ForPatients
by Roche

Hemophilia ASevere Hemophilia A

A study to look at how safe emicizumab treatment is and how well it works to prevent bleeds in children with haemophilia A (without factor 8 inhibitors) who started emicizumab in their first year of life

A Study to Evaluate the Efficacy, Safety, Pharmacokinetics, and Pharmacodynamics of Subcutaneous Emicizumab in Participants From Birth to 12 Months of Age With Hemophilia A Without Inhibitors

Trial Status	Trial Runs In	Trial Identifier
Active, not recruiting	14 Countries	NCT04431726 2020-001733-12 2023-505964-13-00 MO41787

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 IIIb, Multicenter, Open-Label, Single-Arm Study to Evaluate the Efficacy, Safety, Pharmacokinetics, and Pharmacodynamics of Subcutaneous Emicizumab in Patients From Birth to 12 Months of Age With Hemophilia A Without Inhibitors

Trial Summary:

This is a Phase IIIb, multicenter, open-label, single-arm study of prophylactic emicizumab in previously untreated and minimally treated patients at study enrollment from birth to #12 months of age with severe hemophilia A (intrinsic factor VIII [FVIII] level <1%) without FVIII inhibitors. The study is designed to evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of emicizumab administered at 3 milligrams per kilogram of body weight (mg/kg) once every 2 weeks (Q2W) for 52 weeks. After 1 year of treatment, participants will continue to receive emicizumab (1.5 mg/kg once every week [QW], 3 mg/kg Q2W or 6 mg/kg once every 4 weeks [Q4W]) over a 7-year long-term follow-up period under this study frame.

Hoffmann-La Roche	Phase 3
Sponsor	Phase

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Trial Identifiers

Eligibility Criteria:

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Gender	Age	Healthy Volunteers
All	#0 Months & # 12 Months	No

1. Why is this study needed?

Haemophilia A is a health condition where the blood doesn't clot as it should. People with haemophilia A don't have enough of a select protein, called ‘factor 8’ (sometimes written as ‘FVIII’). This makes them bleed for a longer time after they get a cut or injury. People with haemophilia can also bleed for no clear cause (spontaneous bleeding) in their joints (such as knees, elbows, ankles), muscles and other soft tissues (such as skin or fat), and have difficulties with physical activities. Preventing joint bleeds and maintaining good joint health are key goals when treating haemophilia.

Treatments for haemophilia A focus on providing the missing factor 8 protein, to help blood clot after a cut or injury and prevent or reduce the bleeds associated with the disorder. On-demand and regular factor 8 replacement therapy are used to treat and prevent bleeds. However, it needs to be given directly into a vein. Also, the body’s natural defence (immune system) can develop antibodies that stop the therapy working (these are known as ‘factor 8 inhibitors’).

This study is testing a medicine called emicizumab. It can be given as an injection under the skin and less often (weekly, every other week or every four weeks) than factor 8 replacement therapy. Emicizumab is approved by health authorities (like the U.S. Food and Drug Administration and the European Medicines Agency) for treating haemophilia A in people with or without factor 8 inhibitors, and in all ages. It is used to prevent or reduce the number of bleeding episodes. However, there is limited information available on the use of emicizumab in children when the treatment has started in the first year of life.

This study aims to test how safe and well emicizumab works and to understand how the treatment gets to different parts of the body, and how the body changes and gets rid of it in children without factor 8 inhibitors who have started emicizumab in the first year of life.

2. Who can take part in the study?

Children under 1 year of age with haemophilia A without factor 8 inhibitors can take part in the study.

Children may not be able to take part in this study if they have previously been given certain medicines within a certain time frame before the study, including emicizumab, or if they have certain other medical conditions, such as another bleeding disorder or an autoimmune disease.

3. How does this study work?

Children will be screened to check if they are able to participate in the study. The screening period will take place from 2 weeks before the start of treatment.

Everyone who joins this study will be given emicizumab, as an injection under the skin weekly for the first month. Then every 2 weeks for a year. After 1 year of treatment, participants continued to be given emicizumab every 1, 2 or 4 weeks and will be monitored for another 7 years as part of this study.

This is an open-label study. This means everyone involved, including the participant and the study doctor, will know the study treatment the participant has been given.

During the first year of this study, the study doctor will see participants every week for the first 5 weeks, then every 2 or 4 weeks. They will see how well the treatment is working and any unwanted effects participants may have. Participants will have follow-up visits every 3 months during the next 7 years. Total time of participation in the study will be about 8 years. Participants have the right to stop study treatment and leave the study at any time, if they wish to do so.

4. What are the main results measured in this study?

The main results measured in the study to assess if the medicine has worked are:

- The number of bleeds children have that require a treatment
- The number of all bleeds children have (whether a treatment is given or not)
- The number of bleeds requiring a treatment that do not have a clear cause
- The number of joint bleeds that require a treatment

Other key results measured in the study include:

- Joint health measured using the Hemophilia Joint Health Score (HJHS) and magnetic resonance imaging (MRI) scans during the 7-year follow-up period
- The number and seriousness of any unwanted effects
- How emicizumab gets to different parts of the body, and how the body changes and gets rid of it
- How emicizumab affects the immune system

5. Are there any risks or benefits in taking part in this study?

Taking part in the study may or may not make participants feel better. But the information collected in the study can help other people with similar health conditions in the future.

It may not be fully known at the time of the study how safe and how well the study treatment works. The study involves some risks to the participant. But these risks are generally not greater than those related to routine medical care or the natural progression of the health condition. The parents or carers of children interested in taking part will be

informed about the risks and benefits, as well as any additional procedures or tests they may need to undergo. All details of the study will be described in an informed consent document. This includes information about possible effects and other options of treatment.

Risks associated with the study emicizumab Participants may have unwanted effects of the drug used in this study. These unwanted effects can be mild to severe, even life-threatening, and vary from person to person. During this study, participants will have regular check-ups to see if there are any unwanted effects.

Participants' carers will be told about the known unwanted effects of emicizumab and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines. Known unwanted effects include pain or discomfort in the head, joint pain and a reaction on the skin where it has been pricked with a needle to give a treatment.

Emicizumab will be given as an injection under the skin. Known unwanted effects include redness, swelling or rash on the skin where it has been pricked with a needle to give a treatment.

Inclusion Criteria:

- Age from birth to #12 months at time of informed consent
- Body weight #3 kilograms (kg) at time of informed consent. Patients with a lower body weight can be enrolled after they have reached a body weight of 3 kg. Premature babies (gestational age <38 weeks) may be enrolled as long as they have reached a body weight of 3 kg. For premature babies, the corrected gestational age should be reported.
- Mandatory receipt of vitamin K prophylaxis according to local standard practice
- Diagnosis of severe congenital hemophilia A (intrinsic FVIII level <1%)
- A negative test for FVIII inhibitor (i.e., <0.6 Bethesda units [BU]/mL) locally assessed during the 2-week screening period
- No history of documented FVIII inhibitor (i.e., <0.6 BU/mL), FVIII drug-elimination half-life <6 hours, or FVIII recovery <66%
- Previously untreated patients or minimally treated patients (i.e., up to 5 days of exposure with hemophilia-related treatments, such as plasma-derived FVIII, recombinant FVIII, fresh frozen plasma, cryoprecipitate, or whole blood products)
- Documentation of the details of the hemophilia-related treatments received since birth
- Documentation of the details of the bleeding episodes since birth
- For patients from birth to <3 months of age at the time of study entry: no evidence of active intracranial hemorrhage, as confirmed by a negative cranial ultrasound at screening irrespective of delivery mode
- Adequate hematologic, hepatic, and renal function, as defined in the protocol
- For parents/caregivers: willingness and ability to comply with the study protocol requirements, scheduled visits, treatment plans, laboratory tests, completion of applicable questionnaires, and other study procedures

Exclusion Criteria:

- Inherited or acquired bleeding disorder other than severe hemophilia A
- Use of systemic immunomodulators (e.g., interferon) at enrollment or planned use during the study

- Receipt of any of the following: Prior use of emicizumab prophylaxis including investigational or commercial emicizumab; An investigational drug to treat or reduce the risk of hemophilic bleeds within 5 drug-elimination half-lives of last drug administration; A non-hemophilia-related investigational drug within the last 30 days or 5 drug-elimination half-lives, whichever is shorter; An investigational drug concurrently
- Current active severe bleed, such as intracranial hemorrhage
- Planned surgery (excluding minor procedures, e.g., circumcision, CVAD placement) during the study
- History of clinically significant hypersensitivity associated with monoclonal antibody therapies or components of the emicizumab injection
- Patients who are at high risk for thrombotic microangiopathy (TMA) (e.g., have a previous medical or family history of TMA, such as thrombotic thrombocytopenic purpura, atypical hemolytic uremic syndrome) in the investigator's judgment
- Previous or current treatment for thromboembolic disease (with the exception of previous catheter-associated thrombosis in patients for whom anti-thrombotic treatment is not currently ongoing) or signs of thromboembolic disease
- Any hereditary or acquired maternal condition that may predispose the patient to thrombotic events (e.g., inherited thrombophilias antiphospholipid syndrome)
- Other diseases (e.g., certain autoimmune diseases) that may increase risk of bleeding or thrombosis
- Known infection with HIV, hepatitis B virus, or hepatitis C virus
- Serious infection requiring antibiotics or antiviral treatments within 14 days prior to screening
- Concurrent disease, treatment, abnormality in clinical laboratory tests, vital signs measurements, or physical examination findings that could interfere with the conduct of the study or that would, in the opinion of the investigator or Sponsor, preclude the patient's safe participation in and completion of the study or interpretation of the study results
- Unwillingness of the parent or caregiver to allow receipt of blood or blood products, or any standard-of-care treatment for a life-threatening condition
- Any other medical, social, or other condition that may prevent adequate compliance with the study protocol in the opinion of the investigator