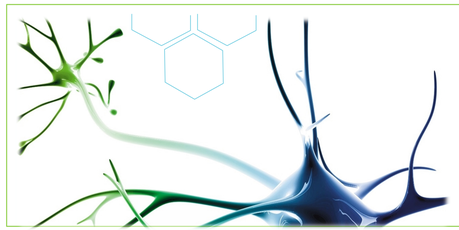


Long-term Rimegepant for the Acute Treatment of Migraine Reduces Use of Analgesics and Antiemetics

David Kudrow, MD[1]; William T. Seidel, PhD[2]; Kate Mullin, MD[3]; Gary Berman, MD[4]; Richard B. Lipton, MD[5,6]; Alexandra Thiry, PhD[2]; Robert Croop, MD[2]; Meghan Lovegren, BS[2]; Vladimir Coric, MD[2]; Christopher M. Jensen, PharmD[2]

1 California Medical Clinic for Headache, Santa Monica, CA, USA; 2 Biohaven Pharmaceuticals, New Haven, CT, USA; 3 New England Institute for Neurology and Headache, Stamford, CT, USA; 4 Clinical Research Institute, Minneapolis, MN, USA; 5 Albert Einstein College of Medicine, Bronx, NY, USA; 6 Montefiore Headache Center, Bronx, NY, USA

Background

- Nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, caffeinated analgesics, and antiemetics are widely used therapies for the acute treatment of migraine
- The clinical benefits that these non-specific drugs provide can be inadequate for severe migraine pain and associated symptoms; these drugs also have safety issues and the potential to cause medication-overuse headache[1]
- Reducing use of non-specific migraine medications may reduce total medication exposure, risk of adverse events, and medication overuse
- Rimegepant is an orally administered, small-molecule calcitonin gene-related peptide receptor antagonist that has demonstrated efficacy and safety in the acute and preventive treatment of migraine[2-5]

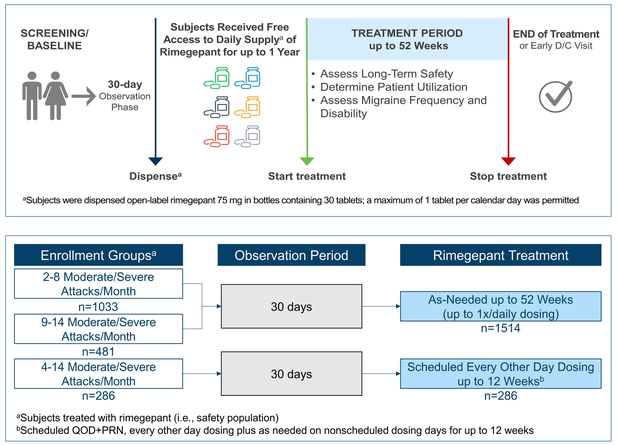
Purpose

- This post hoc analysis of data from a 52-week safety study of rimegepant 75 mg was conducted to determine if long-term use of rimegepant for migraine reduced the use of analgesics and antiemetics

Methods

- This was a multicenter, open-label, long-term safety study (NCT03266588) of rimegepant 75 mg oral tablet dosed up to once daily for up to 1 year (Figure 1)

Figure 1. Study Design



- Subjects were instructed to self-administer treatment as follows:
  - As needed (PRN) enrollment groups: rimegepant 75 mg up to once daily as needed to treat attacks of any pain intensity for 52 weeks
  - Scheduled dosing group (every other day): rimegepant 75 mg every other day (QOD) with patients allowed to take PRN dosing if needed on nonscheduled dosing days to treat attacks of any pain intensity for 12 weeks
- Subjects were allowed to use standard of care analgesic and antiemetic medications for migraine if needed during the study; triptan use was allowed during the observation period but was not permitted during the rimegepant treatment period
- Subjects recorded use of non-study acute medications in a paper diary

Subjects

- Aged ≥18 years, with ≥1-year history of migraine with or without aura
- Two to 14 moderate or severe monthly migraine attacks during the 3 months prior to the screening visit
- If using migraine preventive medication, stable dose for ≥3 months

Methods *cont.*

Assessments

- Subject demographics and migraine history, rimegepant 4-week and total exposure, and concomitant medication use were assessed

Statistical Analysis

- In this post hoc analysis, use of the most common over-the-counter or prescription analgesics and antiemetics (select analgesics and antiemetics) was analyzed during the 30-day observation period and over time in the rimegepant long-term treatment period
- Among subjects who used select analgesics and antiemetics in the observation period, 100% reductions in the use of these medications were evaluated

Results

Subjects

- In total, 1800 subjects were treated with rimegepant 75 mg (PRN 2-8 n=1033, PRN 9-14 n=481, every other day dosing n=286)
- Most subjects (89.4%) were female; mean age was 43.1 years, and 3.7% of subjects were ≥65 years of age; according to their migraine history, subjects had 6.7 mean monthly moderate to severe migraine attacks (Table 1)

Table 1. Baseline Demographics and Migraine History

	PRN (2-8)[a] n (%) (n=1033)	PRN (9-14)[a] n (%) (n=481)	Every Other Day[b] (n=286)	Overall n (%) (N=1800)
DEMOGRAPHICS				
Age, years, mean (SD)	44.0 (11.8)	42.4 (12.4)	41.1 (12.7)	43.1 (12.2)
Sex, n (%)				
Female	917 (88.8)	444 (92.3)	248 (86.7)	1609 (89.4)
Male	116 (11.2)	37 (7.7)	38 (13.3)	191 (10.6)
Race, n (%)				
White	847 (82.0)	394 (81.9)	234 (81.8)	1475 (81.9)
Black or African American	149 (14.4)	66 (13.7)	35 (12.2)	250 (13.9)
Other[c]	37 (3.6)	21 (4.4)	17 (5.9)	75 (4.2)
Weight, kg, mean (SD)	83.6 (22.0)	81.7 (22.9)	69.8 (11.7)	80.9 (21.5)
BMI, kg/m^2, mean (SD)	30.4 (7.8)	29.7 (7.7)	25.2 (3.5)	29.4 (7.5)
MIGRAINE HISTORY				
Moderate-severe attacks/month, mean (SD)	4.9 (1.8)	10.8 (1.6)	6.8 (2.6)	6.7 (3.1)
Duration of untreated attacks, hours, mean (SD)	33.7 (22.2)	34.5 (21.9)	33.5 (23.2)	33.9 (22.3)
Primary migraine type				
Without aura	674 (65.2)	311 (64.7)	215 (75.2)	1200 (66.7)
With aura	359 (34.8)	170 (35.3)	71 (24.8)	600 (33.3)

[a]PRN, as needed dosing up to 52 weeks.
[b]Scheduled QOD+PRN, every other day dosing plus as needed on nonscheduled dosing days for up to 12 weeks.
[c]Includes American Indian or Alaskan native, Asian, Hawaiian native or other Pacific Islander, or subjects of multiple races.

Exposure

- Overall, 112,014 doses of rimegepant 75 mg were administered across 1800 subjects; mean (SD) exposure was 7.7 (4.6) tablets per 4 weeks
- Rimegepant exposure data by enrollment group are shown in Table 2

Results *cont.*

Table 2. Rimegepant Exposure During the Long-term Treatment Period

	PRN (2-8)[a] n (%) (n=1033)	PRN (9-14)[a] n (%) (n=481)	Every Other Day[b] (n=286)	Overall n (%) (N=1800)
Mean (SD) doses per 4 weeks	5.6 (3.5)	8.5 (4.2)	13.7 (2.9)	7.7 (4.6)
Median doses per 4 weeks	4.9	7.8	14.2	6.5
Total rimegepant 75 mg doses	61,837	38,841	11,336	112,014

[a]PRN, as needed dosing up to 52 weeks.
[b]Scheduled QOD+PRN, every other day dosing plus as needed on nonscheduled dosing days for up to 12 weeks.

Use of Analgesics/Antiemetics

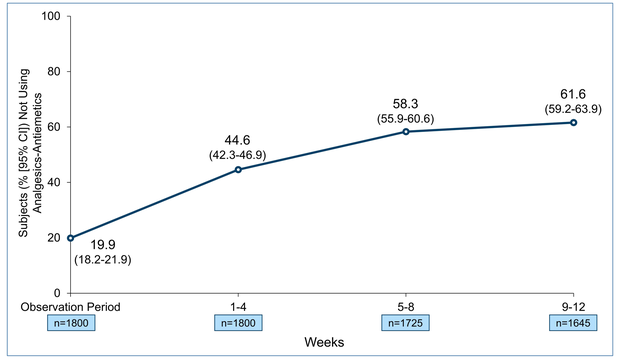
- In total, 80% of subjects took select analgesics and antiemetics during the observation period (Table 3)
- Freedom from using select analgesics and antiemetics increased over the first 12 weeks of rimegepant treatment (Figure 2)
- During Weeks 49-52, 67.6% of subjects reported no use of select analgesics and antiemetics

Table 3. Use of Select Analgesics and Antiemetics During the Observation Period

	PRN (2-8)[a] n (%) (n=1033)	PRN (9-14)[a] n (%) (n=481)	Every Other Day[b] (n=286)	Overall n (%) (N=1800)
Analgesics or antiemetics	828 (80.2)	388 (80.7)	225 (78.7)	1441 (80.1)
Analgesics	814 (78.8)	379 (78.8)	222 (77.6)	1415 (78.6)
Ibuprofen	418 (40.5)	199 (41.4)	122 (42.7)	739 (41.1)
AAC[c]	368 (35.6)	184 (38.3)	104 (36.4)	656 (36.4)
Acetaminophen	162 (15.7)	95 (19.8)	52 (18.2)	309 (17.2)
Naproxen	141 (13.6)	61 (12.7)	38 (13.3)	240 (13.3)
Antiemetics[d]	52 (5.0)	40 (8.3)	14 (4.9)	106 (5.9)

[a]PRN, as needed dosing up to 52 weeks.
[b]Every other day dosing plus as needed on nonscheduled dosing days for up to 12 weeks.
[c]Fixed combination analgesic containing acetaminophen, aspirin, and caffeine (AAC).
[d]Dimenhydrinate, meclozine, meclozine hydrochloride, metoclopramide, ondansetron, ondansetron hydrochloride, prochlorperazine, prochlorperazine edisylate, or promethazine.

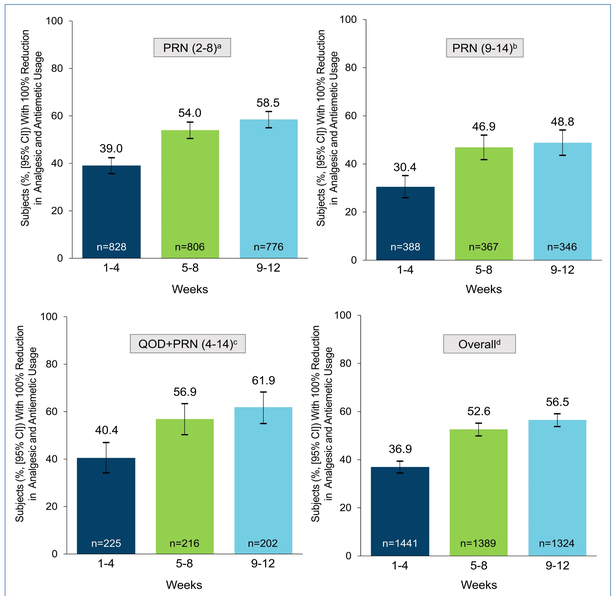
Figure 2. Freedom From Using Select Analgesics and Antiemetics: Observation Period through Week 12



Results *cont.*

- The percentages of subjects with a 100% reduction in analgesic and antiemetic use consistently increased with rimegepant treatment (Figure 3)
- Percentages (95% CI) of subjects with 100% reductions in analgesic and antiemetic use continued to increase during Weeks 49 to 52: PRN (2-8) 62.7% (58.6, 66.6); PRN (9-14) 57.8% (51.2, 64.0); and overall 61.3% (57.8, 64.6)

Figure 3. 100% Reduction in Use of Analgesics and Antiemetics From the Observation Periods



Conclusions

- The majority of participants eliminated the use of common analgesic and antiemetic medications during long-term treatment with rimegepant
- Reductions in the use of analgesics and antiemetics were noted within the first month of rimegepant treatment and increased over time
- As needed dosing and scheduled QOD dosing of rimegepant were associated with significant reductions in analgesic and antiemetic use; the QOD dosing group had the greatest rates of analgesic and antiemetic freedom

References: 1. Marmura M et al. *Headache*. 2015;55(1):3-20. 2. Lipton R et al. *Headache*. 2018;58:1336-1337. [Poster #PS123LB]. 3. Lipton RB et al. *N Engl J Med*. 2019;381(2):142-149. 4. Croop R et al. *Lancet*. 2019;394(10200):737-745. 5. Croop R et al. *Lancet*. 2021;397(10268):51-60.

Disclosures: This study was sponsored by Biohaven Pharmaceuticals. DK, KM, GB, and RBL have received honoraria and/or research support from Biohaven Pharmaceuticals; RBL is also a stockholder. WTS, AT, RC, ML, VC, and CMJ are employed by and own stock/stock options in Biohaven Pharmaceuticals.

American Society of Neuroimaging and NeuroNet Pro Joint Annual Meeting 2022 | Poster #32

To download a copy of this poster, scan QR code.