Pan European Prospective Observational Study of Fremanezumab effectiveness in patients with chronic or episodic migraine in the Real-World: PEARL study

First published: 07/05/2020

Last updated: 21/05/2025

Study | Finalised

Administrative details

EU PAS number

EUPAS35111

Study ID

35112

DARWIN EU® study

No

Study countries

Czechia

Denmark

Finland

Greece
Italy
Norway
Portugal
Spain
Sweden
Switzerland
United Kingdom

Study description

This was a 45-month (21-month recruitment and 24-month follow-up), multicenter, multicountry (pan-European), prospective observational study to describe evidence of outcomes of fremanezumab treatment according to the SmPC in real-world clinical practice.

The study was aimed to address the impact of fremanezumab treatment in European real-world clinical practice and to generate information about real-world effectiveness, safety, tolerability, treatment adherence, and treatment persistence.

Primary endpoint: The proportion of patients reaching at least 50% reduction in the monthly average number of migraine days during the 6-month period after the first dose of fremanezumab.

Secondary effectiveness endpoints include mean change from baseline in MMD across months 1, 3, 6, 9, 12, 15, 18, 21, and 24, acute migraine medication use, and migraine-related disability scores.

Safety is evaluated based on adverse events (AEs) reported in clinical practice.

Study status

Finalised

Research institutions and networks

Institutions

Danish Headache Center

First published: 01/02/2024

Last updated: 01/02/2024

Institution

INEP - Institut neuropsychiatrické péče

Thomayer Hospital

Motol University Hospital Prague

Nemocnice Jihlava

Neurologická klinika Olomouc

Vesctra Clinics s.r.o

Rigshospitalet Glostrup

University Hospital Odense, Hovedpineklinik

Southwest Jutland University Hospital

Pohjola Sairaala Oulu

Terveystalo Jyväskylä

Tampere University Hospital

Saaristokaupungin Lääkäriasema Oy

Helsinki University Hospital

Aeginition Hospital

ATTIKON University Hospital

401 Military Hospital Athens

Mediteraneo Hospital

Euromedica "Geniki Kliniki"

Aristotle University

IRCCS C. Mondino

SST Spedali Civili di Brescia

Ospedale Sant'Andrea

AOU Città della Salute e dela Scienza

Azienda Ospedaliero-Universitaria Modena

Ospedale SS Filippo e Nicola

POLICLINICO “PAOLO GIACCONE”

Azienda Ospedaliera "Pugliese - Ciaccio"

Ospedal S.Maria Della Misericordia

IRCCS Ospedale Policlinico San Martino

Sant'Anna University Hospital

IRCCS Istituto delle Scienze Neurologiche

IRCCS Neuromed

IRCCS San Raffaele

Università di Napoli Federico II of Naples

Azienda Ospedaliero-Universitaria Careggi

Headache Center, Via Roma 67, Pisa

IRCCS Carlo Besta Neurological Institute

Ospedale G.Moscati di Avellino

Istituto Auxologico San Luca

SITE CLOSED - Ospedale San Bortolo

Az. Ospedaliera Universitaria Bari

Clinica Neurologia AOU Policlinico San Marco Catania

Ospedale Santa Maria della Misericordia

AOU Ospedali Riuniti di Ancona

Campus Biomedico Roma

Az. Ospedaliera Universitaria Vanvitelli

Sapienza University of Rome Polo Pontino

Ospedale Cattinara-Ospedali Riuniti

Ospedale San Carlo Milano

Oslo Hodepinesenter AS

Sandvika Nevrosenter AS

Hodeverket Headache Clinic

Frisk Utvikling Helse AS

Hodepineklinikken

Hospital de Santa Maria, Lisboa

Hospital de Egas Moniz, Lisboa

Hospital Prof. Doutor Fernando Fonseca, Amadora

Hospital Universitario Vall d'Hebron

Hospital Universitary de Bellvitge

Hospital Clínico Universitario de Santiago

Hospital Universitario Virgen del Rocío

Hospital Universitario Virgen de Valme

Skåneuro AB, Lund

Stortorgets Neurologmottagning

St Görans Hospital Neuro Center

Rehdo AB, Göteborg

Läkarhuset Vällingby

VO Närsjukvård

Neurology Clinic Stockholm, Sophiahemmet, Box 5605

Neuroenheten Utsikten

Inselspital, University Hospital Bern

Kantonsspital St. Gallen

Neurologie am Löwenplatz

Cabinet de Neurologie, Sion, Valais

Ospedale Regionale di Lugano

Kopfwehzentrum Hirslanden AG

Hospitalier Universitaire Vaudois

RehaClinic Bad Zurzach

Luzerner Kantonsspital

Hôpital du Valais

Newcastle Acute Hospitals

Brighton and Sussex

Queens Medical Centre

King's College Hospital

St Thomas's Hospital

Hull University Teaching Hospitals

Contact details

Study institution contact

Faisal Amin FAISAL@DADLNET.DK

Study contact

FAISAL@DADLNET.DK

Primary lead investigator

Messoud Ashina 0000-0003-0951-5804

Primary lead investigator

ORCID number:

0000-0003-0951-5804

Study timelines

Date when funding contract was signed

Planned: 31/10/2019

Actual: 23/12/2019

Study start date

Planned: 31/01/2020

Actual: 07/08/2020

Data analysis start date

Planned: 08/08/2024

Actual: 08/08/2024

Date of final study report

Planned: 26/02/2025

Actual: 08/04/2025

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Teva Pharmaceuticals Europe B.V.

Regulatory

Was the study required by a regulatory body?

No

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

Not applicable

Other study registration identification numbers and links

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Drug utilisation

Effectiveness study (incl. comparative)

Evaluation of patient-reported outcomes

Safety study (incl. comparative)

Data collection methods:

Primary data collection

Study design:

This was a 45-month (21-month recruitment and 24-month follow-up), multicenter, multicounty (pan-European), prospective observational study to describe evidence of outcomes of fremanezumab treatment according to the Summary of Product Characteristics (SmPC) in real-world clinical practice.

Main study objective:

To evaluate the effectiveness of fremanezumab in adult patients with CM or EM who have at least 4 migraine days per month, including a proportion of patients reaching a 50% reduction in the monthly average number of migraine days during a 6 month period after the first dose of fremanezumab, in real world clinical practice

Study Design

Non-interventional study design

Other

Non-interventional study design, other

Prospective observational study in real-world clinical practice

Study drug and medical condition

Medicinal product name

AJOVY

MIGRAINE RELIEF

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

FREMANEZUMAB

Anatomical Therapeutic Chemical (ATC) code

(N02CD03) fremanezumab

fremanezumab

Medical condition to be studied

Migraine

Additional medical condition(s)

Chronic migraine (CM) and Episodic migraine (EM)

Population studied

Short description of the study population

The study population was composed of male and female patients, aged 18 years and older, diagnosed with CM or EM, and had been prescribed fremanezumab according to the SmPC as a treatment decision of their physician before enrollment in this study.
Patients included might have received acute or other preventive migraine treatments before the start of this study and might have continued these treatments, changed or unchanged, throughout the study period.
Up to 30% of patients enrolled were allowed to have previously taken preventive migraine treatment with other monoclonal antibodies targeting the CGRP pathway.
Patients who switched from another monoclonal antibody targeting the CGRP pathway were recommended to wait until their next scheduled dose before starting fremanezumab. The number of actually enrolled subjects was 1140 patients.

Age groups

- **Adult and elderly population (≥18 years)**
  - Adults (18 to < 65 years)
    - Adults (18 to < 46 years)
    - Adults (46 to < 65 years)

- Elderly (≥ 65 years)
  - Adults (65 to < 75 years)
  - Adults (75 to < 85 years)
  - Adults (85 years and over)

Estimated number of subjects

1140

Study design details

Setting

The study took place between 07/08/2020 and 17/04/2024 in 11 European countries.

Patients were included in the study if all of the following inclusion criteria were fulfilled:

a. The patient has signed the informed consent.

b. The patient is male or female and 18 years of age or older.

c. The patient has a diagnosis of CM or EM.

d. The patient has been prescribed fremanezumab as a treatment decision of their physician according to the SmPC and their first dose of fremanezumab was within 3 months (+ 7 days) of the day of enrollment.

e. The patient has been maintaining a daily headache diary as part of their routine disease management per their treating physician and has maintained a headache diary for at least 21 days in the 28 days prior to fremanezumab treatment initiation.

f. For patients with fremanezumab treatment initiation at least 28 days before enrollment, the patient has maintained a headache diary for at least 21 days per month since fremanezumab treatment initiation.

g. The patient’s headache diary ideally captures information on headache duration, headache severity, and headache characteristics.
h. The patient understands and is willing to keep records in their electronic or paper headache diary for the course of the study.

Exclusion Criteria
Patients were excluded from the study for any of the following reasons:
a. The patient is not treated according to the SmPC.
b. Up to 30% of patients enrolled may have previously taken preventive migraine treatment with other monoclonal antibodies targeting the CGRP pathway.
c. The patient is participating in an interventional clinical trial in EM or CM

Comparators
Not applicable

Outcomes
Primary objective:
• To evaluate the effectiveness of fremanezumab administered in adult patients with chronic migraine (CM) or episodic migraine (EM) who have at least 4 migraine days per month, including the proportion of patients reaching at least 50% reduction in the monthly average number of migraine days during the 6-month period after the first dose of fremanezumab, in real-world clinical practice.
Secondary objectives:
• To evaluate measures of effectiveness of fremanezumab, including monthly average number of migraine days, and disability scores, in real-world clinical practice
• To evaluate the use of concomitant acute migraine medications in real-world

clinical practice
• To evaluate patient adherence to and persistence with fremanezumab treatment in real-world clinical practice
• To evaluate measures of effectiveness of fremanezumab in real-world clinical practice in patients who have no prior exposure to a monoclonal antibody targeting the calcitonin gene-related peptide (CGRP) pathway
Exploratory objectives:
• To evaluate the impact of fremanezumab on reducing migraine severity in real-world clinical practice
• To assess the number and classes of concomitant preventive and acute migraine medications used in real-world clinical practice
• To evaluate outcomes following fremanezumab cessation and any subsequent reinitiation of fremanezumab treatment in real-world clinical practice
• To evaluate the reasons for fremanezumab cessation and reinitiation in real-world clinical practice
• To evaluate measures of effectiveness of fremanezumab in real-world clinical practice in patients who have prior exposure to a monoclonal antibody targeting the CGRP pathway

---

Data analysis plan

All variables will be summarized descriptively. For continuous variables, descriptive statistics (n, mean, standard deviation, standard error of mean, median, minimum, and maximum) will be provided for actual values and changes from baseline to each visit. For categorical variables, frequency and percentage will be provided.
The 95% confidence intervals will be provided for point estimate, if appropriate. Nominal p-values for comparisons to baseline or for testing some other hypotheses may be provided as well.
This approach will apply to all interim analyses and the final analysis. Data analyses will be performed based on the data available from individual patient

diaries. Data from monthly and quarterly fremanezumab dosing groups will be combined for all analyses.
Analyses of monthly and quarterly fremanezumab dosing subgroups and for EM and CM subgroups will be also provided. Analyses for patients who do not miss any doses up to a certain timepoint will be also provided

Documents

Study, other information

PEARL Study Protocol a Real-World Study of Fremanezumab Effectiveness in Patients with Chronic or Episodic Migraine.pdf (1.09 MB)

https://www.tandfonline.com/doi/epdf/10.2217/pmt-2021-0015?needAccess=true

Study publications

https://journals.sagepub.com/doi/epub/10.1177/03331024231214987

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), other

Not applicable

Data sources (types)

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

Unknown

Data characterisation moment

after data extraction