EPO-325

Real-World Study of Migraine Patients Treated With Galcanezumab or Topiramate in the German NeuroTransData Network

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BACKGROUND

- Migraine is estimated to affect 1.04 billion individuals globally and is associated with 45.1 million years of life lived with disability,[1] a high direct and indirect economic burden on payer and society,[2,3] and impaired health-related quality of life (HRQoL) among patients.[4]
- NeuroTransData (NTD) is a network working on the digitalisation of personalised healthcare and has been running a registry database since 2008.
- Treatments for migraine include acute medications and prophylactic therapies. The use of acute medications has been associated with adverse events[5,6] and overuse,[7] which can lead to migraine progression.[8,9] Prophylactic treatments should be considered for patients with frequent migraine and/or reduced HRQoL to reduce the occurrence of acute attacks and use of acute medications, and to improve HRQoL.[10]
- A number of therapies have been used as prophylactic treatments for migraine, including anticonvulsant medications (e.g. topiramate, valproate), tricyclic antidepressants (e.g. amitriptyline), beta-blockers (e.g. propranolol, metoprolol) and botulinumtoxin for chronic migraine (CM).
- As some calcitonin-gene-related-peptide (CGRP) monoclonal antibodies (mAbs) are available on the market in Germany since 2018-2019 (erenumab, galcanezumab, fremanezumab), their use in the real-world setting becomes of interest.
- Topiramate is a validated migraine prophylaxis in randomized controlled trials (PROMPT,[11] TOPCHROME[12]) and was therefore chosen as a standard-of-care molecule for comparisons in this descriptive study.

OBJECTIVES

- **Objective 1:** To identify cohorts of adult migraine patients prescribed galcanezumab or topiramate and describe patients' socio-demographic and clinical characteristics, including disease severity and prior treatments.
- **Objective 2:** To evaluate real-world switching patterns from one type of CGRP mAb to another.

KEY RESULTS

Table 1. Patient history comparison

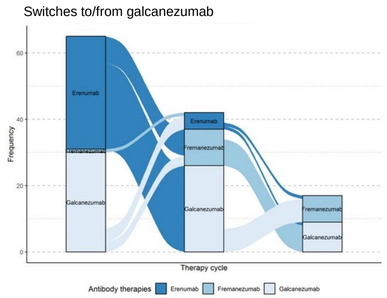
Variable	Statistic	Galcanezumab	Topiramate
Sample size	n	**65**	**111**
Gender	Man	7 (10.8)	19 (17.1)
	Woman	58 (89.2)	92 (82.9)
	P-value (global test)**	0.4	
Age at migraine diagnosis	mean	27.0	27.9
	sd	11.8	12.5
	missing	1	2
	P-value*	0.6	
Employment status n (percent)	education	1 (1.6)	3 (3.6)
	employed (full time)	23 (37.1)	50 (59.5)
	employed (part time)	18 (29.0)	17 (20.2)
	retired	14 (22.6)	2 (2.4)
	homemaker	2 (3.2)	7 (8.3)
	unemployed	4 (6.5)	5 (6.0)
	missing	3 (4.6)	27 (24.3)
	P-value (global test)**	< 0.001	
Body mass index (BMI)	mean	25.7	25.2
	sd	4.5	5.5
	missing	16	40
	P-value*	0.3	
Type of migraine (based on diagnosis)	migraine without aura (G43.0)	32 (50.8)	78 (72.2)
	migraine with aura (G43.1)	11 (17.5)	17 (15.7)
	status migraenosus (G43.2)	1 (1.6)	1 (0.9)
	chronic migraine (G43.3)	19 (30.2)	12 (11.1)
	missing	2 (3.1)	3 (2.7)
	P-value (global test)**	0.026	
Acute medications***	migraine specific acute medication	64 (98.5)	103 (92.8)
	non migraine specific acute medication	57 (87.7)	88 (79.3)
	None	0 (0)	1 (0.9)
Prior prophylactic medication***	antidepressants	58 (89.2)	40 (36.0)
	betablocker	53 (81.5)	62 (55.9)
	botulinum toxin	40 (61.5)	15 (13.5)
	ca-channel blocker	43 (66.2)	24 (21.6)
	None	0 (0)	31 (27.9)

Table 2. Observations during the baseline period

Variable	Statistic	Galcanezumab	Topiramate
Sample size	n	**65**	**111**
Monthly migraine days (MMDs)	mean	13.2	9.7
	sd	6.5	4.8
	missing	-	-
	P-value*	< 0.001	
Monthly headache days (MHDs)	mean	14.4	11.1
	sd	7.4	5.5
	missing	-	-
	P-value*	< 0.01	
Type of migraine (inferred based on MMDs|MHDs during the baseline period) n (percent)	CM	25 (38.5)	21 (18.9)
	HFEM	26 (40.0)	48 (43.2)
	IFEM	14 (21.5)	42 (37.8)
	P-value (global test)**	< 0.01	
Monthly acute medication days	mean	8.6	8.1
	sd	4.0	4.3
	missing	-	4
	P-value*	0.2	
Average pain intensity (self-rating scale from 0 to 10)	mean	5.7	5.5
	sd	1.6	1.7
	missing	28	53
	P-value*	0.4	
Average headache duration (hours)	mean	4.9	3.4
	sd	5.3	3.5
	Missing	41	58
	P-value*	0.3	

LEGEND FOR TABLES 1, 2 AND 6
CM: 8-14 MMDs and at least 15 MHDs or at least 15 MMDs
HFEM (High-frequency episodic migraine): 8-14 MMDs and < 15 MHD
IFEM (Intermediate-frequency episodic migraine): 4-7 MMDs
n: number of observations for this outcome
sd: standard deviation
* P-values based on Wilcoxon rank sum test with continuity correction
** P-values based on Pearson's Chi-squared test
*** No p-value given, because due to reimbursement requirements in Germany, galcanezumab patients were required to have several failed prior therapies

Figure 2. CGRP switching patterns of the 65 NTD patients in the galcanezumab cohort



Galcanezumab was mostly used as the first (n=30) or second (n=26) CGRP mAb. When comparing switching patterns, it is important to consider that not all molecules entered the market at the same time, and that switches from the first-to-market molecule erenumab to other CGRP mAbs are, naturally, most commonly observed.

Variable	Galcanezumab given as…	1st line	2nd line	3rd line
Therapy pathway	Galcanezumab	23		
	Erenumab to Galcanezumab		19	
	Erenumab to Galcanezumab to Fremanezumab		7	
	Erenumab to Fremanezumab to Galcanezumab			8
	Fremanezumab to Erenumab to Galcanezumab			1
	Galcanezumab to Erenumab	3		
	Galcanezumab to Fremanezumab	3		
	Galcanezumab to Erenumab to Fremanezumab	1		
	Sum	30	26	9

CONCLUSIONS

- We identified 65 patients treated with galcanezumab and 111 with topiramate.
- Core socio-demographic data showed that the age at diagnosis was similar in the two groups while employment status differed (Tables 1 and 2).
- Exploratory comparisons of clinical characteristics revealed that galcanezumab-treated patients had more baseline monthly migraine days (MMDs) and monthly headache days (MHD) and were more likely to suffer from chronic migraine (CM) (Table 2).
- Pre-treatment assessments of health-related quality of life (HRQoL) and pain showed similar values between groups, but interpretation is limited due to incomplete responses.
- Galcanezumab was mostly used as the first (n=30) or second (n=26) CGRP mAb.
- In summary, this real-world study revealed similarities (e.g., HRQoL, pain) and differences (e.g., migraine frequency) between patient groups receiving galcanezumab and the conventional prophylactic treatment topiramate when including patients with ≥4 MMDs.
- Future studies on comparative real-world effectiveness will need to take these characteristics into account.

LIMITATIONS

- The small sample size (due to relatively short availability of galcanezumab) and substantial numbers of missing values for some of the variables (e.g., HRQoL, pain) limit the robustness and interpretation of the results of this exploratory study.

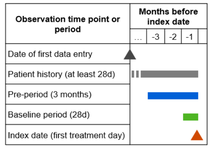
METHODS

Key Inclusion Criteria

Eligible patients should:

- have received either galcanezumab or topiramate as a migraine prophylactic treatment (any dosage)
- have entered the registry at least 4 weeks before the first dose of galcanezumab or topiramate and between May 1, 2018, and November 16, 2021, and have at least 4 monthly migraine days (MMDs) in the 4-week baseline period prior to the first dose
- be aged ≥ 18 years at the time of the initiation of galcanezumab or topiramate
- not be pregnant at treatment initiation and during treatment.

Figure 1. Study design and index date definition



Study time points and periods of interest
The first day of treatment with galcanezumab or topiramate was considered to be the index date. The baseline period was defined as the 28-day period before the index, while the pre-period, during which patient-relevant outcomes (PROs) were assessed, was 3 months long. Patient history could reach as far into the past as possible and included at least the 28 days of the baseline period (Figure 1).

Statistical analysis
We conducted a descriptive assessment of baseline characteristics in each group reporting counts, percentages, means, and standard deviations (sd), as appropriate. Exploratory p-values for between-group comparisons were calculated using the Wilcoxon rank sum test with continuity correction for continuous variables and Pearson's Chi-squared test for categorical variables. P-values are reported as nominal results without correction for multiple testing.

Assessment of treatment switching
CGRP-antibody switching patterns were assessed in all patients who received galcanezumab by searching for treatment cycles with erenumab or fremanezumab (the two other mAbs available in the study period) before or after the galcanezumab cycle (Figure 2).

Table 3. Attrition based on inclusion criteria

	Galcanezumab	Topiramate	Total
(a) Substance	100	1092	1192
(b) Study period	100	485	585
(c) Registry entry	87	257	344
(d) MMDs at baseline	65	114	179
(e) >= 18 years	65	111	176
(f) Not pregnant	65	111	176

- Table 3 shows the number of included patients in the study after each inclusion criterion (a-f) has been applied
- The biggest hurdle for inclusion were the restriction to the study period and registry entry for topiramate and the availability of documentation of four monthly migraine days (MMDs) at baseline for both treatments.

Table 4. Doses used during index cycle

	Galcanezumab (N = 65)		Topiramate (N = 111)	
Dosing (N, [percent])	120mg	22 (33.8)	25mg	64 (57.7)
	240mg	42 (64.6)	50mg	27 (24.3)
	Missing	1 (1.5)	75mg	4 (3.6)
			100mg	14 (12.6)
			Missing	2 (1.8)

- Galcanezumab 240mg was exclusively given as a loading dose in first injection of 1st-line treatment. The dosage of 120mg was given on consecutive monthly injections or as first injection of 2nd line treatment after mAbs switch in 22 patients due to intended reduction of interaction effects.

ADDITIONAL RESULTS

Table 5. Treatment duration in case of overlap periods

Variable	Statistic	1 week	2 weeks	3 weeks	4 weeks	5 weeks	6 weeks	8 weeks	8+ weeks
Pool of topiramate patients	24								
Prophylactic medication (multiple entries per patient possible)	all available	7	1	4	3	2	1	1	9
	antidepressants	3	0	1	0	2	0	1	4
	betablocker	4	1	2	1	0	1	0	3
	botulinum toxin	0	0	0	1	0	0	0	2
	ca-channel blocker	0	0	1	1	0	0	0	0

Variable	Statistic	1 week	2 weeks	3 weeks	4 weeks	5 weeks	6 weeks	8 weeks	8+ weeks
Pool of galcanezumab patients	28								
Prophylactic medication (multiple entries per patients possible)	all available	1	0	0	2	1	1	1	33
	antidepressants	0	0	0	1	0	1	1	14
	betablocker	0	0	0	0	0	0	0	6
	botulinum toxin	0	0	0	1	0	0	0	2
	ca-channel blocker	0	0	0	0	1	0	0	2
	topiramat	1	0	0	0	0	0	0	9

- 24 topiramate patients and 28 galcanezumab patients have an overlap with other prophylactic treatments.
- This overlap varies from 1 to 8+ weeks.
- The most frequently found overlapping treatments were antidepressants.

Table 6. Quality of life measurements during the 3-months pre-period were comparable between groups

Missing data patterns need further investigation before drawing conclusions on HRQoL in the two groups.

Variable	Statistic	Galcanezumab	Topiramate
Sample size	n	65	111
MIDAS, total score	mean	57.6	55.2
	sd	36.5	42.7
	missing	27	65
	P-value*	0.6	
HIT-6, total score	mean	64.8	64.1
	sd	5.3	6.0
	missing	31	64
	P-value*	0.6	
EQ5D, LQ-VAS	mean	61.5	64.9
	sd	23.4	23.4
	missing	26	59
	P-value*	0.4	
HADS, depression score	mean	5.9	7.1
	sd	3.4	4.9
	missing	35	64
	P-value*	0.3	
HADS, anxiety score	mean	6.7	7.7
	sd	3.9	4.3
	missing	35	64
	P-value*	0.4	
WPAI, productivity score	mean	4.5	4.0
	sd	1.8	3.0
	missing	43	81
	P-value*	0.4	
WPAI, daily task score	mean	5.4	5.6
	sd	2.5	3.0
	Missing	28	74
	P-value*	0.5	

Included instruments for measurements of PROs
Headache/migraine type, frequency, intensity, duration, and acute medication used (captured in the patient diary), Migraine Disability Assessment Test (MIDAS) total score, Headache Impact Test (HIT-6) total score, EQ-5D Visual Analogue Scale (VAS), Hospital Anxiety and Depression Scale (HADS), and Work Productivity and Activity Impairment (WPAI) work productivity and impact on daily activities scores.

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DISCLOSURES

Authors performed the work as employees of companies shown in affiliations under contract with Eli Lilly and Company, who funded the study. Past consulting fees: Janssen-Cilag and Novartis (M.K.); Novartis, TEVA, Allergan/Abbvie, and Eli Lilly (H. I.-W).

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