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A Phase III trial evaluating the response to belimumab after rituximab in lupus patients who have high levels of IgA2 anti-DNA antibodies

Submission date
21/01/2026

Recruitment status
Recruiting

Registration date
10/08/2026

Overall study status
Ongoing

Last Edited
16/10/2026

Condition category
Skin and Connective Tissue Diseases

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

Plain English summary of protocol

Background and study aims
People with systemic lupus erythematosus (SLE) who are not responding to usual treatments like steroids are normally prescribed rituximab. STRATIFY lupus is based on a previous trial, BEAT-lupus, which showed that participants who were treated with belimumab after rituximab had fewer severe flares (worsening of symptoms) compared to treatment with rituximab alone. Autoantibodies are produced by the immune system in people with SLE and cause damage and inflammation to the body. Research on samples from BEAT-lupus participants identified an autoantibody called IgA2 anti-dsDNA that predicts which SLE patients may respond better to the combination treatment of rituximab followed by belimumab.

Who can participate?
Patients aged 16 to 75 years with active SLE who are not responding to standard treatment, are being considered for rituximab, and are positive for the IgA2 anti-dsDNA antibody.

What does the study involve?
Participants will be randomly allocated to either group A, belimumab intravenous (IV) infusions after rituximab for 48 weeks or group B, placebo IV infusions after rituximab treatment for 48 weeks. Participants will be in the study for a total of 52 weeks. The trial is ‘double blind’, meaning neither the participant nor the trial team will know which group the participant has been randomly allocated to. Participants will attend face-to-face visits, including an IV infusion every 2 weeks and then every 4 weeks until week 48. The final visit at week 52 does not include an IV infusion. Participants will undergo pre-specified assessments, complete questionnaires, and may have optional research blood and stool samples collected.

What are the possible benefits and risks of participating?
A positive trial will help to ensure access to rituximab followed by belimumab for those people who are most likely to respond and improve our understanding of SLE as a result.
The most frequently reported adverse reactions for systemic lupus erythematosus (SLE) patients

who are treated with belimumab are infection and delayed onset of symptoms of acute hypersensitivity reactions. Participants will be closely monitored after their first and second infusions for a minimum of 3 hours by the site research team. This is because symptoms of hypersensitivity occur more frequently during the first two infusions and then tend to decrease. If necessary, site teams can monitor participants for an extended period at all trial visits. At every trial visit, adverse events will be reviewed by the site research team for any updates, and recurring adverse events or resolutions will be recorded. Any participants with recurring infections or adverse events may be asked to stop trial treatment and/or withdraw from the trial for their own safety. Participants will be informed of all adverse events associated with belimumab and symptoms to look out for. They will also be provided with a card containing contact details for their research team that can be used 24 hours a day, 7 days a week. If necessary, emergency unblinding can also take place 24 hours a day, 7 days per week. The trial location teams will be aware of the risk of these adverse events and provided with the relevant safety information for Belimumab alongside the protocol.
When participants experience flares or symptoms such as photosensitivity, extreme fatigue or joint pain, travelling to trial visits may become difficult, especially for elderly participants. Additionally, younger participants may have other obligations, such as employment or education, which can make trial visits inconvenient. The trial has been designed to minimise the travel burden through only visits 1, 2 and 3 being every 2 weeks; from visit 4 onwards, each visit is every 4 weeks. There are also no additional trial activities for participants to complete outside of the scheduled face-to-face visits. Participants will be informed of the visit schedule, what to expect at each visit and the approximate time for a visit in the participant information sheet. There is an allowance of +/- 3 days for the 2- weekly scheduled treatment visits and +/- 7 days for the 4- weekly scheduled treatment visits, as well as a 4-8 week window from the first screening visit to randomisation.
Participants who are under the age of 18 years old may find it uncomfortable to complete the scheduled urine pregnancy testing, discuss contraception or complete questionnaires in the presence of their parents/legal guardians. The participant information sheet has a summary of the visit schedule, outlines what to expect at each visit and the requirement for urine pregnancy testing and contraceptive use. Special attention and care will be given to the “sexually active” prompt in participants, as per the clinician's discretion and only if appropriate to do so. The clinicians will ensure there is a safe space at visits to discuss these matters where appropriate. Participants will be given the opportunity to discuss such matters in a private environment.
Biological samples will be shipped to the UCL Department of Medicine at the Rayne Building (Ehrenstein Laboratory) at specified timepoints as per the protocol. There is a risk that these samples get lost when transported. A Sample Management Plan will be followed and provided to sites, there will be full accountability logs for each sample from the point of collection, storage and transfer. Oversight logs will be maintained at sites and reviewed during monitoring and requested for central monitoring by the CCTU.
There is limited data on the effects of belimumab on pregnancy. Participants of childbearing potential must either use a form of contraceptive with a failure rate <1% or be sexually inactive by abstinence. These participants must have a negative serum or urine pregnancy test at screening and will have regular urine pregnancy tests at each trial visit before treatment. Participants who are pregnant, breastfeeding or plan to become pregnant either during the trial period or within 4 months of trial treatment stopping will not be eligible for the trial. Any pregnancies that occur from consent to within 4 months of the last dose of trial treatment must be reported to UCL CCTU for follow-up and trial treatment stopped accordingly as applicable.

Where is the study run from?
University College London (UK)

When is the study starting and how long is it expected to run for?
November 2026 to November 2029

Who is funding the study?
1. Arthritis UK
2. NIHR Efficacy and Mechanism Evaluation Programme (EME) (UK)

Who is the main contact?
STRATIFY lupus trial team, cctu.stratifylupus@ucl.ac.uk

Contact information

Type(s)
Principal investigator, Scientific

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Type(s)
Public

Contact name
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Additional identifiers

Integrated Research Application System (IRAS)
1013219

Central Portfolio Management System (CPMS)
57705

Sponsor's protocol code number

160445

Study information

Scientific Title
A Phase IIIa randomised placebo-controlled biomarker enrichment trial: IgA2 anti-DNA antibodies as a biomarker of response to belimumab after rituximab in systemic lupus erythematosus

Acronym
STRATIFY lupus

Study objectives
Primary objective:
To determine whether clinical response, including prevention of disease flares through to 52 weeks, to belimumab after rituximab therapy is significantly superior to rituximab alone in lupus participants who are due to receive rituximab as part of their NHS standard of care and with high levels of serum IgA2 anti-dsDNA antibodies (≥12.5 AU).

Secondary objective:
To provide safety data, including the occurrence of infections and hypogammaglobulinemia for this combination in biomarker-positive participants during the 52-week trial duration.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 07/08/2026, East of England - Cambridge East Research Ethics Committee (2 Redman Place, Stratford, London, EC20 1JQ, United Kingdom; +44 (0)2071048181; CambridgeEast.REC@hra.nhs.uk), ref: 26/EE/0155

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Placebo

Assignment
Parallel

Purpose
Treatment

Study type(s)

Efficacy, Safety, Treatment

Health condition(s) or problem(s) studied
Systemic lupus erythematosus

Interventions
Participants will be randomised to receive belimumab or placebo (normal saline, sodium chloride 0.9%) using Sealed Envelope. Intravenous administration of belimumab or placebo will be given from randomisation at the recommended standard dosage and intervals: 10 mg/kg at 2-week intervals for the first 3 doses and at 4-week intervals thereafter for 48 weeks. The final assessment visit will occur at week 52. After the first Screening visit, participants will have their first and second rituximab infusion and their eligibility for the trial confirmed during the second Screening and Randomisation visit. During each visit at their trial location, participants will have any medications they are taking reviewed; a physical exam and urine test; vital signs and weight change check; blood samples taken for safety monitoring; complete questionnaires about their lupus activity and how they feel during the trial and the collection of optional blood and stool samples.

Intervention Type
Drug

Phase
Phase III

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

Primary outcome(s)
Modified Major Clinical Response (MCR) at 52 weeks. Modified MCR is defined as a reduction in BILAG–2004 (British Isles Lupus Assessment Group-2004) index A/B scores to BILAG–2004 C/D or remain E in all domains, a reduction in steroid dose to ≤7.5 mg daily and a modified SLEDAI (Systemic Lupus Erythematosus Disease Activity Index 2000) –2K score ≤2 (without including the IgG anti-dsDNA antibody component) and no increase in immunosuppressant dose in the last 3 months before 52 weeks.

Key secondary outcome(s)
1. Modified Major Clinical Response (MCR) at 24 weeks: Reduction in BILAG–2004 (British Isles Lupus Assessment Group-2004) index A/B scores to BILAG–2004 C/D or remain E in all domains, a reduction in steroid dose to ≤7.5 mg daily and a modified SLEDAI (Systemic Lupus Erythematosus Disease Activity Index 2000) –2K score ≤2 (without including the IgG anti-dsDNA antibody component).
2. Major Clinical Response (MCR) at 24 and 52 weeks: Reduction in BILAG–2004 (British Isles Lupus Assessment Group-2004) index A/B scores to BILAG–2004 C/D or remain E in all domains, a reduction in steroid dose to ≤7.5mg daily and a modified SLEDAI (Systemic Lupus Erythematosus Disease Activity Index 2000) –2K score ≤4. For the 52- week outcome: no increase in immunosuppressant in the last 3 months.
3. Time to first incidence of:
3.1. Severe BILAG-2004 A flare (severe flare: a BILAG-2004 A score due to items which are “new” or “worse”; or, in the renal or haematological systems, an A score due to items which didn’t result in an A score last month).
3.2. Severe or moderate BILAG-2004 flares (moderate flare: 2 BILAG-2004 B scores due to items

which are either “new” or “worse”; or, in the renal or haematological systems, B scores due to items which didn’t result in a B score last month) accompanied by an increase in concomitant lupus medication: glucocorticoids, or immunosuppressant through to 24 and 52 weeks.
3.3. Severe or moderate BILAG-2004 flare (moderate flare: 2 BILAG-2004 B scores due to items which are either “new” or “worse”; or, in the renal or haematological systems, B scores due to items which didn’t result in a B score last month).
3.4. BILAG-2004 low disease activity with prednisolone i) ≤5 mg/day (BILAG-2004 LDA-5); ii) ≤7.5 mg/day (BILAG-2004 LDA-7.5), and stable dose of immunosuppressive drugs.
4. Time to achieve:
4.1. BILAG-2004 low disease activity with prednisolone i) ≤5 mg/day; ii) ≤7.5 mg/day and stable dose of immunosuppressive drugs
4.2. Lupus Low Disease Activity State (LLDAS)
4.3. DORIS (Definition of Remission in SLE) remission
5. Proportion of patients at 24, 36 and 52 weeks in:
5.1. BILAG-2004 low disease activity with prednisolone: i) ≤5 mg/day; ii) ≤7.5 mg/day and stable dose of immunosuppressive drugs
5.2. DORIS remission
5.3. LLDAS
6. Cumulative steroid and immunosuppressant doses during treatment from randomisation to 52 weeks measured using case report forms
7. Impact of SLE and the trial treatment measured using Lupus Quality of Life (LupusQoL), SF-36 and EQ5D at 52 weeks
8. IgA2 anti-dsDNA antibody levels measured using ELISA assay at 24 and 52 weeks
9. Proportion of participants with any infectious serious adverse event through to week 52 of the trial.
10. Proportion of participants with any adverse events and proportion with any serious adverse events through to week 52 of the trial.
11. Total serum IgG levels measured using standard automated immunoturbidimetric assay at 52 weeks.

Completion date
30/11/2029

Eligibility

Key inclusion criteria
1. Aged between 16 and 75 years inclusive at screening.
2. Participants who meet the 2019 criteria for SLE according to the European League Against Rheumatism/American College of Rheumatology Classification Criteria for Systemic Lupus Erythematosus.
3. Positive serum IgA2 anti-dsDNA antibodies (≥12.5 AU) at time of screening measured in UCL laboratory. IgA2 results defined in UCL Central laboratory.
4. Participants are due to be treated with the first infusion of B-cell depletion therapy (e.g. Rituximab) 4-8 weeks before randomisation (Day 0, see participant timeline) for active SLE. Previous use of rituximab is allowed prior to this cycle.
5. No contraindications to the use of belimumab.
6. Participants willing and able to provide informed consent.

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
16 Years

Upper age limit
75 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
Current key exclusion criteria as of 16/10/2026:
1. Pregnant or planned pregnancy during the trial and/or breastfeeding.
2. Women of childbearing potential (WOCBP) not willing to use highly effective contraception or abstinence for the duration of the trial and for at least 4 months following the last dose of the study drug.
3. Prior use of biologic/advanced therapy (except rituximab given as part of this trial after screening) less than 6 months before randomisation.
4. Participation in any other interventional trial within the last 6 months before randomisation.
5. eGFR <30 ml/min at screening
6. Active infections, including but not limited to:
6.1. Current or past infection with hepatitis B or C as defined by:
6.1.1. Hepatitis B surface antigen positive
6.1.2. Hepatitis B surface antibody positive and hepatitis B core antibody positive
6.1.3. Hepatitis C antibody positive
6.2. Historically positive HIV test or test positive at screening for HIV
6.3. Active TB
7. Infection history:
7.1. Currently on any suppressive therapy for a chronic infection (such as tuberculosis, pneumocystis, cytomegalovirus, herpes simplex virus, herpes zoster and atypical mycobacteria)
7.2. Hospitalisation for treatment of infection within 30 days prior to randomisation
8. Use of parenteral (IV or IM) antibiotics (antibacterials, antivirals, anti-fungals, or anti-parasitic agents) within 30 days prior to randomisation.
9. Receipt of a live-attenuated vaccine within 3 months prior to randomisation.
10. In the investigator’s opinion, participants that are at high risk for infection (including but not limited to in-dwelling catheter, dysphagia with aspiration, decubitus ulcer, history of prior aspiration pneumonia or recurrent severe urinary tract infection).
11. Primary immunodeficiency.
12. History of malignant neoplasm within 5 years prior to randomisation except for basal cell carcinomas of the skin, squamous cell carcinomas of the skin, and carcinoma in situ of the cervix that have been completely excised and considered cured for >2 years prior to screening.
13. History of cervical dysplasia CIN Grade III cervical high risk human papillomavirus or abnormal cervical cytology other than abnormal squamous cells of undetermined significance (ASCUS) in the last 3 years prior to randomisation. The participant will be eligible after the condition has resolved (e.g., follow-up HPV test is negative, or cervical abnormality has been effectively treated >1 year ago).

14. Severe, progressive, or uncontrolled renal, hepatic, haematological, gastrointestinal, pulmonary, cardiac, or neurological disease or, in the investigator's opinion, any other concomitant medical condition or significant abnormal laboratory value that places the participant at risk by participating in this study except for diseases or conditions related to active SLE.
15. Comorbidities not lupus related currently requiring systemic corticosteroid or immunosuppressant therapy.
16. Evidence of serious suicide risk including having any history of suicidal behaviour in the last 6 months and/or suicidal ideation in the last 2 months, or who in the investigator's judgement, pose a significant suicide risk.
17. History of an anaphylactic reaction to parenteral administration of contrast agents, human or murine proteins or monoclonal antibodies.
18. IgG levels <4.0 g/L or IgA level <10 mg/dL tested no more than 10 days before randomisation.
19. White blood cells (WBC) <1.5 x 10e9/L or Neutrophils <1.0 x 10e9/L measured no more than 10 days before randomisation.
20. Current drug or alcohol abuse or dependence or a history of drug or alcohol abuse or dependence within a year prior to randomisation.

Previous key exclusion criteria:
1. Pregnant or planned pregnancy during the trial and/or breastfeeding.
2. Women of childbearing potential (WOCBP) not willing to use highly effective contraception or abstinence for the duration of the trial and for at least 4 months following the last dose of the study drug.
3. Prior use of biologic/advanced therapy (except rituximab given as part of this trial after screening) less than 3 months before randomisation.
4. Participation in any other interventional trial within the last 6 months before randomisation.
5. eGFR <30 ml/min at screening
6. Active infections, including but not limited to:
6.1. Current or past infection with hepatitis B or C as defined by:
6.1.1. Hepatitis B surface antigen positive
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15. Comorbidities not lupus related currently requiring systemic corticosteroid or immunosuppressant therapy.
16. Evidence of serious suicide risk including having any history of suicidal behaviour in the last 6 months and/or suicidal ideation in the last 2 months, or who in the investigator's judgement, pose a significant suicide risk.
17. History of an anaphylactic reaction to parenteral administration of contrast agents, human or murine proteins or monoclonal antibodies.
18. IgG levels <4.0 g/L or IgA level <1 mg/dL tested no more than 10 days before randomisation.
19. White blood cells (WBC) <1.5 x 10e9/L or Neutrophils <1.0 x 10e9/L measured no more than 10 days before randomisation.
20. Current drug or alcohol abuse or dependence or a history of drug or alcohol abuse or dependence within a year prior to randomisation.

Date of first enrolment
01/11/2026

Date of final enrolment
31/10/2028

Locations

Countries of recruitment
United Kingdom

England

Wales

Study participating centre
University College London Hospital
250 Euston Road
London
England
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Study participating centre
The Royal Glamorgan Hospital
Ynysmaerdy
Pontyclun
Wales
CF72 8XR

Study participating centre
Manchester Royal Infirmary
Oxford Road
Manchester
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M13 9WL

Study participating centre
King's College Hospital
Denmark Hill
London
England
SE5 9RS

Study participating centre
Guy's and St Thomas' Hospitals
Trust Offices
Guy's Hospital
Great Maze Pond
London
England
SE1 9RT

Study participating centre
Royal Free Hospital
Royal Free Hospital
Pond Street
London
England
NW3 2QG

Study participating centre
Royal Hallamshire Hospital
Glossop Road
Sheffield
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S10 2JF

Study participating centre
Doncaster Royal Infirmary
Armthorpe Road
Doncaster
England
DN2 5LT

Study participating centre
Sandwell General Hospital
Lyndon
West Bromwich
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B71 4HJ

Study participating centre
Mile End Hospital
Block 9 Me67
275 Bancroft Road
London
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E1 4DG

Study participating centre
Royal United Hospital
Combe Park
Bath
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Study participating centre
Chapel Allerton Hospital
Chapeltown Road
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LS7 4SA

Study participating centre
Freeman Road Hospital
Freeman Road
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NE7 7DN

Study participating centre
Addenbrooke's Hospital
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CB2 0QQ

Study participating centre
Queen Elizabeth Hospital
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B15 2TH

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Tremona Road
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SO16 6YD

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Liverpool
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L14 3LB

Study participating centre
Nuffield Orthopaedic Centre
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Oxford
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OX3 7HE

Study participating centre
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L9 7AL

Sponsor information

Organisation
University College London

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type

Funder Name
Arthritis Research UK

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
Efficacy and Mechanism Evaluation Programme

Alternative Name(s)
NIHR Efficacy and Mechanism Evaluation Programme, Efficacy and Mechanism Evaluation (EME), EME

Funding Body Type
Government organisation

Funding Body Subtype
National government

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.0	11/12/2025	06/02/2026	No	Yes
Participant information sheet	version 2.0	29/07/2026	12/08/2026	No	Yes
Protocol file	version 3.0	09/09/2026	16/10/2026	No	No