Erenumab Versus Topiramate for the Prevention of Migraine: Results of a Randomized Active-controlled Double-dummy Trial

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One Sentence Summary: HER-MES is the first and largest randomized controlled study that directly compared an antibody targeting the CGRP pathway (erenumab) to a standard of care preventive migraine treatment (topiramate). The study demonstrated superior tolerability profile and a significantly higher efficacy of erenumab versus topiramate.

Background: Migraine is one of the most common causes of disability worldwide. In 2018, the US Food and Drug Administration and European Medicines Agency approved erenumab (erenumab-aooe in the US), a fully human monoclonal antibody binding to the calcitonin gene-related peptide (CGRP) receptor, as the first medication specifically developed for migraine prevention. HER-MES is the first **H**ead-to-head study of **E**renumab against topi**R**amate-**M**igraine study to assess tolerability and efficacy in a pati**E**nt-centered **S**etting (NCT03828539).

Methods: HER-MES was a randomized, multicenter, controlled trial in a German cohort of 777 adult migraine patients with at least 4 monthly migraine days (MMD). The study comprised a

24-week double-blind, double-dummy treatment epoch (DBTE) in which patients received (1) either erenumab 70 mg or 140 mg monthly subcutaneous (investigator's choice) and an oral placebo or (2) a subcutaneous placebo and the maximally tolerated dose of oral topiramate (50-100 mg/daily; control group). The primary endpoint of tolerability was assessed by the rate of treatment discontinuation due to adverse events (AEs). The secondary endpoint addressing efficacy was assessed by the proportion of patients achieving at least a 50% reduction from baseline MMD over months 4, 5 and 6 of the DBTE.

Results: Both primary and secondary endpoints were met, showing a significant difference between erenumab and topiramate. During the DBTE 10.6% of patients receiving erenumab and 38.9% of patients receiving topiramate discontinued the study treatment due to AEs. Additionally, the 50% responder rate was significantly higher for erenumab compared to topiramate.

Conclusion: The results of this first head-to-head trial of a therapy targeting the CGRP pathway compared to a preventive standard-of-care therapy will provide guidance to inform clinical decision-making for the preventive treatment of migraine.

Funding: This study was funded by Novartis. Erenumab is co-developed by Amgen and Novartis.

MLR ID (128609)