A SINGLE-ARM, MULTICENTER PHASE IIIB CLINICAL TRIAL TO EVALUATE THE SAFETY AND TOLERABILITY OF PROPHYLACTIC EMICIZUMAB IN HEMOPHILIA A PATIENTS WITH INHIBITORS

Published: 03-07-2017
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The study will investigate the safety and efficacy of emicizumab in patients with hemophilia A with inhibitors against FVIII.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Blood and lymphatic system disorders congenital
Study type	Interventional

Summary

ID

NL-OMON47443

Source
ToetsingOnline

Brief title
STASEY (MO39129)

Condition

- Blood and lymphatic system disorders congenital

Synonym
Bleeder's disease

Research involving
Human

Sponsors and support

Primary sponsor: Roche Nederland B.V.
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: Emicizumab, Hemophilia A

Outcome measures

Primary outcome

The primary endpoint of this study is to evaluate the overall safety and tolerability of prophylactic administration of emicizumab in patients with hemophilia A. The specific focus will be to characterize any thromboembolic events, microangiopathic hemolytic anemia, thrombotic microangiopathy (TMA) (e.g. hemolytic uremic syndrome), and hypersensitivity reactions that may occur in patients with hemophilia A treated with emicizumab.

Secondary outcome

The secondary objective of this study is to evaluate the efficacy of prophylactic administration of emicizumab. As part of this objective, the number of bleeds over time will be recorded for all of the enrolled patients.

Study description

Background summary

Hemophilia A is a rare bleeding disorder that is attributable to a congenital absence or hypofunctioning of Factor VIII (FVIII). The gene that encodes FVIII is located on the X chromosome. Genetic defects are expressed through X-linked recessive inheritance or de novo FVIII mutations, and more than 99% of hemophilia patients are males.
The absence or functional deficiency of FVIII leads to a lifelong bleeding tendency. Common clinical signs of hemophilia A include easy bruising;

prolonged bleeding after trauma or surgery; spontaneous bleeding into joints, muscles, or soft tissues; and intracranial hemorrhage.
For patients with hemophilia A who are diagnosed with inhibitors, permanent eradication of these inhibitors is currently the ultimate aim of therapy. This can be achieved by means of intensive FVIII administration over many months with immune tolerance induction (ITI), and for those patients with inhibitors who are unable to eradicate their inhibitors or are not candidates for ITI, bypassing agents are required to treat or prevent bleeds.

Given the hemostatic management challenges with the current treatment options in adults and children with inhibitors, there is a clinical need for therapeutics that have a lower treatment burden, more reliable efficacy, and an extended t1/2 that can be used for preventing bleeding in patients with hemophilia A.

Study objective

The study will investigate the safety and efficacy of emicizumab in patients with hemophilia A with inhibitors against FVIII.

Study design

Single-arm, multicenter, open label Phase IIIb clinical study

Intervention

Patients will receive treatment with emicizumab during this study. Emicizumab is administered through the use of an injection just beneath the surface of the skin. You will receive one dose of emicizumab every week. You will initially receive a dose of 3 mg per kilogram of body weight (so a 70 kg person would receive 210 mg of emicizumab), for a total of 4 doses. After 4 weeks, your dose will be halved to 1.5 mg per kilogram of body weight (a 70 kg person would receive 105 mg of emicizumab). You will then receive the same dose of emicizumab every week for the rest of the 2-year treatment period, unless you are told otherwise by your doctor.

Study burden and risks

Emicizumab is not approved, and clinical development is ongoing. Thus, the complete safety profile is not known at this time. The safety plan for patients in this study is based on clinical experience with emicizumab in completed and ongoing studies. The anticipated important safety risks for emicizumab are outlined in protocol section 5.1. Please refer to the emicizumab Investigator's Brochure for a complete summary of safety information.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- As per the investigator's judgment, willingness and ability to comply with scheduled visits, treatment plans, laboratory tests, and other study procedures, including the patient-reported outcome (PRO) questionnaires and bleed diaries through the use of an electronic device or paper
- Aged 12 years or older at the time of informed consent
- Body weight ><=40 kg at the time of screening
- Diagnosis of congenital hemophilia A with persistent inhibitors against FVIII
- Documented treatment with bypassing agents or FVIII concentrates in the last 6 months (on-demand or prophylaxis). Prophylaxis needs to be discontinued the latest by a day before starting emicizumab

- Adequate hematologic, hepatic, and renal function
- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use a highly effective contraceptive method with a failure rate of <1% per year during the treatment period and for at least five elimination half-lives (24 weeks) after the last dose of emicizumab

Exclusion criteria

- Inherited or acquired bleeding disorder other than hemophilia A
- Ongoing (or plan to receive during the study) immune tolerance induction (ITI) therapy (prophylaxis regimens with FVIII and/or bypassing agents must be discontinued prior to enrollment). Patients receiving ITI therapy will be eligible following the completion of a 72-hour washout period prior to the first emicizumab administration
- History of illicit drug or alcohol abuse within 12 months prior to screening, as per the investigator*s judgment
- High risk for thrombotic microangiopathy (TMA) (e.g., have a previous medical or family history of TMA), as per the investigator*s judgment
- Previous (in the past 12 months) or current treatment for thromboembolic disease (with the exception of previous catheter-associated thrombosis for which antithrombotic treatment is not currently ongoing) or current signs of thromboembolic disease
- Other conditions (e.g., certain autoimmune diseases) that may increase the risk of bleeding or thrombosis
- History of clinically significant hypersensitivity reaction associated with monoclonal antibody therapies or components of the emicizumab injection
- Known human immunodeficiency virus (HIV) infection with CD4 count <200 cells/*L within 6 months prior to screening
- Use of systemic immunomodulators (e.g., interferon or rituximab) at enrollment or planned use during the study, with the exception of antiretroviral therapy
- Concurrent disease, treatment, or abnormality in clinical laboratory tests 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
- Receipt of:
*Emicizumab in a prior investigational study
*An investigational drug to treat or reduce the risk of hemophilic bleeds within five half-lives of last drug administration
*A non-hemophilia-related investigational drug within last 30 days or five half-lives, whichever is shorter
*Any concurrent investigational drug.
- Pregnancy or lactation, or intent to become pregnant during the study
- Positive serum pregnancy test result within 7 days prior to initiation of emicizumab (females only)

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-05-2018
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Emicizumab
Generic name:	Emicizumab

Ethics review

Approved WMO Date:	03-07-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	09-11-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	29-01-2018
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	14-02-2018
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	18-06-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	17-07-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	05-12-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	09-12-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	16-12-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	17-01-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2016-004366-25-NL
CCMO	NL61146.041.17