ISRCTN94958652 https://doi.org/10.1186/ISRCTN94958652

This study is looking at a potential new treatment, secukinumab for patients diagnosed with non-ocular Behçet's Syndrome. Phase II wants to evaluate how safe and how effective secukinumab might be. Patients will be assigned to either the study drug (secukinumab) or placebo arm for 16 weeks, followed by 36 weeks of treatment for both groups. Double blind trial means that neither the patient nor the study team will be able to tell which arm the patient is allocated to.

Submission date 19/03/2022	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 19/07/2022	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 06/06/2025	**Condition category** Circulatory System	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims

This study is looking at a potential new treatment, secukinumab for patients diagnosed with non-ocular Behçet's Syndrome. This is a phase II, proof of principle trial and wants to evaluate how safe and how effective secukinumab might be for this group of patients.

Who can participate?

We are aiming to recruit 64 patients over a 24 months period.

The patient population we would like to include into this study are patients who have previously not responded to first line therapy with topical steroid (mouth wash or skin cream), colchicine or azathioprine.

What does the study involve?

Patients will be randomly assigned to either the placebo or the study drug (secukinumab) arm. Each patient will either receive 300mg subcutaneous (under the skin) injection of secukinumab

or matched placebo up to week 16. Injections will be self-administered once a week for four weeks (weeks 0, 1, 2, 3, 4), then once every four weeks at week 8 and 12. From week 16 we will not use placebo anymore and all patients will receive 300mg secukinumab every 4 weeks up to and including week 48.
Patients will be required to attend 6 scheduled clinic visits and also have 6 follow-up telephone calls. The total duration of each patient's time in the study will be approximately 1 year.
The screening visit includes physical examination, medical history check, current medication and collection of demographic data such as gender and race. Blood samples will be collected (this will be routine clinical tests and will include HIV, hepatitis and tuberculosis testing) and urine samples. Other assessments will include blood pressure, respiration rate, temperature and an ECG test (which measures the electrical activity of the heart). Height and weight will also be measured.

What are the possible benefits and risks of participating?
Benefits:
Not provided at time of registration
Risks:
Whilst secukinumab is widely used in conditions such as psoriatic arthritis and psoriasis, it has not formally been evaluated in Behçet's Syndrome, and is not licensed for this condition. It is possible that there are unknown adverse events in this disease.
The volume of blood being taken over the course of the trial should not cause any problems for healthy adults. There may be some temporary mild discomfort, such as bruising and tenderness at the site where the blood samples are taken. Patients may experience faintness as a result of the blood test.
If abnormal results or undiagnosed conditions are found during the course of the study these will be discussed with the patient and, if the patient agrees, their GP (or a hospital specialist, if more appropriate) will be informed.

Where is the study run from?
Liverpool Hospital NHS Trust (UK)

When is the study starting and how long is it expected to run for?
March 2022 to April 2025

Who is funding the study?
Novartis Pharmaceuticals UK Limited

Who is the main contact?
Dr Robert Moots, Robert.moots@liverpoolft.nhs.uk

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2022-000255-37

IRAS number
1005007

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
SP0422, IRAS 1005007, CPMS 52281

Study information

Scientific Title
A phase II, multicentre, randomised, double blind, placebo controlled parallel group study, followed by a 36 week active treatment phase to evaluate the efficacy and safety of secukinumab in patients with non-ocular Behçet's Syndrome

Study objectives
Primary objective:
To evaluate the change in oral ulcer severity score following 16 weeks of treatment.

Secondary objectives:
1. To assess Behçet's Disease Current Activity Form (BDCAF): Behçet's Disease Current Activity Index (BDCAI) at weeks 16 and 52
2. To assess Behçet's Disease Current Activity Form ((BDCAF): Patient's Perception of Disease Activity at weeks 16 and 52

3. To assess change in outcome measure Behçet's Disease Current Activity Form (BDCAF): Clinician's Overall Perception of Disease Activity from baseline to weeks 16 and 52

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/05/2022, North West - Haydock Research Ethics Committee (3rd Floor - Barlow House, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)2071048032; haydock.rec@hra.nhs.uk), ref: 22/NW/0113

Study design
Interventional double blind placebo controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a participant information sheet.

Health condition(s) or problem(s) studied
Behçet's syndrome

Interventions
This study is looking at a potential new treatment, secukinumab for patients diagnosed with non-ocular Behçet's Syndrome. This is a phase II, proof of principle trial and wants to evaluate how safe and how effective secukinumab might be for this group of patients. We are aiming to recruit 64 patients over a 24 months period. The patient population we would like to include into this study are patients who have previously not responded to first line therapy with topical steroid (mouth wash or skin cream), colchicine or azathioprine .Patients will be randomly assigned to either the placebo or the study drug (secukinumab) arm. Each patient will either receive 300 mg subcutaneous (under the skin) injection of secukinumab or matched placebo up to week 16. Injections will be self-administered once a week for four weeks (weeks 0, 1, 2, 3, 4), then once every 4 weeks at week 8 and 12. From week 16 we will not use placebo anymore and all patients will receive 300 mg secukinumab every 4 weeks up to and including week 48. Patients will be required to attend 6 scheduled clinic visits and also have 7 follow-up telephone calls. The total duration of each patient's time in the study will be approximately 14 months. The screening visit includes physical examination, medical history check, current medication and collection of demographic data such as gender and race. Blood samples will be collected (this will be routine clinical tests and will include HIV, hepatitis and tuberculosis testing) and urine samples. Other assessment will include blood pressure, respiration rate, temperature and an

ECG test (which measures the electrical activity of the heart). Height and weight will also be measured. Clinic visits days will include routine bloods and urine samples as well as genital and oral ulcer assessments and some questionnaires (quality of life, pain, disease activity and symptoms). Telephone consultation will be to check compliance and if any adverse events happened. Randomisation via IWRS.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Secukinumab

Primary outcome measure
1. Change from baseline in Behçet's oral ulcer severity score at 16 weeks. (An improvement of 20% is considered to be clinically meaningful). The USS incorporates six ulcer characteristics: number, size, duration, ulcer-free period, site, and pain. It is scored by the clinician, based on patient reported details. There is a continuous scale between 0 (no problems) to 84 (most severe problems).

Secondary outcome measures
1. Change from baseline in Disease Activity as Measured by (BDCAF) at week 16 and week 52 end of study
2. Change from baseline in patient's perception of disease, as measured by BDCAF: patient's perception of disease activity at weeks 16 and 52
3. Change from baseline in Disease Activity as Measured by BDCAF: Clinician's Overall Perception of Disease Activity at Week 16 and 52

Overall study start date
17/03/2022

Completion date
17/04/2025

Eligibility

Key inclusion criteria
1. Patient must be able to understand and communicate with the investigator and comply with the requirements of the study and must give a written, signed and dated informed consent before any study assessment is performed
2. Male or non-pregnant, non-lactating female patients at least 18 years of age
3. Diagnosis of Behçet's Syndrome as defined by the 1990 International Study Group (ISG) and who have failed to respond to at least first line treatment with topical steroid (mouth wash or skin cream) and colchicine (≤ 500microg twice/day), azathioprine (≤2.5 mg/kg/day), or a single TNFα inhibitor (if due to inefficacy, after a trial of 3 months. If due to intolerance, at any stage).
4. Patients must have either signs of skin manifestations (including papulopustular lesions, erythema nodusum or vasculitis), mucosal ulceration, and/or joint tenderness that the investigator considers to be caused by active BS at randomization.

5. At least one active oral ulcer is required
6. Failure to respond to first line therapy with topical steroid (mouth wash or skin cream), colchicine (≤ 500microg twice/day) or azathioprine (≤2.5 mg/kg/day).
7. Patients taking corticosteroids must be on a stable dose of no more than 5 mg/day prednisone or equivalent for at least 2 weeks before randomization and can continue this during the study
8. Patients taking azathioprine (≤2.5 mg/kg/day) are allowed to continue their medication if the dose is stable for at least 4 weeks before randomization.
9. Patients taking topical steroid (as mouth wash or skin cream) can continue with this medication as required.
10. Patients taking colchicine must be on a stable dose (≤500mcg twice/day) for at least two weeks before randomization and can continue with this medication.
11. Prior exposure to a maximum of one TNFα inhibitor is permitted if due to TNFi inefficacy (after a trial of 3 months) or if due to intolerance (at any stage).

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
64

Total final enrolment
64

Key exclusion criteria
1. History of Behçet's related active central nervous system, peripheral nervous system, vascular disease, gastrointestinal system, or inflammatory ocular disease requiring systemic therapy over the preceding 12 months.
2. If there is chest X-ray or chest MRI with evidence of ongoing infectious or malignant process, obtained within 3 months prior to screening and evaluated by a qualified physician.
3. Patients taking high potency opioid analgesics (e.g. methadone, hydromorphone, morphine)
4. Previous exposure to secukinumab or other biologic drug directly targeting IL-17 or IL-17 receptor
5. Use of any investigational drug and/or devices within 4 weeks before randomization or a period of 5 half-lives of the investigational drug, whichever is longer
6. History of hypersensitivity to the study drug or its excipient or to drugs of similar chemical classes.
7. Any intramuscular or intravenous corticosteroid treatment within 4 weeks before randomization
8. Any therapy by intra-articular injections (e.g. corticosteroid) within 4 weeks before randomization
9. Patients who have previously been treated with more than 3 different TNF-a inhibitors

(investigational or approved)
10. Patients who have ever received biologic immunomodulating agents except for those targeting TNFα, investigational or approved
11. Previous treatment with any cell-depleting therapies including but not limited to anti-CD20, investigational agents (e.g., CAMPATH, anti-CD4, anti-CD5, anti-CD3, anti-CD19)
12. Pregnant or nursing (lactating) women, where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive urine pregnancy test
13. Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unwilling to use effective contraception during the study and for 16 weeks after stopping treatment. Effective contraception is defined as either: a. Barrier method: Condom or Occlusive cap (diaphragm or cervical/vault caps) with spermicide (where available). Spermicides alone are not a barrier method of contraception and should not be used alone
The following methods are considered more effective than the barrier method and are also acceptable:
13.1. Total abstinence: When this is in line with the preferred and usual lifestyle of the patient [Periodic abstinence (e.g. calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception]
13.2. Female sterilization: have had a surgical bilateral oophorectomy (with or without hysterectomy) or tubal ligation at least six weeks before taking study treatment. In case of oophorectomy alone, only when the reproductive status of the woman has been confirmed by follow up hormone level assessment
13.3. Use of established oral, injected or implanted hormonal methods of contraception, intrauterine device (IUD) or intrauterine system (IUS). In case of use of oral contraception women should have been stabile on the same pill for a minimum of 12 weeks before taking study treatment.
NOTE: Women are considered post-menopausal and not of child bearing potential if they have had 12 months of natural (spontaneous) amenorrhea with an appropriate clinical profile (e.g. age appropriate, history of vasomotor symptoms) or six months of spontaneous amenorrhea as defined by the Central Lab FSH and/or oestradiol levels
14. Active ongoing inflammatory diseases other than Behçet's syndrome that might confound the evaluation of the benefit of secukinumab therapy
15. Underlying metabolic, hematologic, renal, hepatic, pulmonary, neurologic, endocrine, cardiac, infectious or gastrointestinal conditions which in the opinion of the investigator immunocompromises the patient and/or places the patient at unacceptable risk for participation in an immunomodulatory therapy
16. Significant medical problems or diseases, including but not limited to the following: uncontrolled hypertension (≥160/95 mmHg), congestive heart failure [New York Heart Association status of class Ill or IV], uncontrolled diabetes
17. History of clinically significant liver disease or liver injury as indicated by abnormal liver function tests such as SGOT (AST), SGPT (ALT), alkaline phosphatase, or serum bilirubin. The investigator should be guided by the following criteria:
17.1. Any single parameter may not exceed 2 x upper limit of normal (ULN). A single parameter elevated up to and including 2 x ULN should be re-checked once more as soon as possible, and in all cases, at least prior to enrolment/randomization, to rule out lab error
17.2. If the total bilirubin concentration is increased above 2 x ULN, total bilirubin should be differentiated into the direct and indirect reacting bilirubin. In any case, serum bilirubin should not exceed the value of 1.6 mg/dl (27 µmol/L)
18. Estimated creatinine clearance less than 30 mL/min

Date of first enrolment

30/04/2022

Date of final enrolment
17/04/2025

Locations

Countries of recruitment
United Kingdom

Study participating centre
Aintree University Hospital
Department of Rheumatology
Liverpool University Hospitals
Liverpool
United Kingdom
L9 7AL

Study participating centre
Barts and the London NHS Trust
Dental Institute
London
United Kingdom
E1 1BB

Sponsor information

Organisation
Royal Liverpool and Broadgreen University Hospital NHS Trust

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Longmoor Lane
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England
United Kingdom
L9 7AL
+44 151 706 2000 ext 3702
RGT@liverpoolft.nhs.uk

Sponsor type
Hospital/treatment centre

Website

http://www.rlbuht.nhs.uk/Pages/RoyalHome.aspx

ROR
https://ror.org/009sa0g06

Funder(s)

Funder type
Industry

Funder Name
Novartis Pharmaceuticals UK Limited

Alternative Name(s)
Novartis UK, NOVARTIS UK LIMITED

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Peer reviewed scientific journals
Conference presentation
Publication on website
Submission to regulatory authorities
The CI and Sponsor will have jurisdiction over the release of the final trial dataset and site investigators will have access to the full dataset if a formal request describing their plans is approved by the CI and Sponsor.

Intention to publish date
31/12/2025

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from RGT@liverpoolft.nhs.uk

IPD sharing plan summary
Available on request

Study outputs

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