Benefit of Migraine Prevention With Erenumab in Patients Receiving Background Standard-of-Care Acute Treatment

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INTRODUCTION

- Erenumab (in the United States, erenumab-aooe) is a fully human monoclonal antibody that selectively targets and blocks the canonical calcitonin gene-related peptide receptor,[1] and is approved as a preventive treatment for migraine in adults in the United States and Europe[2,3]
- The efficacy (up to 1 year) and safety (up to 3 years) of erenumab has been established in episodic (EM) and chronic migraine (CM)[4–7]
  - However, the additional benefit of erenumab in patients using acute migraine-specific medications (AMSM) has not been established

OBJECTIVE

- To assess the effect of erenumab in combination with AMSM over AMSM only in patients with EM and CM with frequent use of AMSM at baseline

METHODS

Episodic Migraine Study (STRIVE; NCT02456740)[4]

Key inclusion criteria
- Adults with migraine for ≥ 12 months
- In three months before screening
  - ≥ 4 and < 15 migraine days per month
  - < 15 headache days per month

Key exclusion criteria
- > 50 years at migraine onset
- No response to > 2 preventive treatments*

Patients (N = 955) randomized (1:1:1):
- Placebo (n = 319)
- Erenumab 70 mg QM SC (n = 317)
- Erenumab 140 mg QM SC (n = 319)

Endpoints evaluated over months 4–6 of 6-month DBTP

Chronic Migraine Study (NCT02066415)[5]

Key inclusion criteria
- Adults
- In three months before screening
  - ≥ 15 headache days per month
  - ≥ 8 migraine days per month

Key exclusion criteria
- > 50 years at migraine onset
- CM with continuous pain
- No response to > 3 preventive treatments*

Patients (N = 667) randomized (3:2:2):
- Placebo (n = 286)
- Erenumab 70 mg QM SC (n = 191)
- Erenumab 140 mg QM SC (n = 190)

Endpoints evaluated over last 4 weeks of 3-month DBTP

*No reduction in frequency, duration or severity of headache after ≥ 6 weeks of treatment at generally accepted doses of the preventive treatment
DBTP, double-blind treatment phase; QM, once monthly; SC, subcutaneous

Post Hoc Analysis

Subgroup of patients with ≥ 4 days of AMSM (ie, triptans and ergot derivatives) use during the 4-week baseline period
- Excluded patients who used migraine prophylactic medication treatment at baseline or on study
- Patients continued AMSM as needed throughout the study

Outcomes compared between
- Patients receiving preventive treatment (erenumab 70 mg or 140 mg) plus AMSM
- Patients receiving AMSM only (ie, patients in the placebo arm of the double-blind studies)

Outcomes assessed over months 4–6 for EM study and over month 3 for the CM study included change from baseline in:
- Monthly migraine days (MMD)
- ≥ 50% responder rate
- Monthly AMSM use days
- 6-Item Headache Impact Test (HIT-6) score
- Migraine Disability Assessment (MIDAS) score

RESULTS

In patients already using AMSMs, the addition of effective prevention with erenumab to acute treatment appears to be associated with clinical benefit compared with acute treatment only

Addition of Erenumab Significantly Improved Efficacy Across a Range of Measures Among AMSM Users versus AMSM Alone in Patients with EM and CM

EM:	AMSM only (N = 142)	Erenumab 70 mg (N = 131)	Erenumab 140 mg (N = 139)
Change in MMDs	–1.0 days	–3.1 days‡	–4.0 days‡
≥ 50 Responder	17.6%	37.4%‡	47.5%‡
Change in AMSM Days	–0.8 days	–2.7 days‡	–3.5 days‡
Change in HIT-6 Score	–3.8	–6.7‡	–7.5‡
MIDAS Score	–13.5	–21.5†	–25.2‡

CM:	AMSM only (N = 200)	Erenumab 70 mg (N = 122)	Erenumab 140 mg (N = 135)
Change in MMDs	–3.7 days	–5.8 days‡	–7.0 days‡
≥ 50 Responder	18.5%	33.6%†	41.5%‡
Change in AMSM Days	–3.1 days	–5.6 days‡	–6.7 days‡
Change in HIT-6 Score	–3.0	–5.2†	–5.6‡
MIDAS Score	–8.6	–21.8†	–19.4*

*P < 0.05 versus AMSM only; †P < 0.01 versus AMSM only; ‡P < 0.001 versus AMSM only; nominal *P* values
AMSM, acute migraine-specific medication; HIT-6, 6-item Headache Impact Test; MMD, monthly migraine days; N, number of patients in analysis dataset; not all patients may have had data for every endpoint.

Patients with CM had a Greater Burden of Disease Than Those with EM

		Age, Female, White	MMDs	Monthly AMSM Use Days	HIT-6 Score	MIDAS Score
Episodic migraine	AMSM only (N = 142)	43.7 y, 86.6%, 95.1%	8.7 (2.6)	7.6 (2.3)	60.1 (6.3)	44.3 (37.5)
	Erenumab 70 mg + AMSM (N = 131)	45.1 y, 84.7%, 97.7%	8.8 (2.4)	8.0 (2.4)	59.9 (6.1)	46.4 (40.3)
	Erenumab 140 mg + AMSM (N = 139)	42.4 y, 87.8%, 95.7%	8.7 (2.4)	8.0 (2.4)	59.1 (6.3)	40.0 (31.5)
Chronic migraine	AMSM only (N = 200)	43.7 y, 78.0%, 95.5%	18.3 (4.4)	16.8 (5.6)	63.1 (5.2)	68.3 (51.8)*
	Erenumab 70 mg + AMSM (N = 122)	43.4 y, 88.5%, 95.9%	18.0 (4.1)	16.7 (4.8)	63.8 (4.4)	68.4 (41.1)*
	Erenumab 140 mg + AMSM (N = 135)	45.1 y, 91.1%, 97.8%	17.7 (4.2)	16.2 (4.5)	62.6 (5.8)	63.7 (53.3)*

N = Number of subjects with acute migraine specific medication treatment days ≥ 4 at baseline in the analysis set
Data are mean (SD)
AMSM, acute migraine-specific medication; HIT-6, 6-item headache impact test; MIDAS, Migraine Disability Assessment; MMD, monthly migraine day
*Not all patients had MIDAS scores reported at baseline

CONCLUSIONS

- A post hoc analysis of AMSM users from two pivotal EM and CM trials demonstrated that preventive treatment with erenumab plus AMSM as needed significantly reduced MMDs and AMSM use versus AMSMs only
- **The percentage of patients achieving a ≥ 50% reduction** in MMDs was significantly higher in patients receiving preventive treatment with erenumab plus AMSM as needed versus AMSMs only
- Measures of disability (HIT-6 and MIDAS scores) were also reduced by preventive treatment with erenumab plus AMSM versus AMSMs only

LIMITATIONS

- Neither study was designed to compare treatment modalities. We cannot be certain that AMSM use followed a similar pattern and frequency of use in both groups despite the similar total number of AMSM days at baseline
- Although the placebo arm in this analysis served as a surrogate for an AMSM-only treatment paradigm, there may still be effects of the placebo intervention that are not taken into consideration. However, the treatment effect reported here is likely underestimated if considering the potential preventive effects of a placebo intervention
- The clinical relevance must be carefully considered as the endpoints of this analysis were preventive therapy goals rather than acute therapy goals. Thus, use of an acute therapy early in an attack, while consistent with use in standard of care, automatically considers the episode to be a migraine day despite not being certain that an attack aborted by acute therapy would have qualified as a migraine, thereby potentially inflating the MMD endpoint

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DISCLOSURES

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