Incidence of Inpatient Constipation Among Migraine Patients Treated With Erenumab: A Retrospective Cohort Study in a US Electronic Health Record Database

V Hoffman[1], KS Gill[2], CA Szekely[2], G Reznor[1], SM Ezzy[1], AS Park[2], R Urman[2], RK Hernandez[2], M Navetta[2], S Lopez-Leon[3], DE Chou[2], F Xue[2], FT Wang[1]

[1]Optum, Boston, MA, USA; [2]Amgen Inc., Thousand Oaks, CA, USA; [3]Novartis Pharmaceuticals Corp, East Hanover, NJ, USA

Migraine Trust Virtual Symposium, 3–9 October, 2020

This study was supported by Amgen, Inc and was carried out under a research collaboration/contract between Optum and Amgen, Inc. Erenumab is co-marketed by Amgen and Novartis.

Background

- Erenumab (erenumab-aooe in the U.S.) is a calcitonin gene-related peptide (CGRP) receptor antagonist that was approved in the United States (US) on May 2018 as a first in class treatment for migraine prevention in adults
- Constipation was identified as an adverse drug reaction based on data from erenumab clinical trials, and constipation with serious complications has been observed among erenumab users in the post-marketing setting
- Patients with migraine have comorbidities or concomitant medications that increase the risk of developing constipation
- This study describes the incidence of inpatient constipation among all new users of erenumab, and among subsets of new users with select baseline characteristics

Methods

Data source: Optum Electronic Health Record (EHR) Database

- US based, 88+M patients from 2007-2020

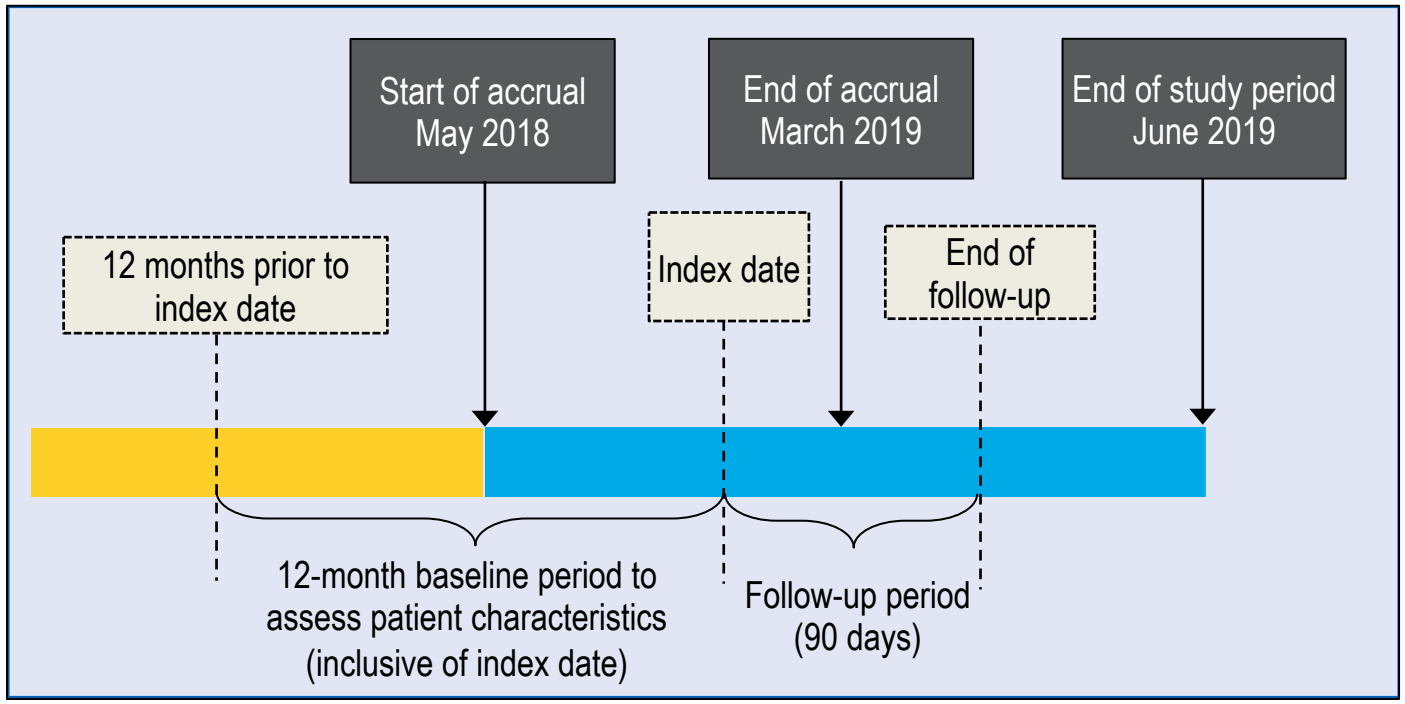
Cohort eligibility

- Prescription order for erenumab during the accrual period; only the first identified prescription order was considered
- Age ≥ 18 years
- At least 1 migraine diagnosis (ICD-10-CM G43.-) or prescription for a triptan/ergotamine in the prior 12 months
- At least 1 outpatient (OP) visit at least 1 year prior to the erenumab prescription to establish the 12-month baseline period
- No use of any monoclonal antibodies targeting the CGRP pathway in the one year prior to the erenumab prescription

Index date

- Date of cohort entry (earliest date of meeting all cohort eligibility criteria)

Figure 1. Cohort study design



Follow-up period

- Starting the day following the index date through the earliest of: 1) occurrence of the outcome, 2) prescription for other CGRP antagonists (galcanezumab or fremanezumab), or 3) end of the 90-day risk evaluation window

Methods (continued)

Outcome: inpatient constipation

- ICD-10-CM K59.0- in an emergency department (ED) or inpatient (IP) visit
- Any constipation event occurring during an inpatient hospital or ED visit was counted, regardless of the primary reason for the visit.
- Only the first (incident) event identified during the follow-up period was counted in the analysis

Analysis

- The 90-day incidence proportion was calculated as the number of incident events identified during the 90-day outcome risk window after the index date, divided by the number of cohort members at risk at the start of follow-up
- 95% CIs for the incidence proportions were also calculated
- Incidence proportions among all new users of erenumab, and among subsets of new users by select baseline characteristics, are presented

Results

Table 1. Incidence of inpatient constipation among new users of erenumab, by select patient characteristics

Baseline characteristics		New users of erenumab	Inpatient constipation	
		N (%)	N	90-day incidence proportion (%, 95% CI)
Overall		**9,994 (100.0)**	**55**	**0.55 (0.42 – 0.72)**
Age† group (years)	18 – 34	1,793 (17.9)	12	0.67 (0.38 – 1.17)
	35 – 49	4,056 (40.6)	20	0.49 (0.32 – 0.76)
	50 – 64	3,374 (33.8)	15	0.44 (0.27 – 0.73)
	≥ 65	771 (7.7)	8	*1.04 (0.53 – 2.03)**
Sex	Female	8,731 (87.4)	51	0.58 (0.44 – 0.77)
	Male	1,263 (12.6)	4	0.32 (0.12 – 0.81)
BMI (kg/m^2)	< 18.5	172 (1.7)	1	0.58 (0.10 – 3.22)
	18.5 – 24	2,374 (23.8)	13	0.55 (0.32 – 0.93)
	25 – 29	2,303 (23.0)	5	0.22 (0.09 – 0.51)
	≥ 30	3,723 (37.3)	28	0.75 (0.52 – 1.08)
	Unknown	1,422 (14.2)	8	0.56 (0.29 – 1.11)

Abbreviations: BMI: body mass index; kg/m^2: kilogram / square meter
*90-day incidence proportions in red font represent those > 1%.
† Mean age (standard deviation): 46.6 (12.7) years;

Results (continued)

Table 2. Incidence of inpatient constipation among new users of erenumab, by select baseline constipation risk factors

Baseline characteristics		New erenumab users	Inpatient constipation	
		N (%)	N	90-day incidence proportion (%, 95% CI)
Prior constipation or complications	Any constipation (OP, IP, ED)	638 (6.4)	20	*3.13 (2.04 – 4.79)**
	Inpatient constipation (IP, ED)	181 (1.8)	12	*6.63 (3.83 – 11.23)**
	Complications of constipation (IP, ED)†	52 (0.5)	6	*11.54 (5.40 – 22.97)**
Potential risk factors for constipation	Irritable bowel syndrome	743 (7.4)	12	*1.62 (0.93 – 2.80)**
	Diverticular disease	331 (3.3)	5	*1.51 (0.65 – 3.49)**
	Hemorrhoids (not due to pregnancy)	433 (4.3)	9	*2.08 (1.10 – 3.90)**
	Diabetes	952 (9.5)	12	*1.26 (0.72 – 2.19)**
	Autonomic neuropathy	73 (0.7)	3	*4.11 (1.41 – 11.40)**
	Multiple sclerosis	161 (1.6)	1	0.62 (0.11 – 3.43)
Medications that may cause constipation	Opioids	4,793 (48.0)	46	0.96 (0.72 – 1.28)
	NSAIDs (prescription and OTC)	5,503 (55.1)	44	0.80 (0.60 – 1.07)
	Anticholinergics	5,649 (56.5)	44	0.78 (0.58 – 1.04)

Abbreviations: ED: emergency department; IP: inpatient; NSAIDs: nonsteroidal anti-inflammatory drugs; OP: outpatient; OTC: over the counter medications
90-day incidence proportions in red font represent those > 1%.
†Includes intestinal impaction, megacolon, anal/rectal prolapse, fissure, fistula, ulcer, and ileus in outpatient, inpatient, and emergency department (ED) visits.

Results (continued)

Table 3. Incidence of inpatient constipation among new users of erenumab, by select characteristics related to migraine

Baseline characteristics		New erenumab users	Inpatient constipation	
		N (%)	N	90-day incidence proportion (%, 95% CI)
Comorbidities related to migraine	Asthma	1,467 (14.7)	12	0.82 (0.47 – 1.42)
	Hypertension	2,633 (26.4)	24	0.91 (0.62 – 1.35)
	Anxiety	3,512 (35.1)	33	0.94 (0.67 – 1.32)
	Depression	2,940 (29.4)	30	*1.02 (0.72 – 1.45)**
	Non-migraine headache	4,657 (46.6)	43	0.92 (0.69 – 1.24)
	Chronic pain	5,072 (50.8)	48	0.95 (0.71 – 1.25)
	Insomnia	1,875 (18.8)	17	0.91 (0.57 – 1.45)
	Thyroid disorder	1,879 (18.8)	17	0.90 (0.57 – 1.44)
Migraine preventive agents	Botulinum toxin	3,052 (30.5)	22	0.72 (0.48 – 1.09)
	Anti-epileptics†	6,042 (60.5)	42	0.70 (0.51 – 0.94)
	Anti-depressants‡	5,317 (53.2)	36	0.68 (0.49 – 0.94)
	Anti-hypertensives§	3,989 (39.9)	32	0.80 (0.57 – 1.13)

*90-day incidence proportions in red font represent those > 1%.

†Includes carbamazepine, gabapentin, levetiracetam, pregabalin, topiramate, valproate sodium, valproic acid, divalproex sodium, and zonisamide.

‡Includes duloxetine, desvenlafaxine, venlafaxine, amitriptyline, desipramine, doxepin, imipramine, nortriptyline, protriptyline, escitalopram, citalopram, and sertraline.

§Includes atenolol, bisoprolol, metoprolol, nadolol, nebivolol, pindolol, propranolol, timolol, verapamil, candesartan, clonidine, and lisinopril.

Conclusions

- The overall 90-day incidence proportion of inpatient constipation among new users of erenumab (0.55%) was similar to the incidence of serious constipation (0.63%) reported in migraine patients in a real-world setting (Chia et al., 2019)
- The incidence proportion was higher in patients ≥65 years (1.04%), patients with prior constipation or prior complications of constipation (3.13 – 11.54%), and patients with baseline constipation risk factors (1.26 – 4.11%) other than multiple sclerosis
- The majority of patients who experienced inpatient constipation had pre-existing risk factors for constipation (e.g., 46 of 55 patients with events had opioid use during the baseline period).
- Further research on the incidence of inpatient constipation in non-erenumab users with migraine and older age or baseline constipation risk factors may be helpful to contextualize these findings

Reference:

Chia V, Park A, Goli V, et al. Incidence of constipation in patients treated with commonly used migraine medications. Cephalalgia. 2019;39(1_suppl):376