



Real-World Evidence of CGRP Dual Blockade: Clinical and Biomarker Insights From Combined Therapy in Chronic Migraine

Laura Marino¹, M. Lioi¹, M. Trimboli²

¹ Department of Neurology — Magna Graecia University — Catanzaro

² Institute of Neurology — AOU Renato Dulbecco — Catanzaro

Backgrounds and aims

Chronic migraine is a highly disabling condition, often refractory to conventional preventive treatments. OnabotulinumtoxinA (onabotA) and CGRP receptor antagonists act on complementary mechanisms and may exert synergistic effects when combined.

The objective of this study was to evaluate, in a real-world setting, the comparative efficacy and tolerability of atogepant, onabotulinumtoxinA, and their combination in refractory chronic migraine.

Materials and methods

This observational analysis included nine adult patients with refractory chronic migraine (ICHD-3). Patients received atogepant, onabotulinumtoxinA, or the combination of both. Clinical assessments were performed at baseline, 1 month, and 3 months.

Endpoints included monthly migraine and headache days, headache intensity (NRS), acute medication use, MIDAS and HIT-6. Statistical analysis was carried out with Type III ANOVA, considering $p < 0.05$ as significant.

Results

Preliminary Analysis of Nine patients with refractory chronic migraine indicates that all treatment groups showed clinical improvement over time. In patients treated with atogepant, a statistically significant reduction was observed in monthly headache days at 1 month compared with baseline, in MIDAS scores at 3 months, and in acute medication days at both 1 and 3 months. In the group receiving combination therapy (onabotulinumtoxinA + atogepant), a significant time×group interaction for HIT-6 ($p = 0.01$) was found, indicating a progressive and strengthening reduction in headache-related disability over time. Across all treatment groups, a general trend toward improvement in headache frequency, intensity, and impact was observed, more evident in the combination group at 3 months.

Outcome	Atogepant Baseline	Atogepant 1M	Atogepant 3M	onabotA Baseline	onabotA 1M	onabotA 3M	Atogepant + onabotA Baseline	Atogepant + onabotA 1M	Atogepant + onabotA 3M	Global p (Time×Group)
Monthly Migraine Days	9.2 ± 4.0	6.8 ± 3.3	5.8 ± 6.0	15.0 ± —	8.0 ± —	7.0 ± —	26.0 ± —	11.0 ± —	15.0 ± —	0.943
Monthly Headache Days	14.2 ± 5.1	9.8 ± 5.8	10.5 ± 8.2	15.0 ± —	12.0 ± —	15.0 ± —	4.0 ± —	7.0 ± —	2.0 ± —	0.702
Headache Intensity (NRS)	8.3 ± 1.0	7.3 ± 2.3	5.6 ± 2.5	10.0 ± —	8.0 ± —	5.0 ± —	10.0 ± —	8.0 ± —	8.0 ± —	0.732
MIDAS	134.0 ± 84.3	75.8 ± 56.8	42.6 ± 54.4	232.0 ± —	117.0 ± —	105.0 ± —	74.0 ± —	39.0 ± —	3.0 ± —	0.805
HIT-6	69.4 ± 6.3	63.0 ± 11.4	52.0 ± 22.2	68.0 ± —	63.0 ± —	54.0 ± —	69.0 ± —	22.0 ± —	76.0 ± —	0.01
Acute Medication Days	14.6 ± 6.1	7.5 ± 5.8	5.8 ± 5.1	15.0 ± —	7.0 ± —	10.0 ± —	26.0 ± —	11.0 ± —	15.0 ± —	0.762

Clinical outcomes over time in patients with chronic migraine treated with atogepant, onabotulinumtoxinA (onabotA), or their combination. Data are presented as mean ± SD; p-values refer to Time×Group interaction.

Discussion

These preliminary findings suggest that both atogepant and onabotulinumtoxinA are effective in reducing headache burden and disability in patients with refractory chronic migraine. The combination therapy showed the most consistent and progressive improvement, supporting the hypothesis of a synergistic effect through dual blockade of the CGRP pathway. Overall, the combination of onabotulinumtoxinA and atogepant appears to be a valid and effective therapeutic option for patients who remain refractory to standard monotherapies. Treatment was well tolerated, and no serious adverse events were reported.

Conclusions

This preliminary analysis provides real-world evidence supporting the potential of dual CGRP blockade as a promising therapeutic strategy for refractory chronic migraine. The study is ongoing and will enroll additional patients to increase statistical power and confirm these preliminary findings.

References

- Melo-Carrillo A, Strassman AM, Schain AJ, Adams AM, Brin MF, Burstein R. Combined onabotulinumtoxinA/atogepant treatment blocks activation/sensitization of high-threshold and wide-dynamic range neurons. *Cephalalgia*. 2021;41:17–32.
- Ashina M, Hansen JM, Do TP, et al. Migraine and the trigeminovascular system: 40 years and counting. *Lancet Neurol*. 2019.



24-28 Ottobre 2025
Padova Congress

55° CONGRESSO
SOCIETÀ ITALIANA
DI NEUROLOGIA