Rimegepant for Acute Treatment of Migraine Across BMI Categories: Pooled Analysis of 4 Phase 3 Randomized Clinical Trials

DISCLOSURES: MSR has presented at congresses and/or participated in scientific boards for Eli Lily, Lundbeck, Novartis, Teva, and Pfizer; serves as the second-vice president of the European Headache Federation and as a review editor on the editorial board of *Headache* and *Neurogenic Pain* (a specialty section of *Frontiers in Neurology*). TF, GP, and AC are employees of and own stock/options in Pfizer.

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INTRODUCTION

- Rimegepant is an oral small-molecule calcitonin gene-related peptide receptor antagonist indicated for acute treatment of migraine and for preventive treatment of episodic migraine in adults.[1,2]
- The efficacy and safety of rimegepant for acute treatment of migraine was demonstrated in 3 randomized, double-blind, placebo-controlled trials in the United States (NCT03235479, NCT03237845, NCT03461757) and 1 in China and South Korea (NCT04574362).[3-5]

OBJECTIVE

- This post hoc subgroup analysis assessed the efficacy and safety of rimegepant for the acute treatment of migraine across sub-populations of varying body mass index (BMI) using pooled data from studies NCT03235479, NCT03237845, NCT03461757, and NCT04574362.

METHODS

PARTICIPANTS AND TREATMENT

- Each study enrolled participants aged ≥18 years with a ≥1-year history of migraine, 2–8 attacks of moderate or severe pain intensity per month, and attacks lasting an average of 4–72 h if untreated.
- Participants were provided a single dose of rimegepant 75 mg or placebo to treat a single migraine attack of moderate or severe pain intensity within 45 days after enrollment.
- Preventive migraine medications were permitted if dosing was stable for ≥3 months prior to screening. Rescue medication (aspirin, ibuprofen, acetaminophen up to 1000 mg/day, NSAIDs, antiemetics, or baclofen) was allowed after 2 h post dose.

ENDPOINTS AND ANALYSIS

- The co-primary endpoints in each study were pain freedom and freedom from the most bothersome symptom (MBS) at 2 h post dose.
- Secondary endpoints included pain relief at 2 h, return to normal function at 2 h (among those with disability at time of dosing), use of rescue medication within 24 h, and sustained pain freedom from 2–24 and 2–48 h post dose.
- Treatment comparisons (rimegepant vs placebo) were conducted in each BMI cohort (<25, ≥25 to <30, and ≥30 kg/m^2) using Mantel–Haenszel risk estimation with stratification by study in randomized participants who took study therapy, had a migraine of moderate or severe intensity at the time of treatment, and provided ≥1 post-treatment efficacy data point. All P values are nominal.
- On-treatment adverse events (AEs) were summarized in all treated participants.

RESULTS

PARTICIPANTS

- 2439 participants received rimegepant and 2456 received placebo.
- In each BMI cohort, demographics were similar among participants receiving rimegepant and those receiving placebo (**Table 1**).

Table 1: Participant demographics according to BMI category[a]

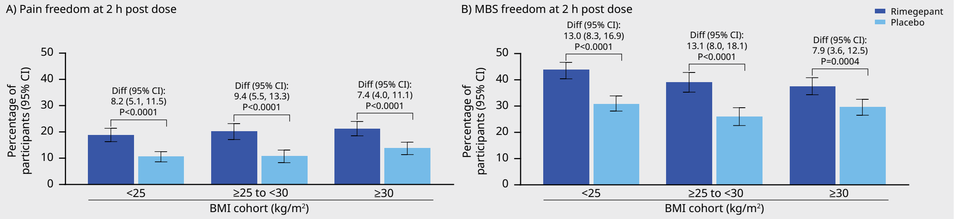
BMI category[b]	Rimegepant n=2439	Placebo n=2456
BMI <25 kg/m^2, n (%)	**907 (37.2)**	**953 (38.8)**
Age, mean (SD), y	38.0 (11.4)	38.4 (12.1)
Sex, n (%)		
Male	140 (15.4)	135 (14.2)
Female	767 (84.6)	818 (85.8)
BMI, mean (SD), kg/m^2	21.62 (2.06)	21.76 (2.01)
No. of moderate to severe attacks per month, mean (SD)	4.1 (1.7)	4.1 (1.7)
Primary migraine type, n (%)		
With aura	187 (20.6)	180 (18.9)
Without aura	720 (79.4)	773 (81.1)
BMI ≥25 to <30 kg/m^2, n (%)	**661 (27.1)**	**636 (25.9)**
Age, mean (SD), y	41.6 (12.2)	41.1 (12.1)
Sex, n (%)		
Male	141 (21.3)	134 (21.1)
Female	520 (78.7)	502 (78.9)
BMI, mean (SD), kg/m^2	27.20 (1.43)	27.25 (1.44)
No. of moderate to severe attacks per month, mean (SD)	4.4 (1.74)	4.4 (1.71)
Primary migraine type, n (%)		
With aura	182 (27.5)	165 (25.9)
Without aura	479 (72.5)	471 (74.1)
BMI ≥30 kg/m^2, n (%)	**869 (35.6)**	**865 (35.2)**
Age, mean (SD), y	40.7 (11.4)	40.6 (11.1)
Sex, n (%)		
Male	103 (11.9)	90 (10.4)
Female	766 (88.1)	775 (89.6)
BMI, mean (SD), kg/m^2	37.05 (6.50)	37.09 (6.73)
No. of moderate to severe attacks per month, mean (SD)	4.6 (1.81)	4.6 (1.76)
Primary migraine type, n (%)		
With aura	264 (30.4)	306 (35.4)
Without aura	605 (69.6)	559 (64.6)

[a] Includes all treated participants.
[b] 2 participants in the rimegepant group and 2 participants in the placebo group did not have a BMI reported.
BMI=body mass index; No.=number

EFFICACY

- Across all BMI cohorts, rimegepant demonstrated improvements over placebo for the co-primary endpoints of pain freedom (**Figure 1A**) and MBS freedom (**Figure 1B**) at 2 h post dose.
- Rimegepant also demonstrated improvements over placebo, across all BMI cohorts, for all secondary endpoints including pain relief at 2 h, return to normal function at 2 h, rescue medication use through 24 h, and sustained pain freedom from 2–24 and 2–48 h post dose (**Table 2**).

Figure 1: Summary of the co-primary efficacy endpoints according to BMI category[a]



[a] Includes randomized participants who took study therapy, had a migraine of moderate or severe intensity at the time of treatment, and provided ≥1 post-treatment efficacy data point.
Comparisons used Mantel–Haenszel risk estimation with stratification by study.
P values are nominal.
BMI=body mass index; diff=difference; MBS=most bothersome symptom

Table 2: Summary of secondary efficacy endpoints according to BMI category[a]

	Rimegepant		Placebo			
Endpoint[b]	n/N	% (95% CI)	n/N	% (95% CI)	Risk difference[c]	P value[d]
Pain relief at 2 h						
BMI <25 kg/m^2	573/900	63.7 (60.5, 66.7)	431/945	45.6 (42.5, 48.9)	18.1 (13.4, 22.4)	<0.0001
BMI ≥25 to < 30 kg/m^2	375/654	57.3 (53.4, 61.0)	281/630	44.6 (40.7, 48.4)	12.7 (7.3, 18.1)	<0.0001
BMI ≥30 kg/m^2	507/859	59.0 (55.8, 62.4)	385/855	45.0 (41.6, 48.3)	14.0 (9.4, 18.8)	<0.0001
Return to normal function at 2 h[e]						
BMI <25 kg/m^2	272/785	34.6 (31.5, 38.1)	166/833	19.9 (17.2, 22.6)	14.7 (10.7, 19.2)	<0.0001
BMI ≥25 to < 30 kg/m^2	189/593	31.9 (27.9, 35.4)	119/564	21.1 (17.7, 24.4)	10.8 (5.6, 15.6)	<0.0001
BMI ≥30 kg/m^2	269/802	33.5 (30.4, 36.9)	177/796	22.2 (19.3, 25.0)	11.3 (7.2, 15.9)	<0.0001
Rescue medication use within 24 h						
BMI <25 kg/m^2	121/900	13.4 (11.1, 15.5)	268/945	28.4 (25.6, 31.3)	–15.0 (–18.7, –11.6)	<0.0001
BMI ≥25 to <30 kg/m^2	96/654	14.7 (12.1, 17.6)	182/630	28.9 (25.2, 32.2)	–14.2 (–18.3, –9.5)	<0.0001
BMI ≥30 kg/m^2	157/859	18.3 (15.7, 20.9)	254/855	29.7 (26.7, 32.8)	–11.4 (–15.4, –7.4)	<0.0001
Sustained pain freedom 2–24 h						
BMI <25 kg/m^2	127/900	14.1 (11.9, 16.5)	58/945	6.1 (4.7, 7.7)	8.0 (5.3, 10.8)	<0.0001
BMI ≥25 to <30 kg/m^2	102/654	15.6 (12.8, 18.3)	42/630	6.7 (4.7, 8.6)	8.9 (5.5, 12.3)	<0.0001
BMI ≥30 kg/m^2	122/859	14.2 (11.9, 16.5)	73/855	8.5 (6.6, 10.3)	5.7 (2.8, 8.7)	0.0002
Sustained pain freedom 2–48 h						
BMI <25 kg/m^2	115/900	12.8 (10.7, 15.1)	51/945	5.4 (4.0, 6.9)	7.4 (4.8, 10.0)	<0.0001
BMI ≥25 to <30 kg/m^2	91/654	13.9 (11.2, 16.5)	40/630	6.3 (4.4, 8.2)	7.6 (4.3, 10.8)	<0.0001
BMI ≥30 kg/m^2	99/859	11.5 (9.4, 13.7)	65/855	7.6 (5.8, 9.3)	3.9 (1.2, 6.8)	0.0045

[a] Includes randomized participants who took study therapy, had a migraine of moderate or severe intensity at the time of treatment, and provided ≥1 post-treatment efficacy data point.
[b] All endpoints are postdose.
[c] Mantel–Haenszel risk estimation with stratification by study.
[d] All P values are nominal.
[e] Among those with some level of disability at time of dosing.
BMI=body mass index

SAFETY

- The proportion of participants reporting an AE of any severity was similar across treatment groups and across BMI cohorts (rimegepant, 9.2–12.9%; placebo, 8.8–10.9%; **Table 3**).
- Most AEs were mild, and the proportion of participants reporting a severe AE was ≤0.5% in all treatment groups and BMI cohorts.
  - Severe AEs reported by participants treated with rimegepant included the following:
    - BMI <25 kg/m^2 cohort: rash maculo-papular (n=1), and anaphylactic reaction (n=1).
    - BMI ≥25 to <30 kg/m^2 cohort: blood creatine phosphokinase increased (n=1), nausea (n=1).
    - BMI ≥30 kg/m^2 cohort: diarrhea (n=2), hematemesis (n=1), back pain (n=1), and pain in extremity (n=1).

Table 3: Summary of on-treatment AEs according to BMI category[a]

BMI category	Rimegepant n=2437	Placebo n=2454
BMI <25 kg/m^2, n	**907**	**953**
AE of any severity, n (%)	98 (10.8)	104 (10.9)
Mild AE, n (%)	23 (2.5)	35 (3.7)
Moderate AE, n (%)	12 (1.3)	17 (1.8)
Severe AE, n (%)	1 (0.1)	0
AE severity not reported, n (%)	65 (7.2)	57 (6.0)
BMI ≥25 to <30 kg/m^2, n	**661**	**636**
AE of any severity, n (%)	61 (9.2)	56 (8.8)
Mild AE, n (%)	34 (5.1)	24 (3.8)
Moderate AE, n (%)	16 (2.4)	12 (1.9)
Severe AE, n (%)	2 (0.3)	1 (0.2)
AE severity not reported, n (%)	14 (2.1)	20 (3.1)
BMI ≥30 kg/m^2, n	**869**	**865**
AE of any severity, n (%)	112 (12.9)	76 (8.8)
Mild AE, n (%)	79 (9.1)	49 (5.7)
Moderate AE, n (%)	33 (3.8)	29 (3.4)
Severe AE, n (%)	4 (0.5)	2 (0.2)
AE severity not reported, n (%)	0	5 (0.6)

[a] Includes all treated participants. Participants could be included in more than one AE severity category.
AE=adverse event; BMI=body mass index

CONCLUSION

- A single dose of rimegepant 75 mg for the acute treatment of migraine showed comparable efficacy and a favorable AE profile across all BMI cohorts.

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