Switching Associated with Initiation of Calcitonin Gene-Related Peptide (CGRP) Monoclonal Antibodies (mAbs) Versus non-CGRP mAb Treatments for Prevention of Migraine

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INTRODUCTION AND OBJECTIVE

- Many patients who use oral non-CGRP mAb preventive therapies are unable to achieve optimal efficacy or experience difficulty tolerating the medicine. As a result, more than one-half of patients who receive a prescription migraine preventive medication (oral non-CGRP mAbs) discontinue its use within 6 months of treatment.[1-3]
- The FDA approved calcitonin gene-related peptide (CGRP) monoclonal antibodies (CGRP mAbs) for prevention of migraine. Currently, there is limited data on switching patterns of CGRP inhibitors compared to other preventive migraine treatments.

Objective

- Compare 6-month switching patterns among adult patients with migraine initiating CGRP mAbs versus non-CGRP mAbs.
- Compare 6-month switching patterns among adult patients with migraine initiating galcanezumab versus non-CGRP mAbs.

STUDY DESIGN AND METHODS

Study: Retrospective observational cohort study using administrative claims from the IBM® MarketScan® Commercial and Medicare Supplemental Databases.

Participants: Adults with ≥1 claim (first claim=index) for a CGRP mAb (galcanezumab, erenumab, fremanezumab) or non-CGRP mAb treatment (antidepressants, beta-blockers, anticonvulsants, or neurotoxin) between May 1, 2018 and June 30, 2019 with continuous enrollment in medical and pharmacy benefits for 12 months pre- and 6 months post-index. Additionally, patients had ≥1 inpatient or ≥2 outpatient claims with a migraine diagnosis during the 12 months pre-index period. Patients with evidence of their index drug class during 12-month pre-index period or with evidence of pregnancy, epilepsy, cancer, cluster headache, or treatment for cluster headache during the study period were excluded.

Outcome measures: Switching was defined as the first initiation of a preventive migraine treatment not part of the index regimen after the index drug discontinuation (based on 60-day gap). Time to switch was defined as days from index until the first switch to a non-index migraine treatment (not part of the index treatment regimen) over the post-index period.

Statistical analyses: Descriptive analyses were conducted on all study measures. Chi-square/Fisher's exact tests were conducted for categorical variables and Student's t-test for continuous variables. After completing the descriptive analyses and to control for bias, CGRP mAb patients were matched to non-CGRP mAb patients, and galcanezumab patients were matched to non-CGRP mAb patients using propensity score techniques.

KEY RESULTS

- CGRP mAb initiators were less likely to discontinue therapy over the 6-month post-index period compared to non-CGRP mAb initiators; however, out of those that discontinued, CGRP mAb initiators were more likely to switch compared to those on non-CGRP mAbs.
- Galcanezumab initiators were less likely to discontinue therapy over the 6-month post-index period compared to non-CGRP mAb initiators; however, out of those that discontinued, galcanezumab initiators were more likely to switch compared to those on non-CGRP mAbs.

Abbreviations: CGRP mAbs, calcitonin gene-related peptide monoclonal antibodies; GMB, galcanezumab; n, number of patients within each specific category; NSAID, nonsteroidal anti-inflammatory drug; SD, standard deviation

CONCLUSIONS

- CGRP mAb initiators were less likely to discontinue therapy over the 6-month post-index period compared to non-CGRP mAb initiators; however, out of those that discontinued, CGRP mAb initiators were more likely to switch compared to those on non-CGRP mAbs. The average time to switch was longer for those initiating CGRP mAbs compared to non-CGRP mAb initiators.
- Galcanezumab initiators were less likely to discontinue therapy over the 6-month post-index period compared to non-CGRP mAb initiators. Out of those that discontinued, galcanezumab initiators were more likely to switch compared to those on non-CGRP mAbs. The average time to switch was longer for those initiating galcanezumab compared to non-CGRP mAb initiators.

References: 1. Diamond S, et al. *Headache* 2007;47:355-63. 2. Loder E and Rizzoli P. *Headache* 2011;51:1336-45. 3. Berger A, et al. *Pain Pract* 2012;12:541-49.

Patient demographics: CGRP mAbs vs. non-CGRP mAbs

Characteristic	CGRP mAb patients (N=12,681)	non-CGRP mAb patients (N=21,474)	CGRP mAb patients (N= 7,867)	Non-CGRP mAb (N=7,867)
	Pre-Match*		Post-Match	
Age, years, mean (SD)	44.3 (11.6)	41.0 (12.5)	43.6 (11.7)	43.6 (12.0)
Female, n (%)	11,032 (87.0)	18,244 (85.0)	6,754 (85.9)	6,831 (86.8)
Deyo-Charlson Comorbidity Index, mean (SD)	0.4 (0.9)	0.4 (0.9)	0.4 (0.9)	0.4 (0.9)
Chronic Migraine, n (%)	7,789 (61.4)	4,458 (20.8)	3,646 (46.3)	3,420 (43.5)
Provider Type, N (%)				
Neurology	3,816 (30.1)	5,533 (25.8)	2,344 (29.8)	2,396 (30.5)
Primary Care	3,233 (25.5)	9,225 (43.0)	2,333 (29.7)	2,293 (29.1)
Acute Care Hospital, Emergency Room	893 (7.0)	1,118 (5.2)	511 (6.5)	488 (6.2)
Radiology, Laboratory, Pathology	566 (4.5)	580 (2.7)	334 (4.2)	234 (3.0)
Other/Unknown	4,173 (32.9)	5,018 (23.4)	2,345 (29.8)	2,456 (31.2)

* All pre-match comparisons statistically significant p<0.001 except Deyo-Charlson Comorbidity Index p=0.631; All post-match comparisons not statistically significant.

Post-matching population results: CGRP mAbs vs. non-CGRP mAbs

	CGRP mAb patients (N= 7,867)	Non-CGRP mAb (N=7,867)
Discontinuation		
Patients that discontinue index drug (60-day gap), n (%)	2,442 (31.0)	4,825 (61.3)
Patients that restart index after discontinuation (60-day gap), n (%)	429 (17.6)	1,206 (25.0)
Switching		
Patients who switched among those who discontinued, n (%)	868 (35.5)	1,129 (23.4)
Time to 1st Switch (days), mean (SD)	105.9 (39.1)	93.3 (42.8)

*All comparisons statistically significant p<0.001; Sensitivity analyses conducted for discontinuation 45-day gap, 90-day gap and 120-day gap with similar directional results p<0.001

Post-matching population results: Drugs switched to by Class (6 months)

Drug Switched to, by Class	CGRP mAb patients (N=7,867)	non-CGRP mAb patients (N=7,867)
CGRP mAbs (n, %)		
Erenumab*	36 (4.1)	20 (1.8)
Fremanezumab*	86 (9.9)	12 (1.1)
Galcanezumab*	150 (17.3)	19 (1.7)
Non-CGRP mAb Migraine Treatment (n, %)		
ACE inhibitors*	25 (2.9)	83 (7.4)
Alpha-agonists	14 (1.6)	22 (1.9)
Angiotensin receptor blockers	10 (1.2)	20 (1.8)
Antidepressants*	111 (12.8)	239 (21.2)
Antiepileptic drugs*	170 (19.6)	330 (29.2)
Antithrombotics	1 (0.1)	3 (0.3)
Botox*	134 (15.4)	119 (10.5)
Beta-blockers*	98 (11.3)	180 (15.9)
Calcium-channel blockers	32 (3.7)	62 (5.5)
Diuretic (Acetazolamide)	12 (1.4)	13 (1.2)
NSAID (Nabumetone)*	4 (0.5)	22 (1.9)

*Statistically significant p<0.001, NSAI p<0.004

- Over the 6-month post-index period, 31.0% of CGRP mAb and 61.3% of non-CGRP mAb initiators discontinued therapy (p<0.001).
- Among patients who discontinued their index drug, 35.5% of CGRP mAb and 23.4% of non-CGRP-mAb initiators switched to another therapy (p<0.001).
- The average time to switch was longer for those initiating CGRP mAbs (106 days) compared to non-CGRP mAb initiators (93 days).

Patient demographics: Galcanezumab vs. non-CGRP mAbs

Characteristic	GMB patients (N=3,253)	non-CGRP mAb patients (N=21,474)	GMB patients (N=2,986)	Non-CGRP mAb (N= 2,986)
	Pre-Match*		Post-Match*	
Age, years, mean (SD)	43.4 (11.4)	41.0 (12.5)	43.2 (11.5)	43.2 (11.9)
Female, n (%)	2,854 (87.7)	18,244 (85.0)	2,613 (87.5)	2,606 (87.3)
Deyo-Charlson Comorditiy Index, mean (SD)	0.4 (0.9)	0.4 (0.9)	0.4 (0.9)	0.4 (0.9)
Chronic Migraine, n(%)	1,784 (54.8)	4,458 (20.8)	1,543 (51.7)	1,512 (50.6)
Provider Type (N, %)				
Neurology	985 (30.3)	5,533 (25.8)	903 (30.2)	942 (31.5)
Primary Care	961 (29.5)	9,225 (43.0)	908 (30.4)	882 (29.5)
Acute Care Hospital, Emergency Room	238 (7.3)	1,118 (5.2)	212 (7.1)	171 (5.7)
Radiology, Laboratory, Pathology	125 (3.8)	580 (2.7)	115 (3.9)	90 (3.0)
Other/Unknown	944 (29.0)	5,018 (23.4)	848 (28.4)	901 (30.2)

*All pre-match comparisons statistically significant P<0.001; Provider Type statistically significant p=0.0364. All other post-match not statistically significant
*All pre-match comparisons statistically significant P<0.001 except Deyo-Charlson Comorbidity Index p=0.542; Post-match Provider Type statistically significance p=0.036; All other post-match comparisons not statistically significant

Post-matching population results : Galcanezumab vs. non-CGRP mAbs

	GMB patients (N=2,986)	Non-CGRP mAb (N=2,986)
Discontinuation		
Patients that discontinue index drug (60-day gap), n (%)	763 (25.6)	1,826 (61.2)
Patients that restart index after discontinuation (60-day gap), n(%)	130 (17.0)	506 (27.7)
Switching		
Patients who switched among those who discontinued, n(%)	269 (35.3)	478 (26.2)
Time to 1st Switch (days), mean (SD)	101.8 (40.4)	92.9 (43.8)

*All comparisons statistically significant p<0.001

Post-matching population results: Drugs switched to by Class (6 months)

Drug Switched to, by Class	GMB patients (N=2,986)	non-CGRP mAb patients (N=2,986)
CGRP mAbs (n, %)		
Erenumab*	23 (8.6)	8 (1.7)
Fremanezumab*	24 (8.9)	6 (1.3)
Galcanezumab	N/A	9 (1.9)
Non-CGRP mAb Migraine Treatment (n, %)		
ACE inhibitors*	8 (3.0)	36 (7.5)
Alpha-agonists	4 (1.5)	12 (2.5)
Angiotensin receptor blockers	2 (0.7)	9 (1.9)
Antidepressants	42 (15.6)	93 (19.5)
Antiepileptic drugs	57 (21.2)	140 (29.3)
Antithrombotics	1 (0.4)	3 (0.6)
Botox*	65 (24.2)	60 (12.6)
Beta-blockers	31 (11.5)	72 (15.1)
Calcium-channel blockers	14 (5.2)	19 (4.0)
Diuretic (Acetazolamide)	2 (0.7)	7 (1.5)
NSAID (Nabumetone)	1 (0.4)	10 (2.1)

*Statistically significant p<0.001;ACE Inhibitors p<0.011

- Over the 6-month post-index period, 25.6% of galcanezumab and 61.2% of non-CGRP mAb initiators discontinued therapy (p<0.001).
- Among patients who discontinued their index drug, 35.3% of galcanezumab and 26.2% of non-CGRP-mAb initiators switched to another therapy (p<0.001).
- The average time to switch was longer for those initiating galcanezumab (102 days) compared to non-CGRP mAb initiators (93 days).

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