

# A study evaluating the safety, pharmacokinetics, pharmacodynamics, and efficacy of crovalimab for the management of acute uncomplicated vaso-occlusive episodes in participants with sickle cell disease

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| <b>Submission date</b><br>22/02/2022   | <b>Recruitment status</b><br>No longer recruiting     | <input type="checkbox"/> Prospectively registered    |
|  |   | <input type="checkbox"/> Protocol                    |
| <b>Registration date</b><br>07/07/2022 | <b>Overall study status</b><br>Completed              | <input type="checkbox"/> Statistical analysis plan   |
|  |   | <input type="checkbox"/> Results                     |
| <b>Last Edited</b><br>22/10/2024       | <b>Condition category</b><br>Haematological Disorders | <input type="checkbox"/> Individual participant data |
|  |   | <input type="checkbox"/> Record updated in last year |

## Plain English summary of protocol

### Background and study aims

Sickle cell disease (SCD) is a genetic disorder leading to red blood cells that distort into a sickled shape, contributing to painful vaso-occlusive episodes (VOEs). The purpose of this clinical trial is to look at the safety and effectiveness of crovalimab, and to understand the way your body processes (pharmacokinetics) and reacts (pharmacodynamics) to crovalimab.

### Who can participate?

People aged 12 to 55 years with a confirmed diagnosis of sickle cell anemia (HbSS or HbS $\beta$ 0)

### What does the study involve?

Everyone who joins this clinical trial will receive ONLY one dose of either:

Crovalimab as a single infusion into the vein, OR

Placebo as a single infusion into the vein

The patients will have a 2 in 3 (67%) chance of being in the crovalimab group and a 1 in 3 (33%) chance of being in the placebo group.

During the clinical trial, participants can continue to have standard treatment for the pain attack (crisis) as recommended by the clinical trial doctor.

This is a 'placebo-controlled' clinical trial, which means that one of the groups will be given a saline (salt water) infusion with no active ingredients (also known as 'placebo'). A placebo is used as a control, to make sure any health effects are from the clinical trial treatment rather than other factors.

Neither the participant nor the site staff can choose or know which group they are in. An exception is made if the clinical trial doctor needs to know which group the participant is in for safety reasons.

While the participant is in the hospital for treatment for the sickle cell pain attack (crisis), they will be seen by the clinical trial doctor.

After being given treatment with crovalimab or a placebo, the participant will have regular tests and check-ups while hospitalised until they are well enough to go home from the hospital (discharged).

Once the participant is discharged from the hospital, they will have 5 telephone check-ups and 2 clinic visits with the clinical trial doctor to check on their health and any side effects they may be having.

The clinical trial will last for a total of 322 days (approximately 10.5 months) after the participant is given clinical trial treatment (crovalimab or placebo).

What are the possible benefits and risks of participating?

As with any study, there are risks (both known and unknown) associated with the drug or procedures used. Before starting the clinical trial, participants will be told about any risks and benefits of taking part in the trial. The participants will also be told what other treatments are available so that they may decide if they still want to take part. Participants health may or may not improve in this study, but the information that is learned may help other people who have a similar medical condition in the future. The potential side effects related to the study drug, based on laboratory studies, knowledge of similar drugs, or studies in other diseases, are listed below:

1. Increased risk of infection, including Neisseria meningitidis infection
2. Allergic reactions
3. Infusion-related reactions

You may also receive antibiotics while taking part in this study. There may be risks to taking antibiotics:

1. Allergic reactions
2. Clostridium difficile infection
3. Development of resistant (unresponsive to treatment) bacteria in the body

It is possible that side effects of crovalimab which are unknown at this time may occur during the study. Any new information that may affect participants' health or which may make the participants want to stop taking part in the study will be shared with them as soon as it becomes available. There may be a risk in exposing an unborn child to crovalimab, and all risks are not known at this time. Participants cannot take part in the study if they are pregnant or become pregnant.

Participants will be fully informed of the potential risks and burdens involved in taking part in this research study in the Participant Information Sheet and will be given opportunities to ask questions prior to consent and during their participation. Participants will be monitored throughout the study in order to minimize risks.

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?

January 2021 to October 2025

Who is funding the study?

F. Hoffmann-La Roche (Switzerland)

Who is the main contact?

Reference Study ID Number: BO42452; <https://forpatients.roche.com/>, [global-roche-genentechtrials@gene.com](mailto:global-roche-genentechtrials@gene.com)

## Contact information

## Type(s)

Public, Scientific, Principal investigator

## Contact name

Dr . Clinical Trials

## Contact details

Building 1, Grenzacherstrasse 124

Basel

Switzerland

CH-4058

+1 888-662-6728

global-roche-genentech-trials@gene.com

## Additional identifiers

### Clinical Trials Information System (CTIS)

2020-004840-27 / 2022-502546-26-00

### Integrated Research Application System (IRAS)

1005134

### ClinicalTrials.gov (NCT)

NCT04912869

### Protocol serial number

BO42452, CPMS 46764

## Study information

### Scientific Title

A phase Ib randomized, placebo-controlled study evaluating the safety, pharmacokinetics, pharmacodynamics, and efficacy of crovalimab for the management of acute uncomplicated vaso-occlusive episodes (VOE) in patients with sickle cell disease (SCD)

### Study objectives

Current study hypothesis as of 09/02/2023:

The study is designed to evaluate the safety, pharmacokinetics, pharmacodynamics, and efficacy of crovalimab compared with placebo for the management of acute uncomplicated vasoocclusive episodes (VOE) in participants with sickle cell disease (SCD).

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Previous study hypothesis:

### Objectives:

- To evaluate the safety of crovalimab compared with placebo
- To evaluate the pharmacokinetics (PK) of crovalimab
- To evaluate the pharmacodynamics (PD) of crovalimab

- To evaluate the efficacy of crovalimab compared with placebo
- To evaluate the immune response to crovalimab

## **Ethics approval required**

Ethics approval required

## **Ethics approval(s)**

approved 23/05/2022, East of England - Cambridge and Hertfordshire Research Ethics Committee (Equinox House, City link, Nottingham, NG2 4LA, United Kingdom; +44 (0)207 104 8265; cambsandherts.rec@hra.nhs.uk), ref: 22/YH/0061

## **Study design**

Interventional double-blind randomized parallel group placebo controlled trial

## **Primary study design**

Interventional

## **Study type(s)**

Treatment

## **Health condition(s) or problem(s) studied**

Sickle cell disease (SCD); vaso-occlusive episodes in SCD; Pain crisis

## **Interventions**

Current interventions as of 09/02/2023:

1. Crovalimab: Participants will receive a single intravenous (IV) infusion of Crovalimab based on body weight.
2. Placebo: Participants will receive a single IV infusion of a matching Placebo.

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Previous interventions:

Patients who meet all eligibility criteria and have consented for participation in the study will be randomized 2:1 to receive either a single intravenous (IV) tiered weight-based dose of crovalimab or placebo. Patients will be randomised via an online platform hosted by Clinphone.

A 2-step process for screening procedures is encouraged to preliminarily identify and consent patients for the study prior to VOE presentation, Screen Visit #1 (initial screen) is conducted at an outpatient visit (i.e., when the patient is not experiencing a VOE), where the main Informed Consent Form (ICF) is signed and preliminary eligibility is assessed. During this visit, preliminary screening assessments can be conducted, and a steady state SCD exploratory biomarker sample will be collected (only after consent is received). No additional assessments are required until Screen Visit #2. Eligibility at Screen Visit #1 does not guarantee eligibility at Screen Visit #2. Screen Visit #2 (VOE presentation screen) is then conducted when the patient presents with a VOE to the A/E department. The patient consent from Screen Visit #1 must be confirmed prior to starting study assessments (this confirmation must be documented). Once patient consent is confirmed, all remaining eligibility criteria must be assessed, and all screening assessments will be conducted .

Alternatively, if a patient is only first identified for participation in the study at presentation with a VOE, then all consent procedures (main ICF signature) and all screening assessments listed for both Screen Visit #1 and Screen Visit #2 (excluding the steady state SCD exploratory biomarker listed under Screen Visit #1) can be conducted at the same time after the patient presents in A/E.

If the patient meets all eligibility criteria then they are randomised and will receive treatment within 12 hours of presenting to A/E. Patients will be admitted to Hospital, Patients will be followed for the duration of the hospitalization until the time of discharge. After discharge, they will continue to be followed during an observational period on Days 14, 28, 46, 64, and 84 after study treatment administration; Days 14, 46, and 64 are telephone follow-ups and Days 28 and 84 are study site visits. The total duration of the study is 12 weeks (84 days) following administration of study treatment.

### **Intervention Type**

Drug

### **Phase**

Phase I

### **Drug/device/biological/vaccine name(s)**

crovalimab

### **Primary outcome(s)**

Current primary outcome measure as of 09/02/2023:

1. Percentage of participants with adverse events (AEs), measured from Baseline up to Day 322
2. Percentage of participants with infusion-related reactions and hypersensitivity, measured from Baseline up to Day 84

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Previous primary outcome measure:

Incidence and severity of adverse events, with severity determined according to National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events, Version 5.0 (CTCAE v5.0) measured at Screening visit 2, during study treatment, within 30 mins post-infusion, 12 hours post-infusion, day 2 - day 14, day of discharge, post-discharge day 28, day 46, day 64, and day 84

### **Key secondary outcome(s)**

Current secondary outcome measures as of 09/02/2023:

1. Time to improvement of the primary acute uncomplicated VOE, measured from Baseline up to Day 84
2. Total cumulative opioid dose, measured from Baseline up to Day 84
3. Time to discontinuation of all parenteral opioids, measured from Baseline up to Day 84
4. Time to readiness for hospital discharge, measured from Baseline up to Day 84
5. Time to hospital discharge, measured from Baseline up to Day 84
6. Time to a confirmed decrease in pain score of at least 2 points from the maximal pre-dose pain score, measured from Baseline up to Day 84
7. Change in pain score from the maximal pre-dose pain score to the score at hospital discharge,

measured from Baseline up to Day 84

8. Percentage of participants who develop acute chest syndrome (ACS), measured from Baseline up to Day 28

9. Percentage of participants requiring intensive care unit (ICU)/critical care admission for SCD-related complications, measured from Baseline up to Day 84

10. Percentage of participants requiring blood transfusion for SCD-related complications, measured from Baseline up to Day 84

11. Readmission rate for a VOE or VOE-related event within 28 days of discharge of the primary VOE, measured from Baseline up to Day 84

12. Serum concentrations of crovalimab over time, measured from Baseline up to Day 84

13. Change in PD Biomarkers including complement activity (CH50)s over time, measured from Baseline up to Day 84

14. Change over time in free C5 concentration, measured from Baseline up to Day 84

15. Change over time in soluble complement 5b 9 (sC5b-9) concentration, measured from Baseline up to Day 84

16. Percentage of participants with anti-drug antibodies to crovalimab, measured from Baseline up to Day 84

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Previous secondary outcome measures:

Change from baseline in targeted vital signs and clinical laboratory test results :

1. Vital signs (temperature, pulse, and blood pressure) at Screening visit 2, during study treatment, within 30 mins post-infusion, 12 hours post-infusion, day 2 - day 14, day 28, and Day 84

2. Clinical lab tests (Hematology (including reticulocytes), Chemistry (including LDH), Serum PK sample, Serum ADA sample, Plasma and serum PD samples, and Blood sample for clinical genotyping) at screening visit 2, day 2, day6, day 10, day 14, day if discharge, day 28, and day 84

3. Incidence and severity of infusion-related reactions and hypersensitivity, will be measured during the infusion and also post-infusion, depending on the incidence and the severity of the infusion

### **Completion date**

31/10/2025

## **Eligibility**

### **Key inclusion criteria**

Current inclusion criteria as of 15/10/2024:

1. Age  $\geq 12$  to  $\leq 55$  years
2. Body weight  $\geq 40$  kg
3. Confirmed diagnosis of HbSS (SCD genotype of sickle cell anemia) or HbS $\beta$ 0 (SCD genotype of sickle cell beta zero thalassemia)
4. Vaccination against Neisseria meningitidis
5. Vaccinations against H. influenzae type B and S. pneumoniae
6. Participants vaccinated against SARS-CoV-2 are eligible, as long as it has been 3 days or more after inoculation with the vaccine.
7. Diagnosis of an acute uncomplicated VOE, that requires admission to a hospital/acute medical facility and treatment with parenteral opioid analgesics

8. Adequate hepatic and renal function
  9. Hemoglobin  $\geq 5$  grams/deciliter (g/dL)
  10. Platelet count  $\geq 100,000$ /microliter ( $\mu\text{L}$ )
  11. Participants receiving SCD-directed therapies must be on a stable dose for  $\geq 28$  days
  12. For female participants of childbearing potential, an agreement to remain abstinent or use contraception for 6 months after the dose of study treatment
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  2. Body weight  $\geq 40$  kg
  3. Confirmed diagnosis of HbSS (SCD genotype of sickle cell anemia) or HbS $\beta$ 0 (SCD genotype of sickle cell beta zero thalassemia)
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  9. Hemoglobin  $\geq 5$  grams/deciliter (g/dL)
  10. Platelet count  $\geq 100,000$ /microliter ( $\mu\text{L}$ )
  11. Participants receiving sickle cell therapies must be on a stable dose for  $\geq 28$  days
  12. For female patients of childbearing potential, an agreement to remain abstinent or use contraception for 6 months after the dose of study treatment
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Previous inclusion criteria:

1. Signed ICF or Assent Form (as determined by patient's age and individual site and country standards)
2. Age  $\geq 12$  to  $\leq 55$  years
3. Body weight  $\geq 40$  kg
4. Confirmed diagnosis of HbSS (SCD genotype of sickle cell anemia) or HbS $\beta$ 0 (SCD genotype of sickle cell beta zero thalassemia)
5. Vaccination against Neisseria meningitidis
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### **Participant type(s)**

Patient

## Healthy volunteers allowed

No

## Age group

Mixed

## Lower age limit

12 years

## Upper age limit

55 years

## Sex

All

## Key exclusion criteria

Current exclusion criteria as of 15/10/2024:

1. More than 10 VOEs within the last 12 months prior to presentation, that have required a medical facility visit
2. Pain related to the current VOE ongoing for >36 hours
3. Acute pain related to avascular necrosis, hepatic or splenic sequestration, or priapism
4. Pain atypical of an acute uncomplicated VOE
5. Evidence of or suspicion of ACS
6. Evidence or high suspicion of a severe systemic infection
7. Major surgery and/or hospitalization for any reason within 30 days
8. History of Neisseria meningitidis infection within 6 months prior
9. Known HIV infection with a documented CD4 count <200 cells/ $\mu$ L
10. Transfusion or receipt of blood products within 3 months or current participation in a chronic transfusion protocol
11. Immunized with a live attenuated vaccine within 30 days
12. History of hematopoietic stem cell transplant
13. Known or suspected hereditary complement deficiency
14. Pregnant or breastfeeding, or intending to become pregnant during the study or within 322 days (approximately 10.5 months) after the study drug administration.
15. Participation in another interventional treatment study with an investigational agent or use of any experimental therapy within the prior 28 days or within five half-lives of that investigational product, whichever was greater

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Previous exclusion criteria as of 09/02/2023:

1. More than 10 VOEs within the last 12 months prior to presentation, that have required a medical facility visit
2. Pain related to the current VOE ongoing for >48 hours
3. Acute pain related to avascular necrosis, hepatic or splenic sequestration, or priapism
4. Pain atypical of an acute uncomplicated VOE
5. Evidence of or suspicion of ACS
6. Evidence or high suspicion of a severe systemic infection
7. Major surgery and/or hospitalization for any reason within 30 days

8. History of Neisseria meningitidis infection within 6 months prior
9. Known HIV infection with a documented CD4 count <200 cells/ $\mu$ L
10. Transfusion or receipt of blood products within 3 months or current participation in a chronic transfusion protocol
11. Immunized with a live attenuated vaccine within 30 days
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**Date of first enrolment**

26/03/2022

**Date of final enrolment**

31/12/2024

## Locations

**Countries of recruitment**

United Kingdom

Brazil

France

Italy

Kenya

Lebanon

Netherlands

South Africa

Spain

United States of America

**Study participating centre**

**Azienda Ospedaliera di Verona-Policlinico G.B. Rossi; Medicina Interna**

Verona Veneto

Italy

371734

**Study participating centre**

**Hospital General Univ. Gregorio Maranon**

Madrid

Spain

28009

**Study participating centre**

**Hospital Universitario Virgen del Rocio; Servicio de Hematologia**

Sevilla

Spain

41013

**Study participating centre**

**CHU Henri Mondor; Service de médecine interne**

Créteil

France

94010

**Study participating centre**

**Hôpital Saint Eloi; Service de Médecine interne**  
Montpellier  
France  
34295

**Study participating centre**  
**Icahn School of Medicine at Mount Sinai**  
New York City  
United States of America  
10029

**Study participating centre**  
**East Carolina University; Brody School of Medicine**  
Greenville  
United States of America  
27834

**Study participating centre**  
**Hospital Sao Rafael – HSR**  
Salvador  
Brazil  
41253-190

**Study participating centre**  
**Hospital das Clinicas – UFRGS**  
Porto Alegre  
Brazil  
90035-903

**Study participating centre**  
**Hospital de Base de Sao Jose do Rio Preto**  
Sao Jose do Rio Preto  
Brazil  
15090-000

**Study participating centre**  
**The Whittington Hospital**  
Highgate Hill  
London

United Kingdom  
N19 5NF

**Study participating centre**  
**University College Hospital**  
235 Euston Road  
London  
United Kingdom  
NW1 2BU

**Study participating centre**  
**Hospital Universitario Miguel Servet; Servicio Hematologia**  
Zaragoza  
Spain  
50009

**Study participating centre**  
**Children's Healthcare of Atlanta**  
Atlanta  
United States of America  
30322

**Study participating centre**  
**Amsterdam UMC Location VUMC**  
Amsterdam  
Netherlands  
1105 AZ

**Study participating centre**  
**International Cancer Institute (ICI)**  
Eldoret  
Kenya  
30100

**Study participating centre**  
**Gertrude's Children's Hospital**  
Nairobi  
Kenya  
00100

**Study participating centre**  
**American University of Beirut - Medical Center**  
Hazmeih  
Lebanon  
1003

**Study participating centre**  
**Hopital Nini**  
Tripoli  
Lebanon  
-

**Study participating centre**  
**Charlotte Maxeke Johannesburg Hospital; Haemophilia Comprehensive Care Center**  
Johannesburg  
South Africa  
2193

## **Sponsor information**

**Organisation**  
F.Hoffmann-La Roche Ltd.

## **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

All data generated or analysed during this study will be included in the subsequent results publication

## IPD sharing plan summary

Published as a supplement to the results publication

## Study outputs

| Output type                   | Details       | Date created | Date added | Peer reviewed? | Patient-facing? |
|-------------------------------|---------------|--------------|------------|----------------|-----------------|
| <a href="#">Study website</a> | Study website | 11/11/2025   | 11/11/2025 | No             | Yes             |