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The Safety and Efficacy of Dual Calcitonin Gene-Related Peptide Therapies for Migraine Treatment

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Objective
To assess the safety and efficacy of dual CGRP therapies.

Background
Although singular regimens of calcitonin gene-related peptide (CGRP) medications are shown to be effective in treating migraines, a considerable number of patients continue to experience suboptimal outcomes. Adding a second CGRP inhibitor could provide increased relief; however, limited research is available to support this practice.

Design/Methods
This retrospective chart review analyzed 67 patients diagnosed with episodic or chronic migraine and treated with two CGRP medications simultaneously between May 2018 and July 2023. The prescribed CGRP inhibitors were receptor monoclonal antibodies (erenumab), ligand monoclonal antibodies (fremanezumab, galcanezumab, and eptinezumab), or receptor small molecule antagonist (ubrogepant, rimegepant, and atogepant). Variables, including age of onset, current age, sex, race, ethnicity, baseline symptoms, and adverse events, were collected. Pre-treatment severity was reported by patients on a scale of 1-10, along with monthly headache frequency. They were compared to post-treatment results evaluated for 1 to 8 months.

Results
Of the 67 patients, 33 patients experienced a 14% average reduction in headache severity ($p = 4.4 \times 10^{-6}$), while 37 patients showed an average reduction of 5 days in monthly headache frequency ($p = 1.4 \times 10^{-6}$). No major adverse events were reported even when considering different mechanisms of action or whether the medications were used acutely or prophylactically. While statistically insignificant, dual-CGRP therapies involving small molecule antagonists are consistently associated with a lower incidence of adverse events compared to combinations with monoclonal antibodies only.

Conclusions
The observed reduction in headache severity and frequency suggests a dual blockade is beneficial for migraine symptom control in selected patients. Safety regarding this treatment option is also supported by these findings; specifically, the small molecule antagonists appear to be the safest option to include in dual regimens.