ForPatients
by Roche

Paroxysmal nocturnal hemoglobinuria (PNH)

A clinical trial to compare how effective and safe crovalimab is in comparison to eculizumab in people with paroxysmal nocturnal hemoglobinuria (PNH) not previously treated with complement inhibitors.

A Study Evaluating the Efficacy and Safety of Crovalimab Versus Eculizumab in Participants With Paroxysmal Nocturnal Hemoglobinuria (PNH) Not Previously Treated With Complement Inhibitors

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	23 Countries	NCT04434092 2019-004931-21 2023-506498-36-00 BO42162

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, Open-label, Active-controlled, Multicenter Study Evaluating the Efficacy and Safety of Crovalimab Versus Eculizumab in Patients With Paroxysmal Nocturnal Hemoglobinuria (PNH) Not Previously Treated With Complement Inhibitors

Trial Summary:

A study designed to evaluate the non-inferiority of crovalimab compared with eculizumab in participants with PNH who have not been previously treated with complement inhibitor therapy.

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

NCT04434092 2019-004931-21 2023-506498-36-00 BO42162
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#2 Years	No

1. Why is the COMMODORE 2 clinical trial needed?

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Paroxysmal nocturnal hemoglobinuria (PNH) is a genetic blood disorder that leads to the breakdown of red blood cells (‘haemolysis’) causing anaemia (low levels of haemoglobin) where damage is caused to red blood cells. This can lead to symptoms like tiredness, headaches, trouble breathing, less appetite, difficulty exercising or concentrating, and stomach or chest pain. If haemolysis destroys too many red blood cells, a person may need to receive blood from a donor (a blood transfusion). People with PNH also have a higher risk of blood clots. PNH is currently treated with medicines called C5 inhibitors (eculizumab or ravulizumab), which reduce the destruction of blood cells. However, this treatment means life-long drip infusions into a vein. Only some people benefit from this treatment, and better treatment options are needed. Crovalimab is also a C5 inhibitor, but it is given as injection under the skin (subcutaneous injection) every four weeks. Crovalimab can be self-administered or given by a caregiver at home, administered by your caregiver or can be given by your doctor. Crovalimab is an experimental drug, which means it has not been approved by health authorities for treating PNH. This clinical trial aims to compare how safe and effective crovalimab is compared with eculizumab in people with PNH not previously treated with C5 inhibitors.

2. How does the COMMODORE 2 clinical trial work?

This clinical trial has recruited people with PNH. People who take part in this clinical trial (participants) will be given the clinical trial treatment crovalimab (Groups A and C) or eculizumab (Group B) for up to 6 months. The clinical trial doctor will see them regularly. These hospital visits will include checks to see how the participant responds to crovalimab treatment and any side effects they may have. After the 6-month treatment period, there may be the opportunity to continue crovalimab treatment (Groups A and C) or switch to crovalimab (Group B) for an extension period if the clinical trial doctor thinks it is in the participant’s best interest. Crovalimab may be given in the extension period for up to 5 years. The total time of participation in the clinical trial will be up to about 6 and half years including a safety follow-up. Participants can stop trial treatment and leave the clinical trial at any time, the trial doctor will advise how this can be done safely.

3. What are the main endpoints of the COMMODORE 2 clinical trial?

The main clinical trial endpoints (the main results measured in the trial to see if the drug has worked) are the number of participants who do not require a blood transfusion after 6 months of treatment and who have a controlled level of red blood cell breakdown during treatment.

The other clinical trial endpoints include:

- The number of participants who have:
    - At least one new or worsening symptom or sign of PNH
    - Stable levels of a blood protein (haemoglobin)

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    - Reduced symptoms of tiredness
- The number and seriousness of any side effects
- How the body processes crovalimab and eculizumab over time
- How crovalimab affects the immune system
- Any change in certain molecules (biomarkers) in the blood

4. Who can take part in this clinical trial?

People can take part in this trial if they have been diagnosed with PNH, weigh at least 40kg and have not been treated with C5 inhibitors, such as eculizumab or ravulizumab, before.

People may not be able to take part in this trial if they have previously not received certain vaccinations or have certain other medical conditions including certain types of cancer in the last 5 years, certain infections, or are pregnant or breastfeeding.

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

Everyone who joins this clinical trial will join 1 of 3 groups depending on their age.

Patients aged 18 years and older will be placed randomly (by chance) into two groups:

- **Group A:** will receive crovalimab, given as an infusion (into the vein) once on Day 1 of the trial, then as an injection under the skin (subcutaneous) on Day 2 and every week for 3 more weeks. From Week 5, crovalimab will be given as a subcutaneous injection once a month for a total of 6 months and may be self-administered (or by a caregiver) from Week 9
- OR **Group B**: will receive eculizumab, given as an infusion into the vein once a week for 4 weeks, followed by once every 2 weeks for a total of 6 months.

Participants will have a 2 in 3 chance of being placed in Group A. Participants aged less than 18 years will be included in Group C:

- **Group C**: will be given crovalimab as an infusion (into the vein) once on Day 1 of the trial, then as an injection under the skin (subcutaneous) on Day 2 and every week for three more weeks. From Week 5, crovalimab will be given as a subcutaneous injection once a month for a total of 6 months and may be self-administered (or by a caregiver) from Week 9.

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?

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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 drug

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 crovalimab and eculizumab, and possible side effects based on human and laboratory studies or knowledge of similar drugs. Crovalimab and eculizumab will be given as infusions and/or subcutaneous injections. Participants will be told about any known side effects of infusions and subcutaneous injections.

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:

- Body weight # 40 kg at screening (pediatric participants with body weight < 40 kg)
- Willingness and ability to comply with all study visits and procedures
- Documented diagnosis of PNH, confirmed by high sensitivity flow cytometry
- LDH level # 2x ULN at screening (as per local assessment)
- Vaccination against Neisseria meningitidis serotypes A, C, W, and Y< 3 years prior to initiation of study treatment; or, if not previously done, vaccination administered no later than one week after the first drug administration
- Women of childbearing potential: agreement to remain abstinent or use contraception during the treatment period and for 10.5 months after the final dose of crovalimab or for 3 months after the final dose of eculizumab (or longer if required by the local product label)

Exclusion Criteria:

- Current or previous treatment with a complement inhibitor
- History of allogeneic bone marrow transplantation
- History of Neisseria meningitidis infection within 6 months prior to screening and up to first study drug administration
- History of myelodysplastic syndrome with Revised International Prognostic Scoring System (IPSS-R) prognostic risk categories of intermediate, high and very high

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- Pregnant or breastfeeding, or intending to become pregnant during the study, within 10.5 months after the final dose of crovalimab, or 3 months after the final dose of eculizumab (or longer if required by the local product label)
- Participation in another interventional treatment study with an investigational agent or use of any experimental therapy within 28 days of screening or within 5 half-lives of that investigational product, whichever is greater
- Concurrent disease, treatment, procedure or surgery, or abnormality in clinical laboratory tests that could interfere with the conduct of the study, may pose any additional risk for the participant, or would, in the opinion of the Investigator, preclude the participant's safe participation in and completion of the study
- Splenectomy < 6 months before screening
- Positive for Active Hepatitis B and C infection (HBV/HCV)
- History of or ongoing cryoglobulinemia at screening

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