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A study of JNJ-80948543 in combination with other CD3 T-cell engagers in participants with relapsed/refractory B-cell non-Hodgkin lymphoma (R/R B-Cell NHL)

Submission date
09/08/2024

Recruitment status
Recruiting

Registration date
25/10/2024

Overall study status
Ongoing

Last Edited
19/11/2024

Condition category
Cancer

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Refractory or relapsed B-cell non-Hodgkin lymphoid (R/R B-cell NHLs) malignancies are cancers that start in white blood cells called B-lymphocytes. While curative treatments are available, the majority of patients' cancers can come back after treatment or can be resistant to standard treatment. There is a need for continued development of effective treatments. A T-cell redirecting trispecific (CD79b x CD20 x CD3) antibody is a novel treatment for patients with B-cell malignancies developed by drug companies. Upon binding to tumor cells, T-cell redirecting antibodies* guide T-cells to the tumor, resulting in T-cell activation and tumor cell killing. In this study, researchers want to find out the recommended phase 2 regimen (RP2R) and safe dose of JNJ-80948543 when used in combination with other CD3-targeting T-Cell engagers (TCEs) for the treatment of R/R B-cell NHL. The investigational treatment, JNJ-80948543, is a novel T-cell redirecting trispecific antibody that will be combined with JNJ-75348780, an investigational bi-specific antibody (CD22 x CD3).
*Type of protein that finds and binds to other proteins and fights off an infection.

Who can participate?
Participants aged 18 years or older with R/R B-cell NHLs

What does the study involve?
The study will consist of the following:
1. Screening phase: Participants will be screened to confirm eligibility.
2. Treatment phase: Part 1 (Dose Escalation): Participants will be enrolled into different groups. The first group will receive the starting doses of JNJ-80948543 in combination with JNJ-75348780. If this dose is found to be safe, subsequent groups will receive higher doses of JNJ-80948543. This process will be repeated until serious side effects of JNJ-80948543 occur that prevent a tolerated dose.
Part 2 (Dose Expansion): Participants will receive treatment at RP2R selected in Part 1 until worsening of disease, serious side effects, or withdrawal.

1. Follow-up phase: Participants will be followed up to monitor their health.
Safety assessments include blood & urine tests, physical exams, vital signs, and electrocardiograms.

What are the possible benefits and risks of participating?
It is unknown whether participants will receive any benefit from taking part in this study, but the information collected may help people with R/R B-NHL cancer in the future.
This is a Phase 1b dose confirmation study. Each of the drugs used in this study has been studied in previous clinical trials to confirm what doses and side effects are expected when the drugs are used by themselves.
The expected risks for the RP2R dose of JNJ-80948543 in combination with JNJ-75348780 are based on how the drug works and results from each drug's individual Phase I clinical trials. Expected side effects can include but are not limited to: injection site reactions, cytokine release syndrome (inflammation condition that may occur after treatment with some types of immunotherapy, such as monoclonal antibodies), neurological side effects (including headaches or a condition of the brain), tumor lysis syndrome, systemic administration related reaction, cytopenias (reduction in blood cells), serious infections, hypogammaglobulinemia (low protein in blood that fights infection) and hepatitis B virus reactivation.
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 Research & Development

When is the study starting and how long is it expected to run for?
August 2024 to September 2026

Who is funding the study?
Janssen Research & Development

Who is the main contact?
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Contact information

Type(s)
Scientific

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ClinicalTrials.gov (NCT)
NCT06660563

Integrated Research Application System (IRAS)
1010515

Central Portfolio Management System (CPMS)
63575

Protocol serial number
80948543LYM1002

Study information

Scientific Title
A Phase Ib study of JNJ-80948543 in combination with other CD3 T-cell engagers in participants with relapsed/refractory B-cell non-Hodgkin lymphoid malignancies

Study objectives

Primary objectives:
1. To find the effective recommended phase 2 regimen (RP2R) of JNJ-80948543 when given with JNJ-75348780
2. To further check the safety of JNJ-80948543 at RP2R when given with JNJ-75348780

Secondary objectives:
To assess the following when JNJ-80948543 is given with JNJ-75348780:
1. The process by which the drug gets absorbed, distributed in the body, and excreted (pharmacokinetics)
2. Immune response against the study drugs (immunogenicity)
3. To determine the initial effectiveness (preliminary clinical activity) of JNJ-80948543 when given with JNJ-75348780

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 17/10/2024, East of England - Essex Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; -; essex.rec@hra.nhs.uk), ref: 24/EE/0194

Study design
Phase Ib investigational dose-escalation dose-expansion study

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Relapsed/refractory B-cell non-Hodgkin lymphoid malignancies

Interventions
JNJ-75348780 will be administered as a subcutaneous (SC) injection and JNJ-80948543 will be administered as a subcutaneous (SC) or an intravenous (IV) injection.

Participants will receive JNJ-80948543 in combination with JNJ-75348780 to determine the recommended Phase II regimen (RP2R) in Part 1 (dose escalation). JNJ-80948543 will be dosed in an escalation manner in combination with fixed doses of JNJ-75348780. In Part 2 (dose expansion) participants will receive RP2R of JNJ-80948543 as determined in Part 1 in combination with JNJ-75348780.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
JNJ-80948543, JNJ-75348780

Primary outcome(s)
1. Number of participants with dose-limiting toxicity (DLT) will be reported up to 1 year and 10 months. DLTs are defined as any of the treatment-related toxicities: any toxicity that would require discontinuation of treatment; Fatal toxicity; Non-hematologic toxicity (Grade 3 toxicity or higher with exceptions); and Hematologic Toxicity (Grade 4 neutrophil count decrease; Grade 4 febrile neutropenia; Grade 3 febrile neutropenia that does not recover with best supportive care within 7 days; Grade 4 platelet count decrease for >=7 days or Grade >3 with Grade >=2 bleeding; Grade 4 anemia).
2. Number of participants with adverse events (AEs) will be reported up to 1 year and 10 months. An AE is any untoward medical occurrence in a clinical study participant administered a pharmaceutical (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the intervention.

Key secondary outcome(s))
1. Serum concentration-time profiles and PK parameters for JNJ-8094853 and JNJ-75348780 will be reported up to 1 year and 10 months and will be measured and reported as descriptive statistics using available serum concentrations.
1.1. Time to Reach Cmax (Tmax) for JNJ-80948543 and JNJ-75348780 will be assessed up to 1 year and 10 months and will be measured and reported as descriptive statistics using available serum concentrations. Tmax is the time to reach the maximum observed serum concentration for JNJ-80948543 and JNJ-75348780.
1.2. Maximum Serum Concentration (Cmax) for JNJ-80948543 and JNJ-75348780 will be reported up to 1 year and 10 months and will be measured and reported as descriptive statistics using available serum concentrations.
1.3. Area Under the Curve (AUCtau) for JNJ-80948543 and JNJ-75348780 will be assessed up to 1 year and 10 months and will be measured and reported as descriptive statistics using available serum concentrations.
2. The number of participants with the presence of anti-JNJ-80948543 and anti-JNJ-75348780 antibodies assessed up to 1 year and 10 months and will be measured and reported as descriptive statistics using available serum concentrations.
3. Overall Response Rate (ORR), Complete Response Rate (CRR) and Duration of Response (DoR), where the response will be assessed by the investigator based on standard response criteria up to 1 year and 10 months.

Completion date
21/09/2026

Eligibility

Key inclusion criteria
1. Histologic documentation of diffuse large B-cell lymphoma (DLBCL), including high-grade B-cell lymphoma and DLBCL arising from indolent lymphoma.
2. All participants must have received at least 2 prior lines of therapy
3. Participants must have measurable disease as defined by the appropriate disease response criteria
4. Have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1
5. Hematologic laboratory parameters must meet the required criteria's and the values must be without a transfusion or growth factors for at least 7 days prior to the first dose of the study drug
6. Participants of childbearing potential must have a negative highly sensitive serum pregnancy test (beta (β)-human chorionic gonadotropin) at screening and within 24 hours before the first

dose of study treatment and must agree to further serum or urine pregnancy tests during the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Known active central nervous system involvement (CNS) or leptomeningeal involvement
2. Prior solid-organ transplantation
3. Autoimmune or inflammatory disease requiring systemic steroids or other immunosuppressive agents (for example, methotrexate or tacrolimus) within 1 year before the first dose of the study drug
4. Toxicity from prior anticancer therapy has not resolved to baseline levels or to Grade <= 1 (except alopecia, vitiligo, peripheral neuropathy, or endocrinopathies that are stable on hormone replacement, which may be Grade 2)
5. Clinically significant pulmonary compromise defined as the need for supplemental oxygen to maintain adequate oxygenation
6. Evidence of clinically significant and/or symptomatic infection (viral, bacterial, or fungal) at the time of study drug initiation. Anti-microbial treatment for infection must be discontinued at least 7 days before the first dose of study drug

Date of first enrolment
05/11/2024

Date of final enrolment
20/09/2026

Locations

Countries of recruitment
United Kingdom

England

Australia

Spain

Taiwan

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

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 and Johnson is available at https://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