Patient Global Impression of Change Related to Improvement in Most Bothersome Symptom Following Treatment With Eptinezumab

Richard B. Lipton[1], Lora McGill[2], Joe Hirman[3], David Biondi[4], Roger Cady[4]

[1]Albert Einstein College of Medicine, Bronx, NY, USA; [2]CNS Healthcare, Memphis, TN, USA; [3]Pacific Northwest Statistical Consulting, Inc., Woodinville, WA, USA; [4]Alder BioPharmaceuticals, Inc., Bothell, WA, USA

Disclosures

Relevant: *Consultant, advisory board member, and/or has received honoraria:* Alder BioPharmaceuticals

Other: *Consultant, advisory board member, and/or has received honoraria:* Allergan, American Academy of Neurology, American Headache Society, Amgen, Avanir Pharmaceuticals, Biohaven Pharmaceuticals, Dr. Reddy's Laboratories, electroCore Medical, Eli Lilly, eNeura Therapeutics, GlaxoSmithKline, Merck, Pernix, Pfizer, Teva Pharmaceuticals, Trigemina, Vector, Vedanta; *Stock or stock options:* Biohaven Pharmaceuticals; *Research support:* Allergan, Amgen, Biohaven Pharmaceuticals, Dr. Reddy's, Migraine Research Foundation, National Headache Foundation.

Introduction

- Migraine is a disabling and costly neurological disorder characterized by episodic attacks of head pain and associated symptoms (e.g., nausea, photophobia, and phonophobia)[1]
- Typical endpoints for migraine preventive studies do not consider migraine associated and interictal symptoms or the patient's global impression of change (PGIC)
- In a randomized trial of eptinezumab in the preventive treatment of chronic migraine (CM), we assessed:
  - PGIC
  - Self-reported most bothersome migraine-associated symptom (MBS)

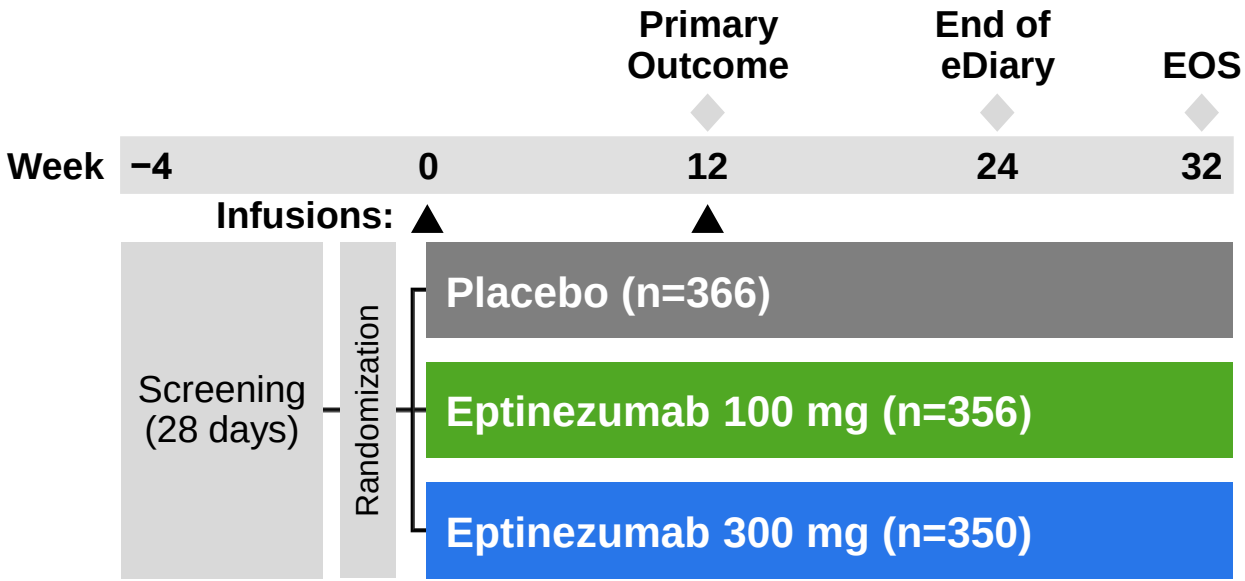
1. Headache Classification Committee of the IHS. *Cephalalgia*. 2013. doi: 10.1177/0333102413485658.

PROMISE-2: phase 3, multicenter, parallel-group, double-blind, randomized, placebo-controlled trial (NCT02974153)

Eptinezumab (ALD403) is an IgG1 anti-CGRP monoclonal antibody administered quarterly by IV infusion, providing 100% bioavailability at the end of infusion

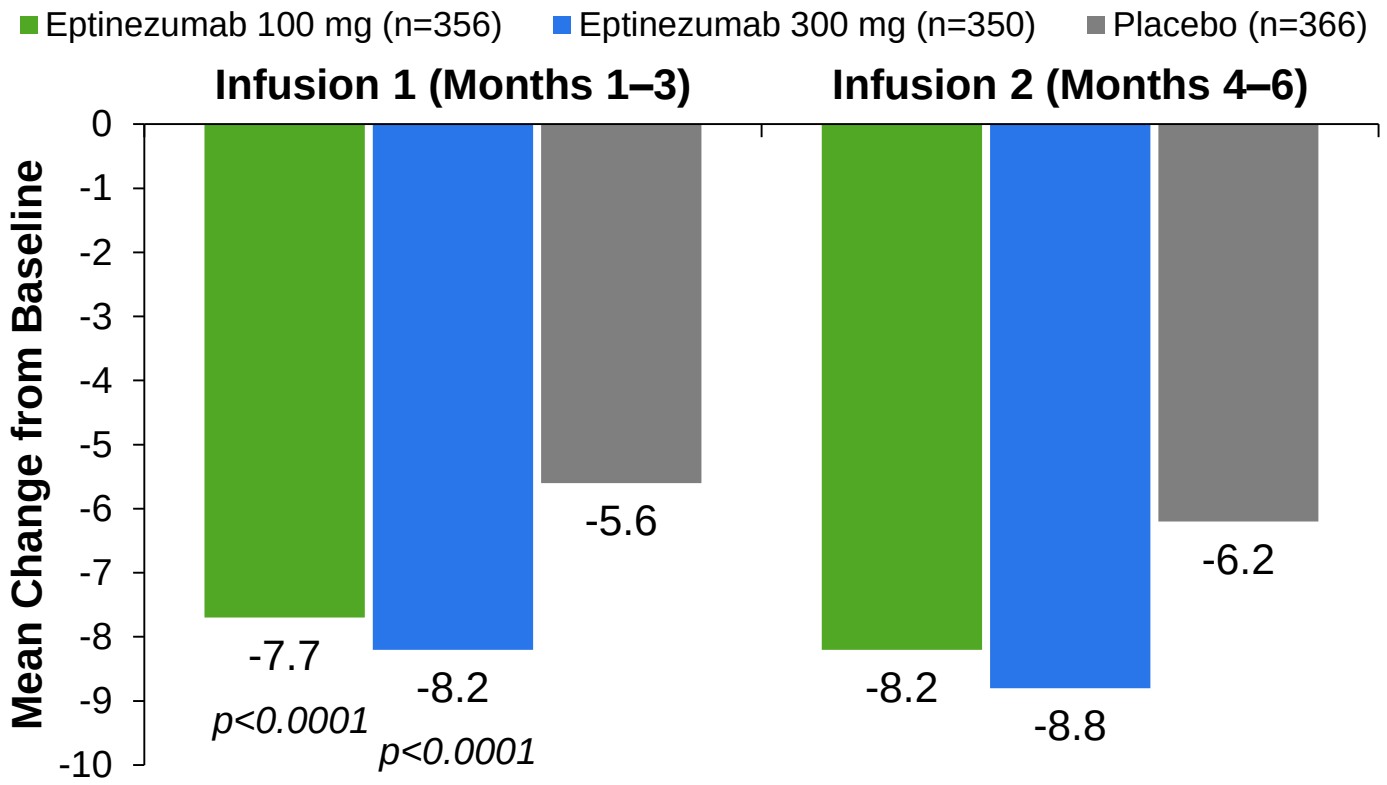
Inclusion/Exclusion Criteria

- Patients aged 18–65 yrs
- Diagnosis of migraine (ICHD-3β) at age ≤50 yrs
- 15–26 headache days/month, including ≥8 migraine days/month in previous 12 months and during screening period
- No use of botulinum toxin for any indication within 4 months prior to screening and during the screening period



EOS, end of study

Eptinezumab significantly reduced MMDs across Months 1–3 (primary endpoint), with further reductions after an additional infusion



MMDs, monthly migraine days. Months 4–6 not included in prespecified statistical algorithm (p<0.0001 vs placebo, post hoc)

Patients were asked to designate their MBS at screening from a predefined list

Patients, n (%)	**Eptinezumab 100 mg** n=356	**Eptinezumab 300 mg** n=350	**Placebo** n=366
Light sensitivity	64 (18.0%)	63 (18.0%)	66 (18.0%)
Nausea	48 (13.5%)	38 (10.9%)	52 (14.2%)
Pain with activity	52 (14.6%)	44 (12.6%)	49 (13.4%)
Sound sensitivity	19 (5.3%)	27 (7.7%)	26 (7.1%)
Mental cloudiness	11 (3.1%)	10 (2.9%)	6 (1.6%)
Vomiting	7 (2.0%)	8 (2.3%)	9 (2.5%)
Fatigue	7 (2.0%)	11 (3.1%)	7 (1.9%)
Mood changes	5 (1.4%)	3 (<1%)	2 (<1%)
Other	143 (40.2%)	146 (41.7%)	149 (40.7%)

MBS in clinical trials for acute migraine treatment is generally limited to nausea (with or without vomiting), photophobia, or phonophobia[1]

1. FDA Guidance for Industry. February 2018. Available at https://www.fda.gov/downloads/drugs/guidances/ucm419465.pdf

MBS and PGIC were captured at similar time points and measured with identical scales

Most Bothersome Symptom

- Identified from a predefined list at screening
- Patients rated the change (improvement or worsening since the start of the study) in this symptom every month beginning with Day 0

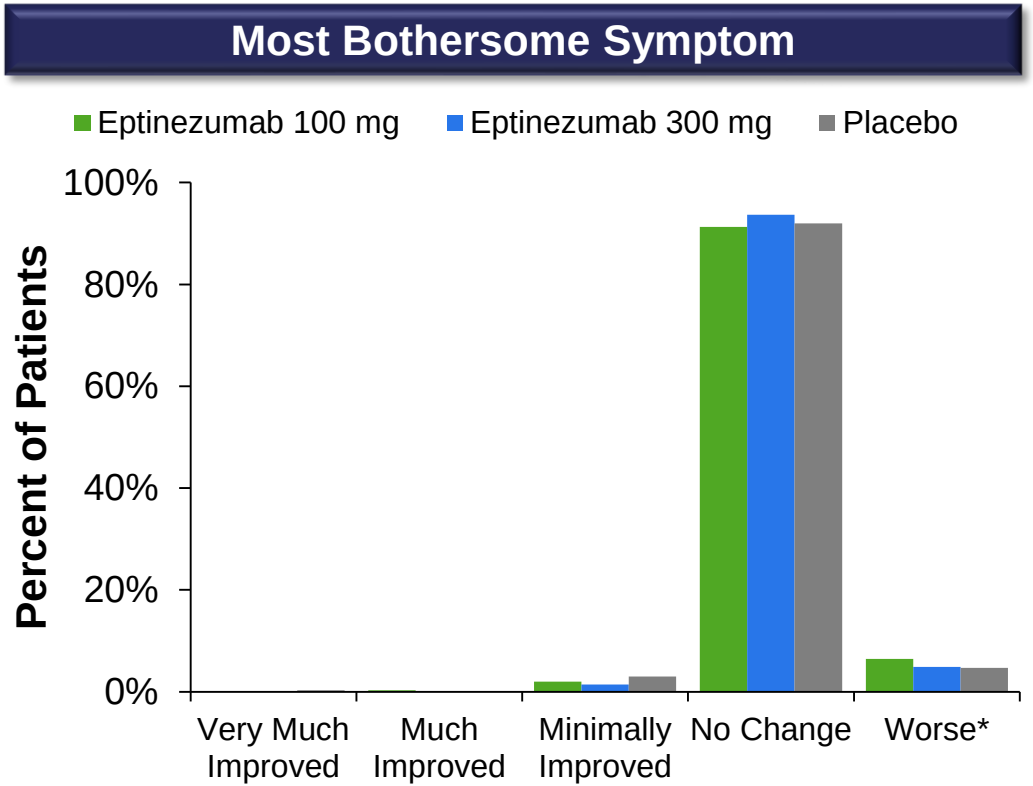
Patient Global Impression of Change

- Captured every month beginning with Month 1
- Comprises a single question concerning the patient's impression of the overall change in their disease status since the start of the study

Rated using an identical 7-point scale:

Very Much Improved	Much Improved	Minimally Improved	No Change	Minimally Worse	Much Worse	Very Much Worse

MBS assessment after the 28-day run in period reveals stability

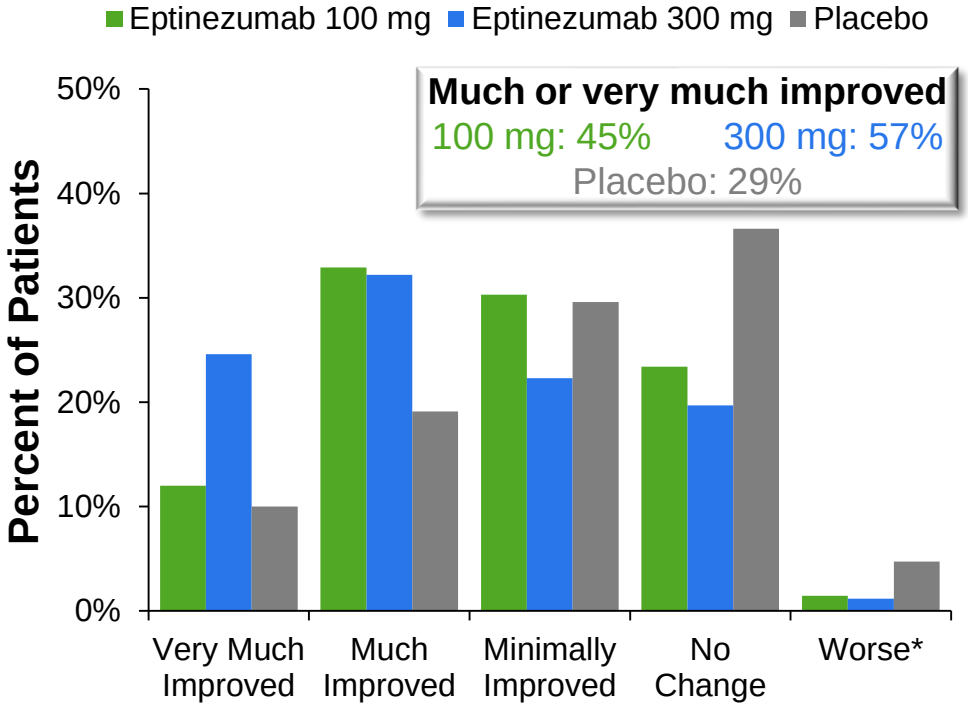


- At Day 0 (prior to treatment), >90% of patients in each treatment group indicated “no change” in their MBS for the 28-day baseline period
- If change in MBS was indicated, it was primarily minimal

*Worse includes “minimally worse”, “much worse”, and “very much worse”

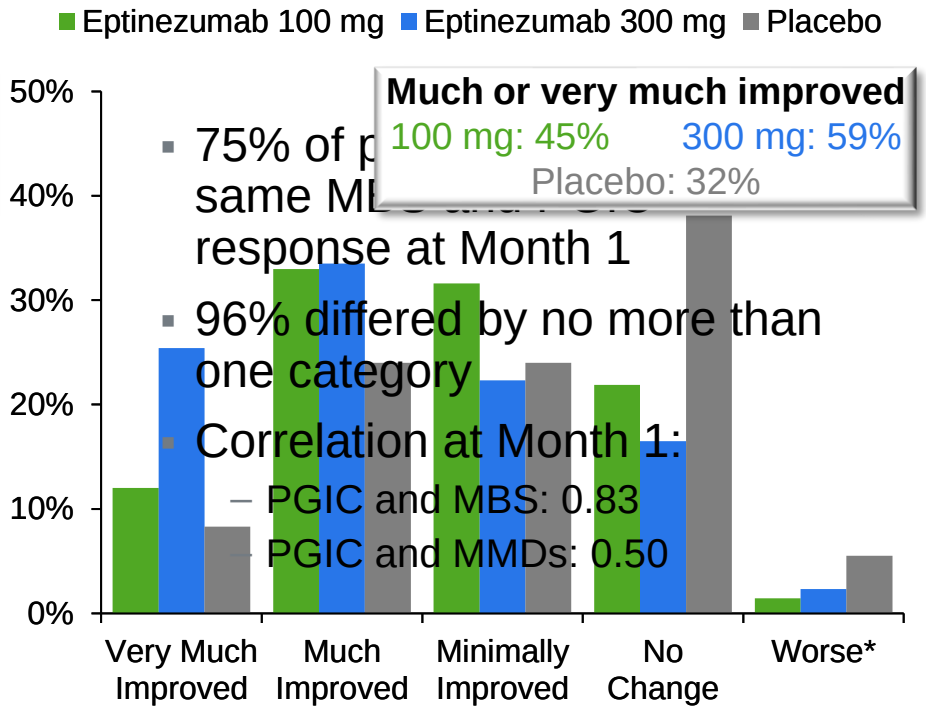
Most eptinezumab-treated patients (75%–82%) indicated some level of improvement by Month 1 after treatment vs placebo (56%–59%)

Most Bothersome Symptom



*Worse includes “minimally worse”, “much worse”, and “very much worse”

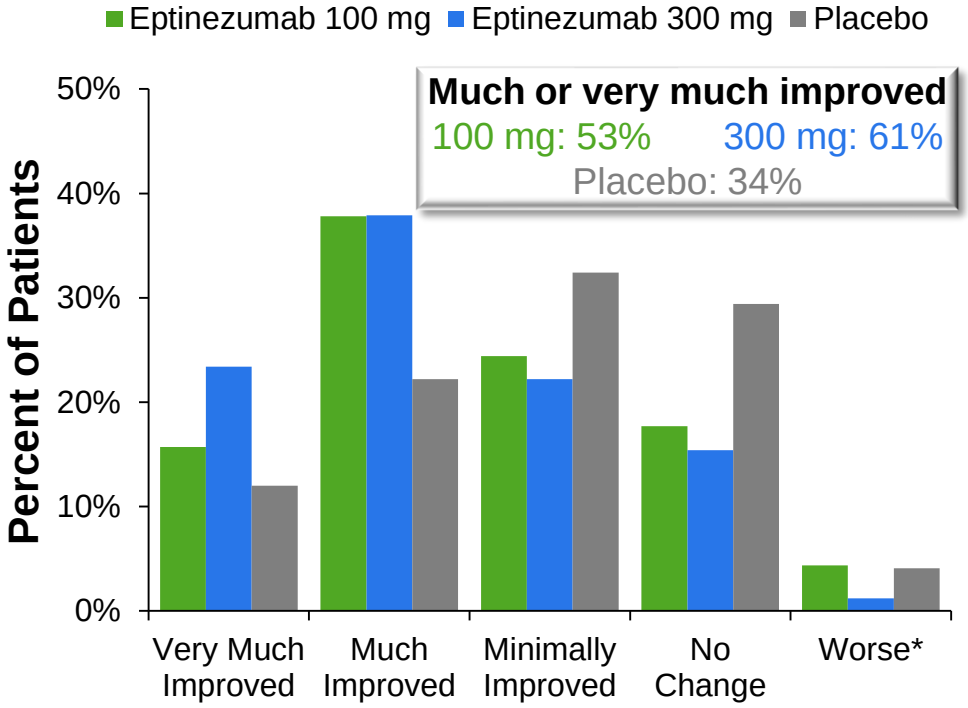
Patient Global Impression of Change



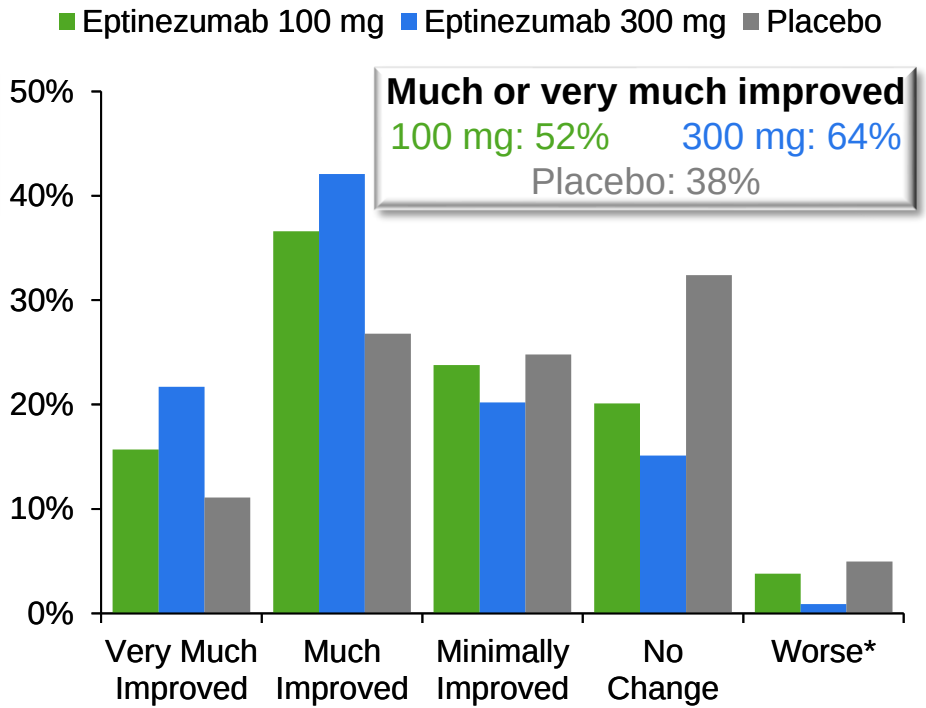
- 75% of p… same MB… response at Month 1
- 96% differed by no more than one category
- Correlation at Month 1:
  - PGIC and MBS: 0.83
  - PGIC and MMDs: 0.50

Ratings of improvement were similar by Month 3 (end of 1st infusion), with ~40% of placebo-treated experiencing no change or worsening

Most Bothersome Symptom



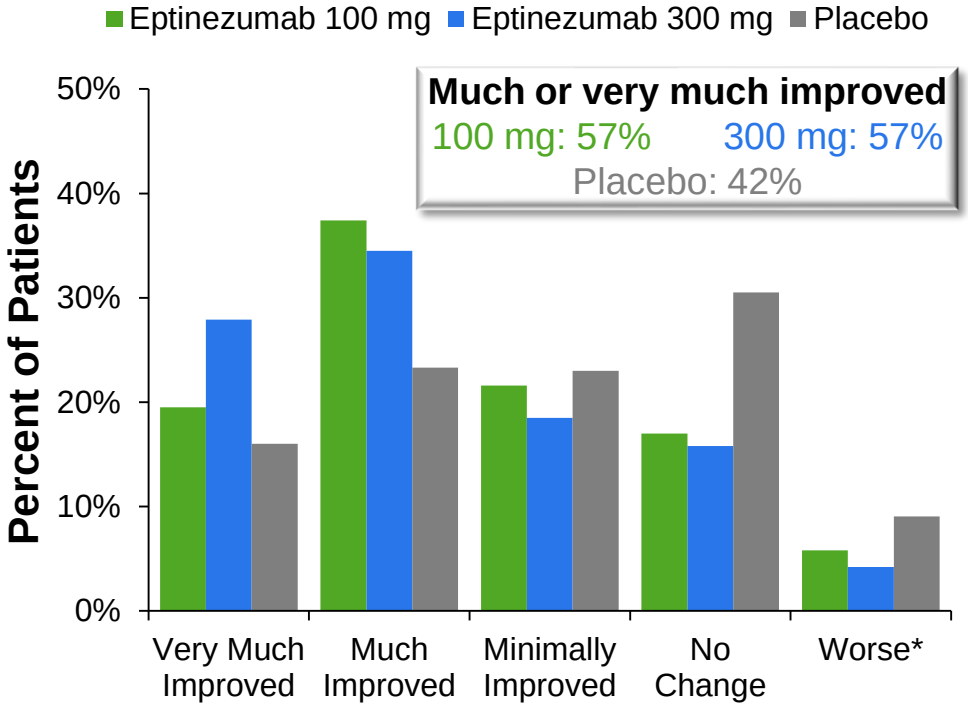
Patient Global Impression of Change



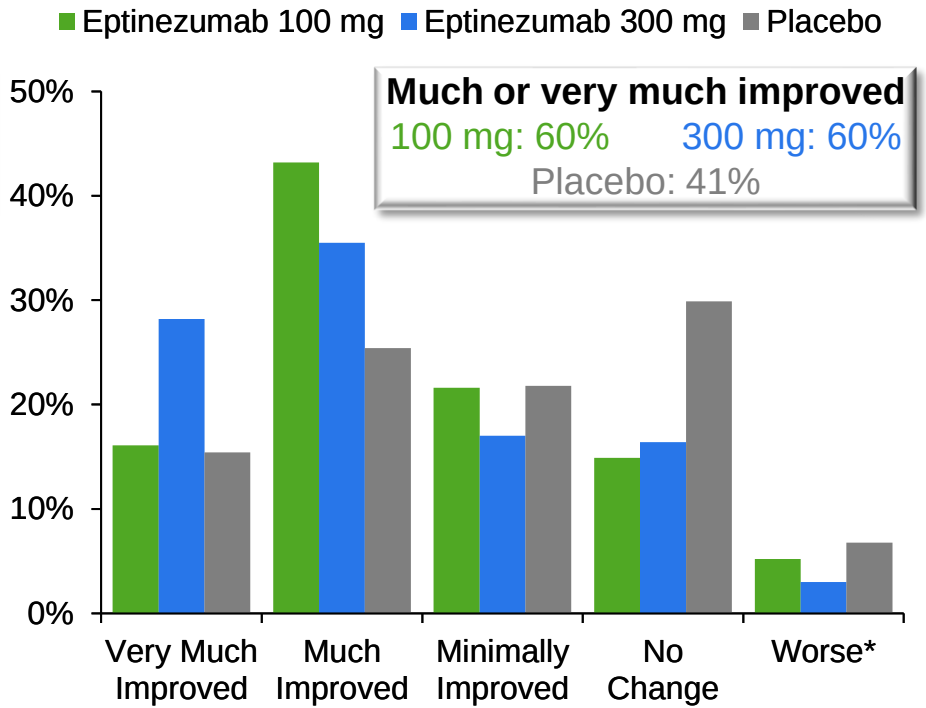
*Worse includes “minimally worse”, “much worse”, and “very much worse”

At Month 6 (end of 2nd infusion), ~80% of eptinezumab-treated patients indicated ≥1 categorical level of improvement in MBS and PGIC

Most Bothersome Symptom



Patient Global Impression of Change



*Worse includes “minimally worse”, “much worse”, and “very much worse”

Conclusions

- Improvements in both MBS and PGIC were apparent by Month 1 and were sustained or increased through 2 quarterly infusions to 6 months
- The distribution of ratings for MBS improvement and PGIC were similar across time points, suggesting that the two identically-rated measures in patients with chronic migraine move in parallel
- These data suggest that improvements in non-headache migraine symptoms experienced with CM are highly correlated with patients' perception of an improved disease status