Efficacy of Ubrogepant in the Acute Treatment of Migraine With Mild Pain vs Moderate or Severe Pain

Richard B. Lipton, MD, David W. Dodick, MD, Peter J. Goadsby, MD, et al.

Correspondence
Dr. Lipton
richard.lipton@einsteinmed.edu

Study Question
Does the treatment of migraine with ubrogepant when pain is mild vs moderate or severe increase the probability of freedom from pain, associated symptoms, and disability?

What Is Known and What This Paper Adds
Acute treatment trials require treatment of migraine when pain is moderate or severe, yet clinical guidance recommends treatment when pain is mild. The primary hypothesis was that treatment of migraine with ubrogepant when pain is mild would increase the likelihood of achieving positive outcomes, relative to treatment of moderate or severe pain, in adults with migraine. This trial provides Class III evidence that treatment of migraine with ubrogepant when pain is mild vs moderate or severe increases the likelihood of achieving pain freedom, absence of symptoms, and normal function within 2 hours postdose.

Methods
This was a post hoc analysis of a phase 3, open-label, dose-blinded, 52-week extension trial. Adults with migraine with or without aura were randomized (computer-generated) 1:1:1 to ubrogepant 50 mg, ubrogepant 100 mg, or usual care and treated up to 8 migraine attacks at any pain intensity every 4 weeks. Data for 19,291 treated attacks from 808 participants who were aged on average 42 years, majority female and White, were included. Efficacy outcomes (only collected for ubrogepant) included 2-hour pain freedom rates in attacks treated with mild vs moderate or severe pain. A generalized linear mixed model with binomial distribution and logit link function was used to perform subgroup comparisons based on all treated attacks. Each participant was treated as a random effect in the generalized linear regression model with the migraine attacks nested within participants.

Results and Study Limitations
At 2 hours postdose, rates of pain freedom were higher for attacks treated when pain was mild vs moderate or severe for ubrogepant 50 mg (47.1% vs 23.6%; adjusted odds ratio [95% CI]: 2.89 [2.57–3.24]) and ubrogepant 100 mg (55.2% vs 26.1%; 3.50 [3.12–3.92]; p < 0.001). Rates of 2-hour freedom from photophobia, phonophobia, and nausea were significantly higher after the treatment of mild vs moderate or severe pain (p < 0.001 all symptoms, both doses). A significantly higher proportion of treated attacks had normal function at 2 hours when treated while pain was mild vs moderate or severe for ubrogepant 50 mg (66.6% vs 34.3%; 3.83 [3.40–4.30]) and ubrogepant 100 mg (70.1% vs 37.2%; 3.95 [3.50–4.46]; p < 0.001 both doses). The most common adverse event was upper respiratory tract infection (~11% both doses). Serious adverse events were seen in 2% and 3% of ubrogepant 50 and 100 mg participants, respectively. Study limitations include absence of a placebo comparison and the open-label trial design.

Registration, Study Funding, and Competing Interests
This study (ClinicalTrials.gov, NCT02873221) was sponsored by AbbVie. The authors report competing interests. Go to Neurology.org/N for full disclosures.
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Neurology 2022;99:e1905-e1915 Published Online before print August 17, 2022
DOI 10.1212/WNL.00000000000201031

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