ForPatients
by Roche

Atypical Hemolytic Uremic Syndrome (aHUS)

A clinical trial to look at how well crovalimab works in adults and adolescents with atypical hemolytic uremic syndrome (aHUS)

A Study Evaluating the Efficacy, Safety, Pharmacokinetics and Pharmacodynamics of Crovalimab in Adult and Adolescent Participants With Atypical Hemolytic Uremic Syndrome (aHUS)

Trial Status	Trial Runs In	Trial Identifier
Recruiting	19 Countries	NCT04861259 2020-002475-35 2023-505089-27-00 BO42353

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, Multicenter, Single-Arm Study Evaluating the Efficacy, Safety, Pharmacokinetics, and Pharmacodynamics of Crovalimab in Adult and Adolescent Patients With Atypical Hemolytic Uremic Syndrome (aHUS)

Trial Summary:

This study aims to evaluate the efficacy and safety of crovalimab in adult and adolescent participants with aHUS.

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

NCT04861259 2020-002475-35 2023-505089-27-00 BO42353
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#12 Years	No

1. HOW DOES THE BO42353 CLINICAL TRIAL WORK?

This clinical trial is recruiting adults and adolescents who have a particular type of disease called atypical hemolytic uremic syndrome (aHUS).

The purpose of this clinical trial is to test the effects of crovalimab in two different groups of patients, based on whether or not they have previously received a specific type of treatment for aHUS.

2. HOW DO I TAKE PART IN THIS CLINICAL TRIAL?

To be able to take part in this clinical trial, you must have been diagnosed with aHUS. You must be at least 12 years of age and weigh at least 40 kilograms.

You must not have a history of kidney disease or any other condition, apart from aHUS, that causes your kidneys to not work as well as they should. You may not be able to take part in the study if you have been diagnosed with certain conditions in the past, if you previously received certain treatments, or if you are pregnant or breastfeeding.

If you think this clinical trial may be suitable for you, and you would like to take part, please talk to your doctor. If your doctor thinks that you might be able to take part in this clinical trial, he/she may refer you to the closest clinical trial doctor. The clinical trial doctor will give you all the information you need to make your decision about taking part in the clinical trial. You can also find the clinical trial locations on this page.

You will have further tests to make sure you will be able to take the treatments given in this clinical trial. Some of these tests or procedures may be part of your regular medical care. They may be done, even if you do not take part in the clinical trial. If you have had some of these tests recently, they may not need to be repeated.

Before starting the clinical trial, you will be told about any risks and benefits of taking part in the trial. You will also be told what other treatments are available so that you may decide if you still want to take part.

If you are a woman and not currently pregnant but can become pregnant, you will need to either not have heterosexual intercourse or take contraceptive medication.

3. WHAT TREATMENT WILL I BE GIVEN IF I JOIN THIS CLINICAL TRIAL?

Everyone who joins this clinical trial will be given crovalimab. Your first treatment will be given as an infusion into a vein, followed by injections under the skin, as follows:

Week 1:

Day 1: Crovalimab as an injection into a vein (infusion)

Day 2: Crovalimab as an injection under the skin

Weeks 2–4:

Crovalimab as an injection under the skin once a week

Week 5 onwards:

Crovalimab as an injection under the skin every 4 weeks.

The first few doses (up to Week 5) will be given in the clinic or hospital. During these visits, doctors will show you and/or your caregiver how to administer the injections so that you can continue treatment outside of the clinic. However, you still have the option to come to the clinic to receive treatment, if you prefer.

4. HOW OFTEN WILL I BE SEEN IN FOLLOW-UP APPOINTMENTS AND FOR HOW LONG?

You will be given crovalimab for a minimum of 25 weeks, and you may continue longer if you and your clinical trial doctor determine that it is working well for you.

While you are receiving study treatment, you will be seen regularly by the clinical trial doctor (once a week initially, followed by every 2 weeks and then every 4 weeks). If you continue to take crovalimab after the first 24 weeks (6 months), the clinical trial doctor will continue to see you every 8 weeks until Week 49. Thereafter, he/she will see you every 16 weeks for as long as you remain in the study. These visits will include checks to see how you are responding to the treatment and any side effects that you may be having. Your study center may organize for some visits to be done in your home if you would like to, on Week 13, 21 and 33.

If crovalimab works well for you, it is intended to be a life-long treatment but you are free to stop this treatment at any time. If you received crovalimab treatment for at least 25 weeks and your disease improved, but you or your clinical trial doctor decide to stop treatment, you may be able to re-start treatment at a later date if your disease gets worse.

If you decide to stop treatment with crovalimab and switch to a different treatment (eculizumab or ravulizumab), your clinical trial doctor will ask to see you every 1–2 weeks for 10 weeks to check on any side effects you may have during this time. You will also be asked to return for a safety clinic visit after 6 months, and will receive a safety telephone call 11 months after your last dose of crovalimab to monitor your health.

5. WHAT HAPPENS IF I AM UNABLE TO TAKE PART IN THIS CLINICAL TRIAL?

If this clinical trial is not suitable for you, you will not be able to take part. Your doctor will suggest other clinical trials that you may be able to take part in or other treatments that you can be given. You will not lose access to any of your regular care.

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For more information about this clinical trial see the **For Expert** tab on the specific ForPatient page or follow this link to ClinicalTrials.gov: https://clinicaltrials.gov/ct2/show/NCT04861259

Trial-identifier: NCT04861259

Inclusion Criteria:

- Body weight >= 40 kg at screening.
- Vaccination against Neisseria meningitidis serotypes A, C, W, and Y; vaccination against serotypes B, according to national vaccination recommendations.
- Vaccination against Haemophilus influenzae type B and Streptococcus pneumoniae, according to national vaccination recommendations.
- For participants continuing to receive other therapies concomitantly with crovalimab (e.g., immunosuppressants, corticosteroids, mammalian target of rapamycin inhibitor (mTORi) , or calcineurin inhibitors): stable dose for >=28 days prior to screening and up to the first crovalimab administration.
- For female participants of childbearing potential: an agreement to remain abstinent or use contraception.
- Female participants of childbearing potential must have a negative serum pregnancy test result within 7 days prior to initiation of crovalimab.
- Participants with a prior kidney transplant are eligible if they have a known history of complement-mediated aHUS prior to the kidney transplant.
- Onset of initial TMA presentation within 28 days prior to the first dose of crovalimab (for Naive Cohort only).
- Documented treatment with either eculizumab or ravulizumab (for Switch Cohort only).
- Clinical evidence of response to a C5 inhibitor (for Switch Cohort only).
- Known C5 polymorphism (for C5 SNP Cohort only).
- Poorly controlled TMA following treatment with another C5 inhibitor (for C5 SNP Cohort only).

Exclusion Criteria:

- TMA associated with non-aHUS related renal disease.
- Positive direct Coombs test.
- Chronic dialysis within 90 days prior to first crovalimab administration and/or end stage renal disease.
- Identified drug exposure-related TMA.
- Presence or history of a condition that could trigger TMA, such as malignancy, bone marrow or organ transplant (other than kidney transplant) or autoimmune disease.
- History of a kidney disease, other than aHUS.
- History of Neisseria meningitidis infection within 6 months of study enrollment.
- Known or suspected immune deficiency (e.g., history of frequent recurrent infections).
- Positive Human Immunodeficiency Virus (HIV) test.
- Active systemic bacterial, viral, or fungal infection within 14 days before first crovalimab administration
- Presence of fever (>= 38°C)
- Multi-system organ dysfunction or failure.
- Recent intravenous immunoglobulin (IVIg) treatment.
- Pregnant or breastfeeding or intending to become pregnant.
- Participation in another interventional treatment study with an investigational agent or use of any experimental therapy within 28 days of screening or within five half lives of that investigational product, whichever is greater.
- Recent use of tranexamic acid.

- Current or previous treatment with a complement inhibitor (for Naive Cohort only).
- First initiation of plasma exchange/plasma infusions (PE/PI) should not be more than 28 days prior to first crovalimab administration (for Naive Cohort only).
- Last PE/PI completed less than 2 hours prior to first crovalimab administration (for Naive Chorot only).
- Receiving PE/PI within 8 weeks of the first crovalimab administration (Switch Cohort only).
- Positive for active Hepatitis B and C infection (HBV/HCV) (for Switch Cohort and C5 SNP Cohort participants who recently received C5 inhibitor treatment).
- Cryoglobulinemia at screening (for Switch Cohort and C5 SNP Cohort participants who recently received C5 inhibitor treatment).
- Diagnosis of condition leading to non-aHUS TMA: Thrombotic Thrombocytopenic Purpura (TTP), Shiga Toxin producing Escherichia Coli (STEC)
- TMA, Pneumococcal HUS, TMA secondary to cobalamin C defect and TMA related to a known DGKE nephropathy.