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Eptinezumab Demonstrated Early and Sustained Reductions in HIT-6 Total and Item Scores Over Time in Patients With Chronic Migraine in the PROMISE-2 Trial

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KEY POINTS

- Longitudinal modeling was applied to HIT-6 data from PROMISE-2 in order to determine whether the effect of eptinezumab on headache-related impact on daily functioning occurred early during treatment and if that effect was sustained over continued treatment.
- Eptinezumab 100 mg and 300 mg were associated with greater decreases in headache-related impact on daily functioning—as measured by HIT-6 total and item scores—over the first month of treatment compared with placebo, with improvements generally stable over 8 months.

CONCLUSIONS

- The stability of the reductions in HIT-6 total and item scores over Months 1–8 suggest that early treatment response may provide longer-term benefits to patients' everyday functioning across a variety of impact areas.
  - At all post-baseline time points, the mean change in the HIT-6 total scores in the eptinezumab groups met the threshold for clinically meaningful change.
- By focusing on item-level information, the current study provided novel insights regarding how eptinezumab relates to a variety of specific migraine impact areas, which are relevant to clinical practice.

Introduction

- Migraine broadly impacts daily life, with negative effects on activities related to occupational, academic, social, familial, and personal roles.[1-3]
- Migraine preventive treatment has many goals, including the reduction of headache and migraine frequency and the reduction of their negative impact on daily life and functioning.[4]
- Eptinezumab is an intravenously administered monoclonal antibody that inhibits calcitonin gene-related peptide and is indicated for the preventive treatment of migraine in adults.[5]
- Eptinezumab significantly reduced monthly migraine frequency vs placebo in patients with chronic migraine in the phase 3, randomized, double-blind, placebo-controlled, parallel-group PROMISE-2 study.[6]

Objective

- To describe the effect of eptinezumab on headache-related impact on daily functioning, as measured by short-form Headache Impact Test (HIT-6) total and item scores, in patients with chronic migraine in the PROMISE-2 study

Methods

- The HIT-6 is intended to measure the impact of headache on the daily lives of individuals **(Table 1)**.[7,8]
- Total score:
  - Potential range: 36–78
  - Greater scores indicative of greater life impact
  - Reduction of ≥6 points considered clinically meaningful[3]
- Item scores simplified to:
  - 1 = never
  - 2 = rarely
  - 3 = sometimes
  - 4 = very often
  - 5 = always
- HIT-6 data came from PROMISE-2 (NCT0297153) **(Figure 1)**.[6]
- The HIT-6 was administered at baseline and at Months 1, 3, 4, 6, and 8.
- This analysis examined longitudinal changes from baseline **(Figure 2)**.
- The ANCOVA model controlled for stratification factors of migraine days during the screening period (<17 vs ≥17 days) and previous prophylactic medication use (yes vs no).
- All *P* values are descriptive (post hoc analyses).

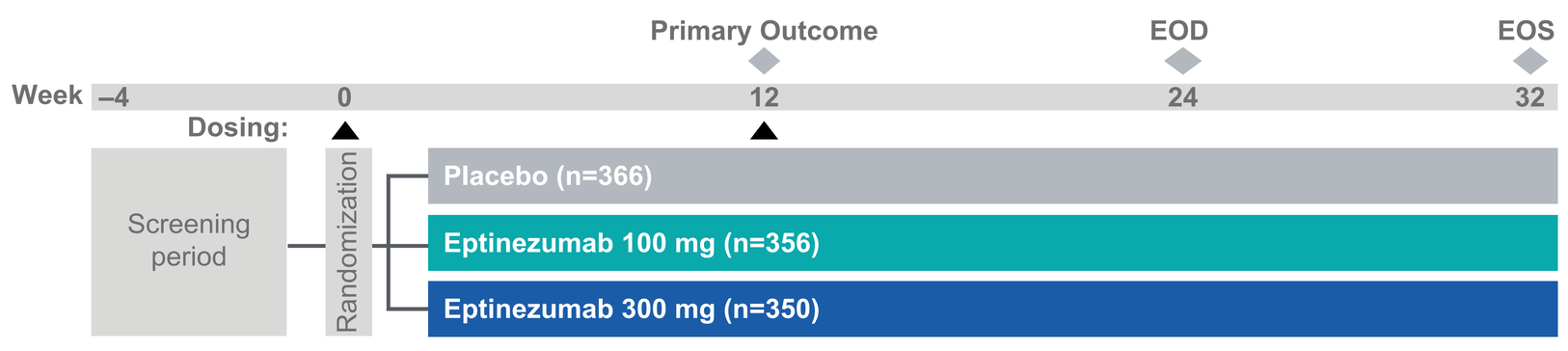
Results

- Baseline headache impairment was similar across treatment groups.
- Total scores decreased from baseline to Month 1 in all 3 groups (*P*<0.0001 vs baseline); reductions with eptinezumab were significantly greater than with placebo (*P*<0.0001 vs placebo) **(Figure 3)**.
- From Month 1 to 8, all groups demonstrated stable HIT-6 total scores, with eptinezumab scores lower than placebo at all time points (*P*<0.05 vs placebo).
- Scores for all individual HIT-6 items declined from baseline to Month 1 in all treatment groups; reductions with eptinezumab were significantly greater than with placebo (*P*<0.01 vs placebo) **(Figure 4)**.
- For all groups, item scores were generally stable from Month 1 to 8.

Table 1. Items of the HIT-6

Item 1	When you have headaches, how often is the pain severe?
Item 2	How often do headaches limit your ability to do usual activities including household work, work, school, or social activities?
Item 3	When you have a headache, how often do you wish you could lie down?
Item 4	In the past 4 weeks, how often have you felt too tired to do work or daily activities because of your headaches?
Item 5	In the past 4 weeks, how often have you felt fed up or irritated because of your headaches?
Item 6	In the past 4 weeks, how often did headaches limit your ability to concentrate on work or daily activities?

Figure 1. PROMISE-2 Study Design



EOD, end of eDiary; EOS, end of study

Figure 2. Post hoc Two-Piece Linear Mixed-Effects Model

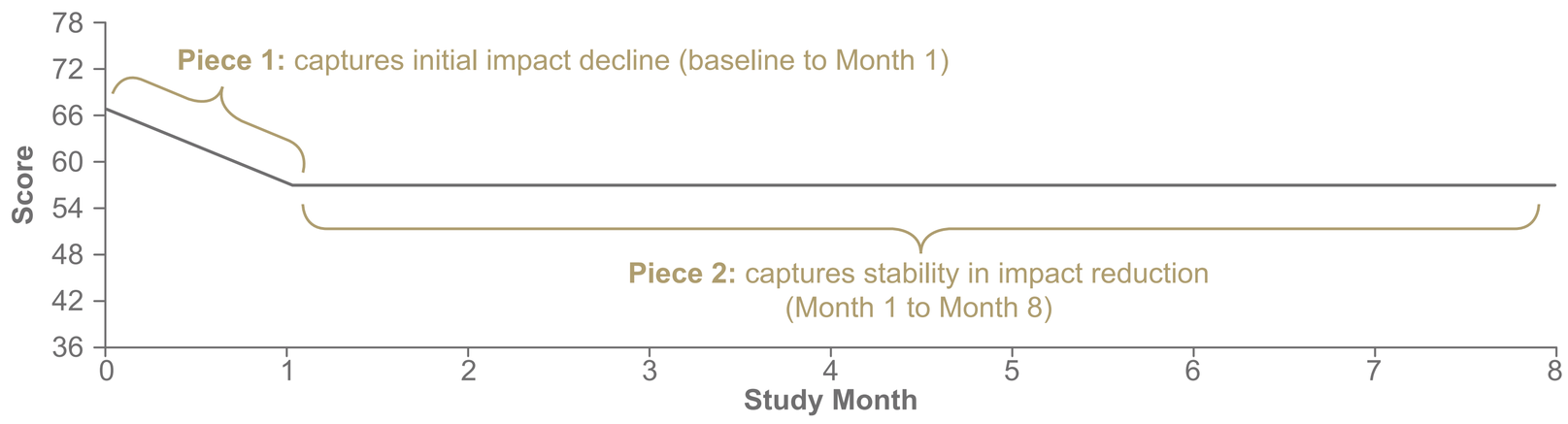
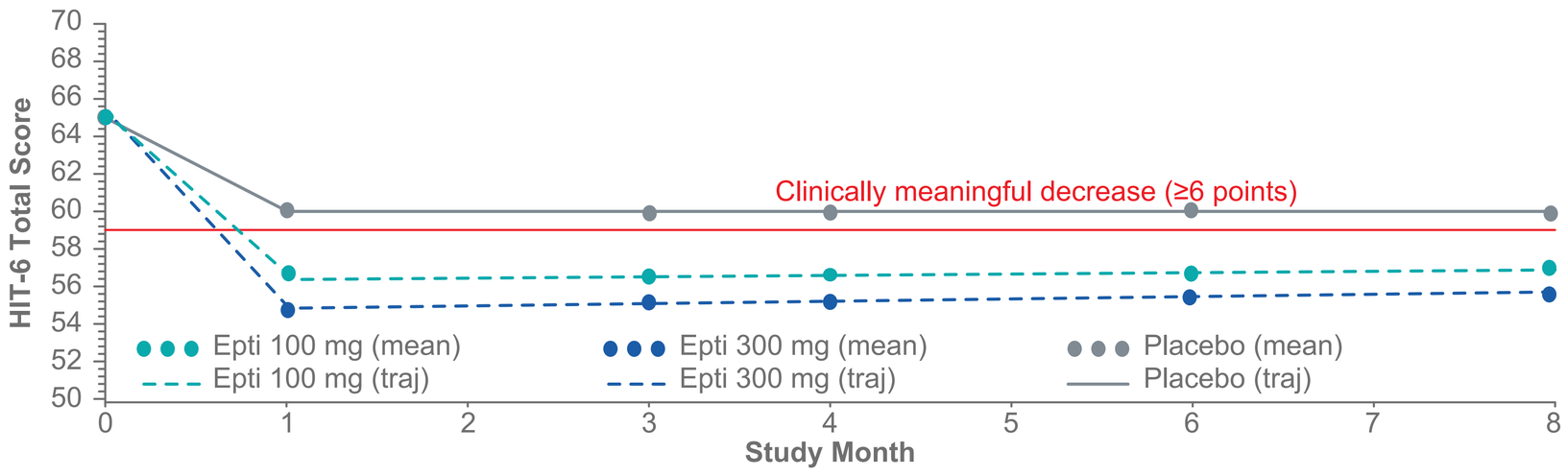
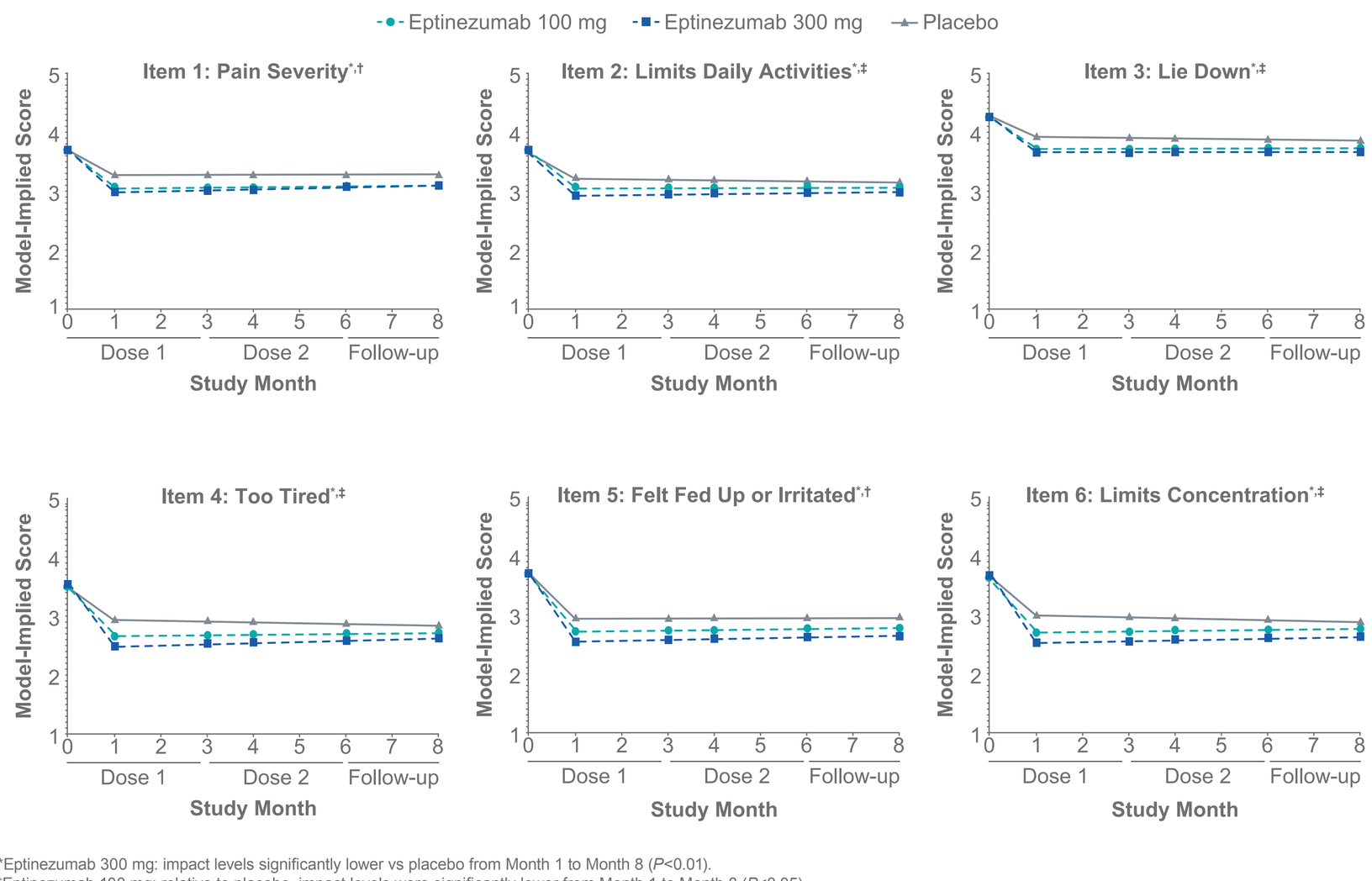


Figure 3. HIT-6 Total Score: Model-Implied Treatment Differences (Lines) Overlaying Observed Mean Values (Dots)



Model-implied treatment differences (lines) overlaying observed mean values (dots). Red line indicates an approximate 6-point mean decrease from baseline (clinically meaningful change threshold). Epti, eptinezumab; traj, model-implied trajectory.

Figure 4. HIT-6 Item Scores: Model-Implied Treatment Differences Over Time



*Eptinezumab 300 mg: impact levels significantly lower vs placebo from Month 1 to Month 8 (*P*<0.01).
†Eptinezumab 100 mg: relative to placebo, impact levels were significantly lower from Month 1 to Month 8 (*P*<0.05).
‡Eptinezumab 100 mg: relative to placebo, impact levels were significantly lower from Month 1 to Month 6 (*P*<0.05).

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