ForPatients
by Roche

Systemic Lupus Erythematosus

A clinical trial to compare different doses of mosunetuzumab in people with systemic lupus erythematosus (SLE)

A Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Subcutaneously Administered Mosunetuzumab to Participants With Systemic Lupus Erythematosus

Trial Status	Trial Runs In	Trial Identifier
Completed	3 Countries	NCT05155345 2021-001565-20 GA43191

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 Ib, multicenter, open-label, dose-escalation study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of subcutaneously administered mosunetuzumab to participants with systemic lupus erythematosus

Trial Summary:

This study will evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of mosunetuzumab in participants with systemic lupus erythematosus (SLE).

Hoffmann-La Roche Sponsor	**Phase 1** Phase

NCT05155345 2021-001565-20 GA43191
Trial Identifiers

Eligibility Criteria:

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

1. Why is the GA43191 clinical trial needed?

Systemic lupus erythematosus (SLE) is an autoimmune disease, which means the immune system attacks the body by mistake. This causes damage and inflammation and can affect the joints, skin, brain, lungs, kidneys and blood vessels. In SLE, one type of

cells of the immune system called B cells produce antibodies (blood proteins normally made to help defend the body against infection) that attack the body's own tissues by mistake (also known as 'autoantibodies'). Symptoms flare up when SLE is in an 'active' state when more autoantibodies may be produced (also known as 'relapsing'). Symptoms reduce when SLE is not active (known as 'remitting'). Standard treatment aims to reduce inflammation and suppress the immune system and includes steroids, antimalarials, immunosuppressants and antibody therapies that lower levels of B cells. Some people also have unacceptable side effects to treatment, or treatment may stop working (known as 'refractory' disease). New treatments for SLE are needed.

Mosunetuzumab is an experimental antibody therapy – which means it is not approved for treating SLE. Mosunetuzumab sticks to B cells marking them for destruction by other immune cells to stop the harmful autoantibodies being made. Mosunetuzumab may work better than other antibody therapies against SLE.

This clinical trial aims to test the safety of mosunetuzumab at different doses and to understand how the body processes mosunetuzumab.

2. How does the GA43191 clinical trial work?

This clinical trial is recruiting people with active SLE. People who take part in this clinical trial (participants) will be given either one dose of the clinical trial treatment, mosunetuzumab, or two doses 1 week apart. Participants are required to stay in the hospital for 3 days after being given mosunetuzumab so that their health can be observed closely. . All participants will be seen by the clinical trial doctor every week for the first month, followed by monthly visits up to and including Month 6, then every 3 months (Months 9 and 12). If the number of B cells in a participants' blood remains low at Month 12, they will have further visits every 6 months until the number of B cells recovers or until the clinical trial ends, whichever occurs first. These clinic visits will include checks to see how the participant responds to the treatment and any side effects they may have. The total time of participation in the clinical trial will be at least 1 year. Participants can stop trial treatment and leave the clinical trial at any time.

3. What are the main endpoints of the GA43191 clinical trial?

The main clinical trial endpoint (the main result measured in the trial to see how safe mosunetuzumab is and how well participants can handle different doses) is the number and seriousness of side effects.

The other clinical trial endpoints include:

- The level of mosunetuzumab in the blood at certain times during the trial
- How the body breaks down and gets rid of mosunetuzumab
- The number of B-cells in the blood at certain times during the trial

- The amount of time that the level of B-cells in the blood stays lower than levels were before mosunetuzumab treatment
- How mosunetuzumab affects the body's 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 and have been diagnosed with SLE for more than 3 months according to certain criteria (this may be confirmed with tests to look for autoantibodies in the blood). Participants must also currently be receiving at least one standard treatment for SLE, and both men and women (if they can become pregnant) will need to either not have heterosexual intercourse or will need to use reliable contraception for safety reasons.

People may not be able to take part in this trial if they have SLE that affects the brain or nerves, a low level of B-cells before joining the study, have been given certain medicines such as those that affect B-cells within the last year, or have certain other medical conditions such as infections, cancer in the last 5 years, or they are pregnant or breastfeeding.

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

Everyone who joins this clinical trial will be placed into one treatment group depending on when they join the trial, and given either:

- Group 1: one dose of mosunetuzumab, given as an injection (under the skin) on Day 1
- Group 2: two doses of mosunetuzumab, given as an injection (under the skin) on Days 1 and 8

Participants will only join Group 2 once Group 1 has finished treatment. Participants may also receive another medicine called tocilizumab as an infusion into the vein if they experience certain side effects during the clinical trial.

This is an open-label trial, which means everyone involved, including the participant and the clinical trial doctor, will know the clinical trial treatment the participant has been given.

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

The safety or effectiveness of the experimental treatment 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 mosunetuzumab and tocilizumab 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 injections under the skin (subcutaneous injections) and infusions into the 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 Classification Criteria at least 12 weeks or more prior to screening
- Presence of one or more of the following SLE autoantibodies documented within the 12 months prior to screening or during screening: positive ANA (greater than or equal to 1:160); anti dsDNA above the upper limit of normal (ULN); anti-Sm above the ULN
- Active SLE disease, as demonstrated by a SLEDAI-2K total score of greater than or equal to 4 at screening
- Current receipt of one or more of the following classes of standard therapies for the treatment of SLE at stable doses: oral corticosteroids (OCSs), antimalarial agents, conventional immunosuppressants
- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraception as defined by the protocol
- For men on mycophenolate mofetil (MMF): With a female partner of childbearing potential, men who are not surgically sterile must remain abstinent (refrain from heterosexual intercourse) or use contraception as defined by the protocol

Exclusion Criteria:

- Pregnant or breastfeeding, or intending to become pregnant during the study or within 3 months after the final dose of mosunetuzumab and 3 months after the final dose of tocilizumab
- Active severe or unstable lupus-associated neuropsychiatric disease that is likely to require treatment with protocol-prohibited therapies
- Active overlap syndrome with mixed connective tissue disease or systemic sclerosis within 12 months prior to screening or during screening
- Catastrophic or severe antiphospholipid syndrome within 12 months prior to screening or during screening

- Presence of significant lupus-associated renal disease and/or renal impairment that is likely to require treatment with protocol-prohibited therapies
- Peripheral CD19+ B-cell count < 25 cells/uL
- Receipt of an investigational therapy within 30 days or 5 drug-elimination half-lives (whichever is longer) prior to initiation of study treatment and during the study
- Receipt of any of the following excluded therapies: any anti-CD19 or anti-CD20 therapy such as blinatumomab, obinutuzumab, rituxumab, ocrelizumab, or ofatumumab less than 12 months prior to screening or during screening; inhibitors of JAK, Bruton tyrosine kinase, or tyrosine kinase 2, including baricitinib, tofacitinib, upadacitinib, filgotinib, ibrutinib, or fenebrutinib, or any investigational agent within 30 days prior to screening or during screening; tacrolimus, ciclosporin, or voclosporin within 30 day prior to screening or during screening; cyclophosphamide or a biologic therapy such as but not limited to belimumab, ustekinumab, anifrolumab, secukinumab, or atacicept during 2 months prior to screening or during screening; any live or attenuated vaccine during 28 days prior to screening or during screening
- High risk for any clinically significant bleeding or any condition requiring plasmapheresis, IV immunoglobulin, or acute blood product transfusions
- Significant or uncontrolled medical disease that would preclude participation
- HIV infection, acute or chronic hepatitis B virus (HBV), acute or chronic hepatitis C (HCV) infection, tuberculosis (TB) infection, known or suspected chronic active Epstein-Barr virus (EBV) infection, or cytomegalovirus (CMV) infection
- Active infection of any kind, excluding fungal infection of the nail beds
- Any major episode of infection that fulfills any of the following criteria: requires hospitalization during 8 weeks prior to screening or during screening; requires treatment with IV antibiotics (or anti-infective medications) during 8 weeks prior to screening or during screening; requires treatment with oral antibiotics (or anti-infective medications) during 2 weeks prior to screening or during screening
- History of serious recurrent or chronic infection
- History of progressive multifocal leukoencephalopathy (PML)
- History of cancer, including solid tumors, hematological malignancies, and carcinoma in situ, within the past 5 years
- Major surgery requiring hospitalization during 4 weeks prior to screening or during screening or any planned surgery or procedure requiring hospitalization during 12 weeks following study drug administration
- Current alcohol or drug abuse or history of alcohol or drug abuse within 12 months prior to screening or during screening
- Intolerance or contraindication to study therapies including history of severe allergic or anaphylactic reactions to monoclonal antibodies or known hypersensitivity to any component of mosunetuzumab injection
- Positive serum human chorionic gonadotropin measures at screening
- Any of the following laboratory parameters: aspartate transaminase (AST) or alanine transaminase (ALT) > 2.5 x upper limit of normal (ULN); total bilirubin > 1.5 x ULN; absolute neutrophil count (ANC) < 2.0 x 10^9/L (< 2000/mm^3); platelet count < 100 x 10^9/L (100,000 mm^3); hemoglobin < 100 g/L (10 g/dL); estimated glomerular filtration rate (eGFR) < 30 ml/min/1.73 m^2 calculated according to the Chronic Kidney Disease Epidemiology Collaboration equation; positive serum human chorionic gonadotropin measured at screening