

SUSTAINED CLINICAL RESPONSE TO ATOGEPANT AFTER FAILURE OF FOUR ANTI-CGRP MONOCLONAL ANTIBODIES IN HIGHLY RESISTANT CHRONIC MIGRAINE

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Background. Chronic migraine (CM) resistant to multiple preventive therapies remains a major therapeutic challenge, particularly in patients with medication overuse headache (MOH) and psychiatric comorbidities. Although monoclonal antibodies (mAbs) targeting the calcitonin gene related peptide (CGRP) pathway have significantly improved migraine prevention, some patients show inadequate or transient responses. Atogepant may provide clinical benefit after mAb failure owing to their distinct pharmacological profile.

Methods. We report the case of a 51-year-old man with highly resistant CM, MOH, and psychiatric comorbidities, including anxiety disorder and mood disorder with obsessive compulsive features and dysphoric mood. Previous preventive treatments included topiramate, valproate, propranolol, flunarizine, amitriptyline, onabotulinumtoxinA, and four anti-CGRP mAbs (galcanezumab, fremanezumab, erenumab, and eptinezumab), all with inadequate efficacy. Peripheral nerve blocks, repetitive transcranial magnetic stimulation, behavioral therapies, and medical cannabis were also unsuccessful. Eptinezumab (October 2024–July 2025) produced only partial and transient benefit. From August 2025, migraine frequency progressively worsened, with near-daily attacks and severe disability (MIDAS 90). Atogepant 60 mg once daily was initiated in October 2025. Outcomes included monthly migraine days (MMDs), pain intensity (Numerical Rating Scale, NRS), MIDAS score, and acute medication use.

Results. At baseline, the patient reported 28 MMDs, severe disability (MIDAS 90), and triptan use on 15 days/month, consistent with MOH. After three months of atogepant, MMDs decreased to 9, mean pain intensity improved to 6/10, MIDAS score decreased to 30, and triptan use was reduced to 6 days/month. Treatment was well tolerated, with no adverse events. Clinical benefits were sustained throughout follow-up.

Conclusions. This case demonstrates the effectiveness of atogepant in a patient with highly resistant CM after failure of multiple preventive therapies, including four anti-CGRP mAbs. The observed clinical benefit may reflect its distinct mechanism of action, characterized by sustained intracellular inhibition of CGRP receptor signaling following receptor co-internalization. These findings suggest that switching to a gepant may represent an effective, mechanism-based strategy for patients with refractory CM, particularly in the presence of MOH and psychiatric comorbidities.