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A study of JNJ-90014496 in relapsed or refractory B-Cell non-Hodgkin lymphoma (r/r B-NHL)

Submission date
19/01/2024

Recruitment status
Recruiting

Registration date
18/04/2024

Overall study status
Ongoing

Last Edited
03/12/2024

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-cell non-Hodgkin lymphoma (NHL) is a cancer that starts in a specific type of white blood cell called B lymphocytes. The symptoms include lymph nodes (part of the body's immune system) that are larger than normal, fever, and weight loss. Although treatments are available, it can come back after treatment (relapse) or can be resistant to standard treatment (refractory). There is a need for the continued development of safe and effective treatments. The study treatment, JNJ-90014496, is made by using a type of white blood cells (T-cells) from the participant. These cells are changed in the laboratory so that they attack cancer cells when they are put back into the participant's blood. The purpose of this study is to see if JNJ-90014496 can be used in future studies for the treatment of B-cell NHL in adults. During the study, side effects caused by the study drug will be followed closely, as well as how long the study drug stays in the body and how the body responds to it.

Who can participate?
Adults with recurrent/resistant aggressive B-cell non-Hodgkin lymphomas (r/r B-NHL), follicular lymphoma or marginal zone lymphoma after standard treatment.

What does the study involve?
This study will be conducted in 2 parts which consist of run-in and dose expansion phases.
Run In: The participants will undergo lymphodepletion and then receive JNJ-90014496 through intravenous infusion on Day 1.
Expansion: Participants will receive JNJ-90014496 infusion at the recommended phase 2 dose(s) confirmed after the run-in.

Participants will be monitored for their long-term follow-up period after the post-treatment follow-up. Participants will undergo study assessments and tests, such as blood tests, and vital signs. Scans of the participants' bodies will also be done to monitor disease status.

What are the possible benefits and risks of participating?
Participants may experience some benefit from participation in the study. The information

learned from the study may help people with r/r B-NHL, follicular lymphoma or marginal zone lymphoma in the future.

This is a phase Ib dose confirmation study. The expected risks for JNJ-90014496, based on how the drug works and results from laboratory studies 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, and subsequent primary malignancy.

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 NV

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

Who is funding the study?
Janssen Research and Development

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

Contact information

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Additional identifiers

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IRAS number
1008775

ClinicalTrials.gov number
NCT05421663

Secondary identifying numbers
90014496LYM1001, IRAS 1008775, CPMS 58328

Study information

Scientific Title

A phase Ib multicenter, open-label, study of JNJ-90014496, an autologous CD19/CD20 Bi-specific CAR-T cell therapy in adult participants with relapsed or refractory 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 multicenter open-label study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Safety, Efficacy

Participant information sheet

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

Pharmaceutical study type(s)
Pharmacokinetic, Pharmacodynamic, Dose response, Therapy

Phase
Phase I

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

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

Secondary outcome measures
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

Overall study start date
17/01/2024

Completion date
28/10/2027

Eligibility

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

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
92

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
30/12/2026

Locations

Countries of recruitment
Australia

Canada

Denmark

France

Germany

Netherlands

Spain

United Kingdom

Study participating centre
University College London Hospitals NHS Foundation Trust
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Study participating centre
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Janssen-Cilag International NV

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Sponsor type
Industry

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

Publication and dissemination plan
Peer reviewed scientific journals
Internal report
Conference presentation
Submission to regulatory authorities
Results of the study will be available to the wider scientific community via publication in scientific journals and presentation at scientific meetings. Study results summary will also be published in the ISRCTN Registry and may be available on the HRA website's Research Summaries page.

Intention to publish date
28/10/2028

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are not expected to be made available due to commercial confidentiality.

IPD sharing plan summary

Not expected to be made available