
Interventional

Study type(s)
Diagnostic, Safety, Efficacy

Health condition(s) or problem(s) studied
Calreticulin (CALR)-mutated myeloproliferative neoplasms

Interventions
JNJ-88549968 is the study drug. JNJ-88549968 will be administered in the following:
Part 1: Dose Escalation-Participants will receive JNJ-88549968. The dose will be escalated sequentially to determine the recommended phase 2 dose (RP2D) and optimal dosing schedule (s) based on safety, pharmacokinetic, pharmacodynamic, and preliminary assessment of efficacy across several dose regimens.
Part 2: Cohort Expansion: Essential Thrombocythemia (ET)- Participants will receive JNJ-

88549968 at the RP2D regimen(s) determined in Part 1.
Part 2: Cohort Expansion: Myelofibrosis (MF)- Participants will receive JNJ-88549968 at the RP2D regimen(s) determined in Part 1.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
JNJ-88549968 [JNJ-88549968]

Primary outcome(s)
1. Part 1: Number of Participants With Dose Limiting Toxicity (DLT) approximately up to 35 days after the first dose of study treatment. DLTs are specific adverse events and are defined as any of the following: high-grade non-hematologic toxicity, or hematologic toxicity
2. Part 1 and 2: Number of Participants with Adverse Events (AEs). AEs- up to 2 years. 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 under study
3. Part 1 and 2: Number of Participants with Adverse Events (AEs) by Severity. Severity- up to 2 years, according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 5. The 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. Cytokine release syndrome (CRS) and associated neurologic toxicity events immune effector cell-associated neurotoxicity syndrome events [ICANS]) graded according to American Society for Transplantation and Cellular Therapy (ASTCT) guidelines.

Key secondary outcome(s))
1. Part 1 and 2: Serum Concentration of JNJ-88549968 evaluated up to 2 years serum will be analysed to determine concentrations of JNJ-88549968
2. Part 1 and 2: The number of participants with the presence of anti-drug antibodies to JNJ-88549968 will be evaluated for up to 2 years
3. Part 1 and 2: Overall Response Rate (defined as the percentage of participants who achieve partial response (PR) and complete response (CR)) will be evaluated for up to 2 years - according to the modified International Working Group-Myeloproliferative Neoplasm Research and Treatment (IWG-MRT) criteria and the modified European Leukemia Net (ELN) consensus report
4. Part 1 and 2: CR rate (defined as the percentage of participants who achieve the best response to CR according to disease) evaluated for up to 2 years according to modified IWG-MRT and modified ELN consensus report
5. Part 1 and 2: Time to Response (TTR) (defined for participants who achieved PR or CR as the time from the first dose of study treatment to the first response of PR or CR) evaluated for up to 2 years, according to modified IWG-MRT and modified ELN consensus report
6. Part 1 and 2: Duration of Response (DOR) (defined for participants who achieved PR or CR as the time between the date of initial documentation of PR or CR to the date of first documented evidence of disease progression) evaluated up to 2 years, according to modified IWG-MRT and modified ELN consensus report.
7. Part 2: Change from baseline in myeloproliferative neoplasm (MPN) symptom burden evaluated from baseline up to 2 years and MPN symptom burden assessed using patient-reported outcome (PRO) questionnaire will be reported in this outcome measure

Completion date
31/12/2026

Eligibility

Key inclusion criteria
Each potential participant must satisfy all of the following criteria to be enrolled in the study:
1. Be greater than or equal to (>=) 18 years of age (or the legal age of majority in the jurisdiction in which the study is taking place, whichever the greater) at the time of informed consent
2. Positive for a calreticulin (CALR) driver mutation of essential thrombocythemia (ET) or myelofibrosis (MF)
3. Have received prior therapy(ies): ET: At least 2 lines of prior cytoreductive therapy, at least 1 of which must have been hydroxyurea (HU); MF: At least 1 prior JAK inhibitor (JAKi) therapy unless ineligible
4. Have an Eastern Cooperative Oncology Group (ECOG) performance status grade of less than or equal to (<=) 2
5. Have the following clinical hematology laboratory values pre-dose:
5.1. Hemoglobin >=8.0 grams per deciliter (g/dL)
5.2. Neutrophils >=0.75*10^9 per liter (/L) without the assistance of granulocyte growth factors within 4 weeks of the first dose of the study drug
5.3. Platelets >=50*10^9/L without the assistance of thrombopoietic factors or transfusions

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Sex
All

Key exclusion criteria
Any potential participant who meets any of the following criteria will be excluded from participating in the study:
1. Known allergies, hypersensitivity, or intolerance to the excipients of the study treatment
2. Concurrent or recently diagnosed or treated malignancies present at the time of participant screening. Exceptions are squamous and basal cell carcinoma of the skin, carcinoma in situ of the cervix, and any malignancy that is considered cured or has minimal risk of recurrence within 1 year of the first dose of study treatment in the opinion of both the investigator and sponsor’s medical monitor. Participants cured of another malignant disease with no sign of relapse greater than or equal to (>=) 3 years after treatment ended are allowed to enter the study
3. Prior solid organ transplantation- Either of the following regarding hematopoietic stem cell transplantation:
3.1. Prior treatment with allogenic stem cell transplant less than or equal to (<=) 6 months

before the first dose of JNJ-88549968 or
3.2. Evidence of graft versus host disease (GVHD) that requires immunosuppressant therapy
4. History of clinically significant cardiovascular disease within 6 months prior to the first dose of study treatment

Date of first enrolment
11/12/2023

Date of final enrolment
12/05/2026

Locations

Countries of recruitment
United Kingdom

Canada

France

Germany

Spain

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
Janssen Research & Development, LLC

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 the Yale Open Data Access (YODA) Project site at https://yoda.yale.edu/.

IPD sharing plan summary
Available on request