ForPatients
by Roche

Atypical Hemolytic Uremic Syndrome (aHUS)

A clinical trial to look at how safe and effective crovalimab is in children and adolescents with atypical haemolytic uraemic syndrome (aHUS)

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

Trial Status	Trial Runs In	Trial Identifier
Recruiting	14 Countries	NCT04958265 2020-002437-15 BO42354

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, multicentre, single-arm study evaluating the efficacy, safety, pharmacokinetics, and pharmacodynamics of crovalimab in paediatric patients with atypical haemolytic uraemic syndrome (aHUS)

Trial Summary:

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

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

NCT04958265 2020-002437-15 BO42354
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#28 Days & # 17 Years	No

1. HOW DOES THE COMMUTE-p (BO42354) CLINICAL TRIAL WORK?

This clinical trial is recruiting people who have a type of disease called atypical haemolytic uraemic syndrome (aHUS). In order to take part, you must be less than 18 years old and have been diagnosed with aHUS.

The purpose of this clinical trial is to test how safe and effective crovalimab is and to understand the way your body processes this medicine.

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

To be able to take part in this clinical trial, you must be less than 18 years old (infants must be at least 28 days old and weigh at least 5 kg). You must also be up to date with certain vaccinations in order to take part in this clinical trial.

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 must not have had any organ transplants (other than kidney) or have received dialysis treatment for more than four weeks. If you have certain other medical conditions or have received certain other treatments, you may also not be able to take part in this clinical trial.

If you and your caregiver 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. They will give you all the information you need to make your decision about taking part in this clinical trial. You can also find the clinical trial locations on this page.

You will have some 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 and your caregiver 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.

While taking part in the clinical trial, female patients who could become pregnant will need to either not have heterosexual intercourse or take contraceptive medications for safety reasons.

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

Everyone who joins this clinical trial will be given crovalimab. Crovalimab treatment will be split into two parts: the loading dose series and the maintenance doses (for at least 24 weeks) but the doses and timings will vary depending on the individual patient’s weight.

In patients who weigh at least 12 kg, crovalimab will be given as an injection into the vein (infusion) on Day 1, and as an injection under the skin on Day 2 during Week 1 of the loading dose series. During Weeks 2, 3 and 4, crovalimab will be given as an injection under the skin once a week.

After this, for the maintenance doses (starting at Week 5), crovalimab will be given as an injection under the skin every two or four weeks (depending on the patient's weight) until the end of the clinical trial.

In patients who weigh less than 12 kg, crovalimab will be given as an injection into the vein (infusion) on Day 1 and as an injection under the skin on Day 2 during Week 1 of the loading dose series. Maintenance doses of crovalimab will then be given every two weeks as injections under the skin, from Week 3 onwards.

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

You will be given crovalimab for at least 24 weeks, and you may continue treatment for longer, if you and your doctor determine that it is working well for you. You are free to stop this treatment at any time. For the first 5 weeks of treatment, you will need to go to a hospital or clinic, so that your doctor can teach you and/or your caregiver how to give your injections. After this, you and/or your caregiver will have the option to give yourself your injections, if preferred. You will still be seen regularly by your doctor during and after treatment. During treatment, you will be seen regularly by your 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-week period, your doctor will continue to see you every 4 months. These clinical visits will include checks to see how you are responding to the treatment and if you are having any side effects.

Your study center may organize for some visits to be done in your home if you would like to, on Week 13, 21 and 41.

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 For Patient page or follow this link to ClinicalTrials.gov https://clinicaltrials.gov/search?intr=NCT04958265
Trial-identifier: NCT04958265

Inclusion Criteria:

- Body weight >= 5 kg at screening.
- Vaccination against Neisseria meningitis serotypes A, C, W, and Y; vaccination against serotype B, according to national vaccination recommendations.
- Vaccination against Haemophilus influenzae type B and Streptococcus pneumoniae, according to national vaccination recommendations.
- For patients 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.
- 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).
- Poorly controlled TMA following treatment with another C5 inhibitor (for C5 SNP participants in the Pretreated Cohort only).
- Known C5 polymorphism (for C5 SNP participants in the Pretreated 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 HIV test.
- Active systemic bacterial, viral, or fungal infection within 14 days before first crovalimab administration.
- Presence of fever (>= 38°C) before the first crovalimab administration (If fevers are solely due to the underlying aHUS pathology, and there is no evidence or suspicion of a systemic infection, participants may enroll).
- 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 Cohort only).
- Receiving PE/PI within 8 weeks of the first crovalimab administration (Switch Cohort only).
- Normalization of serum creatinine values at baseline (<97.5th percentile for age), (for Naive Cohort only).
- Positive for active Hepatitis B and/or C infections (HBV/HCV) (for Switch Cohort and switching C5 SNP Pretreated 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 a 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 (as demonstrated by either increased total blood homocysteine levels or MMACHC gene mutation) and TMA related to Diacylglycerol kinase # (DGKE) nephropathy.