ISRCTN16927703 https://doi.org/10.1186/ISRCTN16927703

A study to evaluate nipocalimab and certolizumab combination therapy in participants with active rheumatoid arthritis

Submission date
02/08/2023

Recruitment status
No longer recruiting

Registration date
20/10/2023

Overall study status
Completed

Last Edited
26/10/2026

Condition category
Musculoskeletal Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Rheumatoid arthritis (RA) is an autoimmune and inflammatory disease, which means that immune system attacks healthy parts in individual's body by mistake, and causes swelling, pain, and stiffness in joints.
The study drug, nipocalimab is an antibody* that targets a specific receptor (protein that binds to specific molecule) called neonatal fragment crystallizable receptor (FcRn). Nipocalimab blocks FcRn receptor and prevents binding of IgG, thereby resulting in decrease of IgG levels.
Certolizumab, another study drug, binds to and blocks the activity of tumor necrosis factor alpha (TNF-alpha), that decreased joint inflammation resulting in decreased joint damage.
*Antibody is a type of protein that can recognize and bind to antigens in the body.
The aim of this study is to see how effective and safe the combination therapy of nipocalimab and certolizumab is compared to certolizumab alone in participants with moderately to severely active RA despite of earlier therapies.

Who can participate?
Patients aged 18 to 75 years who have moderately to severely active RA and who has not responded to the earlier advanced therapy.

What does the study involve?
The study will be conducted in three periods:
1. Screening period (up to 6 weeks): Participants will be screened to confirm if they can take part in study.
2. Double-blind treatment period (up to 22 weeks): Participants will be randomly divided into two groups nipocalimab and certolizumab (combination therapy) and certolizumab alone. Participants receiving certolizumab will also receive placebo to maintain the blind.
3. Follow-up period (up to 8 weeks): Participants will be monitored for their health after last dose of study drug until the study ends.
Participants will undergo study assessments and tests, such as blood tests and urinalysis. All side effects will be recorded until study ends (up to 36 weeks). The total study duration of study is about 9 months.

What are the possible benefits and risks of participating?
There is no established benefit to participants of this study. Based on scientific theory, taking nipocalimab and certolizumab combination therapy may improve RA. However, this cannot be guaranteed because nipocalimab and certolizumab combination therapy is still under investigation as a treatment and it is not known whether nipocalimab and certolizumab combination therapy will work.
If participants are put in the comparator group (certolizumab only), they will not receive nipocalimab and certolizumab combination therapy but treatment already on the market.
Participants may experience some benefit from participation in the study that is not due to receiving nipocalimab and certolizumab combination therapy, but due to regular visits and assessments monitoring overall health. Participation may help other people with RA in the future.
Participants may have side effects from the drugs or procedures used in this study that may be mild to severe and even life-threatening, and they can vary from person to person. The most common, known risks are getting symptoms such as (lack of clinical benefit or clinical worsening of RA, potential increase risk for infection due to decreased serum IgG, activation of latent virus due to decreased IgG concentrations, reduced effectiveness of routine vaccines due to decreased IgG, clinical manifestations (clear) of hypoalbuminemia, infusion reaction, drug-drug interaction, increased lipids, placental infarction, Low IgG in infants born to mothers with early onset severe hemolytic disease of the fetus and newborn receiving nipocalimab during pregnancy, serious infections and reactivation of latent infections, malignancies and lymphoproliferative disorders (complication of immune dysregulation syndromes), chronic heart failure, hematological reactions, neurological events, hypersensitivity reactions, including serious hypersensitivity reactions and anaphylaxis, autoimmunity or lupus-like syndrome, elevated activated partial thromboplastin clotting time) after getting the study drug. There are other, less frequent risks.
The participant information sheet and informed consent form, which will be signed by every participant agreeing to participate in the study, includes a detailed section outlining the known risks to participating in the study.
Not all possible side effects and risks related to nipocalimab and certolizumab combination therapy are known at this moment. During the study, the sponsor may learn new information about nipocalimab and certolizumab combination therapy. The study doctor will tell participants as soon as possible about any new information that might make them change their mind about being in the study, such as new risks.
To minimize the risk associated with taking part in the study, participants are frequently reviewed for any side effects and other medical events. Participants are educated to report any such events to the study doctor who will provide appropriate medical care. Any serious side effects that are reported to the sponsor are thoroughly reviewed by a specialist drug safety team.
There are no costs to participants to be in the study. The sponsor will pay for the nipocalimab and certolizumab combination therapy and tests that are part of the study. The participant will receive reasonable reimbursement for study-related costs (e.g., travel/parking costs).

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

When is the study starting and how long is it expected to run for?
August 2023 to October 2024

Who is funding the study?
Janssen-Cilag International NV (Netherlands)

Who is the main contact?
Dr James Galloway, james.galloway@nhs.net

Contact information

Type(s)
Scientific, Public

Contact name
None - Medical Information and Product Information Enquiry

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Additional identifiers

Clinical Trials Information System (CTIS)
2023-504045-31

Integrated Research Application System (IRAS)
1008163

Central Portfolio Management System (CPMS)
55693

Protocol serial number
80202135ARA2002

Study information

Scientific Title
A Phase 2a multicenter, randomized, double blind, parallel, proof of concept study evaluating the efficacy and safety of nipocalimab and certolizumab combination therapy in participants with active rheumatoid arthritis despite prior treatment with advanced therapies (bDMARD or tsDMARD)

Acronym
DAISY

Study objectives
Primary objective:
To evaluate the efficacy of combination therapy with nipocalimab and certolizumab compared to certolizumab monotherapy in participants with moderately to severely active RA despite ≥1 advanced therapy (bDMARDs or tsDMARDs).

Secondary objectives:
1. To evaluate effectiveness of the combination therapy with nipocalimab and certolizumab compared to certolizumab alone in participants with moderately to severely active RA.
2. To evaluate the safety and tolerability of combination therapy with nipocalimab and certolizumab.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 16/10/2023, Seasonal REC (Health Research Authority) (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; None available; seasonal.rec@hra.nhs.uk), ref: 23/LO/0721

Primary study design
Interventional

Study design
Double-blind randomized controlled parallel-group trial

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Rheumatoid arthritis

Interventions
1. Certolizumab + Placebo, active comparator. Participants will receive placebo intravenously (IV) and certolizumab dose 1 subcutaneously at Week 0, 2, and 4 followed by placebo IV and certolizumab dose 2 subcutaneously at Weeks 6 to 22.

2. Certolizumab + Nipocalimab, Experimental. Participants will receive nipocalimab IV and certolizumab dose 1 subcutaneously at Week 0, 2, and 4 followed by nipocalimab IV and certolizumab dose 2 subcutaneously at Weeks 6 to 22.

Treatment allocation will be controlled by IWRS.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Nipocalimab, certolizumab pegol

Primary outcome(s)
Disease Activity Index Score 28 using C-reactive Protein (DAS28-CRP) at baseline and week 12

Key secondary outcome(s)
1. Percentage of Participants Achieving American College of Rheumatology (ACR) 20 Response at Week 12
2. Percentage of Participants Achieving ACR 50 Response at Week 12
3. Percentage of Participants Achieving ACR 70 Response at Week 12
4. Percentage of Participants Achieving ACR 90 Response at Week 12
5. Percentage of Participants Achieving DAS28-CRP Remission at Week 12
6. Percentage of Participants Achieving DAS28-CRP Low Disease Activity (LDA) at Week 12
7. Change From Baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) Score at Week 12
8. Change From Baseline in Clinical Disease Activity Index Score (CDAI) at Week 12
9. Number of Participants With Treatment-emergent Adverse Events (TEAEs), up to week 30
10. Number of Participants With Treatment-emergent Serious Adverse Events (SAEs), up to week 30
11. Number of Participants With TEAEs Leading to Discontinuation of Study Intervention, up to week 30
12. Number of Participants With Adverse Events of Special interests (AESIs), Up to Week 30

Completion date
29/10/2024

Eligibility

Key inclusion criteria
1. Diagnosis of rheumatoid arthritis (RA) and meeting the 2010 American college of rheumatology (ACR) or European League Against Rheumatism (EULAR) criteria for RA for at least 3 months before screening
2. Has moderate to severe active RA as defined by persistent disease activity with at least 6 of 66 swollen joints and 6 of 68 tender joints at the time of screening and at baseline
3. Is positive for anti-citrullinated protein antibodies (ACPA) or rheumatoid factor (RF) by the central laboratory at the time of screening
4. Has C-reactive protein (CRP) greater than or equal to (>=) 0.3 milligram per deciliter (mg/dL) by the central laboratory at the time of screening
5. If has received prior biological disease-modifying antirheumatic drugs (bDMARDs) (or biosimilars) other than anti-tumor necrosis factor (anti-TNF) agent in RA, has demonstrated inadequate response (IR) or intolerance to the therapy based on one of the following:
5.1. IR to at least 1bDMARD (or the biosimilars) other than anti-TNF agents, as assessed by the treating physician, after at least 12 weeks of therapy including but not limited to abatacept,

anakinra, tocilizumab, and sarilumab or at least 16 weeks of therapy with rituximab Documented IR may include inadequate improvement or loss in response after initial improvement in joint counts or other parameters of disease activity
5.2. Intolerance to bDMARD (or biosimilars) other than anti-TNF agent, as assessed by the treating physician. Documented intolerance includes side effects and injection or infusion reactions
6. If has received prior anti-TNF agent (including biosimilars), has demonstrated IR to >=1 anti-TNF agent (including biosimilars), as assessed by the treating physician:
6.1. After at least 12 weeks dosage of etanercept, adalimumab, golimumab (including biosimilars), and/or
6.2. After at least 14 weeks dosage (example, at least 4 doses) of infliximab (including biosimilars) Documented IR may include inadequate improvement or loss in response after initial improvement in joint counts or other parameters of disease activity

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
104

Key exclusion criteria
1. Has a confirmed or suspected clinical immunodeficiency syndrome not related to treatment of RA or has a family history of congenital or hereditary immunodeficiency unless confirmed absent
2. Is (anatomically or functionally) asplenic
3. Has experienced myocardial infarction, unstable ischemic heart disease, or stroke less than or equal to (<=) 12 weeks of screening
4. Has a diagnosis of congestive heart failure including medically controlled, asymptomatic congestive heart failure
5. Has a history of known demyelinating disease such as multiple sclerosis or optic neuritis

Date of first enrolment
19/02/2024

Date of final enrolment
23/02/2024

Locations

Countries of recruitment
United Kingdom

Argentina

Germany

Hungary

Poland

United States of America

Study participating centre
Kings College Hospital
Denmark Hill
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Study participating centre
Western General Hospital
Crewe Road South
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Study participating centre
Medway Maritime Hospital
Windmill Road
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ME7 5NY

Sponsor information

Organisation
Janssen-Cilag International NV

Funder(s)

Funder type

Industry

Funder Name
Cilag

Alternative Name(s)
Janssen-Cilag, Cilag AG

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.
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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other unpublished results		24/03/2025	21/10/2025	No	No