Impact of Atogepant on Migraine Headache Severity for the Preventive Treatment of Episodic Migraine: A Post-Hoc Analysis of the 12-Week ADVANCE and 52-Week Open-Label Trials

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OBJECTIVE

Evaluate the impact of atogepant 60 mg once daily (QD) on migraine headache day severity in participants with episodic migraine (EM)

CONCLUSIONS

Atogepant treatment reduced the mean number of monthly moderate to severe migraine headache days and mean pain severity of migraine headache days compared with placebo at all timepoints in the 12-week ADVANCE trial

Reductions in the mean number of monthly moderate to severe migraine headache days and mean pain severity of migraine headache days were consistent compared to baseline across 52 weeks in the long-term open-label trial

Atogepant was safe and well tolerated in both trials (previously reported[1,2])

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INTRODUCTION

- Atogepant is an oral, calcitonin gene-related peptide (CGRP) receptor antagonist approved for the preventive treatment of migraine[3,4]
- ADVANCE was a phase 3, randomized, double-blind, placebo-controlled, 12-week trial evaluating atogepant 60 mg QD for the preventive treatment of EM[1]
- The long-term trial was a phase 3, randomized, 52-week, open-label trial evaluating atogepant 60 mg QD for the preventive treatment of EM[2]
- This post-hoc analysis used clinical trial data from both trials to evaluate the impact of atogepant on migraine headache day severity

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2.Ashina M et al. Headache. 2023;63:79-88
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METHODS

Study Design and Participants

- This post hoc analysis included participants with EM from the 12-week ADVANCE trial and 52-week, open-label trial
  - Outcomes are presented for atogepant 60 mg QD dose and placebo (in ADVANCE)
- The modified intent-to-treat (mITT) population consisted of all randomized participants who received ≥1 dose of study intervention, had an evaluable baseline period of eDiary data, and had ≥1 evaluable post-baseline 4-week period of eDiary data during the double-blind or open-label treatment periods

Outcomes

- Change from baseline in the mean number of monthly moderate to severe migraine headache days
  - Migraine headache pain severity was defined as the worst pain intensity participants reported on any headache day with a scale of 1 (mild), 2 (moderate), and 3 (severe)
- Change from baseline in mean pain severity of migraine headache days
  - If the number of monthly migraine headache days at any post-baseline period were reduced from baseline, a pain severity score of 0 was imputed for the resolved migraine headache days

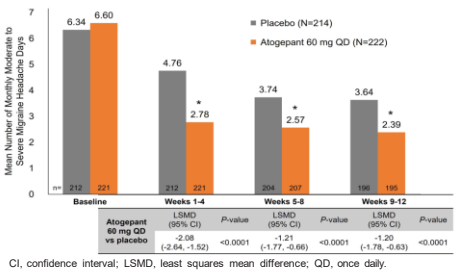
Statistical Analyses

- Atogepant vs placebo comparisons were analyzed using a mixed-effects model for repeated measures (MMRM) for change from baseline. The model includes baseline monthly moderate/severe migraine days as a covariate, prior exposure to migraine prevention medications (Y/N), treatment group and visit (month) as fixed factors, and treatment group-by-visit and baseline-by-visit as interaction terms, with an unstructured covariance matrix. *P*-values are from the test between the atogepant dose group and placebo

RESULTS

Moderate to Severe Migraine Headache Days (mITT Population)

Figure 1: Mean Number of Monthly Moderate to Severe Migraine Headache Days at Baseline and Weeks 1-4, 5-8, and 9-12 (ADVANCE)

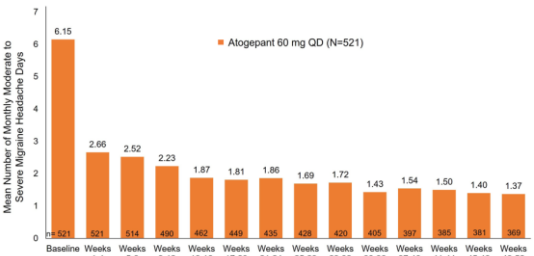


Atogepant 60 mg QD vs placebo	LSMD (95% CI)	*P*-value	LSMD (95% CI)	*P*-value	LSMD (95% CI)	*P*-value
	-2.08 (-2.64, -1.52)	<0.0001	-1.21 (-1.77, -0.66)	<0.0001	-1.20 (-1.78, -0.63)	<0.0001

CI, confidence interval; LSMD, least squares mean difference; QD, once daily.

- At Weeks 9–12 in ADVANCE, the number of monthly moderate to severe migraine headache days was reduced by 64% with atogepant treatment compared to baseline (vs. 43% reduction with placebo)

Figure 2: Mean Number of Monthly Moderate to Severe Migraine Headache Days at Baseline and 4-Week Intervals (52-Week Open-Label Trial)

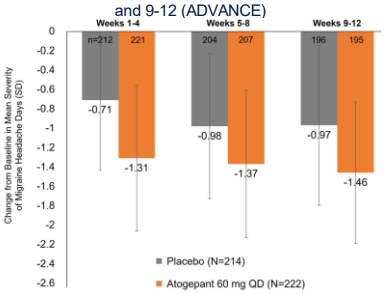


CI, confidence interval; LSMD, least squares mean difference; QD, once daily.

- In the open-label trial, the mean number of monthly moderate to severe migraine headache days was reduced by 57% at Weeks 1–4 compared to baseline, which improved to a 78% reduction at Weeks 49–52

Mean Pain Severity of Migraine Headache Days (mITT Population)

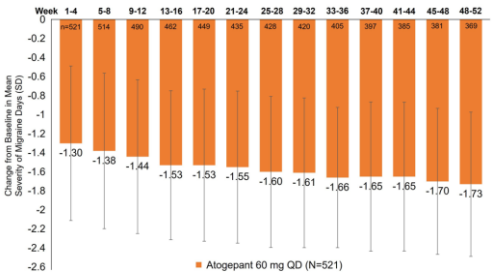
Figure 3: Change from Baseline in Mean Pain Severity of Migraine Headache Days, Including Resolved Migraine Days, at Weeks 1-4, 5-8, and 9-12 (ADVANCE)



SD, standard deviation; QD, once daily.

- Mean baseline (SD) in pain severity for placebo was 2.14 (0.40) and for atogepant, 2.15 (0.40)
- The change from baseline in mean pain severity of migraine headache days, including resolved days, was-1.46 for atogepant and -0.97 for placebo at Weeks 9-12

Figure 4: Change from Baseline in Mean Pain Severity of Migraine Headache Days, Including Resolved Migraine Days, at 4-Week Intervals (52-Week Open-Label Trial)



SD, standard deviation; QD, once daily.

- Mean baseline (SD) in pain severity was 2.17 (0.43)
- The change from baseline in mean pain severity of migraine headache days, including resolved days, was 1.30 at Weeks 1–4 and decreased to -1.73 at Weeks 49–52

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