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

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Study MO41787 will evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of emicizumab administered at 3 mg/kg Q2W for a period of 52 weeks in previously untreated patients (PUPs) and minimally treated patients (MTPs) at study...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Coagulopathies and bleeding diatheses (excl thrombocytopenic)
Study type	Interventional

Summary

ID

NL-OMON51172

Source
ToetsingOnline

Brief title
HAVEN7 MO41787

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
Hemophilia A

Research involving
Human

Sponsors and support

Primary sponsor: Roche Nederland B.V.
Source(s) of monetary or material Support: F. Hoffmann-La Roche Ltd

Intervention

Keyword: Babies, Emicizumab, Hemophilia A, Open label

Outcome measures

Primary outcome

The efficacy objective for this study is to evaluate the efficacy of emicizumab

on the basis of the following endpoints:

- Number of treated bleeds over time (i.e., treated bleed rate)

- Number of all bleeds over time (i.e., all bleed rate)

- Number of treated spontaneous bleeds over time (i.e., treated spontaneous

bleed rate)

- Number of treated joint bleeds over time (i.e., treated joint bleed rate)

- Joint health, as assessed through use of the Hemophilia Joint Health Score

(HJHS) and magnetic resonance imaging (MRI) score of specific joints at

specified timepoints only during the 7-year LTFU period

Secondary outcome

The safety objective for this study is to evaluate the safety of emicizumab on

the basis of the following endpoints:

- Incidence and severity of adverse events, with severity determined according

to

WHO Toxicity Grading Scale (see Appendix 5)

- Incidence of thromboembolic events

- Incidence of thrombotic microangiopathy (TMA)

- Change from baseline in physical examination findings

- Change from baseline in vital signs

- Incidence of laboratory abnormalities

- Incidence and severity of injection-site reactions

- Incidence of adverse events leading to drug discontinuation

- Incidence of severe hypersensitivity, anaphylaxis, and anaphylactoid events

See protocol section 2 for Pharmacokinetic, biomarker and Immunogenicity

objectives

Study description

Background summary

Infant patients with hemophilia A constitute a vulnerable population with high unmet medical need.

In children, the current standard of care is primary prophylaxis with regular FVIII infusions (starting from the first joint bleed onward or earlier), focusing on joint preservation with optimally, no bleeds and the prevention of long-term consequences such as joint damage. Because of difficulties in venous access in newborns and infants, replacement therapy often necessitates the placement of central venous access devices (CVADs). However, long-term CVAD use requires considerable commitment from caregivers and parents, and serious

complications can occur, including thrombosis, bleeding, mechanical dysfunction, and most commonly, infection.

The administration of prophylactic factor concentrate at birth is recommended because it is highly efficacious to prevent bleeds, but the risks of FVIII inhibitor development from early factor exposure of newborns and infants remain. The development of FVIII inhibitors represents a challenging and costly complication of treatment. See part 1 of protocol

Study objective

Study MO41787 will evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of emicizumab administered at 3 mg/kg Q2W for a period of 52 weeks in previously untreated patients (PUPs) and minimally treated patients (MTPs) at study enrollment from birth to <= 12 months of age with severe hemophilia A (intrinsic FVIII level < 1%) without FVIII inhibitors. After 1 year of treatment, patients will continue to receive emicizumab (1.5 mg/kg QW, 3 mg/kg Q2W, or 6 mg/kg Q4W) over a 7-year LTFU period, which will evaluate long-term safety of emicizumab and describe the natural history of these patients, including the preservation of joint health over time. Study MO41787 is a descriptive study with no formal hypothesis testing. Specific objectives and corresponding endpoints for the study are outlined in part 2 of the protocol.

Study design

Study MO41787 is a Phase IIIb, multicenter, open-label, single-arm study of emicizumab in PUPs and MTPs at study enrollment from birth to * 12 months of age with severe hemophilia A (intrinsic FVIII level * 1%) without FVIII inhibitors. The study is designed to evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of emicizumab administered at 3 mg/kg Q2W for 52 weeks. After 1 year of treatment, patients will continue to receive emicizumab (1.5 mg/kg QW, 3 mg/kg Q2W or 6 mg/kg Q4W) over a 7-year LTFU period under this study frame. Study MO41787 is a descriptive study with no formal hypothesis testing. See part 3 of protocol

Intervention

Emicizumab will be administered at 3 mg/kg Q2W for a period of 52 weeks. After 1 year of treatment, patients will continue to receive emicizumab (1.5 mg/kg QW, 3 mg/kg Q2W, or 6 mg/kg Q4W) over a 7-year LTFU period

Study burden and risks

The general burden on the patients consists, among other things, of blood sampling (each visit), visit to the site every week the first 5 weeks, every 4

weeks the first year, and every year the next 7 years. Also the administration of the study drug (every 2 weeks for the first year, thereafter every week, two weeks or four weeks). that may lead to various adverse events.

Contacts

Public
Roche Nederland B.V.

Beneluxlaan 2a
Woerden 3446 GR
NL
Scientific
Roche Nederland B.V.

Beneluxlaan 2a
Woerden 3446 GR
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

Inclusion criteria:
* Age from birth to <<= 12 months at time of informed consent
* Body weight ><= 3 kg at time of informed consent
* 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 for all patients

* For PUPs or MTPs, 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 ICH, as confirmed by a negative cranial ultrasound at screening irrespective of delivery mode
* Adequate hematologic, hepatic, and renal function

Exclusion criteria

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:
* 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 ICH
* Planned surgery during the study
* History of clinically significant hypersensitivity associated with monoclonal antibody therapies or components of the emicizumab injection
* Previous or current treatment for thromboembolic disease or signs of thromboembolic disease
* Any hereditary or acquired maternal condition that may predispose the patient to thrombotic events
* 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

Study design

Design

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Hemlibra
Generic name:	emicizumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	15-12-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-02-2021
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-05-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-09-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2020-001733-12-NL
ClinicalTrials.gov	NCT04431726
CCMO	NL75360.056.20