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Novel Method of Adjustment for Heterogeneous Routes of Administration Within a Cost-Effectiveness Analysis: A Case Study in Migraine

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KEY POINTS

- Medications approved for the preventive treatment of migraine have different routes of administration (ROA).
- Placebo (PBO) effects due to ROA are important to consider when comparing effectiveness of different medications.
- A method for addressing the different PBO effects associated with migraine treatment ROAs (intravenous [IV], intramuscular [IM], and subcutaneous [SC]) and application to a network meta-analysis (NMA) of migraine outcomes are described.

CONCLUSIONS

- This study demonstrated the potential importance of the difference in PBO effects due to ROA observed in clinical trials of comparative effectiveness outcomes.
- Consideration of PBO ROA differences could have substantial effects on payer assessments and allocation of limited healthcare resources.
- Additional research regarding PBO effects due to ROA on treatment outcomes and appropriate incorporation into economic evaluations are required.

Introduction

- Eptinezumab,[1] onabotulinum toxin A,[2] erenumab,[3] fremanezumab,[4] and galcanezumab[5] are approved for the preventive treatment of migraine but have different ROAs.
- Comparison of the effectiveness of approved treatments for migraine prevention via NMA should account for differences related to PBO ROA.
  - PBO effects have been shown to influence outcomes in migraine and pain studies.[6,7]
  - Studies of migraine and osteoarthritis pain have shown that differences in PBO ROA can affect treatment outcomes.[8,9]
- For adequate comparisons of migraine treatments (eg, for cost-utility models that compare to no intervention), methods to estimate differences based on contribution of PBO response are needed.

Objective

- To develop an NMA to compare the change in monthly migraine days that adjusts for ROA PBO effects

Methods

- An NMA evaluated the consequences of ROA PBO effect adjustment (vs no adjustment) on monthly migraine days outcomes at 4 and 12 weeks.
- Randomized clinical trials of preventive treatments for patients with chronic migraine were identified by literature review.
- Adjustments to the clinical trial data for PBO effects due to ROA were modeled using a 2-step approach **(Figure 1)**.
  - The effect of PBO adjustment on observed outcomes was modeled as the additive effect of PBO and treatment.

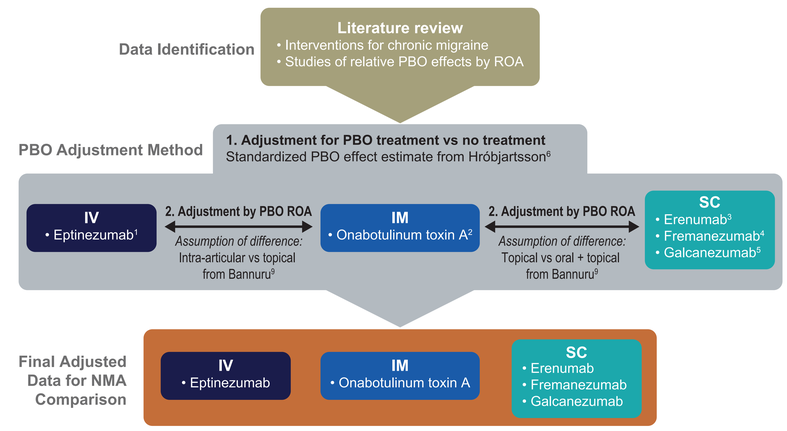
Results

- PBO adjustment by ROA resulted in improved treatment effects (ie, reductions in mean monthly migraine days vs unadjusted) with IV (eptinezumab) and IM (onabotulinum toxin A) treatments **(Figure 2)**.
- Decreased treatment effects (ie, increases in mean monthly migraine days vs unadjusted) were noted for all SC treatments.

Limitations

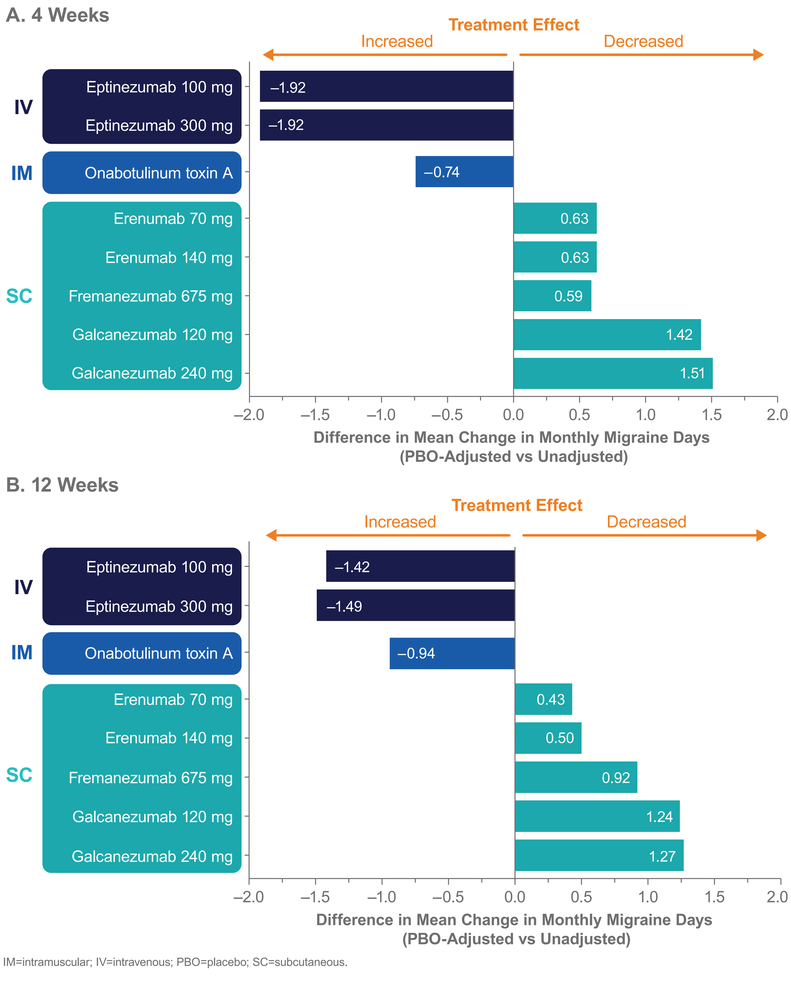
- This study relied on the assumption that ROA PBO relative effects (oral, topical, and intra-articular) identified in an osteoarthritis study are applicable to migraine data and associated ROA (IV, IM, and SC), but there is no empirical basis for this assumption.
- Limited studies were available to examine the IV ROA.

Figure 1. Approach to Adjusting for PBO Effects by ROA



IM=intramuscular; IV=intravenous; NMA=network meta-analyses; PBO=placebo; ROA=route of administration; SC=subcutaneous.

Figure 2. Effect of PBO Adjustment on Treatment Effects



IM=intramuscular; IV=intravenous; PBO=placebo; SC=subcutaneous.

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