Inpatient Constipation in Migraine Patients Prescribed Preventive Medications in a U.S. Electronic Health Record Database

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INTRODUCTION

- Erenumab, an anti-calcitonin gene-related peptide (CGRP) pathway monoclonal antibody (mAb), was approved in the United States in May 2018 as a first-in-class treatment for migraine prevention in adults.
- Other mAbs approved for the prevention of migraine in adults include: galcanezumab, fremanezumab, and eptinezumab.
- Constipation was identified as an adverse drug reaction based on data from erenumab clinical trials. In the post-marketing setting, constipation with serious complications was reported following erenumab use and was added to the Warnings and Precautions in the product label in October 2019 (1).

OBJECTIVE

- To estimate and compare the risk of inpatient constipation among migraine patients prescribed erenumab, other anti-CGRP pathway mAbs, and standard of care anti-epileptic drugs (AEDs).

METHODS

Data Source

- The study population was drawn from Optum's Electronic Health Record (EHR) Research Database, a patient-level database that integrates multiple electronic medial record systems with medical claims, prescription, and practice management data. This EHR database represents a geographically diverse US patient population and included 32 million patients in 2019.

Study Population

- Patients with migraine who initiated erenumab, other anti-CGRP pathway mAbs, and AEDs (carbamazepine, gabapentin, topiramate, valproate sodium/valproic acid/divalproex sodium, zonisamide) were identified from May 2018 through March 2020.
- The index date was set as the date of the earliest prescription order that met all of the eligibility criteria. See Figure 1 for full list of eligibility criteria.
- Erenumab initiators were propensity score (PS)-matched separately to initiators of other anti-CGRP pathway mAbs and AEDs.

Outcome: Inpatient Constipation

- Inpatient constipation was defined as constipation (ICD-10-CM code K59.0-) recorded during an emergency department or inpatient visit.
- The *a priori* defined risk window for outcome assessment was 90 days following treatment initiation.
- Inpatient constipation was evaluated only in patients who initiated treatment by December 2019 to allow for sufficient follow-up to identify outcomes.

Statistical Analysis

- Risk (i.e., incidence proportion) and 95% confidence intervals (CIs) were calculated as the number of incident events identified during the 90-day risk window divided by the number of patients at risk at the start of follow-up.
- Odds ratios (ORs) were calculated comparing risk of inpatient constipation among PS-matched erenumab initiators relative to PS-matched comparators.
- Risk of inpatient constipation was also calculated after stratifying on the use of constipation-causing medications during the baseline period.

RESULTS

Figure 1. Formation of Erenumab, Other Anti-CGRP Pathway mAb, and AED Initiator Cohorts, Optum EHR Research Database

Patients with a prescription order from 17 May 2018 through 31 March 2020
Erenumab N = 29,372; Other anti-CGRP mAbs N = 21,962; AEDs N = 243,183

↓

Known age/sex information and ≥ 18 years of age on the index date
Erenumab N = 28,922; Other anti-CGRP mAbs N = 21,629; AEDs N = 232,747

↓

At least 2 diagnosis codes for migraine on different days or at least one diagnosis code for migraine plus a prescription for a triptan/ergot in the 12 months prior to the index date
Erenumab N = 22,650; Other anti-CGRP mAbs N = 16,432; AEDs N = 130,850

↓

At least 2 outpatient visits prior to the index date†
Erenumab N = 18,220; Other anti-CGRP mAbs N = 13,557; AEDs N = 84,728

↓

No prescription order for the cohort-defining drug or anti-CGRP pathway mAbs in the 12 months prior to the index date
Erenumab initiators N = 17,902; Other anti-CGRP mAb initiators N = 13,404; AED initiators N = 49,497

↓

Patients who initiated treatment between 17 May 2018 and 31 December 2019
Erenumab initiators N = 15,983; Other anti-CGRP mAb initiators N = 11,345; AED initiators N = 43,810

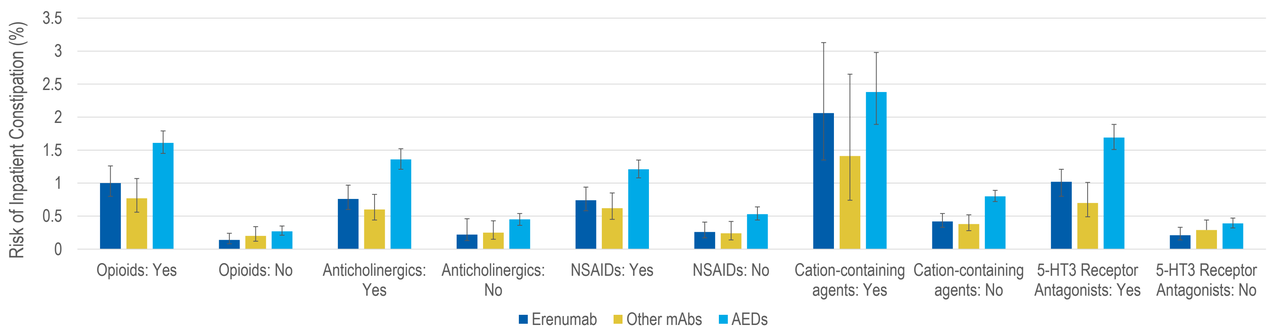
† Including one visit ≥ 12 months prior to prescription order date (to establish a baseline period)

Table 1. Risk of Inpatient Constipation Among Erenumab, Other Anti-CGRP Pathway mAb, and AED Initiators, Pre- and Post-Propensity Score Matching, Optum EHR Research Database

	Initiators†	Inpatient Constipation‡	Risk of Inpatient Constipation		Odds Ratio (95% CI)§
	N	*N*	%	95% CI	
Pre-Propensity Score Matching					
Erenumab	15,983	84	0.53	0.42 - 0.65	---
Other mAbs	11,345	50	0.44	0.33 - 0.58	---
AEDs	43,810	398	0.91	0.82 - 1.00	---
Post-Propensity Score Matching					
Erenumab-Other mAbs Comparison					
Erenumab	11,670	54	0.46	0.35 - 0.60	1.06 (0.72 - 1.55)
Other mAbs	11,172	49	0.44	0.33 - 0.58	1.00 (reference)
Unmatched Erenumab Initiators	4,313	30	0.70	0.49 - 0.99	---
Erenumab-AEDs Comparison					
Erenumab	13,669	72	0.53	0.42 - 0.66	0.69 (0.51 - 0.94)
AEDs	13,752	104	0.76	0.62 - 0.92	1.00 (reference)
Unmatched Erenumab Initiators	2,314	12	0.52	0.30 - 0.90	---

† This table includes initiators identified from 17 May 2018 - 31 December 2019.
‡ Inpatient constipation events were identified within a 90-day risk window following the index date, starting from the day after the index date through the earliest of: end of the 90-day risk window, switching of migraine preventive therapy, or end of the study period (31 March 2020).
§ Odds ratio comparing propensity score-matched erenumab initiators to propensity-score matched comparators.

Figure 2. Risk of Inpatient Constipation† Among Erenumab, Other Anti-CGRP Pathway mAb, and AED Initiators‡, Stratified by the Presence of Baseline Use of Medications Associated with Constipation Risk



† Inpatient constipation events were identified within a 90-day risk window following the index date, starting from the day after the index date through the earliest of: end of the 90-day risk window, switching of migraine preventive therapy, or end of the study period (31 March 2020).
‡ This figure includes initiators identified from 17 May 2018 - 31 December 2019, pre-propensity score matching.

Abbreviations: AED: antiepileptic drug; CGRP: calcitonin gene-related peptide; CI: confidence interval; EHR: electronic health record; mAbs: monoclonal antibodies; OR: odds ratio; PS: propensity score.

Summary of Key Results

- We identified 15,983 erenumab, 11,345 other anti-CGRP pathway mAb, and 43,810 AED initiators (Figure 1).
- Among matched initiators, the risk of inpatient constipation comparing erenumab to other mAbs was similar (OR 1.06 [95 %CI: 0.72-1.55]) while the risk for erenumab was lower than for AEDs (OR 0.69 [95% CI: 0.51-0.94]) (Table 1).
- Risk of inpatient constipation was higher among patients with baseline use of medications associated with constipation risk (Figure 2).

CONCLUSIONS

- Risk of inpatient constipation within 90 days of treatment initiation was similar among patients prescribed erenumab and other anti-CGRP pathway mAbs, and lower in patients prescribed erenumab versus patients prescribed AEDs.

REFERENCES

1. Erenumab Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761077s011lbl.pdf

DISCLOSURES

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