



# Oral Calcitonin Gene-related Peptide Antagonists: A painfully long name for the acute treatment of migraines.

## CLINICAL QUESTION

**What are the risks and benefits of ubrogepant for the acute treatment of episodic migraines?**

## BOTTOM LINE

**Ubrogepant is an oral calcitonin gene-related peptide (CGRP) antagonist approved for the acute treatment of episodic migraines. At 2 hours, ubrogepant is more effective than placebo for freedom from pain (21% versus 13%) or pain relief (61% versus 49%). Ubrogepant is well tolerated; safety in people with co-morbidities is unclear.**

## EVIDENCE

- Results statistically significant unless stated.
- 11 systematic reviews<sup>1-11</sup> of the same 2-3 industry-funded randomized controlled trials (RCTs).<sup>12-14</sup> Participants with 2-8 migraines/month (with or without aura) given ubrogepant or placebo for acute moderate-severe migraine.
  - Focusing on one systematic review<sup>1</sup> of all 3 RCTs (25-100mg) with usable ubrogepant results (3326 participants, ~24% on prophylaxis (non-CGRP):<sup>12,13</sup>
    - Pain free at 2 hours: 21% versus 13% (placebo).
      - No difference between 25, 50 and 100mg doses.
    - Relief at 2 hours (from moderate/severe pain to mild/no pain): 61% versus 49% (placebo)
    - Absence of the most bothersome symptom at 2 hours: 37% versus 28% (placebo).

- Normal functioning at 2 hours: 42% versus 32% (placebo).
  - Sustained pain relief at 24 hours: 37% versus 22% (placebo).
- Limitations: Single dose trials, industry funded.
- Other systematic reviews showed similar.<sup>2-11</sup>
- No difference in adverse events.<sup>1-3,7</sup> One systematic review<sup>3</sup> found more ear, nose and throat-related adverse events but no absolute numbers reported.
- A one-year, open-label RCT evaluated safety of ubrogepant versus usual care (1230 participants, 31968 doses).<sup>15</sup>
  - Discontinuation due to adverse events 2-3% with ubrogepant, similar to usual care. No statistical comparison.

## CONTEXT

- Ubrogepant (Ubrovelvy®) is the only CGRP antagonist approved in Canada for acute migraine treatment.<sup>16</sup> Costs ~\$15/dose.<sup>17</sup>
- No direct comparison available but triptans appear more effective [~30-40% pain free at 2 hours versus 21% (ubrogepant)].<sup>1,3,4,11,18</sup>
  - Response to ubrogepant independent from response to triptans.<sup>19,20</sup>
- Based on 1 RCT, ubrogepant likely effective at preventing headache when taken during prodrome [no moderate-severe headache at 24 hours: 46% versus 29% (placebo)].<sup>21</sup>
- Efficacy in chronic migraines,<sup>12,13</sup> role with concomitant prophylactic CGRP antagonists,<sup>22,23</sup> long-term safety,<sup>24,25</sup> safety in people with cardiovascular disease<sup>26,27</sup> unclear.

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