Emicizumab Use in Pediatric Patients in the Real World: an Analysis of the PedNet Registry

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Last updated: 01/10/2025

Study Finalised

Administrative details

EU PAS number

EUPAS31954

Study ID

48526

DARWIN EU® study

No

Study countries

- Austria
- Belgium
- Canada
- Czechia

- Denmark
- Finland
- France
- Germany
- Greece
- Ireland
- Israel
- Italy
- Netherlands
- Norway
- Portugal
- Spain
- Sweden
- Switzerland
- United Kingdom

Study description

The main aim of this non-interventional, secondary data use, post-authorization safety study (PASS) is to assess safety of emicizumab prophylaxis in real-world conditions, among pediatric patients with hemophilia A enrolled in the European Pediatric Network for Haemophilia Management (PedNet) Registry.

PedNet Registry is the largest registry in the world for pediatric patients with hemophilia. Currently, 19 countries with approximately 34 treatment centers participate. The registry includes all age groups and severities (Factor VIII <25%), which provides substantial coverage and an adequate representation of the pediatric patient population.

The primary safety events of interest in this study are thromboembolic events (TEs), thrombotic microangiopathy (TMA), and anaphylaxis. However, all safety

events collected in the PedNet Registry are reported.
In addition to safety, effectiveness of emicizumab is evaluated by the annual bleeding rate, as reported in the PedNet Registry. The following criteria describe the population eligible for this study, which is a subset of the overall population participating in the PedNet Registry.

Inclusion criteria for inclusion in the PedNet Registry:
- Diagnosis of haemophilia A
- Factor VIII (FVIII) activity <25%
- Treated in one of the participating centers.
Additional inclusion for emicizumab-specific analysis:
- Received prophylactic treatment with emicizumab.

Exclusion criteria for the PedNet Registry:
- Referral to a participating center after development of FVIII inhibitors
- Informed consent for participation in the PedNet Registry not obtained.
Exclusion criteria for emicizumab-specific analysis:
- Inherited or acquired bleeding disorder other than haemophilia A.

The PedNet Registry extracts and analyzes data according to the protocol and provides the Marketing Authorization Holder (MAH) with annual emicizumab-specific reports.

Study status
Finalised

Research institutions and networks

Institutions

PedNet Haemophilia Research Foundation

Netherlands

First published: 01/02/2024

Last updated: 01/02/2024

Institution | Not-for-profit

F. Hoffmann-La Roche

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Institution

Contact details

Study institution contact

Letizia Polito global.clinical_trial_registry@roche.com

Study contact

global.clinical_trial_registry@roche.com

Primary lead investigator

Letizia Polito

Primary lead investigator

Study timelines

Date when funding contract was signed
Actual: 24/03/2019

Study start date
Planned: 30/11/2019

Actual: 03/12/2019

Date of final study report
Planned: 30/09/2025

Actual: 22/08/2025

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

F. Hoffmann-La Roche, Ltd.

Study protocol

Prot MO40685 (PEDNET) emicizumab v1_Redacted.pdf (593.4 KB)

MO40685 (PEDNET)-Protocol v2_Redacted.pdf (284.5 KB)

Regulatory

Was the study required by a regulatory body?

No

Is the study required by a Risk Management Plan (RMP)?

EU RMP category 3 (required)

Other study registration identification numbers and links

MO40685, NCT02979119

PedNet Registry

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Effectiveness study (incl. comparative)

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Main study objective:

The primary objective for this study is to evaluate the overall safety and tolerability of emicizumab administration in all pediatric patients with haemophilia A in real-world conditions, and in subgroups determined by age and inhibitor status, as well as by severity for patients without inhibitors

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

HEMLIBRA

Study drug International non-proprietary name (INN) or common name

EMICIZUMAB

Anatomical Therapeutic Chemical (ATC) code

(B02BX06) emicizumab

emicizumab

Medical condition to be studied

Haemophilia A without inhibitors

Haemophilia A with anti factor VIII

Population studied

Age groups

- **Paediatric Population (< 18 years)**
  - Term newborn infants (0 – 27 days)
  - Infants and toddlers (28 days – 23 months)
  - Children (2 to < 12 years)
  - Adolescents (12 to < 18 years)

Estimated number of subjects

743

Study design details

Setting

PedNet Registry is the largest registry in the world for pediatric patients with hemophilia. Currently, 19 European countries, comprising 17 European countries (including the United Kingdom), Israel, and Canada, with approximately 34 hemophilia treatment centers (HTCs) participate in the registry. The Registry includes all ages groups up to age 18 years and all severities of hemophilia, including mild hemophilia A patients with Factor VIII <25 IU/dL. This setting provides substantial coverage and is an adequate representation of the pediatric patient population.

The following criteria describe the population eligible for this study, which is a subset of the overall population participating in the PedNet Registry.

Inclusion criteria for inclusion in the PedNet Registry:
- Diagnosis of hemophilia A
- Factor VIII activity <25 IU/dL

- Treated in one of the participating HTCs

Additional inclusion for emicizumab-specific analysis:

- Received prophylactic treatment with emicizumab

Exclusion criteria for the PedNet Registry:

- Referral to a participating HTC after development of Factor VIII inhibitors
- Informed consent for participation in the PedNet Registry not obtained

Exclusion criteria for emicizumab-specific analysis:

- Inherited or acquired bleeding disorder other than hemophilia A

Outcomes

Primary safety endpoints:

- Frequency and incidence of thromboembolic events (TEs), thrombotic microangiopathy (TMA), and anaphylaxis (including terms of systemic hypersensitivity, anaphylaxis, and anaphylactoid events), overall and in subgroups determined by age and inhibitor status, as well as by severity of hemophilia A for patients without inhibitors.

Secondary safety endpoints:

- Frequency and incidence of any adverse events (overall, and by age, inhibitor status, and severity of hemophilia A).

Effectiveness endpoints (overall, and by age, inhibitor status, and severity of hemophilia A):

- Annual bleeding rate (ABR) for all bleeds* and percentage of patients with zero bleeds*;
- ABR for joint bleeds and major bleeds
- Bleeds count for all bleeds, major bleeds, minor and major joint bleeds, and minor non-joint bleeds.

*As per PedNet data collection, all bleeds reported are treated bleeds.

Data analysis plan

This is a secondary data use non-interventional study. There is no pre-defined hypothesis testing and all analyses are regarded as exploratory.

The Marketing Authorisation Holder (MAH) receives aggregate level data of patients treated with emicizumab from the PedNet Registry on an annual basis. Based on the number of patients, number of adverse events (AEs), and exposure to emicizumab provided by the PedNet Registry, the MAH performs analyses of frequencies/incidence of AEs overall and grouped by age during emicizumab initiation, severity, and inhibitor status. The youngest age group is newborns (birth to 28 days). Other age groups include: 29 days to less than(<)6 months, 6 months–<2 years, 2 years–<6 years, 6 years–<12 years, and 12 years–18 years. The MAH reports annual bleeding rate (ABR) for all bleeds, percentage of patients with zero bleeds, ABR for joint bleeds and major bleeds overall and grouped by age, severity, and inhibitor status as sent by the PedNet Registry. As per PedNet data collection, all bleeds reported are treated bleeds.

Summary results

Since the beginning of the PedNet Registry up until the clinical cutoff date of 31-Dec-2024, 743 patients with hemophilia A received treatment with emicizumab. Of these, 578 patients with updated follow-up until 1-Jul-2023 were included in this report. Among them, 532 patients with a treatment period of a minimum of 6 consecutive months were included for a reliable negative binomial regression model-based ABR calculation.

Overall, no TMA or anaphylaxis was reported in the 578 patients through the study period. The following 15 AEs were reported cumulatively as of the final report:

- One case of antibodies against emicizumab, 2 local subcutaneous (SC) reactions, and 1 death unrelated to the study drug reported in the 2nd interim report;
- One injection site reaction reported in the 4th interim report;
- One TE following sepsis and port-a-cath removal, 2 local SC reactions, 2 cases of redness at injection site, and 3 other AEs reported in the 5th interim report;
- Two local SC reactions reported in the 6th (final) report.

Following a median duration of emicizumab exposure of 28.1 months (inter-quartile range: 16.6–41.9) in 578 patients, 264 patients (46%) had zero bleeds and 436 (75%) had zero joint bleeds. Of the 993 bleeds reported, 277 (28%) were major bleeds and 716 (72%) were minor bleeds. Moreover, 321 (32%) were joint bleeds.

The model-based ABR for the 532 patients with a minimum 6 consecutive months of treatment was 0.7 (95% CI: 0.6–0.8) for all bleeds, 0.2 (95% CI: 0.2–0.2) for major bleeds (joint and non-joint), and 0.2 (95% CI: 0.2–0.3) for joint bleeds (major and minor).

Documents

Study report

Interim_CSR,_Study_MO40685_(PEDNET),_PASS_Annual_Report_30Sep2020,_Published_Ou
1_Redacted.pdf (905.63 KB)
MO40685 (PEDNET)-Interim CSR Synopsis 2, PASS Annual Report_30Sep2021_Redacted.pdf (1.43 MB)
MO40685 (PEDNET)-Interim CSR Synopsis 3_PASS Annual Report_28Sep2022_Redacted.pdf (601.02 KB)
MO40685 (PEDNET)-Interim CSR Synopsis 4_Annual Report_29-Sep-2023_Redacted.pdf (629.55 KB)

MO40685 (PEDNET)-Interim CSR Synopsis 5_Annual Report_17-Sep-2024_Redacted.pdf (492.51 KB)

MO40685 (PEDNET)-Final CSR Synopsis_Redacted.pdf (586.69 KB)

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data source(s)

PedNet Haemophilia registry

Data sources (types)

Disease registry

Other

Data sources (types), other

Prospective patient-based data collection

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No