ForPatients
by Roche

Lupus Nephritis

A Phase I, multicenter, single-arm study to evaluate the pharmacokinetics, pharmacodynamics, and safety of crovalimab in patients with lupus nephritis

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	4 Countries	CA43761

The source of the below information is the publicly available website ClinicalTrials.gov. It has been summarised and edited into simpler language.

Trial Summary:

Phase I study to evaluate the effects of the body on crovalimab and, safety and the effects of crovalimab in participants with lupus nephritis

F. Hoffmann-La Roche Ltd (USA)	Phase I
Sponsor	Phase

CA43761
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
Both	18 - 65 years	No

Background and study aims:

Systemic lupus erythematosus (SLE) is an autoimmune disease (a disease that causes the immune system to attack the body's own cells) that occurs primarily in women of childbearing age causing widespread inflammation (swelling) and tissue damage (injury to the tissues). Lupus Nephritis (LN) is the most common organ-threatening characteristic sign of SLE. People with biopsy-proven LN (i.e., LN proven by examination of cells or tissues removed from the body) have a high risk of progression to end-stage kidney disease (ESKD), even with standard of care (SOC) treatment.

Crovalimab is a new drug, that has not yet been approved by the health authorities for the treatment of LN in any country. Crovalimab is an antibody. An antibody is a large protein that is normally produced by the body's immune system to identify and neutralize (counteract) foreign objects, such as bacteria and viruses. Crovalimab is developed to

specifically bind to a protein called complement protein 5 (C5) and inhibit its activity. Crovalimab may help to stop damage to kidneys in people suffering from lupus nephritis.

The purpose of this first-in-human study is:

1. To determine how crovalimab is processed by the body, that is how it will be absorbed, distributed, and finally eliminated from the body (pharmacokinetics [PK]).

2. To determine the safety of crovalimab when given at different doses

3. To evaluate the immune response that crovalimab will bring about in the body. Immune response is how the body recognizes and defends itself against bacteria, viruses, and substances that appear foreign and harmful.

4. To evaluate how crovalimab will affect the body (pharmacodynamic effect) and the complement system in the body after administration of multiple doses of this drug. Complement system is a group of proteins that are present in blood or on the surface of some cells that helps the immune system to protect the body from infections and harmful foreign material.

Who can participate?

People who are between 18 to 65 years of age and weigh 40 kilograms (kg) or more with confirmed diagnosis of Lupus Nephritis

What does the study involve?

Participants will be asked to be a part of this study for 48 weeks (11 months).

This study has three parts:

1. A Screening Period, up to 28 days before the start of the study, where certain tests would be done along with the evaluation of participant's medical history and ongoing medications to determine if the participant is eligible to participate in the study.

2. A Treatment Period, of 24 weeks, wherein participants will have to visit the clinic on specified days to receive crovalimab. The dose of crovalimab administered will depend on the participants' body weight. The first dose of the study drug will be given as an intravenous (IV; into the vein) infusion. Participants will be observed during the IV infusion (about 60 to 90 minutes), and for 1 hour after completion of IV infusion. From the second dose onwards, participants will receive crovalimab as an injection under the skin (subcutaneous [SC]). Participants will be observed for at least 1 hour after the first three of these injections under the skin.

During this study, participants will have to visit the clinic to receive crovalimab on Day 1 and Day 2 of the first week, then weekly visits until Week 4, and then every 4 weeks (Weeks 8, 12, 16, 20, and 24). Visits may last 2-4 hours.

3. Follow-up Period during which participants will have to report to the clinic for a check-up approximately 12 weeks (Week 32) and 24 weeks (Week 48) after receiving the last dose of crovalimab.

Participants will have to get vaccinated against Neisseria meningitidis (meningococcal), Haemophilus influenzae type B, and Streptococcus pneumoniae at or before screening.

What are the possible benefits and risks of participating?

Participants may or may not receive any benefit in this study, but the information that is learned during the study may help other people who have a similar medical condition in the future.

Participants may have side effects from the drugs or procedures used in this study, these can be mild to severe, and they can vary from person to person. As crovalimab is a new experimental drug that has not yet been tested in humans, there may be side effects that are not known at this time.

The side effects potentially associated with crovalimab and other drugs that will be used in this study are listed below.

1. Side effects/Risks potentially associated with crovalimab:

- Neisseria meningitidis Infection: Treatment with crovalimab may increase the risk of infection by the bacteria Neisseria meningitidis which causes meningococcal infections (infection of the meninges, a thin layer of tissue that covers the brain and spinal cord).

- Any Other Infections: Crovalimab acts by blocking a part of the immune system and hence there can be an increased risk of getting infections with medications that are like crovalimab, especially infections with a certain subtype of bacteria called encapsulated bacteria (bacteria having a polysaccharide capsule around it)

- Allergic Reactions: These can be in the form of itching, difficulty in breathing, a skin rash, and/or dizziness or feeling faint

- Infusion-related Reactions: This risk is associated with intravenous (into the vein) crovalimab administration. Symptoms may include but are not limited to fever, shivering or chills, nausea, vomiting, high blood pressure, disturbed heart rhythm, breathing difficulties (rapid breathing or shortness of breath), headache, low blood pressure, pain, restlessness,

diarrhea, dizziness, sweating, flushing, skin rash, and sudden reddening of the face, neck, or chest.

- Injection-site Reactions: These range in severity from slight irritation, redness, rash, discomfort, pain, or itching to necrosis (open skin wound)

2. Risks associated with preventative antibiotic treatment for Crovalimab:

If any participant receives antibiotics to prevent infections, depending on which antibiotic, the participant may experience side effects associated with antibiotic therapy.

- Allergic reactions, ranging from a mild rash to severe life-threatening anaphylaxis.

- Risk of developing Clostridium difficile infection, which is a gastrointestinal infection (infection of the digestive system) characterized by abdominal pain, diarrhea, and fever.

- Antibiotics leading to the development of resistant (unresponsive to treatment) bacteria in the body. This could lead to an infection, which may be difficult to treat and, in rare cases, could be fatal.

3. Side effects or risks associated with Mycophenolate Mofetil (MMF) when administered with drugs that inhibit the activity of the immune system are listed below.

- Very Common Side Effects: Bacterial infections, viral infections, asthenia (weakness), edema (swelling), headache, pyrexia (fever), cough, dyspnea (shortness of breath), hypertension (high blood pressure), abdominal pain, constipation, diarrhea, dyspepsia (indigestion), nausea, vomiting, hematuria (blood in urine), anemia (low red blood cell count), leukopenia (low white blood cell count), hypercholesterolemia (high blood cholesterol level), hypophosphatemia (low level of phosphate in the blood)

- Common Side Effects: Fungal infections, abnormal growth of tissue (neoplasm), ecchymosis (bruise), acidosis (too much acid in body fluids), hyperglycemia (high blood glucose), gout, weight decreased, confusion, depression, insomnia (difficulty sleeping), anxiety, hypertonia (muscle tightness), paresthesia (pins and needles sensation), somnolence (drowsiness), tremors, convulsions (seizures),tachycardia (fast heart rate), hypotension (low blood pressure), venous thrombosis (blood clots in vein), vasodilation (flushing), abdominal distension (bloating), colitis (inflammation of the colon), decreased appetite, esophagitis (heartburn), flatulence (gas), stomach inflammation, gastrointestinal hemorrhage (bleeding in digestive tract), stomach ulcer, gingival hyperplasia (enlargement of gums), Ileus (lack of movement in intestines which could cause painful obstruction), mouth ulcer and/or sores, hepatitis (inflammation of liver), hyperbilirubinemia (high blood bilirubin level), acne, alopecia (hair loss), rash, skin hypertrophy (abnormal wound healing causing thick raised scars), arthralgia (joint pain), muscle weakness, renal impairment (impaired kidney function), chills, hernia, malaise (feeling unwell), pain

- Uncommon Side Effects: Protozoal infections (infection by a parasite protozoa), cancer of lymph nodes, uncontrolled production of white blood cells, aplasia pure red cell (bone marrow disorder), bone marrow failure, pseudolymphoma (skin lesion mimicking lymphoma), agitation, abnormal thoughts, dizziness, dysgeusia (sense of taste changed), lymphocele (swelling due to collection of fluid within the body), bronchiectasis (enlargement of airways in lungs), interstitial lung disease (progressive scarring of lung tissue), pleural effusion (fluid around lungs), Eructation (burping), pancreatitis (swelling of the pancreas), hypersensitivity, hypogammaglobulinaemia (low levels of antibodies in the blood), jaundice (yellowing of skin/eyes indicative of liver disease), blood urea increased (abnormal kidney test)

- Very Rare Side Effects: Pulmonary fibrosis (lungs becoming damaged and scarred)

4. Risks associated with vaccination procedures:

- The most common side effects are pain, redness or swelling at the injection site, muscle aches, feeling tired, headache, nausea, and joint pain.

- Allergic reactions ranging from mild to severe may also occur.

- Signs and symptoms of the lupus or lupus nephritis disease may be temporarily increased

5. Risks associated with procedure of kidney tissue sample (biopsy) collection:

- The biopsy procedures may cause pain, redness, swelling, excessive bleeding, bruising, or draining at the needle site.

- Abnormal wound healing, fever, infection, and allergic reaction to the medication used to numb the skin over the biopsy site may also occur

There may be a risk in exposing an unborn child to study drug, and all risks are not known at this time. Women and men must take precautions to avoid exposing an unborn child to study drug. Participants who are pregnant, become pregnant or are currently breastfeeding, cannot take part in this study.

Where is the study run from?

F. Hoffmann-La Roche Ltd (USA)

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

September 2021 to December 2023

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Who is funding the study?

F. Hoffmann-La Roche Ltd (USA)

Who is the main contact?

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