Treatment persistence and effectiveness of CGRP monoclonal antibodies versus high evidence conventional oral preventive treatments in adolescents with high-burden migraine: an exploratory retrospective analysis of depersonalized real-world-data from the German Pain e-Registry (GPeR). (PRIME-Teen)

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Study Finalised

Administrative details

EU PAS number

EUPAS1000000879

Study ID

1000000879

DARWIN EU® study

No

Study countries

Germany

Study description

This is an observational cohort study taht retrospectively analyzed depersonalized routine care data from adolescents with migraine treated with high evidence conventional oral preventives (HECP) or CGRP-mABs in routine care in the German Pain e-Registry. Patient data sets were included if they provide information on at least one 6-month treatment period, each with baseline (BL) and follow-up documentation, for both treatments to allow intraindividual comparisons. Primary endpoint (PE) was achievement of a composite of treatment persistence and ≥50% reduction in monthly migraine days (MMD). Secondary outcomes included changes in MMD with acute medication, (MMDAM), migraine-related sick leave days (MMSLD), disability (MIDAS), sleep, psychological burden, and quality of life.

Study status

Finalised

Research institutions and networks

Institutions

Institute for Neurological Sciences (IFNAP)

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Institution

Networks

German Pain e-Registry

Contact details

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Primary lead investigator

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Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 01/10/2025

Actual: 01/10/2025

Study start date

Planned: 02/10/2025

Actual: 02/10/2025

Data analysis start date
Planned: 02/10/2025

Actual: 02/10/2025

Date of final study report
Planned: 31/10/2025

Actual: 31/10/2025

Sources of funding

- No external funding

Regulatory

Was the study required by a regulatory body?

No

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

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Effectiveness study (incl. comparative)

Data collection methods:

Secondary use of data

Study design:

Retrospective, exploratory analysis of depersonalized routine care data from the GPeR, a web-based, non-interventional registry designed to harmonize and aggregate information on real-world pain care in outpatient practices across Germany.

Main study objective:

The primary endpoint was a composite of two clinically central aspects of migraine prevention. First, the treatment episode had to be continued over the entire 6-month observation period without discontinuation due to adverse drug reactions (ADRs) or insufficient efficacy. Second, the patient had to achieve a reduction in monthly migraine days (MMD) of at least 50% from baseline to end of month six. Data on MMDs were derived from patient-reported information on migraine days in the respective observation window. Monthly migraine days with acute medication use (MMDAM) and monthly migraine-related school or work disability days (MMSLD) were assessed in an analogous manner. Secondary endpoints included absolute and relative changes in MMD, MMDAM and MMSLD from baseline to month six, as well as the distribution of patients

across migraine frequency categories [chronic migraine (CM), high-frequency episodic migraine (HFEM), low-frequency episodic migraine (LFEM) and very low-frequency episodic migraine (VLFEM)] at baseline and follow-up. Disability and functional impact were assessed with the Migraine Disability Assessment (MIDAS); migraine-related sleep impairments were evaluated via subitem #6 of the modified Pain Disability Index (mPDI6); health-related quality of life was measured with the physical and mental component scores of the VR-12; analyses of the degree of migraine-related depression, anxiety and stress were performed based on data gathered with the Depression, Anxiety and Stress Scale (DASS-21), and the Marburg Questionnaire on Habitual Health Findings (MQHHF) has been used for the evaluation of the general wellbeing of patients. For the primary endpoint, the proportion of patients who continued their preventive treatment over the 6-months evaluation period were assessed (component #1 of the PE) and for the MMD (PE component #2) absolute and relative changes were calculated and the proportions of patients with a clinically meaningful improvement vs. baseline (≥50%) were determined.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

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

AMITRIPTYLINE

PROPRANOLOL HYDROCHLORIDE

METOPROLOL

FLUNARIZINE

TOPIRAMATE

VALPROIC ACID

ERENUMAB

FREMANEZUMAB

GALCANEZUMAB

EPTINEZUMAB

Anatomical Therapeutic Chemical (ATC) code

(N06AA09) amitriptyline

amitriptyline

(C07AA05) propranolol

propranolol

(C07AB02) metoprolol

metoprolol

(N07CA03) flunarizine

flunarizine

(N03AX11) topiramate

topiramate

(N03AG01) valproic acid

valproic acid

(N02CD01) erenumab

erenumab

(N02CD03) fremanezumab

fremanezumab

(N02CD02) galcanezumab

galcanezumab

(N02CD05) eptinezumab

eptinezumab

Medical condition to be studied

Migraine

Population studied

Short description of the study population

For the present analysis, data of adolescents aged 12-17 years with a physician diagnosis of migraine were identified at the cut-off date of 30 June 2024.

Age groups

- **Paediatric Population (< 18 years)**
  - Neonate
    - Preterm newborn infants (0 – 27 days)
    - 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

422

Study design details

Setting

Patients served as their own comparators, as we evaluated within-subjects differences with respect to the response due to a) high evidence conventional migraine preventives vs. b) calcitonin-gene-related receptor antagonists (CGRP-mABs)

Comparators

High evidence conventional migraine preventive treatments (with beta-blocking agents, tricyclic antidepressants, flunarizine, topiramate or valproic acid) and CGRP-mABs (erenumab, fremanzumab, galcanezumab, eptinezumab).

Outcomes

Absolute and relative changes in monthly migraine days (MMD), monthly migraine days with acute medication (MMDAM) and monthly migraine sick-leave days (MMSLD) from baseline to month six, as well as the distribution of patients across migraine frequency categories [chronic migraine (CM), high-frequency episodic migraine (HFEM), low-frequency episodic migraine (LFEM) and very low-frequency episodic migraine (VLFEM)] at baseline and follow-up. Disability and functional impact were assessed with the Migraine Disability Assessment (MIDAS); migraine-related sleep impairments were evaluated via subitem #6 of the modified Pain Disability Index (mPDI6); health-related quality of life was measured with the physical and mental component scores of the VR-12; analyses of the degree of migraine-related depression, anxiety and stress were performed based on data gathered with the Depression, Anxiety and Stress Scale (DASS-21), and the Marburg Questionnaire on Habitual Health Findings (MQHHF) has been used for the evaluation of the general wellbeing of patients.

Data analysis plan

Response to both treatment alternatives was evaluated over 6-month periods and absolute/relative changes vs. baseline were assessed. Continuous variables were characterized by mean, standard deviation (SD), median and range. Categorical variables were summarized as absolute and relative (if necessary adjusted) frequencies. Differences in continuous changes between CGRP-mABs episodes and conventional preventive episodes were evaluated using student´s t-test. For dichotomous endpoints, such as achievement of the primary

composite endpoint or a distinct improvement in a given measure, chi-square analyses, odds ratios (ORs) and relative risks (RR) – both with 95% confidence intervals (CI) – were calculated. From responder proportions, number-needed-to-treat (NNT) or harm (NNH) values were derived to quantify the clinical benefit/risks of CGRP-mABs compared with HECP. Finally, effect size (ES) measures (e.g. Cohen´s d and phi-coefficient) were used to gain insight into the clinical relevance of biometrical differences found.

Summary results

A total of 422 adolescents contributed data on 1448/422 treatment episodes with HECP/CGRP. Premature discontinuation occurred in 68.8 vs. 11.9% of HECP vs. CGRP episodes (p<0.001; OR/RR: 0.06/0.17, ES: 0.571; NNH: 2). Corresponding 6-months treatment persistence was 30.6/88.2% (p<0.001). MMD improved with HECP/CGRP from 11.7/11.6 at BL (p=0.673) to 9.4/4.4 (p<0.001; ES: 0.715). A ≥50% reduction in MMD occurred with HECP/CGRP in 25.4/70.9% (p<0.001; ES: 0.455; NNT: 2), and the PE was reached by 23.7/69.9% (OR/RR: 7.5/3.0; p<0.001; ES: 0.223; NNT: 2). Highest response rates were seen for the CGRP-mAB fremanezumab (75.5%), lowest for the HECP amitriptyline (20.5%; OR/RR: 11.9/3.7; p<0.001). Compared to HECP, CGRPs were followed by significantly larger improvements of MMDAM (60.6 vs. 20.6%; <0.001; ES: 1.196), MMSLD (67.3 vs. 20.5%; p<0.001; ES: 1.408), and MIDAS scores (59.1 vs. 18.9%; p<0.001; ES: 1.294). Psychological, sleep, general wellbeing and quality-of-life outcomes improved in 75.8-93.6% of CGRP episodes, compared with 26.1-31.1% under conventional therapy.

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

German Pain e-Registry (GPeR)

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