ISRCTN99067257 https://doi.org/10.1186/ISRCTN99067257

REASCENT trial: a proof of principle trial to treat active systemic sclerosis via interferon inhibition

Submission date
06/06/2025

Recruitment status
Recruiting

Registration date
20/08/2026

Overall study status
Ongoing

Last Edited
25/09/2026

Condition category
Skin and Connective Tissue Diseases

[_] 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
Systemic Sclerosis (SSc) is a rare autoimmune condition that can affect a patient's whole body. An autoimmune disease occurs when a person’s immune system attacks their own body by mistake, in SSc this activity can lead to scarring of the organs.
SSc is a lifelong condition that can involve the skin, joints, lung, heart, kidneys, blood vessels and the digestive system. Patients may experience many complications as well as a decreased quality of life. Though there has been progress in the understanding of SSc, to date, there are no approved disease-modifying treatments for SSc, making this area of research a deeply unmet clinical need.
Scientific research suggests that a protein called Type I interferon (Type I IFN), could play a major role in SSc. Measuring the amount of Type I IFN in a patient’s blood could be crucial and levels of Type I IFN activity has been linked to how SSc presents clinically, for example, which organs are affected.
The REASCENT trial, led by Professor Francesco del Galdo, is a phase 2b, single arm, open label, proof of principle trial to evaluate the efficacy and safety of anifrolumab. Anifrolumab (Astra Zeneca AB) is a new drug that blocks Type I IFN and is currently licensed in the UK to treat another disease involving Type I IFN, systemic lupus erythematosus.

Who can participate?
We will enroll up to 35 participants, diagnosed with SSc, who have poor hand function, from the active observational study, STRIKE (IRAS ID 178638).

What does the study involve?
Those who consent to participate in REASCENT will receive anifrolumab 300 mg intravenously on a monthly basis, for a period of 52 weeks. The final infusion will receive their anifrolumab infusion on week 48.

What are the possible benefits and risks of participating?
Benefits:
Not provided at time of registration

Risks:
1. Investigational product
Patient safety and tolerability is closely monitored throughout the course of this study through the collection of adverse events (interview in clinic).
1.1. Pregnancy: if a participant (or their female partner) becomes pregnant while receiving trial treatment or immediately after, that the unborn baby could be affected. Females of child bearing potential will undergo a pregnancy test and must receive a negative result prior to receiving trial medications. Female participants of child bearing potential and male participants in the treatment arm will be educated regarding the need for acceptable contraception whilst they are receiving trial drugs.
Non-sterilised males who are sexually active with a female partner of childbearing potential must use two acceptable methods of effective contraception from Day 1 until at least 18 weeks after receipt of the final dose of investigational product. Should a participant become pregnant whilst receiving study treatment, treatment will be stopped immediately and the participant will be withdrawn.
1.2. Adverse events: more than 1800 patients have received anifrolumab in the context of several clinical trials as of July 2023. The most reported adverse reactions during anifrolumab treatment were upper respiratory tract infection (34%), bronchitis (11%), infusion-related reaction (9.4%) and herpes zoster (6.1%). The most common serious adverse reaction was herpes zoster (0.4%).
A list of the reported adverse reactions is reported below and additional information can be located in the IB and Study Protocol.
Frequencies of occurrence of adverse reactions are defined as: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1 000 to <1/100); rare (≥1/10 000 to <1/1 000); very rare (<1 /10 000) and not known (cannot be estimated from available data).
Hypersensitivity and infusion-related reactions (common)
Respiratory infections (very common)
Herpes zoster (common)
Immunogenicity (common)
Overall, anifrolumab 300 mg administered as an IV infusion is negligibly immunogenic in moderate to severe SLE patients, with no clinically relevant impact on PK/PD and no detectable association with safety events or clinical efficacy. The ADA results in SSc patients were consistent with those in the SLE studies.
1.3. Administration: there is a risk of localised discomfort to patients at the infusion site as is the case with administration of all intravenous medicines. Patients are advised in the PIL that they may experience some pain, redness, itching or a rash. Patients will be observed for 1-2 hours, following the 30 minute infusion.
2. Blood samples: venous blood sampling may cause bruising or infection at the site where the blood was taken, pain and/or fainting. Where possible, blood samples required for research purposes will be taken at the same time as routine blood sampling to minimise distress and risk to participants.
3. Ionising radiation: participants on this study may receive a chest x-ray at screening to exclude TB. The risk of developing cancer as a consequence of receiving the chest x-rays required by this study is estimated as 0.0003%. For comparison, the natural lifetime cancer incidence in the general population is about 50%.

BURDEN:
1. Hospital visits
As part of the trial additional study visits are required over and above that would occur with standard care alone. It is also possible that additional unscheduled hospital visits will be required to enable all of the relevant safety testing to be carried out, and to check the participants' progress and possible side effects. Though this may be burdensome to the participant, there is

the benefit of increased supervision and disease monitoring. Visits have been kept to a minimum where possible, and investigations grouped to reduce the frequency of visits.

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

When is the study starting and how long is it expected to run for?
September 2026 to August 2028

Who is funding the study?
AstraZeneca UK

Who is the main contact?
Professor Francesco Del Galdo; f.delgaldo@leeds.ac.uk

Contact information

Type(s)
Public, Scientific, Principal investigator

Contact name
Prof Francesco Del Galdo

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Additional identifiers

Clinical Trials Information System (CTIS)
2022-001985-37

Integrated Research Application System (IRAS)
1005954

Central Portfolio Management System (CPMS)
53358

Protocol serial number
RR25/151204

Study information

Scientific Title
REASCENT trial: a proof of principle trial to treat active systemic sclerosis via interferon inhibition

Acronym
REASCENT

Study objectives
Primary objectives:
To evaluate the safety and tolerability of anifrolumab in patients with SSc (Cochin Hand Function score >25)

Secondary objectives:
1. To evaluate the effect of anifrolumab 300 mg on hand function at Week 52
2. To evaluate the effect of anifrolumab 300 mg SC on IFN inducible chemokine score as a measure of active disease at Week 24
3. To evaluate the effect of anifrolumab 300 mg on patient-reported disability at Week 52
4. To evaluate the effect of anifrolumab 300 mg on vascular manifestations of SSc at Week 52
5. To evaluate the effect of anifrolumab 300 mg SC on articular manifestations of SSc at Week 52

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 10/08/2026, London - Central Research Ethics Committee (3rd Floor, 3 Piccadilly Place London Road, Manchester, M1 3BN, United Kingdom; -; londoncentral.rec@hra.nhs.uk), ref: 25/LO/0482

Primary study design
Interventional

Study design
Interventional randomized controlled trial

Study type(s)
Safety

Health condition(s) or problem(s) studied
Systemic sclerosis

Interventions
This is a single-arm, open-label, proof-of-principle trial to evaluate the safety and tolerability of an intravenous (IV) treatment regimen of anifrolumab 300 mg in patients with active systemic sclerosis (SSc) while receiving standard of care (SOC) treatment. Participants enrolled in REASCENT will receive a fixed intravenous dose of anifrolumab 300 mg every 4 weeks (Q4W) for a total of 13 doses (Week 0 to Week 48).

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)

Saphnelo (anifrolumab)

Primary outcome(s)
Safety and tolerability of anifrolumab with endpoints including adverse events (AEs) (including adverse events of special interest [AESIs]), assessments including but not limited to vital signs, physical examination, 12-lead electrocardiograms, clinical laboratory tests (haematology, clinical chemistry, urinalysis) measured using NHS laboratory and/or clinical evaluation from the point of participant consent throughout the treatment and follow-up period

Key secondary outcome(s)
1. Hand function is measured using the Cochin Hand Function Scale (CHFS) at baseline, Week 24, and Week 52
2. Type I interferon (IFN) inducible chemokine activity is measured using serum IFN-inducible chemokine score at baseline, Week 24, and Week 52
3. Inflammatory activity is measured using NHS laboratory evaluation of IFN inducible chemokine score, troponin, CRP, NT-proBNP, complement (C3, C4) at baseline, Week 24, and Week 52
4. Patient-reported disability is measured using the HAQ-DI questionnaire at baseline, Week 24, and Week 52
5. Patient-reported disability is measured using the EULAR ScleroID questionnaire at baseline, Week 24, and Week 52
6. Pain intensity is measured using a visual analogue scale (VAS) at baseline, Week 24, and Week 52
7. Raynaud's phenomenon severity is measured using the Raynaud Condition Score (RCS) at baseline, Week 24, and Week 52
8. Digital ulcer incidence is measured using the proportion of patients with new digital ulcers at baseline, Week 24, and Week 52
9. Digital ulcer activity is measured using a patient-reported visual analogue scale (VAS) at baseline, Week 24, and Week 52
10. Microvascular abnormalities are measured using nailfold videocapillaroscopy at baseline, Week 24, and Week 52
11. Synovitis is measured using musculoskeletal ultrasound at baseline, Week 24, and Week 52
12. Joint stiffness is measured using shear wave elastography at baseline, Week 24, and Week 52
13. Patient-reported joint disease activity is measured using a visual analogue scale (VAS) at baseline, Week 24, and Week 52

Completion date
31/08/2028

Eligibility

Key inclusion criteria
1. Provision of informed consent prior to any study specific procedures (signing informed consent form [ICF])
2. Completion of all screening procedures within 30 days of confirmation of eligibility
3. Adult male or female patient aged 18 to 70 years at the time of screening
4. Weight >40 kg at screening
5. Diagnosis of SSc according to the ACR 2013 classification criteria (van den Hoogen et al. 2013)
6. Patient-reported hand-disability according to CHFS>25 at baseline
7. Modified Rodnan Skin score (mRSS) either: <10 or any mRSS if disease duration >7 years
8. Complete COVID-19 vaccination record according to national guidelines. Negative PCR or antigen test result at screening (according to local guidelines) and no known or suspected

COVID-19 infection or exposure between screening and randomization visits. There must be a minimum of 2 weeks between screening and randomization visits. If suspected infection or known/suspected exposure: Negative re-test result obtained after a minimum of 2 weeks from first test and patient remaining asymptomatic without new exposure. (If positive at screening: RE-screening may be allowed after 3 months provided no development of severe COVID-19 infection or sequalae).
9. Patients on no immunosuppression at screening must remain on no immunosuppression for the duration of treatment.
10. Patients on active immunosuppression at baseline have to have been on stable treatment with either methotrexate (MTX) (≤25 mg/week), hydroxychloroquine (≤400 mg/day), azathioprine (≤150 mg/day), mycophenolate (≤2 g/day), and/or OCS (prednisone-equivalent) (≤10 mg/day) for at least six months at the time of screening.
11. Negative pregnancy (serum β-human chorionic gonadotropin [β-hCG]) test at screening (females of childbearing potential only*).
*where a female of childbearing potential is a fertile female (menarche to post-menopausal) unless permanently sterile. Permanent sterilisation methods include hysterectomy, bilateral salpingectomy and bilateral oophorectomy.
12. Females of childbearing potential must use one effective method of avoiding pregnancy plus a male condom from screening until 18 weeks after the final dose of investigational product unless the subject is surgically sterile (i.e., bilateral tubal ligation, bilateral oophorectomy, or complete hysterectomy), has a sterile male partner, postmenopausal (no menses for 12 months without an alternative medical cause), or practices abstinence. Cessation of birth control after the 18-week follow up period should be discussed with a responsible physician.
12.1. Sustained abstinence is an acceptable practice; however, periodic abstinence, the rhythm method, and the withdrawal method are not acceptable methods of contraception.
12.2. 1 year postmenopausal is defined as at least one year since last menses without an alternative medical cause and the subject has an elevated follicle-stimulating hormone (FSH) level greater than the local participating site NHS Trust laboratory value of post-menopausal at screening.
13. Non-sterilised males who are sexually active with a female partner of childbearing potential must use two acceptable methods of effective contraception (Table 1) from Day 1 until at least 16 weeks after receipt of the final dose of investigational product.
14. Females with an intact cervix must have documentation of a Pap smear with no documented malignancy (e.g., cervical intraepithelial neoplasia grade III [CIN III], carcinoma in situ [CIS], or adenocarcinoma in situ [AIS]) within 2 years prior to Day 1 (see Appendix J I for guidance on abnormal Pap smear results)
15. Confirmed negative test for hepatitis B serology for:
15.1. Hepatitis B surface antigen, OR
15.2. Hepatitis B core antibody (HBcAb) AND hepatitis B virus (HBV) DNA (>169 copies/mL [29 IU /mL]) detected by reflex testing by the participating site's NHS Trust laboratory at screening.
Note: Subjects with HBcAb positivity at screening will be tested every 3 months for HBV DNA. To remain eligible in the study, subject HBV DNA levels must remain ≤169 copies/mL (29 IU/mL) as per the participating site's NHS Trust laboratory.
Confirmed negative test at screening for hepatitis C antibody as confirmed by participating site's NHS Trust laboratory
Herpes zoster infection must have completely resolved > 12 weeks prior to signing the ICF
16. Meets all of the following TB criteria:
16.1. No history of latent (not clinically active TB; asymptomatic and not infectious) or active TB (symptomatic and infectious) prior to screening, with the exception of latent TB with documented completion of appropriate treatment.
16.2. No signs or symptoms suggestive of active TB from medical history or physical examination.
16.3. No recent contact with a person with active TB OR if there has been such contact, referral

to a physician specializing in TB to undergo additional evaluation prior to Week 0 (documented appropriately in source), and, if warranted, receipt of appropriate treatment for latent TB at or before the first administration of investigational product.
16.4. Must meet one of the following criteria:
16.4.1. Negative QuantiFERON-TB Gold [QFT-G] test result for TB obtained from the participating site's NHS Trust laboratory within three months prior to Week 0.
OR
16.4.2. Positive QFT-G test result for TB obtained during the Screening Period from the participating site's NHS Trust laboratory for which active TB has been ruled out and appropriate treatment for latent TB has been initiated prior to the first investigational product administration.
OR
16.4.3. Indeterminate (confirmed on retest) QFT-G test result for TB obtained during the Screening Period from the participating site's NHS Trust laboratory with ongoing QFT-G testing for TB according to the Study Plan.
16.5. A chest radiograph with no evidence of current active infection (e.g., TB) or old active TB, malignancy, or clinically significant abnormalities not due to SSc in the 12 weeks prior to signing the informed consent.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
70 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Unwilling or unable to self-administer the investigational product at any point during the study.
2. Any condition that, in the opinion of the Investigator, would interfere with evaluation of the investigational product or interpretation of subject safety or study results (including Ludwig's angina)
3. Concurrent enrolment in another clinical study with an investigational product
4. Individuals involved with the conduct of the study, their employees, or immediate family members of such individuals
5. Lactating or pregnant females or females who intend to become pregnant anytime from initiation of Screening until the 18-week safety follow-up period following last dose of

investigational product
6. Current alcohol, drug or chemical abuse, or a history of such abuse within one year before Week 0 (Day 1)
7. Pre-operative management of IP: if a non-urgent major surgical procedure becomes necessary during the study, it should be scheduled at least 4 weeks after the last administration of IP, if clinically feasible
8. Spontaneous or induced abortion, still or live birth, or pregnancy ≤4 weeks prior to signing the ICF
9. Any history of severe COVID-19 infection e.g., requiring hospitalization, intensive care unit (ICU) care or assisted ventilation or any prior COVID-19 infection with unresolved sequelae. Confirmed or probable COVID-19 infection (see WHO definitions: www.who.int/publications/i /item/WHO-2019-CoV- Surveillance_Case_Definition-2020.1 based on clinical symptoms and radiologic imaging within 3 months prior to randomization.
10. Failure to comply with all required screening procedures due to circumstances related to pandemic or public health emergency.
11. At screening (within four weeks before Week 0 [Day 1]), any of the following:
11.1. Aspartate aminotransferase (AST) >2.0 × upper limit of normal (ULN)
11.2. Alanine aminotransferase (ALT) >2.0 × ULN
11.3. Total bilirubin >ULN (unless due to Gilbert's syndrome)
11.4. Serum creatinine >2.0 mg/dL (or >181 µmol/L)
11.5. Urine protein/creatinine ratio >2.0 mg/mg (or >226.30 mg/mmol)
11.6. Neutrophil count <1000/µL (or <1.0 × 109/L)
11.7. Platelet count <25000/µL (or <25 × 109/L)
11.8. Haemoglobin <8 g/dL (or <80 g/L)
11.9. Glycosylated haemoglobin (HbA1c) >42 UI at screening (diabetic subjects only)

Exclusion criteria related to medication(s)
12. Receipt of any investigational product (small molecule or biologic agent) within 4 weeks of signing the ICF
13. Prior receipt of anifrolumab
14. Receipt of cyclophosphamide within 24 weeks of signing the ICF.
15. Receipt of IFN therapy (alpha 2a and 2b, beta 1a and 1b, and pegylated IFNs alpha 2a and 2b) within 26 weeks of signing the ICF
16. Receipt of any commercially available biologic agent (including Nintedanib) or biologic immunomodulators prior to signing of the ICF – please confirm permitted washout periods with Chief Investigator and document where required
17. Receipt of B cell-depleting therapy (including but not limited to, epratuzumab, ocrelizumab, or rituximab) ≤26 weeks prior to signing the ICF or if therapy was administered >52 weeks ago absolute B cell less than the lower limit of normal or baseline value prior to receipt of B cell-depleting therapy (whichever is lower)
18. Receipt of immunoglobulin therapy within 4 weeks of signing the ICF
19. A known history of allergy or reaction to any component of the investigational product formulation or history of anaphylaxis to any human gamma globulin therapy
20. Receipt of any of the following:
20.1. Intra-articular, intramuscular or IV glucocorticosteroids within 6 weeks prior to signing the ICF
20.2. Any live or attenuated vaccine within 8 weeks prior to signing the ICF (administration of killed or synthetic vaccines is acceptable, Investigators should ensure all subjects are up to date on required vaccinations, including SARS-CoV (any MHRA approved type) and influenza [inactivated/recombinant] vaccine prior to study entry)
20.3. Bacillus Calmette-Guerin (BCG) vaccine within 1 year of signing the ICF
20.4. Any restricted medication if the washout period is not met

20.5. Blood transfusion within 4 weeks prior to signing the ICF
20.6. Plasmapheresis within 24 weeks of signing the ICF

Exclusion criteria related to Systemic Sclerosis and other conditions
21. History of SSc Renal Crisis in the past 12 months in the opinion of the local investigator or PI
22. Terminal Hand involvement including presence of gangrene, amputation or acrosteolisis or flexure contractions requiring hand surgery or CHFS >75
23. Diagnosis (within one year of confirmation of eligibility) of mixed connective tissue disease or any history of overlap syndromes with SLE or Rheumatoid Arthritis in the previous 12 months
24. History of, or current, inflammatory joint or skin disease other than SSc that, in the opinion of the Investigator, could interfere with the study assessments

Date of first enrolment
27/09/2025

Date of final enrolment
31/08/2028

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Chapel Allerton Hospital
Chapeltown Road
Leeds
England
LS7 4SA

Sponsor information

Organisation
University of Leeds

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Industry

Funder Name
AstraZeneca UK

Alternative Name(s)
AstraZeneca UK Limited, AZ

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date