

Title

Navigating the Acute Migraine Treatment Landscape: Real-World Insights from the **Headache Assessment via a Digital platform in United States (HeAD-US)** Study

Ali Ezzati, Kristina Fanning, Alexandre Urani, François Cadiou, Richard B. Lipton

One sentence summary: This study using 2023 HeAD-US data revealed diverse treatment patterns in individuals with migraine, highlighting gepants' notable effectiveness, especially in patients who use prescription monotherapy.

Background: Individuals with migraine are commonly treated with a combination of acute and/or preventive therapies, and the success of these treatments can vary. Acute treatment has been transformed by the introduction of new classes of pharmacologic agents, particularly gepants. Data on current patterns of acute treatment are limited and often based on electronic health record, medical claims, and pharmacy data, which do not capture the patient voice. This study aims to assess treatment patterns and the efficacy of acute treatments in individuals with episodic migraine (EM, 3 groups based on monthly headache days (MHDs): 0-3, 4-7, 8-14) and chronic migraine (CM, ≥ 15 MHDs) using data collected directly from people living with migraine through a digital platform.

Methods: We used the cross-sectional 2023 data collected as part of the **Headache Assessment via a Digital Platform in the United States (HeAD-US)** Study. The HeAD-US is a cohort of adults with migraine surveyed through the Migraine Buddy application. Eligible participants self-reported a migraine diagnosis and met modified ICHD-3 criteria for migraine. All participants at baseline assessment were surveyed for sociodemographic information, headache features including severity and frequency, and use of acute and preventive treatments. The Migraine Treatment Optimization Questionnaire (mTOQ-4) was used to evaluate the effectiveness of acute treatment. Effective treatment was defined as moderate or maximum treatment efficacy score based on mTOQ-4 scores.

Results:

A total of 6810 participants were eligible for this study. Participants had an average age of 42.0 years (SD=13, range 18-88), 89.9% were female, 4317 (63.4%) met criteria for EM and 2493 (36.6%) met criteria for CM (Table 1). Of the participants, 52.1% were using acute over-the-counter (OTC) medications, 73.2% were using acute prescription medications, 2.3% were using medical devices, and 59.7% were on preventive treatments. There was no significant difference in treatment effectiveness between participants on polytherapy with two or more types of treatments (39.0%) and those on monotherapy (41.1%, $p=0.105$). Among the 2649 patients on monotherapy with acute medications, the most common categories were triptans (42.4%), OTCs (30.2%), and gepants (23.1%). For patients on prescription monotherapy, individuals using gepants reported the highest rate of effective treatment (55.3%) in head-to-head comparison with triptans (49.2%, $p=0.015$), barbiturates (31.6%, $p<0.001$), and opioids (18.8%, $p<0.001$) but not with ergots (37.5%, $p=0.085$). After classifying participants into EM and CM categories, gepants consistently demonstrated the highest rate of effective treatment in each category.

Conclusion: The HeAD-US study presents an opportunity to examine real-world treatment patterns and the effectiveness of each treatment, when used independently and in combination with other treatments. Patients

relying on monotherapy with treatments that are not migraine-specific may face an elevated risk of inadequate treatment.

Table 1. Sample characteristics for the entire sample and by episodic (EM) and chronic (CM) migraine groups.

| | EM | CM | Total |
|---|--------------|--------------|--------------|
| N (%) | 4317 | 2493 | 6810 |
| Age, Mean (SD) | 41.4 (12.9) | 42.4 (13.5) | 41.7 (13.1) |
| Female, Sex (%) | 3861 (89.4%) | 2258 (90.6%) | 6119 (89.9%) |
| Race, Whites (%) | 3664 (84.9%) | 2104 (84.4%) | 5768 (84.7%) |
| Using Preventive therapy, N (%) | 2254 (52.2%) | 1812 (72.7%) | 4066 (59.7%) |
| Not using acute RX/OTC or Preventive medications | 452 (10.5%) | 185 (7.4%) | 637 (9.4%) |
| Not using any acute Rx/OTC medication | 654 (15.1%) | 372 (14.9%) | 1026 (15.1%) |
| Acute medications use | | | |
| Any Acute Medication Treatment | 3663 (84.9%) | 2121 (81.1%) | 5784 (84.9%) |
| Acute Medication Mono Therapy | 1813 (42%) | 836 (33.5%) | 2649 (38.9%) |
| 2 or more acute medications | 1850 (42.9%) | 1285 (51.5%) | 3135 (46%) |
| Total Acute Medication Use | | | |
| OTCs (sold without prescription), such as Aspirin, Acetaminophen, ibuprofen, Excedrin | 2202 (51%) | 1349 (54.1%) | 3551 (52.1%) |
| Opioids, such as Hydrocodone, Vicodin, Oxycodone, OxyContin. | 154 (3.6%) | 194 (7.8%) | 348 (5.1%) |
| Barbiturates, such as Butalbital, Fiorinal | 198 (4.6%) | 189 (7.6%) | 387 (5.7%) |
| Ergots, derivative, e.g., (Dihydro)Ergotamine, Migergot, Cafergot, Migranal | 43 (1%) | 50 (2%) | 93 (1.4%) |
| Gepants, such as Ubrovelvy or Nurtec | 1108 (25.7%) | 855 (34.3%) | 1963 (28.8%) |
| Triptans, such as Zomig, Imitrex, Maxalt, Amerge, Relpax, Axert | 2216 (51.3%) | 1191 (47.8%) | 3407 (50%) |
| Mono Acute Medication Use | | | |
| Only OTC | 564 (31.1%) | 237 (28.3%) | 801 (30.2%) |
| Only Opioid | 12 (0.7%) | 20 (2.4%) | 32 (1.2%) |
| Only Barbiturate | 33 (1.8%) | 24 (2.9%) | 57 (2.2%) |
| Only Ergot | 12 (0.7%) | 12 (1.4%) | 24 (0.9%) |
| Only Triptan | 813 (44.8%) | 311 (37.2%) | 1124 (42.4%) |
| Only Gepant | 379 (20.9%) | 232 (27.8%) | 611 (23.1%) |
| Medical Device Use | | | |
| Total Medical Device | 61 (1.4%) | 98 (3.9%) | 159 (2.3%) |
| Cefaly | 39 (0.9%) | 63 (2.5%) | 102 (1.5%) |
| electroCore noninvasive vagus nerve stimulator (nVS)) | 2 (0%) | 4 (0.2%) | 6 (0.1%) |
| eNeura transcranial magnetic stimulation device (TMS) | 6 (0.1%) | 8 (0.3%) | 14 (0.2%) |
| Nerivio Armband | 22 (0.5%) | 32 (1.3%) | 54 (0.8%) |

Table 2. Headache Characteristics, Comorbidities, & Outcomes in Patients on Monotherapy for Migraine by Acute Medication Class

| | | OTC | Opioids/ Barbiturate | Triptans | Gepants | ANOVA | |
|---|--------------------|-------------|-------------------------|--------------|--------------|------------|--------|
| | | Mean (SD) | Mean (SD) | Mean (SD) | Mean (SD) | F | Sig. |
| Monthly Headache Days | | 10.2 (7.9) | 14.3 (8.8) | 10.8 (7.6) | 13 (8.2) | 46.652 | <0.001 |
| Migraine Symptom Severity Score | | 17.3 (3) | 18 (2.6) | 17.6 (2.8) | 17.8 (2.6) | 8.675 | <0.001 |
| | | N (%) | N (%) | N (%) | N (%) | Chi-Square | P |
| Disability (MIDAS) | None to Mild | 80 (9.9%) | 14 (6.7%) | 266 (9.6%) | 135 (6.9%) | 13.408 | 0.004 |
| | Moderate to Severe | 732 (90.1%) | 195 (93.3%) | 2510 (90.4%) | 1828 (93.1%) | | |
| Anxiety (PHQ-4) | Absent | 429 (52.8%) | 130 (62.2%) | 1648 (59.4%) | 1183 (60.3%) | 15.039 | 0.002 |
| | Present | 383 (47.2%) | 79 (37.8%) | 1128 (40.6%) | 780 (39.7%) | | |
| Depression (PHQ-4) | Absent | 561 (69.1%) | 132 (63.2%) | 2002 (72.1%) | 1423 (72.5%) | 10.92 | 0.012 |
| | Present | 251 (30.9%) | 77 (36.8%) | 774 (27.9%) | 540 (27.5%) | | |
| Monthly Headache Day Frequency | 0-3 | 180 (22.2%) | 21 (10%) | 434 (15.6%) | 226 (11.5%) | 146.285 | <0.001 |
| | 4-7 | 217 (26.7%) | 45 (21.5%) | 745 (26.8%) | 398 (20.3%) | | |
| | 8-14 | 174 (21.4%) | 32 (15.3%) | 695 (25%) | 484 (24.7%) | | |
| | ≥15 | 241 (29.7%) | 111 (53.1%) | 902 (32.5%) | 855 (43.6%) | | |
| Treatment efficacy - based on MTOQ-4 | Very Poor | 107 (13.2%) | 20 (9.6%) | 179 (6.4%) | 127 (6.5%) | 123.092 | <0.001 |
| | Poor | 483 (59.5%) | 136 (65.1%) | 1403 (50.5%) | 986 (50.2%) | | |
| | Moderate | 153 (18.8%) | 35 (16.7%) | 738 (26.6%) | 496 (25.3%) | | |
| | Maximum | 69 (8.5%) | 18 (8.6%) | 456 (16.4%) | 354 (18%) | | |
| Note. OTC = Over the counter; MIDAS = Migraine Disability Assessment, Grades 3 and 4 are categorized as moderate to severe disability; PHQ: Patient Health Questionnaire; MTOQ = Medication Treatment Questionnaire. | | | | | | | |