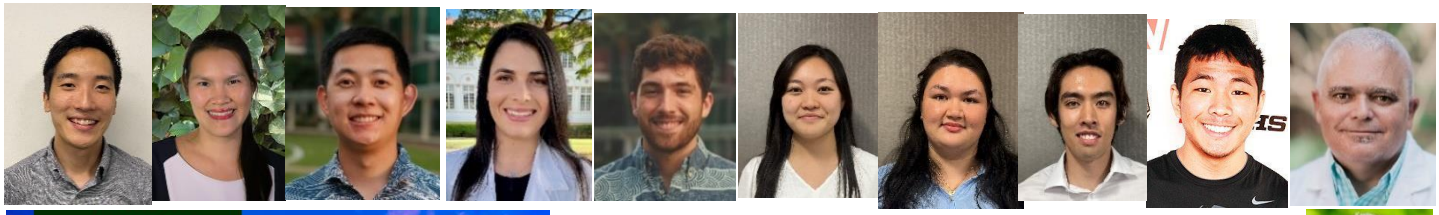

The Safety and Effectiveness of Dual Calcitonin Gene-Related Peptide (CGRP) Therapies for Migraine Treatment: Focus on Small Molecule Antagonist and Ligand Monoclonal Combinations

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Objective To assess the effects of dual-CGRP therapy on patients with synergistic use of small molecule antagonists (SMA) and ligand monoclonal antibodies (L-mAb).

Background Single CGRP regimens may not improve and could worsen migraine outcomes in some patients. Combining SMAs and L-mAbs targets CGRP molecules and receptors, potentially providing increased synergistic relief. Our study aims to garner evidence for this dual-CGRP approach.

Methods A retrospective matched cohort study at a neurological care center analyzed 90 chronic migraine patients aged ≥18 years treated with CGRP inhibitors (L-mAbs: fremanezumab, galcanezumab, eptinezumab; SMAs: ubrogepant, rimegepant, atogepant; or a combination). The study compared dual L-mAb and SMA CGRP treatments with mono-L-mAb or mono-SMA CGRP treatments, matched by age and sex. Variables included age, age at diagnosis, sex, onabotulinumtoxinA use, headache frequency, duration, severity, and associated symptoms before and three months post-treatment. Adverse events were recorded for the dual-treatment group. Statistical analyses were made using Wilcoxon, Kruskal-Wallis, and Fisher's exact tests, with significance set at < 0.05.

Results Patients on dual-CGRP therapy experienced an average reduction of four headache days, with some up to 14 fewer days, while mono-CGRP patients experienced no change ($p = 0.112$). Dual-CGRP therapy also reduced headache severity by 20% compared to a 10% reduction with mono-CGRP therapy ($p = 0.039$). Aura symptoms significantly improved in the dual-CGRP group, with 48% (13 patients) becoming aura-free compared to 20% in the mono-CGRP group ($p = 0.004$). Adverse events in the dual-CGRP group were mild, with three patients experiencing fatigue, drowsiness, or mild constipation. No serious adverse events or discontinuations were reported.

Conclusion Dual-CGRP regimens may enhance migraine symptom control by significantly reducing headache severity and aura symptoms without significant adverse events. These findings, however, need confirmation through randomized placebo-controlled clinical trials.