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ORIGINAL RESEARCH

A National Cross-Sectional Survey on Real-World Experiences of Calcitonin Gene-Related Peptide (CGRP) Monoclonal Antibody Use in Adults with Migraine in Finland

Caroline S. Casey · Mari Pölkki · Elisa K. Suvanen · Ilona Iso-Mustajärvi · Timo Purmonen · Essi J. Peltonen · Camilla K. Appel · Niraj J. Patel · Lill-Brith Von Arx

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ABSTRACT

Introduction: Calcitonin gene-related peptide (CGRP) monoclonal antibodies (mAbs) were the first preventive migraine treatment group to target the underlying cause of migraine. This survey evaluated real-life experiences of adults with migraine in Finland before and after using their current subcutaneous CGRP mAb treatment.

Methods: Adult users of a subcutaneous CGRP mAb for migraine prevention were recruited for an electronic cross-sectional survey by Finnish community pharmacies and Migraine Finland (a patient advocacy group) in 2023. The survey included questions regarding monthly migraine headache days, absenteeism, general disability, pain intensity, treatment patterns, and a validated Migraine-Specific Quality of Life (MSQoL) questionnaire.

Results: The survey was completed by 383 users of subcutaneous CGRP mAb medication, of whom 78 (20.4%) were receiving galcanezumab. Users of galcanezumab, the latest CGRP mAb to be reimbursed in Finland, had more previous CGRP mAb treatment switches than users of other CGRP mAbs. Following any subcutaneous CGRP mAb use, changes were observed in the number of monthly migraine headache days (0–7 experienced by 17/379 participants [4.5%] with data before, versus 302/379 [79.7%] after using treatment; ≥ 12 experienced by 279/379 [73.6%] before, versus 34/379 [9.0%] after), monthly sick leave days (from 139/376 [37.0%] to 15/376 [4.0%] with ≥ 4 monthly sick leave days), overall ability to work or study (from 180/377 [47.7%] to 287/377 [76.1%] able to work or study full time) and average intensity of migraine pain (median [lower–upper quartile] from 8.0 [7.0–9.0] before to 6.0 [4.0–8.0] after). No differences were observed between total MSQoL scores for new (0–6 months CGRP mAb use) versus persistent (≥ 6 months use) users of any CGRP mAb.

Conclusions: Patient experiences of using subcutaneous CGRP mAbs in Finland showed improvements in several migraine-related factors, supporting the potential for CGRP mAbs

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C. S. Casey (✉) · N. J. Patel
Eli Lilly and Company, Lilly House, Basing View, Basingstoke, Hampshire RG21 4FA, UK
e-mail: caroline.casey@lilly.com

M. Pölkki · I. Iso-Mustajärvi · T. Purmonen · E. J. Peltonen
Oriola Finland Oy, Espoo, Finland

E. K. Suvanen
Oy Eli Lilly Finland Ab, Helsinki, Finland

C. K. Appel · L.-B. Von Arx
Eli Lilly Danmark A/S, Herlev, Denmark

to improve the quality of life of adults with migraine.

PLAIN LANGUAGE SUMMARY

Calcitonin gene-related peptide (CGRP) monoclonal antibodies (mAbs) were the first preventive migraine treatments to target a molecule called CGRP, which has been shown to play a key role in the condition. We performed an electronic cross-sectional (single point-in-time) survey to understand the real-life experiences of adults with migraine treated with a subcutaneous CGRP mAb in Finland. The survey was completed by 383 users of subcutaneous CGRP mAb medication. Most people were very satisfied (44.6%) or satisfied (25.1%) with their current CGRP mAb. After initiation of any subcutaneous CGRP mAb, changes were observed in the number of monthly migraine headache days (0–7 experienced by 4.5% of participants with data before, versus 79.7% after treatment; ≥ 12 experienced by 73.6% before, versus 9.0% after), number of monthly sick leave days (from 37.0% to 4.0% with ≥ 4 monthly sick leave days), overall ability to work or study (from 47.7% to 76.1% able to work/study full time) and average intensity of migraine pain (from 8.0 to 6.0, based on a score from 0 [lowest] before to 10 [highest] after). Migraine-Specific Quality of Life scores did not differ between people who had been on their treatment for less than or more than 6 months. Participants reported improvements in several migraine-related factors after using a subcutaneous CGRP mAb, supporting the potential for these medications to improve the quality of life of adults with migraine.

Keywords: CGRP; Erenumab; Fremanezumab; Finland; Galcanezumab; Migraine; Patient-reported experiences; Real-world experiences; Quality of life; Survey

Key Summary Points

Why carry out this study?

Migraine is one of the leading causes of disability and suffering globally.

Calcitonin gene-related peptide (CGRP) monoclonal antibodies (mAbs) were the first preventive migraine treatment group developed to target the underlying cause of migraine, but there is currently limited information on real-world experiences of CGRP mAb use in Finland.

What did the study ask?/What was the hypothesis of the study?

This cross-sectional survey evaluated the real-life experiences of adults with migraine in Finland before and after using their current subcutaneous CGRP mAb treatment, including possible changes in the number of monthly migraine headache days and sick leave days, ability to work or study, and migraine pain intensity; clinical characteristics, treatment patterns and current quality of life were also reported.

What was learned from the study?

Following any subcutaneous CGRP mAb use, participants experienced improvements in the number of monthly migraine headache days and sick leave days, their ability to work or study and the average intensity of migraine pain.

Users of galcanezumab, the latest CGRP mAb to be reimbursed in Finland, had more previous CGRP mAb treatment switches than users of other CGRP mAbs.

INTRODUCTION

Migraine is a complex neurological disorder that often manifests as moderate-to-severe headache attacks combined with various physiological and psychological comorbidities. It is among the most prevalent medical conditions globally, a

leading cause of disability and suffering, and is associated with considerable healthcare resource use and costs [1–3]. As migraine largely affects working-age people, the associated absenteeism and presenteeism may also result in indirect costs [2, 4].

Migraines are classified as episodic if a patient experiences < 15 monthly migraine headache days or as chronic if a patient experiences ≥ 15 monthly migraine headache days for > 3 months with migraine features present on ≥ 8 days per month [5, 6]. Increasing migraine headache frequency is associated with worsening emotional, functional, and societal burden [2], but further real-world data are needed regarding effects of migraine and migraine treatment on overall quality of life (QoL).

Calcitonin gene-related peptide (CGRP) is present throughout the central and peripheral nervous system and is involved in migraine pathophysiology. Elevated CGRP concentrations have been observed in the blood during a migraine attack and infusion of CGRP in people with migraine can induce a migraine attack [7, 8].

CGRP monoclonal antibodies (mAbs) were the first preventive migraine treatment group developed to target the underlying cause of migraine, by preventing CGRP from binding to and activating its receptor [9]. In Europe, three subcutaneous CGRP mAbs are indicated for migraine prevention in adults with ≥ 4 monthly migraine headache days. Erenumab [10] was the first CGRP mAb approved by the European Medicines Agency in July 2018, followed by galcanezumab [11] in November 2018 and fremanezumab [12]. Adherence to preventive treatment is key for its effectiveness, but adherence to treatments available off-label before the introduction of CGRP mAbs has often been poor; reasons for this may be multifactorial but are commonly due to patients reporting a lack of effectiveness or side effects [13, 14].

According to the Social Insurance Institution of Finland [15], reimbursement for CGRP mAbs in Finland can be granted for adults with an average of ≥ 8 monthly migraine headache days when starting CGRP mAb treatment, prior use of ≥ 2 preventive medications without sufficient response, or for whom the preventive medications are contraindicated or are not tolerated [15]. Erenumab became eligible for reimbursement from April 2019, followed by fremanezumab (February 2020) and galcanezumab (October 2020) [16]; however, there is a lack of real-world patient-reported experience data for CGRP mAb use in Finland. Treatment effect (reduction in monthly migraine headache days) is evaluated after 12 weeks of treatment for continued reimbursement [15]. Finnish guidelines recommend switching between CGRP mAbs if the effectiveness of the first CGRP mAb is insufficient.

This survey examined real-world experiences of adults in Finland before and after using their current subcutaneous CGRP mAb treatment, including changes in the number of monthly migraine headache days and sick leave days, migraine pain intensity, and ability to work or study. Clinical characteristics, treatment patterns and current migraine-specific quality of life (MSQoL) were also reported.

METHODS

Study Design and Objectives

This electronic structured cross-sectional survey of former or current users of subcutaneous CGRP mAbs in Finland was developed specifically for this study, incorporating a certified and copyright-protected Finnish version of the MSQoL questionnaire [17, 18]. The analyses reported here focused on current CGRP mAb users only.

Initial questions were developed based on the study objectives and validated by a migraine specialist physician. A pilot study was conducted on 28 eligible adults with migraine recruited by the patient advocacy group Migraine Finland (between March 27 and April 3, 2023) to ensure the questionnaire was easy to understand and to improve its relevance and overall quality. The final survey is provided in the Supplementary Methods section.

The purpose of the survey was to collect patient-reported experiences prior to and/or after using CGRP mAb therapy; for example, number of monthly migraine headache days and sick leave days, ability to work or study, and

intensity of migraine pain. Clinical characteristics, treatment patterns, and current QoL (using the MSQoL; Supplementary Methods section) were also reported.

Patient Recruitment and Data Collection

Survey inclusion criteria were: (1) aged ≥ 18 years old; and (2) former or current users of a subcutaneous CGRP mAb (fremanezumab, erenumab, or galcanezumab) for migraine prevention. There were no specific exclusion criteria for the survey although the analyses reported here are based on current CGRP mAb users only. Patients were recruited across the whole of Finland via Migraine Finland and at community pharmacies between June and September 2023, as described in the Supplementary Methods section.

Participants completed the survey online, either on their own computer or mobile device, responding to the survey questions followed by the MSQoL items. The data were subsequently stored anonymously in a secure digital environment.

Participants reported their current treatment duration based on categories of 0–4 weeks, 1–3 months, 3–6 months, 6–12 months, 1–2 years, or ≥ 2 years. Participants were classified as 'new users' if they had been on their current CGRP mAb for < 6 months or 'persistent users' if they had been on this treatment for ≥ 6 months. In Finland, reimbursement of a CGRP mAb is granted for the first time for 6 months [15]. The effectiveness of the new treatment is first evaluated after 12 weeks and after 16 weeks if the dosing has changed. The reimbursement is renewed if a treatment effect is achieved; therefore, patients with ≥ 6 months of treatment use could be considered as 'persistent'.

Ethics

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki 1964 and its later amendments and that are consistent with Good Pharmacoepidemiology Practices and applicable Finnish laws and regulations. A privacy statement following the European Union General Data Protection Regulation [19] was available online for the respondents. The survey, including the pilot, was conducted according to the guidelines of the Finnish National Advisory Board on Research Integrity which do not require ethics committee approval for surveys targeting respondents aged ≥ 15 years [20].

Participation in the study was anonymous and entirely voluntary. Respondents provided informed consent for the use of their responses in the study (via a checkbox on the electronic survey) and were able to withdraw consent at any time when completing the survey.

Statistical Analyses

Analyses were conducted with R statistical software version 4.3.1. for Windows. As all patients who fulfilled the inclusion criteria were invited to participate, no formal power calculations were performed. The aim was to collect a minimum of 400 responses from current or previous CGRP mAb users.

Demographic and clinical characteristics, migraine-related data (including MSQoL) and treatment patterns were analyzed for all current CGRP mAb users. Galcanezumab was also analyzed separately, as it was the most recent subcutaneous CGRP mAb to become eligible for reimbursement in Finland, so is often prescribed later in the treatment pathway; it also differs from the others by having an initial loading dose of double the regular dose.

Normality of the continuous variables was determined using the Kolmogorov–Smirnov test, together with visual inspection. Differences between categorical and non-normally distributed continuous migraine-related factors before and after current CGRP mAb use were analyzed using McNemar–Bowker or Wilcoxon signed-rank test for paired samples, respectively. Total MSQoL scores were compared between new (i.e., CGRP mAb treatment duration < 6 months) and persistent (duration ≥ 6 months) users of a CGRP mAb using an independent samples *t* test for normally distributed variables. Transitions between current treatment and different combinations of previous treatment were visualized using a Sankey diagram.

Relevant descriptive summary statistics, including frequencies, mean with standard deviation, median with lower and upper quartile (Q1, Q3) and difference in mean values with 95% confidence intervals (CIs) were reported. Appropriate survey question and answer options were grouped based on the availability of collected survey data. Responses with a frequency of less than 5 or 8 were reported as '< 5' or '< 8' to protect patient privacy. Appropriate subgroups of < 5 respondents were combined to enable statistical testing. Missing values were encoded and reported as *n* (%) missing. When calculating the total MSQoL score for patients with a missing response for ≤ 3 MSQoL items, the missing items were scored based on the mean of the items for which responses were available. The MSQoL score was treated as missing if more than three items were missing. *P* values for point estimates of < 0.05 were considered statistically significant, except in the case of multiple testing of migraine-related factors before and after using the current CGRP mAb. Multiple testing was controlled by using the false discovery rate (FDR) method with the threshold level set at 0.05. Here, a result was considered statistically significant if the *p* value was less than the corresponding FDR critical value.

As migraine-related factors from the pre-CGRP mAb period may be subject to recall bias (due to the cross-sectional nature of the survey), differences in migraine-related factors that were reported before and after current CGRP mAb initiation (number of monthly migraine headache days, number of monthly sick leave days, ability to work or study and average intensity of migraine pain) were also analyzed separately for respondents who had been using the current medication for < 6 months or < 12 months as a sensitivity analysis, and results were compared with those obtained for the overall population.

RESULTS

Demographic Characteristics and Treatment Use

The final survey was completed by 418 eligible participants, of whom 383 (91.6%) were current users of CGRP mAb medication. Due to the small number of responses from former CGRP mAb users, the following results only include current users of CGRP mAbs.

Of the 383 current CGRP mAb users, 78 (20.4%) were receiving galcanezumab. Most participants were female (90.9%), aged < 18 years at migraine diagnosis (34.7%) and aged 35–54 years (57.7%) at the time of completing the survey (Table 1). Most respondents were educated to the secondary level (38.6%) or had completed a bachelor's degree or similar qualification (30.5%) and 66.1% were working full-time. Major depressive disorder (single episode) was the most reported comorbidity (23.2%), followed by anxiety (17.8%). Treatment patterns data are presented in Table 2. Approximately one-third of CGRP mAb users (33.9%) initiated their current treatment > 2 years ago and 88.0% had used their current treatment for ≥ 3 months. Among galcanezumab users, 32.1% were CGRP mAb-naive when initiating treatment, whereas this percentage was 62.1% for users of any CGRP mAb.

Treatment Patterns and Satisfaction

Among the 383 CGRP mAb users, fremanezumab was the most prescribed current CGRP mAb (46.7%) and erenumab was the most common previous CGRP mAb (27.9%; Table 2).

Patients currently receiving galcanezumab ($n = 78$) were more likely to report previous use of a CGRP mAb (67.9%), compared with all patients receiving any CGRP mAb (37.9%; Table 2). Fremanezumab was the most common previous treatment for current galcanezumab users (57.7%), although erenumab was also commonly used. The numbers of respondents with zero, one and two CGRP mAb treatment switches were 25 (32.1%), 19 (24.4%) and 34

Table 1 Patient characteristics: current users of any CGRP mAb or galcanezumab

	Any CGRP mAb (*N* = 383) *n* (%)	**Galcanezumab (*N* = 78) *n* (%)**
Sex		
Female	348 (90.9)	70 (89.7)
Male	32 (8.4)	8 (10.3)
Other	< 5	0 (0.0)
Age category at the time of response, years		
18–24	26 (6.8)	< 5
25–34	53 (13.8)	9 (11.5)
35–44	105 (27.4)	26 (33.3)
45–54	116 (30.3)	22 (28.2)
55–64	63 (16.4)	15 (19.2)
≥ 65	20 (5.2)	< 5
Age category at the time of migraine diagnosis, years		
< 18	133 (34.7)	27 (34.6)
18–24	80 (20.9)	22 (28.2)
25–34	63 (16.4)	12 (15.4)
35–44	59 (15.4)	11 (14.1)
45–59	35 (9.1)	< 8
≥ 60	13 (3.4)	0 (0.0)
Main healthcare unit currently responsible for migraine treatment		
Occupational healthcare	114 (29.8)	21 (26.9)
Secondary healthcare	69 (18.0)	17 (21.8)
Primary healthcare	61 (15.9)	< 8
Private healthcare	128 (33.4)	31 (39.7)
Student healthcare (e.g., Finnish Student Healthcare Service)	< 8	< 5
I do not remember	< 5	0 (0.0)
Missing	< 5	< 5
Educational level		
Comprehensive school/elementary school (compulsory education only)	10 (2.6)	0 (0.0)
Secondary education (upper secondary school/high school/vocational education)	148 (38.6)	31 (39.7)
Bachelor's degree or similar qualification	117 (30.5)	27 (34.6)
Master's degree	94 (24.5)	15 (19.2)

Table 1 continued

	Any CGRP mAb (*N* = 383) *n* (%)	Galcanezumab (*N* = 78) *n* (%)
Doctoral degree	10 (2.6)	< 5
Another qualification	< 5	< 5
I do not remember	0 (0.0)	< 5
Missing	< 5	0 (0.0)
Employment status		
Full-time employee/entrepreneur	253 (66.1)	61 (78.2)
Part-time employee/entrepreneur	41 (10.7)	< 5
Subsidized employee/rehabilitative employment activity/work trial	< 5	0 (0.0)
Unemployed/suspended without pay	12 (3.1)	< 5
Parental leave	< 5	< 5
Student	30 (7.8)	< 8
Retired (full old-age pension or disability pension)	29 (7.6)	< 8
Part-time pension	< 5	0 (0.0)
Other	11 (2.9)	0 (0.0)
Comorbidities[a]		
Major depressive disorder, single episode	89 (23.2)	23 (29.5)
Anxiety	68 (17.8)	16 (20.5)
Irritable bowel syndrome	57 (14.9)	18 (23.1)
Recurrent major depressive disorder	48 (12.5)	< 8
Gastroenteritis	< 5	0 (0.0)
Crohn's disease	< 5	0 (0.0)
Ulcerative colitis	< 5	< 5
None of the above	216 (56.4)	38 (48.7)

[a]Multiple answers were allowed

CGRP calcitonin gene-related peptide, *mAb* monoclonal antibody

(43.6%), respectively, for current users of galcanezumab, compared with 119 (66.5%), 53 (29.6%) and < 8 for fremanezumab users and 98 (77.8%), 22 (17.5%) and < 8 for erenumab users (Fig. 1).

Most respondents were very satisfied or satisfied with their current medication (Table 2). The most common reasons for satisfaction with current medication were reduction in monthly migraine headache days (85.6% of users of any CGRP mAb; 78.2% of galcanezumab users), improved QoL (74.2%; 71.8%) and intensity of pain decreased (59.3%; 57.7%). Most respondents had also used their current treatment for > 6 months (74.4% of any CGRP mAb users; 67.9% of galcanezumab users) (Table 2).

Of the users of any CGRP mAb, 269 (70.2%) had no experience of using botulinum toxin treatment, while the corresponding number

Table 2 Treatment patterns for current users of any CGRP mAb and galcanezumab at the time of the survey

Treatment patterns	Any CGRP mAb (*N* = 383) *n* (%)	Galcanezumab (*N* = 78) *n* (%)
Use of botulinum toxin treatment		
No use of botulinum toxin	269 (70.2)	43 (55.1)
Used previously but the treatment ended when biological preventive migraine medication started/for other reasons	85 (22.2)	25 (32.1)
Currently using botulinum toxin	29 (7.6)	10 (12.8)
Current treatment		
Current CGRP mAb treatment		
Fremanezumab	179 (46.7)	0 (0.0)
Erenumab	126 (32.9)	0 (0.0)
Galcanezumab	78 (20.4)	78 (100.0)
Satisfaction with current CGRP mAb		
Very satisfied	171 (44.6)	26 (33.3)
Satisfied	96 (25.1)	20 (25.6)
Somewhat satisfied	75 (19.6)	19 (24.4)
Neither satisfied nor dissatisfied	9 (2.3)	< 5
Somewhat dissatisfied	18 (4.7)	< 8
Dissatisfied	< 8	0 (0.0)
Very dissatisfied	< 5	< 5
Missing	< 5	< 5
Reason for satisfaction with current CGRP mAb[a]		
It has reduced the number of monthly migraine headache days	328 (85.6)	61 (78.2)
It has reduced the intensity of pain	227 (59.3)	45 (57.7)
It has improved my quality of life	284 (74.2)	56 (71.8)
It is easier to administer than my previous biological preventive medication	11 (2.9)	< 5
I have fewer side effects than with my previous medication	128 (33.4)	22 (28.2)
I don't have to take medicine every day	150 (39.2)	26 (33.3)
I have become accustomed to the treatment	59 (15.4)	9 (11.5)
Other	< 5	0 (0.0)
Duration of current CGRP mAb treatment		
I am just about to start	< 5	< 5
0–4 weeks	< 8	< 5

Table 2 continued

Treatment patterns	Any CGRP mAb (*N* = 383) *n* (%)	Galcanezumab (*N* = 78) *n* (%)
1–3 months	34 (8.9)	< 8
3–6 months	52 (13.6)	15 (19.2)
6–12 months	64 (16.7)	22 (28.2)
1–2 years	91 (23.8)	16 (20.5)
≥ 2 years	130 (33.9)	15 (19.2)
Previous treatment		
Previous use of CGRP mAb		
Yes	145 (37.9)	53 (67.9)
No	238 (62.1)	25 (32.1)
Previous CGRP mAb treatment[a]		
Fremanezumab	69 (18.0)	45 (57.7)
Erenumab	107 (27.9)	42 (53.8)
Galcanezumab	24 (6.3)	< 5
I do not remember	< 5	0 (0.0)
None	238 (62.1)	25 (32.1)
Number of other migraine medications		
0	< 5	< 5
1	< 8	< 5
2	54 (14.1)	10 (12.8)
3	101 (26.4)	18 (23.1)
4	83 (21.7)	16 (20.5)
5	54 (14.1)	11 (14.1)
6	22 (5.7)	< 5
7	15 (3.9)	< 5
8	11 (2.9)	< 5
9	< 5	0 (0.0)
10	< 8	< 5
> 10	26 (6.8)	10 (12.8)
Missing	< 5	0 (0.0)
Type of previous preventive medication		

Table 2 continued

Treatment patterns	Any CGRP mAb (*N* = 383) *n* (%)	Galcanezumab (*N* = 78) *n* (%)
Subcutaneous CGRP mAb treatment	72 (18.8)	25 (32.1)
Other preventive medication (e.g., beta-blockers, anti-hypertensives, antidepressants, anti-epilepsy medications)	248 (64.8)	32 (41.0)
Combination of subcutaneous biological preventive migraine medication plus other preventive medication	45 (11.7)	16 (20.5)
Other	18 (4.7)	< 8

[a]Multiple answers were allowed

CGRP calcitonin gene-related peptide, *mAb* monoclonal antibody

was only 43 (55.1%) among galcanezumab users (Table 2). Current botulinum toxin use was reported by 29 participants (7.6%) using any CGRP mAb and by ten participants (12.8%) using galcanezumab.

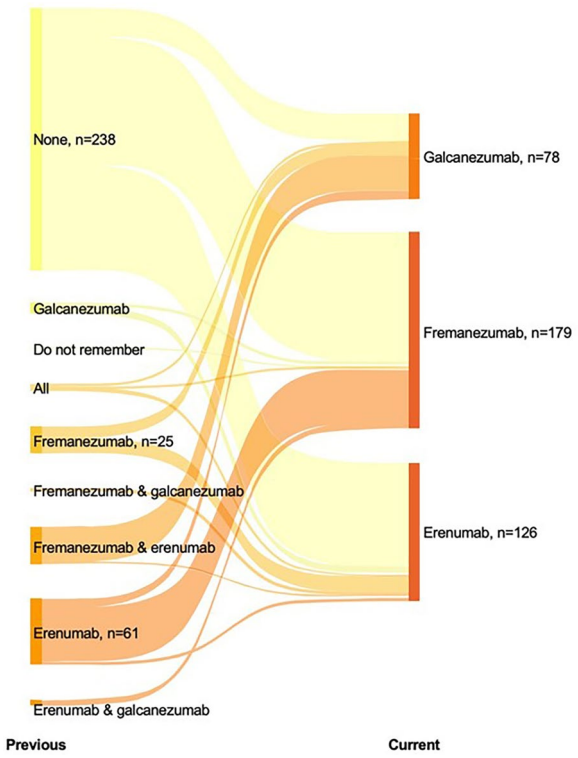

Fig. 1 Previous and current treatments for patients using any CGRP mAb at the time of the survey. Frequencies of < 8 are not reported in the figure. *CGRP* calcitonin gene-related peptide, *mAb* monoclonal antibody

Migraine-Related Factors and Quality of Life

Changes in the number of monthly migraine headache days and sick leave days, overall ability to work or study and average intensity of migraine pain were observed following use of any CGRP mAb or galcanezumab (Fig. 2). For example, the overall proportion of participants in the lowest migraine frequency group of 0–7 monthly migraine headache days shifted from 4.5% (17/379) before any CGRP mAb use to 79.7% (302/379) after use, accompanied by a shift in the proportion experiencing ≥ 12 monthly migraine headache days from 73.6% (279/379) to 9.0% (34/379). The proportion of participants with ≥ 4 monthly sick leave days also changed from 37.0% (139/376) to 4.0% (15/376). Average intensity of migraine pain (on a scale from 0 to 10) reduced from a median (Q1–Q3) of 8.0 (7.0–9.0) before to 6.0 (4.0–8.0) after using any CGRP mAb. Use of social benefits was generally low (data not shown), although there appeared to be a reduction in the number of people receiving sickness allowance from 8.1% (31/383) before to 2.6% (10/383) after CGRP mAb use. Similar findings were observed for people receiving galcanezumab. In the sensitivity analysis, differences in migraine-related factors before and after current CGRP mAb initiation among

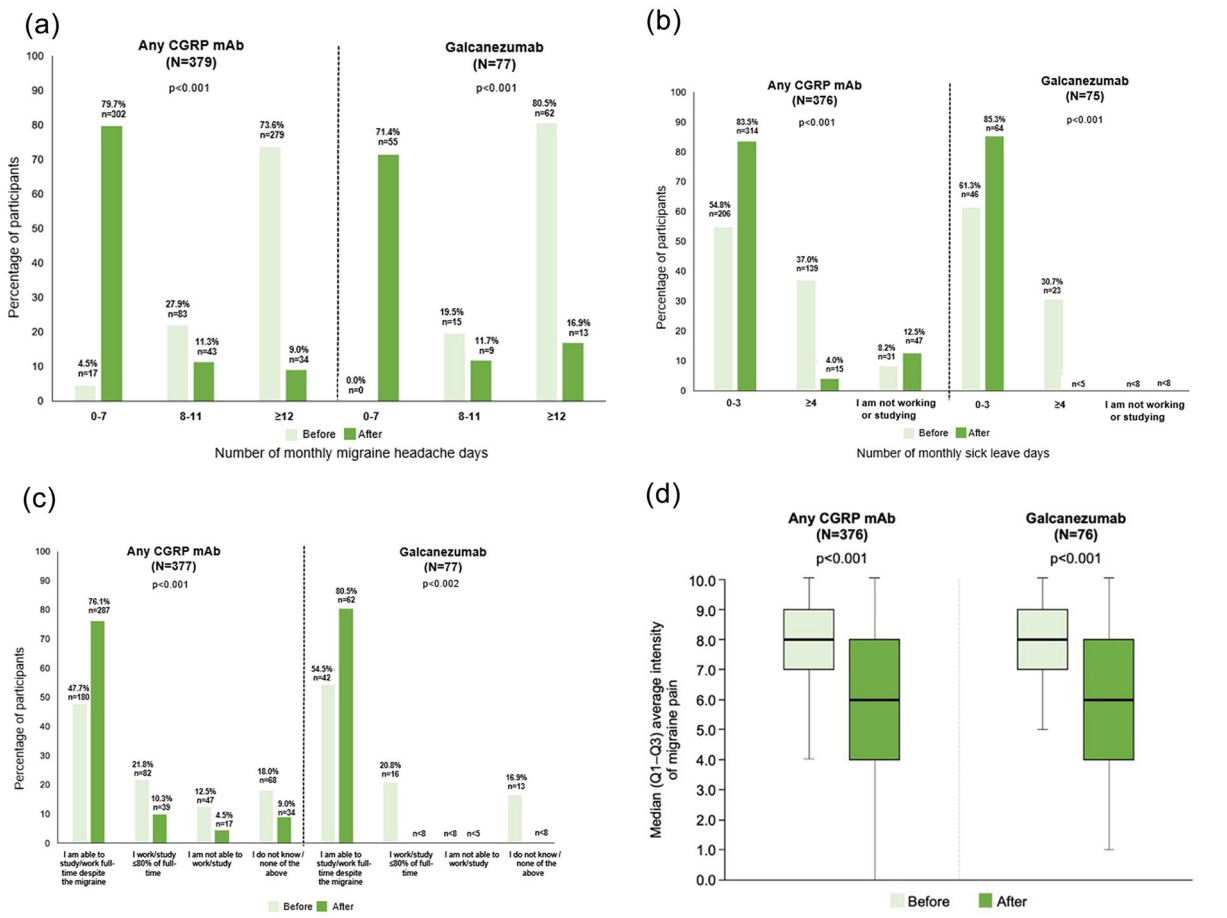

Fig. 2 Migraine-related data before and after current CGRP mAb use[a] **a** Number of monthly migraine headache days. **b** Number of monthly sick leave days[b]. **c** Ability to work or study. **d** Average intensity of migraine pain (on a scale from 0 to 10)[c]. Participants with missing values for either 'before' or 'after' for a particular variable were excluded from the analysis of that variable. [a]*p* values represent differences between data based on before versus after current CGRP treatment use and were obtained using the McNemar–Bowker test for categorical variables and the Wilcoxon signed-rank test for continuous variables; all *p* values presented in this figure were statistically significant after multiple testing correction using the false discovery rate method. [b]'I am not working or studying' represents participants who were not working or studying for any reason (e.g., unemployment, retirement) and is not restricted to those who were not working or studying due to migraine. [c]Participants were asked to describe the average extent of their typical migraine pain when they do not take acute medication, on a scale from 0 to 10, where 0 is no pain and 10 is the worst pain ever experienced; data are presented as medians (*bold horizontal lines within boxes*) with Q1–Q3 (*lower and upper limits of boxes*) and full ranges (*upper and lower limits of whiskers*). *CGRP* calcitonin gene-related peptide, *mAb* monoclonal antibody, *Q1* lower quartile, *Q3* upper quartile

respondents who had received the medication for < 6 months or < 12 months were similar to those in the primary analyses, with no significant changes in results observed when patients who had used their current CGRP mAb for > 6 months or > 12 months were excluded.

No differences were observed in total MSQoL scores between new and persistent users of any CGRP mAb (difference of mean values [95% CI] 2.2 [−0.7, 5.1], $p = 0.136$) or galcanezumab (4.3 [−1.7, 10.3], $p = 0.155$; Table 3).

Table 3 Total MSQoL scores for new and persistent users of current medication

	Overall	New users[a]	Persistent users[b]	Difference (95% CI)	*p* values[c]
Any CGRP mAb, N = 383					
MSQoL score[d]					
Mean (SD)	50.9 (12.6)	49.3 (11.5)	51.5 (12.9)	2.2 (− 0.7, 5.1)	0.136
Median (Q1–Q3)	51.0 (42.0–60.0)	48.5 (40.0–58.8)	52.0 (43.0–61.0)		
Galcanezumab, N = 78					
MSQoL score[d]					
Mean (SD)	49.8 (12.5)	46.9 (10.0)	51.2 (13.4)	4.3 (− 1.7, 10.3)	0.155
Median (Q1–Q3)	48.0 (41.2–59.0)	46.0 (41.0–51.0)	51.0 (43.0–61.0)		

[a]Duration of medication < 6 months; any CGRP mAb *N* = 98, galcanezumab *N* = 25

[b]Duration of medication ≥ 6 months; any CGRP mAb *N* = 285, galcanezumab *N* = 53

[c]*p* values for difference were derived using an independent samples *t* test

[d]Total MSQoL score range 20–80; higher scores indicate a better quality of life

CGRP calcitonin gene-related peptide, *CI* confidence interval, *mAb* monoclonal antibody, *MSQoL* Migraine-Specific Quality of Life, *Q1* lower quartile, *Q3* upper quartile, *SD* standard deviation

DISCUSSION

This study of subcutaneous CGRP mAb users in Finland showed improvements in several migraine-related factors, supporting the potential for CGRP mAbs to improve the QoL of adults with migraine. Our findings support those from clinical trials showing CGRP mAbs to be effective in difficult-to-treat patients who experienced failures of up to four previous migraine preventive medication categories [21–23].

After using their current CGRP mAb, surveyed patients experienced improvements in monthly migraine headache days and sick leave days, their ability to work or study and the average intensity of migraine pain. Although few people reported receiving social benefits, there appeared to be a reduction in the proportion receiving sickness allowance (partial or full) after using their CGRP mAb. No differences in total MSQoL scores were observed for new (treatment duration < 6 months) versus persistent (treatment duration > 6 months) users of any CGRP mAb or galcanezumab, suggesting a possible long-term QoL effect of CGRP mAb use and that benefits may be observed regardless of the position of the CGRP mAb in the treatment pathway.

The changes observed in several migraine-related factors following CGRP mAb use are encouraging, as a previous report from the My Migraine Voice survey (2017–2018) before CGRP mAbs became available highlighted the high emotional, functional and societal burden of migraine in Finland [2]. Participants reported negative effects of migraine on their working life and productivity, with a mean of 2.8 missed working days in the past month for all respondents, increasing to up to 6.0 working days for people with chronic migraine [2]. The study highlighted the need for effective preventive treatments, e.g., CGRP mAbs. According to Finnish treatment guidelines, acute migraine treatment usually includes non-steroidal anti-inflammatory drugs and other simple analgesics such as paracetamol, as well as triptans, which are the recommended first-line therapy for acute migraine [24]. As frequent use of acute migraine drugs often leads to medication-overuse headache, the use of analgesics should be minimized [8], supporting the need for preventive medications. OnabotulinumtoxinA is also approved in Europe for the prevention of chronic migraine

headaches [25, 26]. Other preventive treatments prescribed to patients with chronic or otherwise frequent migraine may include beta-blockers, antiepileptics or anticonvulsants, tricyclic antidepressants or candesartan [8, 27]. However, many of these medicines have no indication as preventive treatment for migraine and are prescribed off-label, with some having limitations in terms of efficacy, tolerability, and adherence [25].

A previous Finnish population survey listed migraine among several chronic conditions with negative effects on health-related QoL (according to the EQ-5D) [28] and more than one-third of respondents (34.9%) in the My Migraine Voice survey reported having mental health-related comorbidities [2]. Our study also found the most common comorbidities were related to mental health, with major depressive disorder reported by 23.9% of participants and anxiety reported by 19.9% of participants. The prevalence of mental health disorders has previously been reported to be higher in people with migraine versus age- and gender-matched controls [29] and the prevalences in our study and the My Migraine Voice survey are higher than those observed for people with several other conditions associated with negative effects on QoL and mental health, although direct comparisons between studies are not possible and higher levels of perceived anxiety have been suggested for people with cardiovascular and metabolic diseases [30, 31]. Negative effects on mental health have been reported for several chronic conditions, with associations being affected by age and sex [32], and the association between several sociodemographic variables and poor mental health also requires consideration [31]. People with migraine experience significant burden, both from migraine itself and from an increased number of comorbidities than those without migraine, although further research is needed to understand the associated pathophysiology [29] and to study the effect of CGRP mAb use on mental health and other comorbidities in general.

To our knowledge, our study is the first real-world analysis describing the association between CGRP mAbs and monthly migraine headache days in Finland. Our data showed a clear shift in the number of monthly migraine headache days experienced following CGRP mAb use, with 79.7% of participants experiencing 0–7 monthly migraine headache days (the lowest migraine frequency group in the survey) after using their current CGRP mAb, compared with only 4.5% before this treatment. Similar results were seen for galcanezumab, albeit based on a smaller sample of patients. The proportions of participants reporting ≥ 12 monthly migraine headache days shifted from 73.6% to 9.0% for users of any CGRP mAb and from 80.5% to 16.9% for galcanezumab users. Accordingly, the proportion of people having ≥ 4 monthly sick leave days shifted from 37.0% to 4.0% for all CGRP mAb users and from 30.7% to < 5 for galcanezumab users. The proportions of participants reporting the ability to work full time also increased. These findings are in accordance with those from a Finnish retrospective registry study that showed a reduction in headache-related sick leave days and healthcare visits in working patients in the 12 months following erenumab treatment initiation [4].

The current study also examined treatment patterns in people using CGRP mAbs. Galcanezumab users were more likely to report previous use of a CGRP mAb (67.9%) compared with the overall population receiving any CGRP mAb (37.9%) and were less likely to have used other classes of preventive medications (41.0% versus 64.8%, respectively). Galcanezumab users were also more likely to have used botulinum toxin for their migraine treatment (44.9%) compared with users of any CGRP mAb (29.8%). This likely reflects that galcanezumab was the latest CGRP mAb to become eligible for reimbursement in Finland, so it is often prescribed later in the treatment pathway. It may also suggest galcanezumab is a possible treatment option for adults with previous failures on other CGRP mAbs, as the treatment benefit after galcanezumab use was in alignment for that seen based on all CGRP mAbs. Fremanezumab was the most common previous treatment for current galcanezumab users, whereas erenumab was the most common previous CGRP mAb treatment for users of any CGRP mAb.

People currently using galcanezumab also reported having more previous CGRP mAb

treatment switches (prior to using galcanezumab) than those currently receiving other CGRP mAbs. This is important as a study performed prior to the introduction of CGRP mAbs found migraine burden increased with increasing numbers of other preventive treatment lines, such as antidepressants, antiepileptics, angiotensin receptor blockers, beta-blockers, or botulinum toxin [27]. Although galcanezumab users in our study showed treatment benefit despite having received this as a later line of treatment than those receiving other CGRP mAbs, this treatment benefit may be further improved by receiving galcanezumab earlier in the treatment pathway. Recent real-world data have shown modest improvements in headache outcomes for patients who switched between CGRP mAbs due to ineffectiveness [33], supporting that patients may benefit from switching from one CGRP mAb to another. Patients may also choose to switch treatment due to adverse events. For example, CGRP is involved in gastric processes and gastrointestinal symptoms in people with migraine may be treatment-related or due to increased CGRP [34].

This study provides important real-world data on subcutaneous CGRP mAb use in Finland, from the patient's perspective. The number of hospital admissions for people with migraine in Finland increased by 4.2% annually between 2004 and 2014, prior to the availability of CGRP mAbs [35], and further data are needed to monitor changes following CGRP mAb use. Most of our survey respondents were very satisfied or satisfied with their current CGRP medication. According to Finnish official drug reimbursement statistics (Statistical Database Kelasto), there were approximately 6,900 CGRP antagonist and mAb users in Finland in 2023 [36] and this number is expected to increase. Data such as those from our current survey provide important insights into patient experiences with subcutaneous CGRP mAbs and will be useful to guide treatment decisions for patients in future. An intravenous CGRP mAb, eptinezumab [37], is also reimbursed in Finland [16] but was used by relatively few patients at the time of this survey [36], which included users of subcutaneous CGRP mAbs only.

Strengths of this study include the use of patient feedback from the pilot survey to inform the final survey, and validation of the survey by a migraine specialist. The study included 383 Finnish adults currently receiving CGRP mAbs, representing approximately 7% of the estimated 5700 CGRP antagonist and mAb users in Finland in 2022 according to Statistical Database Kelasto [36], and most participants (88.0%) had had used their current treatment for ≥ 3 months. The number of missing values was generally low, suggesting that answers were given with care as respondents had the option to skip questions if they wished to do so.

This study is also subject to limitations associated with cross-sectional studies, such as the potential for recall bias. However, our sensitivity analysis for migraine-related factors that were reported before and after current CGRP mAb initiation based on treatment duration (respondents who had been using their current medication for < 6 months or < 12 months) found the risk of recall bias to be low. Data from the MSQoL were not subject to recall bias (or included in the sensitivity analysis) as the MSQoL measures the patient's current QoL only. As the possibility of recall bias cannot be fully excluded in this kind of cross-sectional study setting, further studies could include sensitivity analyses that assess recall bias over longer periods of time and a longitudinal follow-up period to collect real-time data over time following CGRP mAb initiation. The self-reported nature of this study is also a limitation that should be considered when interpreting the results. Surveys such as this also have the potential limitation of reflecting the experiences of people who are more likely to complete surveys and may also include those more familiar with technology required to provide data online. However, we are unable to report survey response rates as we do not have data regarding the overall number of people who were informed of the survey or the demographic distribution of those who did versus did not participate. Although these data likely reflect the experiences of the broader Finnish migraine population using CGRP mAbs, it is not possible to determine how they may differ for other patients or their generalizability to other countries. Future studies are required to examine whether the improvement in migraine-related

factors following CGRP mAb use is reflected in the use of healthcare resources, translating as reduced need for healthcare services.

CONCLUSIONS

Finnish patient experiences of using CGRP mAbs showed improvements in several migraine-related factors, supporting the potential for CGRP mAbs to improve the lives of adults with migraine. The finding of similar MSQoL scores for new and persistent users of CGRP mAbs also suggests QoL benefits are maintained throughout the duration of treatment and may be observed regardless of the position of the CGRP mAb in the treatment pathway. Benefit may therefore be experienced for patients who receive a later-line treatment after the failure of previous treatments, as well as for those who experience migraine improvements with their initial CGRP mAb.

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Data Availability. The analysis datasets generated during and/or analyzed during the current study are not publicly available due to the confidential nature of the data.

Declarations

Conflict of Interest. Caroline Casey and Niraj Patel are employees of Eli Lilly and Company and holders of Eli Lilly stock. Elisa Suvanen is an employee of Oy Eli Lilly Finland Ab and holder of Eli Lilly stock. Camilla Appel and Lill-Brith Von Arx are employees of Eli Lilly Danmark and holders of Eli Lilly stock. Mari Pölkki, Ilona Iso-Mustajärvi, Timo Purmonen, and Essi Peltonen are employees of Oriola Finland Oy.

Ethical Approval. This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki 1964 and its later amendments and that are consistent with Good Pharmacoepidemiology Practices and applicable Finnish laws and regulations. A privacy statement following the European Union General Data Protection Regulation (Intersoft Consulting 2024) was available online for the respondents. The survey, including the pilot, was conducted according to the guidelines of the Finnish National Advisory Board on Research Integrity, which do not require ethics committee approval for surveys targeting respondents aged ≥ 15 years [20].Participation

in the study was anonymous and entirely voluntary. Respondents provided informed consent for the use of their responses in the study (via a checkbox on the electronic survey) and were able to withdraw consent at any time when completing the survey.

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