

LONG-TERM COMBINATION WITH ONABOTULINUMTOXINA AND ATOGEPANT TO ACHIEVE HIGHER STANDARDS OF MIGRAINE CONTROL: A 52-WEEK, PROSPECTIVE, REAL-WORLD EVALUATION (SYNERGY STUDY)

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Background. Patients with chronic migraine (CM) who remain inadequately controlled despite ongoing preventive monotherapy represent a particularly challenging population. Whether the clinical benefit achieved after adding a second preventive therapy can be maintained over the long term remains poorly understood. Herein, we evaluated the 52-week real-world effectiveness of onabotulinumtoxinA (BoNT-A) plus atogepant in the expanded SYNERGY study.

Methods. We prospectively analyzed 143 adults with CM receiving atogepant added to stable BoNT-A (prior exposure mean 11.8±6.7 months), regardless to prior anti-calcitonin gene-related peptide (CGRP) drugs exposure. Outcomes were assessed at baseline and weeks 12, 24, 36, and 52. Co-primary outcomes were change in monthly migraine days (MMDs) from baseline to week 52 and ≥50% MMDs response (RR50%). Secondary outcomes included monthly headache days (MHDs), acute medication days, HIT-6 and effectiveness using the IHS recommendations at 52 weeks. Sensitive analysis were performed including patients that discontinued treatment. All participants give written informed consent.

Results. Participants were mostly female (134/143, 93.7%, mean age±SD, 41.0±11.3) and 88/143 (61.5%) had prior anti-CGRP monoclonal antibody exposure. Baseline MHDs and MMDs were 22.9 ± 5.7 and 16.6 ± 6.6 days, respectively.At week 52, in the 115 patients completing the follow up, MMDs decreased to 8.2±5.8 days ($\chi^2(4)=199.5$, $p<0.001$), with reductions versus baseline at all time points (all $p<0.001$) and RR50% was achieved by 63/108 patients (58.3%). IHS-defined modest or optimal control was achieved by 21/108 (19.4%) and 27/108 (25.0%) individuals respectively. None achieved migraine freedom. In prior anti-CGRP monoclonal antibody failures (n=88), MMDs decreased from 16.7±6.9 to 8.8±6.1 days and RR50% was achieved by 37/67 (55.2%). Discontinuation increased from 8/143 (5.6%) at week 12 to 35/143 (24.5%) at week 52, mainly due to ineffectiveness.

Conclusions. Atogepant add-on to BoNT-A was associated with sustained MMDs reductions over 52 weeks. IHS categories showed that one quarter of subjects achieved optimal control, supporting long-term evaluation of combination prevention in CM with high residual migraine burden.