ForPatients
by Roche

Systemic Lupus Erythematosus

A clinical trial to look at how well obinutuzumab works to reduce certain features of systemic lupus erythematosus (SLE) when compared to placebo

A Study to Evaluate the Efficacy and Safety of Obinutuzumab in Participants With Systemic Lupus Erythematosus

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	14 Countries	NCT04963296 2023-504774-38-00 CA42750

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

A phase III, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy and safety of obinutuzumab in patients with systemic lupus erythematosus

Trial Summary:

This parallel-group, double-blind, placebo-controlled study will evaluate the efficacy and safety of obinutuzumab versus placebo in participants with active, autoantibody-positive systemic lupus erythematosus (SLE) who are treated with standard-of-care therapy.

Hoffmann-La Roche Sponsor	**Phase 3** Phase

NCT04963296 2023-504774-38-00 CA42750
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years & # 75 Years	No

1. Why is the ALLEGORY clinical trial needed?

Systemic lupus erythematosus (SLE) is an autoimmune disease, which means the immune system attacks the body by mistake. This causes inflammation and damage,

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and can affect the joints, skin, brain, lungs, kidneys and blood vessels. In SLE, a type of immune cell called B cells produce antibodies that attack the body (also known as ‘autoantibodies’). Symptoms flare up when SLE is in an ‘active’ state when more autoantibodies may be produced. Symptoms reduce when SLE is not active (known as ‘remission’). Standard treatment aims to suppress the immune system with treatments including steroids (such as prednisone), antimalarials like hydroxychloroquine, immunosuppressants and antibody therapies.

Although treatments are available, people with SLE are more likely than healthy people to have conditions such as heart disease. Some people have treatment side effects they cannot manage, or their treatment may stop working. So, new treatments for SLE are needed. Obinutuzumab is a drug designed to remove B cells in people with SLE. Obinutuzumab is an experimental drug, meaning that health authorities have not approved it as a treatment for SLE. This clinical trial aims to compare the effects, good or bad, of obinutuzumab against placebo in people with SLE. A ‘placebo’ looks like the drug being tested but does not contain any real medicine.

2. How does the ALLEGORY clinical trial work?

This clinical trial is recruiting people with SLE. People can take part if they were diagnosed with SLE at least 3 months previously and have highly active disease. People who take part in this clinical trial (participants) will be given the trial treatment obinutuzumab OR placebo over the course of 1 year. The clinical trial doctor will see them regularly. These visits will include checks to see how the participant responds to the treatment and any side effects they may have. After 1 year of treatment, participants whose SLE has not worsened may be able to be given obinutuzumab for up to 1 more year. After the last dose of treatment, participants will be seen every 6 months until their B cell counts have returned to levels recorded before treatment, or until another B cell-lowering treatment is given as part of their standard SLE treatment. The total time of participation in the clinical trial will be up to around 2 and a half years (30 months). Participants can stop trial treatment and leave the clinical trial at any time.

3. What are the main endpoints of the ALLEGORY clinical trial?

The main clinical trial endpoint (the main result measured in the trial to see if the drug has worked) is the number of participants who have improved symptoms of SLE – known as SRI(4) using the ‘Systemic Lupus Erythematosus Responder Index’ – after 1 year of treatment. The other clinical trial endpoints include the:

- Number of participants:
    - with even greater improvement of SLE symptoms – known as SRI(6)
    - whose treatment with prednisone (or equivalent) is reduced from at least 10mg daily to 7.5mg or less by 9 months with no other steroids given, or at 1 year with SRI(4)

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  - who have improved symptoms of SLE – known as SRI(4) by 6 months, from 9 months to 1 year, or by 1 year when looking at symptoms only
  - who have improved symptoms and no new body parts affected – measured using another score named British Isles Lupus Assessment Group-based Composite Lupus Assessment ('BICLA')
  - who require 5mg or less of prednisone from 9 months to 1 year with no other steroids given
  - who reach a 'low disease activity' status or 'SLE remission' at 1 year
  - who have at least half the number of swollen or tender joints at each visit (for those with more than 4 joints affected at the start of the trial)
  - who have a certain level of skin symptoms at the start of the trial that improve by 50% at each visit
- Time between the start of treatment and the first flare-up of symptoms over 1 year
- The number of flare-ups participants have per year
- Amount of steroids that participants need to take from the start of the trial to 1 year
- Change in the number of swollen or tender joints from the start of the trial to 6 months and 1 year
- Changes in tiredness, pain and physical health from the start of treatment to 6 months and 1 year
- Number and seriousness of side effects, how the body processes obinutuzumab and its effects on the immune system

4. Who can take part in this clinical trial?

People can take part in this trial if they are between 18–75 years old, have been diagnosed with SLE for at least 3 months, and receive at least one standard treatment for SLE, such as oral corticosteroids, immunosuppressants or antimalarials. People may not be able to participate if they have been given certain treatments (including for SLE) within a particular time frame, have SLE that causes severe problems with the kidneys or affects the brain or spinal cord, certain infections, are pregnant or breastfeeding, or are planning to become pregnant within 18 months of the last dose of obinutuzumab or placebo.

5. What treatment will participants be given in this clinical trial?

Everyone who joins this clinical trial will be split into two groups randomly (like flipping a coin) with an equal chance of being placed in either group and given either **obinutuzumab** OR **placebo** as an infusion (into the vein) on Day 1 and Weeks 2, 24 and 26. Participants will receive an infusion of steroids, as well as doses of antihistamine and paracetamol/ acetaminophen, before each obinutuzumab or placebo infusion. They will also be able to continue taking their standard SLE therapy as guided by the clinical trial doctor.

This is a 'placebo-controlled' clinical trial, which means that one of the groups will be given a substance with no active ingredients (also known as a 'placebo'). Comparing results from the different groups helps the researchers know whether any changes seen result from the drug or occur by chance. This is a double-blinded trial, which means that neither

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the participant nor the clinical trial doctor can choose or know the group the participant is in, until the trial is over. This helps to prevent bias and expectations about what will happen. However, the clinical trial doctor can find out which group a participant is in if their safety is at risk. After Week 52, all participants may be given obinutuzumab as an infusion on Weeks 54, 56, 78, and 104 whether they had obinutuzumab or placebo before. This is the open-label phase of the clinical trial – in other words, participants and the clinical trial doctor will know obinutuzumab is being given.

6. Are there any risks or benefits in taking part in this clinical trial?

The safety or effectiveness of the experimental treatment or use may not be fully known at the time of the trial. Most trials involve some risks to the participant. However, it may not be greater than the risks related to routine medical care or the natural progression of the health condition. People who would like to participate will be told about any risks and benefits of taking part in the clinical trial, as well as any additional procedures, tests, or assessments they will be asked to undergo. All of these will be described in an informed consent document (a document that provides people with the information they need to decide to volunteer for the clinical trial).

Risks associated with the clinical trial drugs

Participants may have side effects (an unwanted effect of a drug or medical treatment) from the drugs used in this clinical trial. Side effects can be mild to severe, even life-threatening, and vary from person to person. Participants will be closely monitored during the clinical trial; safety assessments will be performed regularly. Participants will be told about the known side effects of obinutuzumab, and possible side effects based on human and laboratory studies or knowledge of similar drugs. Participants will be told about any known side effects of infusions into a vein (intravenous infusions).

Potential benefits associated with the clinical trial

Participants' health may or may not improve from participation in the clinical trial. Still, the information collected may help other people with similar medical conditions in the future.

Inclusion Criteria:

- Diagnosis of SLE according to the 2019 European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) Classification Criteria >=12 weeks prior to screening
- Anti-nuclear antibody (ANA) >=1:80, or anti-dsDNA and/or anti-Sm antibodies above the upper limit of normal (ULN), as determined by the central laboratory at screening
- Low C3 or low C4 or low CH50 complement as determined by the central laboratory at screening
- High disease activity at screening, based on; BILAG-2004 (Category A disease in >=1 organ system and/or Category B disease in >=2 organ systems), Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) (score >=8) and Physician's Global Assessment (PGA) (score >=1.0 on a 0 to 3 visual analogue scale [VAS])

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- High disease activity on Day 1, based on; SLEDAI-2K (score >=8) and PGA (score >=1.0 on a 0 to 3 VAS)
- Current receipt of >=1 of the following classes of standard therapies for the treatment of SLE at stable doses: oral corticosteroid (OCS), antimalarials, conventional immunosuppressants
- Other inclusion criteria may apply
- The Medical Monitor may be consulted if there are any questions related to eligibility criteria

Exclusion Criteria:

- Pregnancy or breastfeeding
- Presence of significant lupus-associated renal disease and/or renal impairment
- Receipt of an excluded therapy, including any anti-CD20, anti-CD19 therapy less than 9 months prior to screening or during screening; or cyclophosphamide, tacrolimus, ciclosporin, or voclosporin during the 2 months prior to screening or during screening
- Significant or uncontrolled medical disease which, in the investigator's opinion, would preclude patient participation
- Known active infection of any kind or recent major episode of infection
- Intolerance or contraindication to study therapies
- Other exclusion criteria may apply

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