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A trial to investigate the effects of multiple doses of JNJ-67484703 in patients with rheumatoid arthritis, ulcerative colitis and Sjögren's syndrome

Submission date
22/07/2022

Recruitment status
No longer recruiting

Registration date
28/09/2022

Overall study status
Completed

Last Edited
16/04/2026

Condition category
Other

[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
The aim of the PARIS trial is to understand if JNJ-67484703, also referred to as the trial drug, can alter the numbers of disease-associated immune cells in diseased tissue in patients with rheumatoid arthritis (RA), ulcerative colitis (UC) and Sjögren's syndrome (SjS). This will be done by taking a small amount of diseased tissue before and after a 12-week treatment period with the study drug. The numbers of these immune cells can be measured in the biopsy tissue to understand if they are altered by the trial drug. Patients will be closely monitored to see if they feel better or not on treatment and to look for side effects. For patients with RA, biopsy tissue will be obtained by using an ultrasound machine to guide a needle to take samples of the lining of the joint. For patients with UC, bowel tissue will be taken during a camera test of the bowels. For patients with SjS, a small amount of salivary gland tissue will be obtained by a routine lip biopsy. All these biopsy procedures are performed regularly at the hospitals taking part in the study and will be done by someone with the appropriate training and experience. At the end of the trial, we hope to know if the trial drug acts in the way we expect.

Who can participate?
The trial is for patients aged between 18-75 years with either RA, UC or SjS who, based on pre-defined inclusion/exclusion criteria, have active disease and are fit enough to receive multiple doses of the trial drug.

What does the study involve?
All patients will enter a screening period and be assessed using the eligibility criteria. If the patient is eligible, the patient will enter the treatment phase of the trial where they will receive an injection of the trial drug under the skin 7 times over 10 weeks. These injections are injected into the fatty layer just below the skin. 5 patients from each cohort will receive a low dose and 10 will receive a higher dose. After the treatment phase, patients will be followed up at 2 further visits over a 12-week period.

What are the possible benefits and risks of participating?
Patients may not directly benefit from participating in this trial, as the benefit of JNJ-67484703 in patients with RA, UC and SjS is not yet proven. However, by taking part patients will be helping us to see if JNJ-67484703 could be used in the future as a treatment for people with RA, UC and SjS.

Where is the study run from?
University of Birmingham (UK)

When is the study starting and how long is it expected to run for?
January 2020 to July 2026

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

Who is the main contact?
Dr Benjamin Fisher (UK)
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Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-005998-13

Integrated Research Application System (IRAS)
1004476

Central Portfolio Management System (CPMS)
53062

Protocol serial number
RG_21-180

Study information

Scientific Title
Pharmacodynamic activity trial of JNJ-67484703 in rheumatoid arthritis, ulcerative colitis and Sjögren's syndrome (PARIS): a phase II proof of biology trial

Acronym
PARIS

Study objectives
The principal hypothesis of this trial is that treatment with JNJ-67484703 will lead to a dose-dependent alteration in immune cell subsets in disease-relevant tissue.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 24/05/2022, South Central - Berkshire B Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, United Kingdom; +44 (0)207 104 8253; berkshireb.rec@hra.nhs.uk), ref: 22/SC/0128

Primary study design
Interventional

Study design
Multiple-dose parallel multicentre open-label interventional study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Rheumatoid arthritis, ulcerative colitis and Sjögren's syndrome

Interventions
Patients will receive the trial drug JNJ-67484703 at either a low (0.5mg/kg) or high (3mg/kg) dose. Each patient will receive the trial drug at weeks 0, 1 and 2 and then every 2 weeks until week 10. The first 5 participants in each disease cohort will be allocated to the 0.5 mg/kg dosing cohort, and subsequent participants will be allocated to the 3 mg/kg regimen, subject to possible modifications.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
JNJ-67484703

Primary outcome(s)
The biological effects of multiple doses of JNJ-67484703 in disease-relevant tissues (synovium, gut, salivary gland) over time in participants with RA, UC and SjS, measured using cellular analysis techniques at weeks 0, 12

Key secondary outcome(s)
1. Safety and tolerability measured using NCI-CTCAE criterion Version 5 at weeks 0, 1, 2, 4, 6, 8, 10, 12, 16, and 24
2. Disease-relevant immune cell populations measured using cellular analysis techniques at weeks 0, 6, 12, 24
3. Inflammation in target tissue measured using Krenn scoring (RA), Focus score, mean foci area, the percentage area of infiltration, T/B cell organisation and presence of germinal centre-like structures (SjS), Robarts Histopathology Index (RHI) and Nancy Index at weeks 0 and 12
4. Markers of inflammation in peripheral blood measured using immunoassays at weeks 0, 6, 12, and 24
5. Autoantibody levels measured using immunoassays at weeks 0, 6, 12, and 24

6. Clinical measures of disease activity:

6.1. Overall disease activity in RA as measured by:
6.1.1. Disease Activity Score 28 using C-reactive protein (DAS28-CRP) at weeks 0, 6, 12, and 24
6.1.2. Physician global visual analogue scale (VAS) weeks 0, 6, 12, and 24
6.1.3 Response to treatment in RA as measured by:
6.1.3.1. European Alliance of Associations for Rheumatology (EULAR) response weeks 0, 6, 12, and 24
6.1.3.2. Proportion of participants in DAS28-CRP remission (<2.6) and low disease activity (≤3.2) states weeks 0, 6, 12, and 24

6.2. Overall disease activity in SjS as measured by:
6.2.1. Physician global VAS at weeks 0, 6, 12, and 24
6.2.2. Response to treatment in SjS as measured by Composite of Relevant Endpoints for SjS

(CRESS) responders (ultrasound excluded)
6.2.3. Salivary flow in SjS as measured by Unstimulated salivary flow (ml/min; assuming 1g≈1ml) at weeks 0, 6, 12, 24
6.2.4. Stimulated salivary flow (ml/min; assuming 1g≈1ml) at weeks 0, 6, 12, 24
6.2.5. Ocular involvement in SjS as measured by Schirmer's test (mm) at weeks 0, 12

6.3. Overall disease activity in UC as measured by:
6.3.1. Mayo clinic score (MCS) at weeks 0, 12
6.3.2. Partial Mayo Clinic Score at weeks 0, 2, 4, 6, 8, 10, 16, 24
6.3.3. Simple Clinical Colitis Activity Index (SCCAI) at weeks 0, 2, 4, 6, 8, 10, 12, 16, 24
6.3.4. Response to treatment in UC as measured by:
6.3.4.1. Endoscopic healing (Ulcerative Colitis Endoscopic Index of Severity [UCEIS] <1 and Mayo Endoscopic Score [MES] <1) at weeks 0, 12
6.3.4.2. Clinical remission (rectal bleeding [RB]=0 and stool frequency[SF]=0) at weeks 0, 12
6.3.4.3. Clinical response (30% decline in MCS and RB=0 and SF <1 and MES <1) at weeks 0, 12
6.3.4.4. Change detected by artificial intelligence reading of endoscopy videos (Satisfai system) at weeks 0, 12

7. Participant-reported outcomes measured using:
7.1. Health-related Quality of Life as measured by EQ-5D-5L at weeks 0, 6, 12, and 24
7.2. Fatigue as measured by FACIT-Fatigue at weeks 0, 6, 12, and 24
7.3. Patient assessment of overall disease activity as measured by Patient Global Disease Activity VAS at weeks 0, 6, 12, and 24
7.4. Pain in RA as measured by pain VAS at weeks 0, 2, 4, 6, 8, 10, 12, 16, and 24

7.5. Physical function in RA as measured by:
7.5.1. Physical function as assessed by HAQ-DI at weeks 0, 6, 12, and 24
7.5.2. Symptom burden in SjS as measured by EULAR SjS patient Reported index (ESSPRI) at weeks -6, 0, 2, 4, 6, 8, 10, 12, 16, and 24

7.6. Symptom burden in UC as measured by:
7.6.1. Inflammatory Bowel Disease Questionnaire (IBDQ) at weeks 0, 4, 8, and 12
7.6.2. IBD Control at weeks 0, 2, 4, 6, 8, 10, 12, 16, and 24

Completion date
31/07/2026

Eligibility

Key inclusion criteria
Main inclusion criteria for all cohorts:
1. Informed consent must be obtained provided prior to any trial-related procedures being performed
2. Male and female participants aged ≥18 and ≤75 years at the time of enrolment
3. Able to communicate well with the investigator, and to understand and comply with the requirements of the trial
4. Willing to have repeat tissue biopsy relevant to disease group (ultrasound-guided synovial biopsy, minor salivary gland biopsy or endoscopic colonic mucosal biopsy)
5. Body weight within the range of 45.0 kg to 120.0 kg, inclusive

Inclusion criteria for patients with rheumatoid arthritis (RA):
6. Confirmed clinical diagnosis of RA
7. Active RA
8. Joint amenable to biopsy by ultrasound criteria
9. Autoantibody positive
10. Have methotrexate (MTX) inadequate response
11. If using regular non-steroidal anti-inflammatory drugs (NSAIDs) must be on a stable dose

Inclusion criteria for patients with ulcerative colitis (UC):
12. Confirmed clinical diagnosis of UC
13. Moderately to severely active UC on endoscopy
15. Either primary non-response or secondary loss of response to one or more biologic or targeted synthetic therapies
16. Medications/therapies must have been discontinued by the number of stated weeks before Visit 2 (Baseline) as outlined in the protocol.
17. A participant ≥45 years of age must have had a full colonoscopy. Adenomatous polyps must be removed before the first dose of trial intervention
18. A participant who has had extensive colitis for ≥8 years, or disease limited to the left side of the colon for ≥10 years, must have or have had a full colonoscopy to assess for the presence of dysplasia or malignancy at the Screening Visit

Inclusion criteria for patients with Sjögren's syndrome (SjS):
19. A diagnosis of SjS, according to the 2016 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria
20. Autoantibody positive
21. At least "low activity" in the biological domain of EULAR Sjögren's syndrome (SS) disease activity index (ESSDAI)
22. ESSPRI component scores as outlined in the protocol
23. Residual stimulated whole salivary flow

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
75 Years

Sex
All

Total final enrolment
37

Key exclusion criteria

Main exclusion criteria for all cohorts:
1. Prior B cell depletion
2. Other biologic therapy or targeted synthetic disease-modifying antirheumatic drugs (DMARDs)
3. Receipt of any investigational medicinal product within 16 weeks, or approximately 5 half-lives (whichever is longer) prior to Visit 2 (baseline)
4. Any active or ongoing viral, bacterial or other infections
5. Confirmed, suspected, or close contact with a person with known or suspected SARS-CoV-2 infection
6. Major organ, haematopoietic stem cell or bone marrow transplant
7. Any cancer within the previous 5 years,
8. Severe, uncontrolled fibromyalgia symptoms.
9. Treatment with glucocorticoids unless on a stable dose of prednisolone
10. Positive test for HIV, Hepatitis C Virus or Hepatitis B Virus
11. Active cytomegalovirus (CMV) or Epstein–Barr virus (EBV)
12. Live vaccine within 12 weeks of registration
13. Bacillus Calmette-Guérin (BCG) vaccination within 12 months prior to trial drug administration.
14. Evidence of active or latent tuberculosis (TB)
15. Has known allergies, hypersensitivity, or intolerance to JNJ-67484703 or its excipients
16. Any medical, surgical or psychiatric condition that the investigator believes may jeopardise the participant, or the validity of the trial results, were they to participate in the trial
17. Has experienced myocardial infarction, unstable ischaemic heart disease, or stroke within 12 weeks of Screening Visit
18. Female who is pregnant, breastfeeding, intends to become pregnant or is of childbearing potential, not willing to use highly effective contraceptive methods
19. A non-vasectomised male participant who refuses to wear a condom during the trial and for 14 weeks after the last dose of trial treatment when engaging in any activity that allows for passage of ejaculate to another person. An additional method of highly effective method of contraception must also be used.
20. A male participant must agree not to donate sperm for the purpose of reproduction during the trial and for a minimum 14 weeks after receiving the last dose of the trial intervention
21. Screening laboratory test results as specified in the protocol
22. Advised by clinician not to have a tissue biopsy due to clinical reasons or anti-coagulant use
23. Septic arthritis of a native or prosthetic joint in the last 12 months (or indefinitely if the prosthetic joint remains in situ)

Exclusion criteria for patients with rheumatoid arthritis:
24. History of or current inflammatory joint disease other than RA
25. Currently taking anticoagulant medications (not anti-platelet agents) that would contraindicate synovial biopsy
26. DMARD or other immunosuppressive therapy with the exception of methotrexate, sulfasalazine or hydroxychloroquine at stable doses

Exclusion criteria for patients with ulcerative colitis:
27. History of severe extensive colitis
28. Has UC limited to the rectum only
29. Presence or history of a fistula
30. History of colonic mucosal dysplasia.
31. Presence on screening endoscopy of adenomatous colonic polyps, if not removed before trial entry, or history of adenomatous colonic polyps that were not removed

32. Diagnosis of indeterminate colitis, microscopic colitis, ischemic colitis, or Crohn’s disease or clinical findings suggestive of Crohn’s disease

Exclusion criteria for patients with Sjögren’s syndrome:
33. Diagnosis of any other non-SjS sicca syndrome
34. DMARD or other immunosuppressive therapy with the exception of methotrexate, sulfasalazine, hydroxychloroquine, leflunomide or azathioprine
35. Regular use of medications known to cause dry eyes or mouth as a common side effect
36. Topical ocular prescription medications other than artificial tears and lubricating gels
37. Has SjS overlap syndromes where another confirmed autoimmune rheumatic or systemic inflammatory condition is the primary diagnosis
38. Certain eye surgeries:
38.1. Has had cataract surgery prior to dosing and new installation of lacrimal punctal plugs prior to dosing
38.2. Has had a full-thickness corneal transplantation (penetrating keratoplasty); however, participants who have had endothelial keratoplasty are not excluded

Date of first enrolment
30/09/2022

Date of final enrolment
10/01/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
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Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

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
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No