EPTINEZUMAB FOR DIFFICULT TO TREAT MIGRAINE: WHO RESPONDS AND WHO NEED MORE

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INTRODUCTION and PURPOSE

- Eptinezumab, a monoclonal antibody (mAb) targeting the calcitonin gene-related peptide (CGRP), has recently been approved for migraine prevention.[1,2]
- Randomized controlled trials (RCTs) have demonstrated that eptinezumab is both effective and well-tolerated for the preventive treatment of migraine.[3]
- This real-world study evaluated responder and super-responder rates to eptinezumab, explored clinical predictors of dose escalation and assessed its safety and tolerability over a period of 9 months.

METHODS

- A total of 67 migraine patients, who have attended the Headache Clinic at San Raffaele Hospital in Milan from October 2023 to April 2025 , were enrolled.
- Demographic and clinical data, including monthly headache (MHD) and migraine (MMD) days, acute medication use in terms of pills (AMP) and days (AMD), headache intensity (NRS score), disability (MIDAS score), and impact (HIT-6 score), were recorded at baseline and after 3 (M3), 6 (M6), and 9 (M9) months of treatment. Adverse events were assessed at all time-points.
- Responders and Super-Responders were defined by a ≥50% or ≥75% reduction in MMD from baseline, respectively.[4]
- All patients initially received 100 mg of intravenous eptinezumab; for those with a suboptimal response based on the clinician's judgment, the dose was escalated to 300 at M3, M6 or M9.
- Continuous variables were summarized as medians and categorical variables as frequencies. Longitudinal changes in clinical variables were assessed using generalized estimating equations. Baseline predictors of dose escalation were evaluated using univariate generalized linear mixed models (R software).

RESULTS

- A total of 67 patients (85% female, median age: 50 years (IQR, 34–59) were enrolled. Most patients (75%) had chronic migraine and 21% migraine with aura. The cohort was highly treatment-refractory, with a median of 5 failed preventives (IQR 3–6) and 42% previously exposed to anti-CGRP mAbs.
- Significant improvements were observed at all time points in MHD, MMD, AMP, AMD, NRS, MIDAS, and HIT-6 scores (**Table 1**).
- At M3, responders were 46%, including 22% super-responders. At M6 responders were 34%, including 8% super-responders. At M9 responders were 51%, including 16% super-responders (**Fig. 1A**).
- Patients who increased the eptinezumab dosage to 300mg were 70% at M3 and 85% at M6. No further dose escalation were made at M9 (**Fig. 1B**)
- Factors associated with dose escalation included: higher MHD and MMD at baseline (p<0.05), and a prior failure to anti-CGRP mAb (p< 0.04). An 80% predicted probability of dose escalation corresponded to ≥28 baseline MHD in mAb-naïve patients and ≥14 MHD in those previously exposed (**Fig 2**).
- Only two patients permanently discontinued eptinezumab due to tolerability issues. Overall, 23 patients reported adverse events, the most frequent being constipation (n = 11) and mild allergic reactions (n = 8).

	Basale	Mese 3	Mese 6	Mese 9	Basale-Mese 9 (p value)
Monthly Headache Days (MHD)	20 [12-30]	12 [7-27]	12 [8-27.5]	10 [5-20]	< 0.001
Monthly Migraine Days (MMD)	16 [10-20]	9 [5-15]	10 [8-20]	9 [4-10.5]	< 0.001
Acute Medication Pills (AMP)	19 [12-30]	11 [4-17]	12 [8-20]	8 [4-14.5]	0.003
Acute Medication Days (AMD)	14 [9-20]	8 [4-15]	10 [7-17.5]	8 [3-11.5]	< 0.001
MIDAS score	69 [40-120]	32 [16-64]	40.5 [15.5-58.5]	32 [16-52.5]	< 0.001
HIT-6 score	66 [64-68]	64 [61-67]	64 [61-67]	63 [59.5-66.5]	0.003
NRS score	8 [7-8]	7 [6-8]	8 [7-8]	8 [6.5-8]	0.001

Table 1. Median and [IQR] of clinical variables at different timepoints.

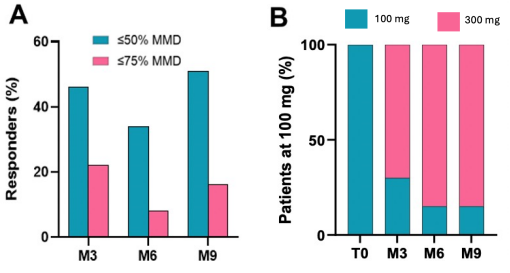

Figure 1. A) Proportions of responders and super-responders across all timepoints. B) Proportions of patients at 100 and 300 mg across all timepoints

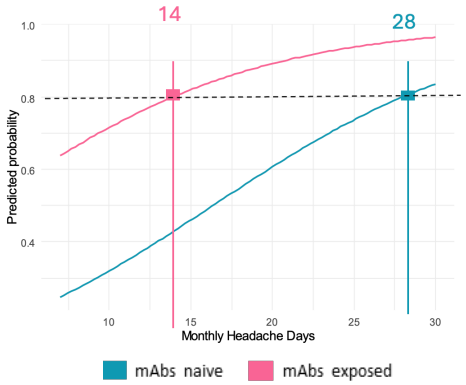

Figure 2. Predicted probability of increasing the dose at 300 mg in patients based on prior anti-CGRP monoclonal antibody exposure and monthly headache days at baseline.

DISCUSSION

- Our findings confirm that eptinezumab is effective and well tolerated in difficult-to-treat migraine patients, with sustained benefits up to nine months of treatment.
- The majority of patients escalate to a 300 mg dose during the course of treatment. Individuals with a higher baseline migraine frequency and a history of prior exposure to anti-CGRP monoclonal antibodies are more likely to require such dose escalation

CONCLUSIONS

Eptinezumab is an effective treatment for migraine. Initiating therapy at 300 mg may be beneficial for patients with prior anti-CGRP mAb failures or higher baseline migraine frequency.

REFERENCES

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