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

Submission date
03/03/2022

Recruitment status
No longer recruiting

Registration date
09/03/2022

Overall study status
Completed

Last Edited
23/01/2026

Condition category
Skin and Connective Tissue Diseases

[X] 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 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. The complement system comprises a group of proteins that are present in blood or on the surface of some cells that help the immune system 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 66 weeks (15 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 32 weeks (Week 52) after receiving the last dose of crovalimab. Participants will also receive a long-term follow-up phone call 66 weeks after enrollment.

Participants may 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 an experimental drug , 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 (Switzerland)

When is the study starting and how long is it expected to run for?
September 2021 to July 2025

Who is funding the study?
F. Hoffmann-La Roche (Switzerland)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-004561-12

Protocol serial number
CA43761

Study information

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

Study objectives
The purpose of this study is to evaluate the pharmacokinetics (PK), pharmacodynamics (PD), and safety of crovalimab in participants with active lupus nephritis (LN) and urinary protein-to-creatinine ratio (UPCR) greater than or equal to 1.5 grams per gram (g/g).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 27/01/2022, Advarra Inc (6100 Merriweather Dr., Suite 600 Columbia, MD, 21044, USA; +1 410-884-2900; rebecca.fisher@advarra.com), ref: Pro00060059

Primary study design
Interventional

Study design
Phase I single-arm multicenter global interventional non-randomized study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Lupus nephritis

Interventions
Crovalimab: Participants will receive crovalimab, intravenously (IV), at an initial loading dose of 1000 mg or 1500 mg on Day 1, based on the participant’s body weight of ≥40 kg to <100 kg or ≥100 kg respectively, followed by crovalimab, 340 mg, administered subcutaneously (SC), on Day 2 and at Weeks 1, 2, and 3. From Week 4 onwards, participants will receive a maintenance dose of crovalimab, SC, 680 mg or 1020 mg every 4 weeks (Q4W) thereafter up to Week 20 (inclusive) based on the bodyweight of ≥40 kg to <100 kg or ≥100 kg respectively.

Intervention Type
Drug

Phase
Phase I

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

Primary outcome(s)
Current primary outcome measures as of 06/12/2022:
1. Maximum observed serum concentration (Cmax) of crovalimab measured using serum samples at specified timepoints from baseline up to 12 weeks after the final dose of study treatment (up to Week 32)

2. Minimum observed serum concentrations (Cmin) of crovalimab measured using serum samples at specified timepoints from baseline up to 12 weeks after the final dose of study treatment (up to Week 32)
3. Trough serum concentration (Ctrough) of crovalimab measured using serum sample at Week 24
4. Incidence of adverse events (AEs) and severity of AEs determined according to National Cancer Institute-Common Terminology Criteria for Adverse Events Version 5.0 (NCI CTCAE v5.0) from screening up to the long-term follow-up telephone visit at Week 66
5. Change in targeted vital signs, including temperature, systolic and diastolic blood pressure, pulse and respiratory rate, from baseline to the long-term follow-up in-person visit at Week 52
6. Change in targeted clinical laboratory test results measured using serum samples from baseline to the long-term follow-up visit in-person at Week 52
7. Percentage of participants with severity of injection-site reactions, infusion-related reactions, hypersensitivity, and infections (including Meningococcal Meningitis) from baseline up to the long-term follow-up visit in-person at Week 52
8. Percentage of participants with AEs leading to crovalimab discontinuation from baseline up to week 24

Previous primary outcome measures:
1. Maximum observed serum concentration (Cmax) of crovalimab measured using serum samples at specified timepoints from baseline up to 12 weeks after the final dose of study treatment (up to Week 32)
2. Minimum observed serum concentrations (Cmin) of crovalimab measured using serum samples at specified timepoints from baseline up to 12 weeks after the final dose of study treatment (up to Week 32)
3. Trough serum concentration (Ctrough) of crovalimab measured using serum sample at Week 24
4. Percentage of participants with adverse events (AEs) and severity of AEs determined according to National Cancer Institute-Common Terminology Criteria for Adverse Events Version 5.0 (NCI CTCAE v5.0) from screening up to the long-term follow-up visit (up to Week 48)
5. Change from baseline in targeted vital signs assessed by measuring temperature, systolic and diastolic blood pressure, pulse and respiratory rate up to the long-term follow-up visit (up to Week 48)
6. Change from baseline in targeted clinical laboratory test results measured using serum samples from screening up to the long-term follow-up visit (up to Week 48)
7. Percentage of participants with severity of injection-site reactions, infusion-related reactions, hypersensitivity, and infections (including Meningococcal Meningitis) from baseline up to the long-term follow-up visit (up to Week 48)
8. Percentage of participants with AEs leading to crovalimab discontinuation from baseline up to 24 weeks of treatment period

Key secondary outcome(s)

Current secondary outcome measures as of 06/12/2022:
1. Percentage of participants with serum anti-drug antibodies (ADAs) measured from serum samples collected at baseline (Day 1) and incidence of ADAs during the study
2. Change over time in PD biomarker-free complement component 5 (C5) measured from serum samples to assess the biologic activity of crovalimab treatment i.e., to measure the interaction of crovalimab against the drug target C5 from baseline (Day 1) up to the long-term follow-up visit (up to Week 52)

3. Change over time in PD biomarkers, including free C5 serum concentrations and CH50 (complement activity) as measured by Liposome Immunoassay (LIA), to assess the biologic activity of crovalimab from baseline (Day 1) up to the long-term follow-up visit (up to Week 52)

Previous secondary outcome measures:
1. Percentage of participants with anti-drug antibodies (ADAs) measured from the serum samples at baseline (Day 1) up to 12 weeks after the final dose of study treatment (up to Week 32)
2. Change over time in PD biomarker-free complement component 5 (C5) measured from serum samples to assess the biologic activity of crovalimab treatment i.e., to measure the interaction of crovalimab against the drug target C5 From baseline (Day 1) up to the long-term follow-up visit (up to Week 48)
3. Change over time in PD biomarker- CH50 (complement activity) as measured by Liposome Immunoassay (LIA), in serum to assess the biologic activity of crovalimab treatment i.e., to monitor total complement activity from baseline (Day 1) up to the long-term follow-up visit (up to Week 48)

Completion date
23/07/2025

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 27/04/2023:
1. Age 18 - 65 years at the time of signing the Informed Consent Form
2. Body weight ≥40 kg at screening
3. Active LN, as evidenced by either: 1) A kidney biopsy demonstrating active proliferative (Class III or IV) and/or membranous (Class V) LN, performed within 12 months of screening or during screening; or 2) biopsy-proven Class III, IV, and/or V LN at anytime before screening and an active LN flare, as determined by the investigator, requiring the equivalent of at least 0.5 mg/kg/day of prednisone during screening.
4. UPCR ≥1.5 g/g on a 24-hour urine collection at screening
5. Vaccination against Neisseria meningitidis (N. meningitidis) serotypes A, C, W, and Y <3 years prior to initiation of study treatment
6. Vaccination against Haemophilus influenzae type B and Streptococcus pneumoniae according to national vaccination recommendations

Previous participant inclusion criteria as of 06/12/2022:
1. Age 18 - 65 years at the time of signing the Informed Consent Form
2. Body weight ≥40 kg at screening
3. Active LN, as evidenced by a kidney biopsy demonstrating active proliferative (Class III or IV) and/or membranous (Class V) LN, performed within 12 months of screening or during screening
4. UPCR ≥1.5 g/g on a 24-hour urine collection at screening
5. Vaccination against Neisseria meningitidis (N. meningitidis) serotypes A, C, W, and Y <3 years prior to initiation of study treatment
6. Vaccination against Haemophilus influenzae type B and Streptococcus pneumoniae according to national vaccination recommendations

Previous participant inclusion criteria:
1. Age 18 - 65 years at the time of signing the Informed Consent Form
2. Body weight ≥40 kg at screening

3. Active LN, as evidenced by a kidney biopsy demonstrating active proliferative (Class III or IV) and/or membranous (Class V) LN, performed within 12 months of screening or during screening
4. UPCR ≥ 1.5 g/g on a 24-hour urine collection at screening
5. Vaccination against Neisseria meningitidis (N. meningitidis) <3 years prior to initiation of study treatment
6. Vaccination against Haemophilus influenzae type B and Streptococcus pneumoniae according to national vaccination recommendations

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
65 Years

Sex
All

Total final enrolment
7

Key exclusion criteria
Current participant exclusion criteria as of 06/12/2022:
1. Pregnant or breastfeeding or intending to become pregnant during the study or within 46 weeks after the final dose of crovalimab or within 6 weeks after the final dose of mycopenolate mofetil (MMF), whichever is longer
2. Severe renal impairment, as defined by estimated glomerular filtration rate < 15 millimetres per minute per 1.73 metres square (mL/min/1.73 m^2), need for dialysis or renal transplantation
3. Presence of rapidly-progressive glomerulonephritis
4. Active or evolving multisystem organ dysfunction or failure
5. Known or suspected hereditary complement deficiency
6. History of N. meningitidis infection within 6 months prior to screening and up to the first drug administration
7. History of serious recurrent or chronic infection
8. Known or suspected immune deficiency
9. Positive Human immunodeficiency virus (HIV) test or known HIV infection
10. Splenectomy < 6 months prior to screening
11. Participants who have a history of malignancy within 5 years prior to screening and up to the first dose of study treatment
12. History of hypersensitivity, allergic, or anaphylactic reactions to any ingredient contained in crovalimab, including hypersensitivity to human, humanized, or murine monoclonal antibodies or known hypersensitivity to any constituent of the product, or to corticosteroids or MMF
13. Current, previous or expected future treatment with a complement inhibitor within 46 weeks

after the final crovalimab administration
14. Lack of peripheral venous access
15. Any condition requiring plasmapheresis

Previous participant exclusion criteria:
1. Pregnant or breastfeeding, or intending to become pregnant during the study or within 6 months after the final dose of crovalimab or within 6 weeks after the final dose of mycopenolate mofetil (MMF), whichever is longer
2. Severe renal impairment, as defined by estimated glomerular filtration rate < 15 millimetres per minute per 1.73 metres square (mL/min/1.73 m²), need for dialysis or renal transplantation
3. Presence of rapidly-progressive glomerulonephritis
4. Active or evolving multisystem organ dysfunction or failure
5. Known or suspected hereditary complement deficiency
6. History of N. meningitidis infection within 6 months prior to screening and up to the first drug administration
7. History of serious recurrent or chronic infection
8. Known or suspected immune deficiency
9. Positive Human immunodeficiency virus (HIV) test or known HIV infection
10. Splenectomy < 6 months prior to screening
11. Participants who have a history of malignancy within 5 years prior to screening and up to the first dose of study treatment
12. History of hypersensitivity, allergic, or anaphylactic reactions to any ingredient contained in crovalimab, including hypersensitivity to human, humanized, or murine monoclonal antibodies or known hypersensitivity to any constituent of the product, or to corticosteroids or MMF
13. Current, previous or expected future treatment with a complement inhibitor within 6 months after the final crovalimab administration
14. Lack of peripheral venous access
15. Any condition requiring plasmapheresis

Date of first enrolment
31/03/2022

Date of final enrolment
15/04/2024

Locations

Countries of recruitment
Argentina

Colombia

Germany

Italy

Spain

United States of America

Study participating centre
Clinica Mayo de U.M.C.B. S.R.L
San Miguel de Tucumán
Argentina
T4000IHE

Study participating centre
Centro Médico IPAM
Rosario
Argentina
S2013SBK

Study participating centre
Hospital Universitario Virgen del Rocio – PPDS
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41013

Study participating centre
Hospital Universitario Vall d'Hebron – PPDS
Barcelona
Spain
8035

Study participating centre
Northwell Health
New York
United States of America
11042-1113

Study participating centre
Amicis Research Center
Los Angeles, CA
United States of America
91324-3138

Study participating centre
Prolato Clinical Research Center
Houston, TX

United States of America
77030-2348

Study participating centre
Hospital Del Mar
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Spain
8003

Study participating centre
Azienda Ospedaliera Spedali Civili di Brescia
Brescia
Italy
25123

Study participating centre
Universitätsmedizin Mainz
Mainz
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Study participating centre
Medizinische Hochschule Hannover
Hannover
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30625

Sponsor information

Organisation
F. Hoffmann-La Roche

Funder(s)

Funder type
Industry

Funder Name
F. Hoffmann-La Roche

Alternative Name(s)
Hoffman-La Roche, F. Hoffmann-La Roche Ltd.

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes