CROSSWALK
BO42451

A clinical trial to evaluate the safety and effectiveness of crovalimab in preventing pain crises, also called vaso-occlusive episodes (VOEs), in people with sickle cell disease

Participants needed for sickle cell study

Roche

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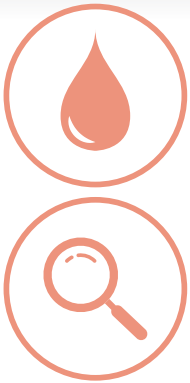
What is this booklet for?



You have been given this booklet because you are interested in the CROSSWALK-c study. We have also given you a document called an Informed Consent Form (ICF; or assent form, if you're under 18 years of age). This brochure contains information from the ICF, but also provides additional information, including what will happen if you decide to take part in this study. If you have additional questions, please contact the medical team at your clinic, and they will be happy to help.

What is CROSSWALK-c?

CROSSWALK-c is a clinical trial, or a research study, for people with sickle cell disease.

The main purpose of the study is to evaluate how effective and safe a study treatment called crovalimab is in preventing pain crises and chronic organ damage in people with sickle cell disease.

Please note that all study-related treatments and assessment will be provided to you at no cost.

If you are reading this booklet on behalf of your child, please note that when this booklet refers to 'you', this should be taken to mean 'your child'.

Why enrol in CROSSWALK-c?

The participation of people, such as yourself, in clinical trials is essential to advancing how medical conditions like sickle cell disease are treated. People enrolled in the CROSSWALK-c study will join a global community of physicians, nurses, and researchers who are dedicated to understanding if a new study treatment, crovalimab, can help improve the lives of people living with sickle cell disease. Your participation in this study will also help advance overall scientific knowledge about sickle cell disease for the full community.

Who can take part in this study?

To be eligible for this trial, you must meet the following criteria:

- Have been diagnosed with sickle cell disease, including sickle cell anaemia or sickle cell beta zero thalassaemia
- Have had at least two (but no more than ten) pain crises requiring a medical visit in the previous year
- Are between 12 and 55 years of age
- Are up to date with certain vaccinations
- Have **not** previously received a stem cell transplant
- Are **not** participating in a chronic transfusion programme
- Are **not** pregnant, breastfeeding or intending to become pregnant during or soon after the clinical trial
- Do **not** have an ongoing infection and have not had a recent infection

You will have some further tests to help determine if you will be able to take the treatments given in this clinical trial.

If you think this clinical trial may be suitable for you and would like to take part, please talk to your doctor.

What are the study treatments in CROSSWALK-c?

In this study, the study treatments are crovalimab and placebo. Crovalimab is being studied to see if it could be beneficial for people with sickle cell disease.

A placebo is a treatment with no active ingredients that looks the same as, and is given the same way as, an active medicine. A placebo group is used in some studies of new medicines to confirm that any health effects are from the active treatment rather than other factors.

How does crovalimab work?

Crovalimab is a study treatment that blocks activation of the complement system in the body. The complement system is a part of the immune system: the body's natural defence against infections. However, the complement system can be overactive in some diseases and cause problems.

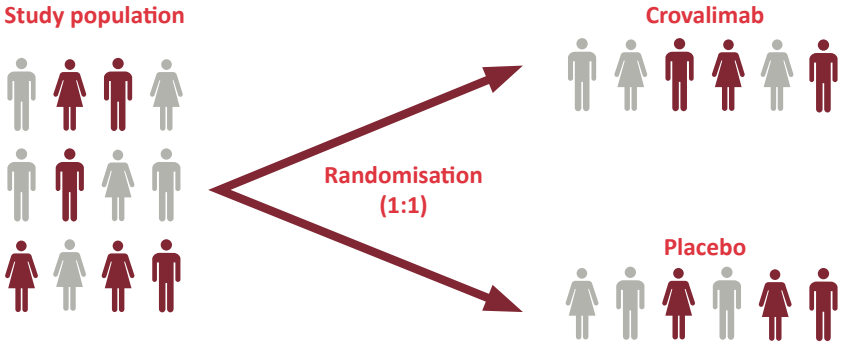
In sickle cell disease, complement overactivity may:

- Add to ongoing inflammation
- Break down red blood cells
- Cause damage to blood vessel walls
- Contribute to blockage of blood vessels, which can lead to pain crises

For this reason, blocking the complement system with crovalimab is being tested as a possible treatment for pain crises in people with sickle cell disease.

What study treatment will I receive?

Everyone who joins this clinical trial will be randomly divided between two groups (like flipping a coin). One group will receive crovalimab and the other group will receive a placebo.



Neither you nor the doctor will know which treatment you will receive. However, your doctor can find out which group you are in if your safety is at risk.

What's important for you to know is that in addition to receiving the study treatment (either crovalimab or placebo), you will also be able to continue receiving your current treatments that have been prescribed by your doctor for sickle cell disease. We understand that stopping current treatments can be concerning for people living with sickle cell disease. This is why we have designed our study in such a way that it does not interfere with your existing treatments.

If you think this clinical trial may be suitable for you and would like to take part, please talk to your doctor.

How is the study treatment administered?

The dose of study treatment (crovalimab or placebo) that you will receive will depend on your body weight.

Initially, for the first 4 weeks, the study treatment will be given weekly at study clinic visits. This initial dose schedule includes a first dose of study treatment administered as an intravenous (into the vein) infusion at the clinic on study day 1. Starting on study day 2, you will have four weekly subcutaneous injections into the abdomen at a study clinic. Your first three subcutaneous doses will be followed by a 60-minute observation period during which a study doctor or nurse will monitor your health. Starting week 5 of the study and thereafter until the end of the study, the study treatment will be given as a subcutaneous injection every 4 weeks.

Some clinics may have mobile nursing available at certain visits. In these clinics, after week 13 of the study, the mobile nurse may give you some of your subcutaneous study treatment doses at home. The administration of treatments will take place at the study site or by a mobile nurse (if available in your country). Study treatment must be administered by a healthcare professional in order to avoid revealing if the study treatment received is the placebo.

See the section on ‘What will the study involve?’ for full details on the dosing and appointment schedule.

How will my safety be ensured throughout the trial?

Your safety as a study participant is our top priority during the study.

Crovalimab works by blocking a part of the immune system. As a result, there can be an increased risk of getting infections, in particular certain bacterial infections. These may include infections caused by the bacteria *Neisseria meningitidis*

(also known as a meningococcal infection), *Haemophilus influenzae* type B, and *Streptococcus pneumoniae*. Some infections may be serious. If you decide to participate in the study, it is important that you observe the following safety measures to help reduce the risk of these infections:

- It is important that you are up to date on the required vaccinations to participate in the study. Your study doctor may decide that you need to take additional preventative treatment with antibiotics
- Safety monitoring for signs and symptoms of infection during the study will be done at regular check-ups at the clinic (or by mobile nursing, if applicable) and by telephone. It is important to attend all these study clinic visits

For information on additional side effects and risks associated with the study treatment and assessments, please see the ICF sections 'Study Treatment Risks' and 'Study Procedures and Potential Risks'.

How long is the study?

This study includes:

Screening period

A 28-day screening period during which we will assess your eligibility for the study.

Study treatment period

A 48-week study treatment period.

Follow-up period

A one-time safety follow-up visit around 24 weeks after your last dose of study treatment.

If you think this clinical trial may be suitable for you and would like to take part, please talk to your doctor.

What kind of support will I have access to?

We understand that participating in a clinical trial is not often easy so we are offering various support services that are designed to help you and your family. The types of support available differ country by country, depending on local regulations and what we are permitted to offer to patients like yourself. These might include financial support for transportation to the clinic, mobile nursing visits, and supportive telephone calls.

The supportive telephone calls are set up to fit your needs so that you can discuss your concerns, your doubts, or anything else about your health or the clinical trial you would like to inform the nurse about. A mobile nurse can call you at a frequency that you choose, however this is fully optional and up to you.

So if you are struggling in any way, please talk to your doctor and they will be able to advise you on what is available in your area.

What will the study involve?

If you join the study, your participation will include attending study clinic visits for treatment administration, to give blood and urine samples for laboratory tests, and other assessments explained on the following pages in more detail.

The following table shows a summary of what will happen during the 48 weeks of study treatment.

If you think this clinical trial may be suitable for you and would like to take part, please talk to your doctor.

Week	1		2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	...	49	Safety FU visit
	D1	D2																											
Study treatment	●	●	●	●	●	●				●				●				●				●				●	Every 4 weeks		
Study clinic visit	●	●	●	●	●	●				●				●				●				●				●	Every 4 weeks		●
Telephone visit								●				●				●				●				●			Every 4 weeks		
Blood samples	●	●	●	●	●	●				●				●				●				●				●	Every 4 weeks		
Urine samples	●					●				●				●				●				●				●	Every 4 weeks		
Ultrasound of the heart	●																									●		●	
Electrocardiogram	●					●																						●	
Questionnaires	●		●	●	●	●				●				●				●				●				●	Every 4 weeks		
Home pain crisis reporting	Sickle cell pain crises reported at home as they occur, or at a minimum every 7 days, in an eDiary (Sickle Cell Pain Crisis Questionnaire)																												
Additional assessments*	●	●	●	●	●	●				●				●				●				●				●	Every 4 weeks		●

*Physical exam, vital signs, pregnancy test and review of medications, transfusions, side effects, pain crises, and hospitalisations since the last visit.
D, Day; FU, follow-up.

Visits

There are different types of visits in this trial:

Study clinic visit

This type of visit will include administration of questionnaires, administration of the study treatment, assessment of any symptoms you may be having, and collection of blood and urine samples and other study assessments. These visits will be at the clinic. Some of the study visits can also be performed in your home by a nurse (called mobile nursing). This is fully optional and up to you. Note that mobile visits are not allowed in all countries because of local regulations. Please talk to your doctor if you are interested in the mobile nursing option.

Telephone monitoring

You will receive a telephone call between study clinic site visits where your doctor will call you to check on your health and see if you have any signs or symptoms of infection.

Assessments

The next few pages will explain what some of the key assessments mean. If you have any questions, please don't hesitate to ask a member of the medical team – they will be more than happy to help. Some of these assessments are important for monitoring your safety during the study and others are for evaluating the effect of the study treatment on your sickle cell disease.

Blood samples

Blood samples will be taken at every visit in order to monitor your safety, how your body is responding to the study medication, and to help understand sickle cell disease biology and potentially support future development of new sickle cell disease therapies.

Urine samples

Urine samples will be taken at most visits to monitor your kidney health and gain additional knowledge about sickle cell disease.

Ultrasound of the heart (echocardiogram)

An echocardiogram is an ultrasound of your heart to measure your heart function, and will be done at the beginning, midpoint and end of the study to measure how your body may be responding to study treatment.

If you think this clinical trial may be suitable for you and would like to take part, please talk to your doctor.

Electrocardiogram

An electrocardiogram, or ECG, is a non-invasive test to measure your heart's rhythm, and will be done at screening, on day 1 (only if screening ECG is abnormal), week 5, and at the end of the study as part of safety monitoring. An electrocardiogram is done by placing small sensors on your chest while you rest quietly.

Questionnaires

You will be asked to complete some questionnaires during the visits about your health and how sickle cell disease is impacting your quality of life.

Sickle Cell Pain Crisis Questionnaire

You will be given a handheld device (similar to a smartphone) to use at home. The device has an electronic Diary ('eDiary') with a short questionnaire, the Sickle Cell Pain Crisis Questionnaire, to help you report any sickle cell pain crises that may occur at home during the study. You will be asked to complete the Sickle Cell Pain Crisis Questionnaire at least every 7 days until the end of the study, even during weeks when you have not had a pain crisis. You will be asked to bring the eDiary device with you to the study clinic visits.

Additionally, at study clinic visits, the site staff will ask you questions from the Sickle Cell Pain Crisis Questionnaire about any pain crisis that you may have had in the past 7 days, similar to the reports you have been making at home on your device.

In addition, at every study clinic visit you will go through these general assessments:

Physical examination: This will be guided by symptoms you may have. You will also be asked about any procedures you have had or any changes in other medical conditions since your last visit.

Vital signs: Your pulse rate, temperature, breathing rate and blood pressure will be measured. Your weight will also be measured at certain visits throughout the study.

Pregnancy test: If you are a woman of childbearing age, a urine or blood sample will be done every 4 weeks to check for pregnancy.

Medication review: You will be asked about any new medications you may be taking, as well as any changes to your current medications. This review includes prescription and non-prescription medications, as well as dietary or herbal supplements.

Transfusion review: You will be asked about any blood transfusions you have had since your last visit.

Side effects: You will be asked about any side effects you may be experiencing throughout the study.

Review of pain crises and hospitalisations: You will be asked about pain crises that required treatment at a medical facility, and any hospitalisation for other sickle cell disease-related complications you may have had since your last visit.

If you think this clinical trial may be suitable for you and would like to take part, please talk to your doctor.

What will happen to any laboratory samples given?

All specimens and samples obtained during this study will be used and kept for the purposes described in the ICF.

What are the possible disadvantages?

It's possible that your condition won't improve during the study or may even get worse. The study treatments may also cause some side effects (listed in the ICF) or affect your health in an unknown way.

What are the possible benefits?

There is no guarantee that you will receive a medical benefit from taking part in this study. The information we gather from this study may, however, help us to treat other people with sickle cell disease in the future.

What will happen if I don't want to carry on with the study?

You may withdraw consent at any time without giving any reason. This will not affect your future treatment or your relationship with the study doctor.

What happens next?

We hope that this booklet was useful to you and that the ICF has answered any questions that you may have.

If you would like to participate or have additional questions, please speak to the medical team for more information.

For further information about sickle cell disease and CROSSWALK-c

CROSSWALK-c is a global study taking place in multiple locations around the world. This is to ensure patient diversity and to contribute to the global effort to better understand and treat people with sickle cell disease.

For more information on trial locations please visit the link below or scan the QR code using your mobile phone camera:

http://tago.ca/Glob_P

To watch an animated video providing further information on this trial, visit the link below or scan the QR code:

https://vimeo.com/565573912/faa0e1bb1e

If you think this clinical trial may be suitable for you and would like to take part, please talk to your doctor.

Thanks for your time!

Medical team contact details:

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