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A phase 1b/2 study of JNJ-90014496 in Adult Participants with B-Cell non-Hodgkin lymphoma

Submission date
19/01/2024

Recruitment status
Recruiting

Registration date
18/04/2024

Overall study status
Ongoing

Last Edited
31/03/2026

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
B-NHL is a specific type of cancer of white blood cell (WBC) called B-lymphocytes. Treatments are available, but it can come back after or can be resistant to standard treatment. There is need for continued development of safe & effective treatments.

Prizlo-cel is a chimeric antigen receptor (CAR) T-cell therapy that targets CD19 & CD20 proteins for treatment of B-NHL or frontline high-risk DLBCL.

The study aims to assess safety & to determine effective doses of prizlo-cel that can be safely given (Phase 1b). Secondly, study aims to determine the effectiveness.

Who can participate?
Adults with relapsed or refractory (r/r) mature aggressive large B-NHL, follicular lymphoma or marginal zone lymphoma or frontline high-risk DLBCL after standard treatment.

What does the study involve?
This study has 2 Phases:
Phase 1b:
- Run In: Prizlo-cel infusion in vein.
- Dose Expansion: Prizlo-cel will be given at the effective dose from Run-In.
Phase 2: Prizlo-cel will be given on Day 1 at dose determined in Phase 1.

Both Phases include:
• Screening (28 days)
• Apheresis/Enrolment: Collect specific WBCs.
• Bridging therapy: Stabilize disease during prizlo-cel production.
• Lymphodepletion: Cyclophosphamide & fludarabine treatment for 3 days.
• Prizlo-cel infusion
• Post-infusion follow-up (FU) (90 days): Assessment for health & drug’s effect on tumor & body.
• Post-treatment FU (every 3 months until EOS or PD): FU for health & drug's effect on tumor.

• Post-treatment FU (every 6 months until EOS): After disease has progressed FU for how long you live until EOS.
• Long-term FU

The study includes laboratory tests, neurological assessments & tumor biopsy. All side effects will be recorded 2 years after last participant is dosed. Afterward, participants may enroll in a 15 years long-term FU study.

What are the possible benefits and risks of participating?
The information obtained from the study may help people with relapsed or refractory B-cell non-Hodgkin lymphomas like follicular lymphoma, marginal zone lymphoma, & Large B-cell lymphoma (LBCL).

This is a phase 1b/2 study. The possible risks for Prizlo-cel are Cytokine release syndrome, Immune Effector Cell-Associated Hemophagocytic Lymphohistiocytosis like Syndrome, Neurologic Toxicities, Cytopenias, Serious Infection, including Viral Reactivation, Hypogammaglobulinemia, Tumor Lysis Syndrome, Hypersensitivity reaction, Pneumonitis, & Subsequent primary malignancy (SPM).

The participant information sheet & informed consent form, which will be signed by every participant agreeing to take part in the study, includes a detailed section outlining the risks with participating in the study. Participants may have none, some, or all the possible side effects listed, & they may be mild, moderate, or severe. To minimize the risk associated with study participation, participants are frequently revaluated for any side effects. If they have any side effects or are worried about them, or have any new or unusual symptoms, participants are encouraged to talk with their study doctor. The study doctor will also be looking out for side effects & will provide appropriate medical care. There may also be side effects that the researchers do not expect or do not know about & that may be serious. Many side effects go away shortly after the intervention ends. However, side effects can sometimes be serious, long-lasting, or permanent. If a severe side effect or reaction occurs, the study doctor will discuss the best way of managing the side effect with the participant. There is always a chance that an unexpected or serious side effect may happen.

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

When is the study starting and how long is it expected to run for?
January 2024 to March 2029

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

Who is the main contact?
Principal Investigator Maeve O'Reilly, maeve.o'reilly@nhs.net

Contact information

Type(s)
Principal investigator

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT05421663

Clinical Trials Information System (CTIS)
2023-506267-33

Integrated Research Application System (IRAS)
1008775

Central Portfolio Management System (CPMS)
58328

Protocol serial number
90014496LYM1001

Study information

Scientific Title
A phase 1b/2 multicenter, open-label, study of JNJ-90014496, an autologous CD19/CD20 Bi-specific CAR-T cell therapy in adult participants with B-cell Non-Hodgkin lymphoma

Study objectives
• To check if JNJ-90014496 is safe and well-tolerated.
• To find the most effective dose (recommended phase 2 dose [RP2D]) of JNJ-90014496.

• To examine JNJ-90014496 in participants with B-cell non-Hodgkin lymphoma cancer that is relapsed (reoccurrence) after or resistant to standard therapies, to check how many people respond well overall (overall response rate), how quickly they respond (time to response) and how long the positive response lasts (duration of response).
• To examine how JNJ-90014496 is absorbed, processed, and eliminated by the body (pharmacokinetic) over time.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 01/03/2024, North East - York Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8079; york.rec@hra.nhs.uk), ref: 24/NE/0006

Study design
Phase Ib/2 multicenter open-label study

Primary study design
Interventional

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Non-Hodgkin lymphoid malignancies

Interventions
This is an open-label, single-drug administration study.
Up to 12 adult participants with r/r aggressive B-cell NHL may be enrolled into a Run-In dose level.
After completion of the Run-In, an aggressive lymphoma and an indolent lymphoma Dose Expansion cohort may open. Up to approx. 40 participants may be enrolled in each Dose Expansion cohort, allowing for up to approx. 92 participants to be enrolled in total.
For both the Run-In and Dose Expansion, the study periods and durations for participants are:

• Screening: <28 days before apheresis
• Apheresis/Enrollment
• Bridging therapy: For participants at high risk of experiencing disease progression during the manufacture of the JNJ-90014496 drug product and before lymphodepletion, a bridging therapy is allowed at the investigator's discretion and the Sponsor's approval.
• Lymphodepletion: Day -5 to Day -3 (window to begin lymphodepletion: Day -7 to Day -5)
• JNJ-90014496 single infusion: Day 1
• Post-infusion follow-up: Beginning after JNJ-90014496 infusion (DLT period: Days 1 to 29) and continuing up to Day 90
• Post-treatment follow-up: Beginning after post-infusion follow-up and continuing 2 years post-infusion
• Long-term follow-up: beginning after post-treatment follow-up

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
JNJ-90014496

Primary outcome(s)
Occurrence of AEs and abnormal laboratory results, including dose limiting toxicities (DLTs) for up to 24 months

Key secondary outcome(s))
1. Overall Response (OR), which includes Partial Response (PR) and Complete Response (CR), for up to 24 months
2. Time to response (TTR), defined as the time from the date of JNJ-90014496 infusion to the first documented CR or PR for up to 24 months
3. Duration of response (DOR), defined as the time from the first documented CR or PR to relapse or death (whichever occurs first) for up to 24 months
4. Amount of JNJ-90014496 in blood over time for up to 24 months

Completion date
29/03/2029

Eligibility

Key inclusion criteria
Current key inclusion criteria as of 31/03/2026:

1. Participant must be greater than or equal to (>=) 18 years of age, at the time of signing informed consent
2. Tumor must be histologically confirmed cluster of differentiation (CD)19 and/or CD20 positive
3. Must meet the indications for each subtype in Phase 1b as specified in protocol and Phase 2 participants must have following:
- Diagnosis of Large B-cell lymphoma (LBCL), Follicular large B-cell lymphoma (FLBCL), or transformation of indolent lymphoma;
- Received at least 2 prior lines of systemic therapy;

- Relapsed or refractory disease defined as 1 or more of the following: Stable disease or Progressive disease (PD) as best response to most recent anti-lymphoma therapy OR disease progression or recurrence after a partial response (PR) or complete response (CR) to most recent anti lymphoma therapy;
- cohort specific requirements as mentioned in protocol.
4. Measurable disease as defined by Lugano 2014 classification
5. Eastern Cooperative Oncology Group (ECOG) performance status of either 0 to 2

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Previous key inclusion criteria:

1. Participant must be greater than or equal to (>=) 18 years of age, at the time of signing informed consent
2. All participants must have relapsed or refractory disease for each histologic subtype - Mature aggressive large B cell NHL and Follicular Lymphoma Grade 3b: Participants must have >= 2 lines of systemic therapy or >=1 line of systemic therapy in case of participants ineligible for high-dose chemotherapy and autologous Hematopoietic stem cell transplantation (HSCT). Participants also must have had exposure to an anthracycline and an anti-CD20 targeted agent- Follicular lymphoma Grade 1-3a and Marginal Zone Lymphoma: Participants must have >=2 prior lines of anti-neoplastic systemic therapy. Participants also must have prior exposure to an anti-CD20 monoclonal antibody
3. Tumor must be cluster of differentiation (CD) 20 positive
4. Measurable disease as defined by Lugano 2014 classification
5. Eastern Cooperative Oncology Group (ECOG) performance status of either 0 or 1

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
150 years

Sex
All

Total final enrolment
0

Key exclusion criteria
Current key exclusion criteria as of 31/03/2026:

1. History of symptomatic deep vein thrombosis or pulmonary embolism within six months of apheresis (line associated deep vein thrombosis is allowed)
2. History of stroke, unstable angina, myocardial infarction, congestive heart failure New York Heart Association (NYHA) class III or IV, severe cardiomyopathy or ventricular arrhythmia requiring medication or mechanical control within six months of apheresis
3. History of a seizure disorder, dementia, cerebellar disease or neurodegenerative disorder
4. Known history or prior diagnosis of optic neuritis or other immunologic or inflammatory disease affecting the central nervous system
5. Current active liver or biliary disease (except for Gilbert's syndrome or asymptomatic gallstones)
6. Evidence of active viral or bacterial infection requiring systemic antimicrobial therapy, or uncontrolled systemic fungal infection
7. Diagnosis of Human herpesvirus 8 positive DLBCL or T cell or histiocyte rich large B cell lymphoma or Burkitt and high grade B cell lymphoma with 11q aberrations (previously Burkitt like lymphoma) or Richter's transformation or lymphomatoid granulomatosis or plasmablastic lymphoma or Waldenstrom's macroglobulinaemia
8. Any prior solid organ or allogeneic stem cell transplantation
9. Autologous stem cell transplant within 12 weeks of apheresis; prior CAR T cell therapy within 12 weeks of apheresis

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Previous key exclusion criteria:

1. Diagnosis of Human herpes virus (HHV) 8-positive Diffuse large B Cell lymphoma (DLBCL)
2. Prior allogeneic Hematopoietic stem cell transplantation (HSCT)
3. Autologous stem cell transplant within 12 weeks of chimeric antigen receptor (CAR) T cell infusion
4. Uncontrolled active infections
5. History of deep vein thrombosis or pulmonary embolism within six months of infusion (except for line associated deep vein thrombosis [DVT])
6. History of stroke, unstable angina, myocardial infarction, congestive heart failure (New York Heart Association [NYHA] Class III or IV), severe cardiomyopathy or ventricular arrhythmia requiring medication or mechanical control within 6 months of screening
7. History of a seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease or neurodegenerative disorder
8. Known history or prior diagnosis of optic neuritis or other immunologic or inflammatory disease affecting the central nervous system
9. Active central nervous system (CNS) involvement by malignancy
10. Current active liver or biliary disease (except for Gilbert’s syndrome or asymptomatic gallstones)

Date of first enrolment
25/04/2024

Date of final enrolment
26/03/2027

Locations

Countries of recruitment

United Kingdom

Australia

Canada

Denmark

France

Germany

Netherlands

Spain

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
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Study participating centre
The Christie NHS Foundation Trust
550 Wilmslow Road
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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