P-696

Time Course of Rimegepant Efficacy for the Acute Treatment of Migraine in Adults Living in China or South Korea

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BACKGROUND

- Consistent and sustained efficacy is important for the acute treatment of migraine.[1-3]
- Patients want complete and sustained freedom from pain and migraine-related symptoms, especially the most bothersome symptom (MBS), and their ability to function restored, with no recurrence and minimal need for repeat dosing or rescue medication.
- Patients with migraine may have insufficient efficacy from or tolerability to triptans.[3,4]
- Rimegepant is an orally administered small-molecule calcitonin gene-related peptide receptor antagonist that is effective for the acute[5,6] and preventive[7] treatment of migraine, with or without aura, in adults.
  - A phase 3 trial demonstrated the efficacy of rimegepant for the acute treatment of migraine in adults living in China or South Korea.[8]

OBJECTIVE

- These analyses assessed the time course of efficacy of rimegepant through 48 h after dosing for the acute treatment of migraine in adults living in China or South Korea.

METHODS

STUDY DESIGN

- Data were from a phase 3, double-blind study (NCT04574362) conducted in China and South Korea of single-dose rimegepant 75 mg or placebo for the acute treatment of migraine.[8]
- Eligibility criteria included aged ≥18 years with ≥1-year history of migraine[9] (with or without aura) and 2–8 migraine attacks per month of moderate or severe pain intensity.
- Participants treated 1 migraine attack of moderate or severe pain intensity with a single oral dose of rimegepant 75 mg or placebo.

EFFICACY ASSESSMENTS

- At migraine onset (before dosing) and at 15 min, 30 min, 45 min, 1 h, 1.5 h, 2 h, 3 h, 4 h, 6 h, 8 h, 24 h, and 48 h post dose, participants rated:
  - Pain intensity (none, mild, moderate, or severe).
  - MBS (presence or absence of nausea, phonophobia, or photophobia).
  - Functional disability (normal, mild, severe, or requires bedrest).
- At each timepoint post dose:
  - Freedom from pain was assessed as the proportion of participants with pain intensity = none.
  - Freedom from MBS was assessed as the proportion of participants with an absence of their MBS.
  - Pain relief was assessed as the proportion of participants with pain intensity = none or mild.
  - Return to normal function was assessed in the subset of participants with any level of functional disability at time of dosing.

STATISTICAL ANALYSES

- Analyses were conducted in the modified intent-to-treat population, comprising those participants who were randomized and took study medication, who had a migraine of moderate or severe intensity at the time of treatment, and provided ≥1 post-treatment efficacy data point.
- Freedom from pain and freedom from MBS at 2 h post dose were co-primary endpoints.
- Pain relief and return to normal function at 2 h post dose were key secondary endpoints and were adjusted using the Hochberg procedure.
- Except for 2 h, all other timepoints were secondary or exploratory endpoints, unadjusted, with nominal P values.
- Failure to report MBS at study migraine onset imputed as failure for MBS analyses.
- Missing data at, or rescue medication use prior to, specified timepoint imputed as failure.
- Common risk differences and associated 95% CI were calculated from Mantel–Haenszel tests, stratified by preventive medication use and country.
- P values were calculated using Cochran–Mantel–Haenszel tests stratified by preventive medication use and country.

RESULTS

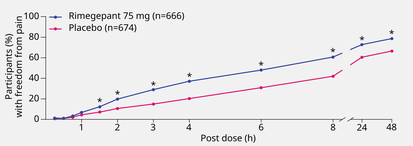
- Overall, 1340 participants (rimegepant n=666; placebo n=674) were included in the analyses; 80.1% were from China and 19.9% from South Korea (**Table 1**).
  - Mean age was 37.8 years, 81.2% of participants were female, and for 89.7% the primary migraine type was without aura.
- The benefits of rimegepant over placebo were first evident at
  - 90 min post dose for freedom from pain (nominal P=0.0012).
  - 45 min post dose for freedom from MBS (nominal P=0.0421).
  - 45 min post dose for pain relief (nominal P=0.0006).
  - 60 min post dose for return to normal function (nominal P=0.0023).
- The benefits of rimegepant over placebo were evident at all subsequent time points through 48 h post dose, including freedom from pain (**Figure 1**), freedom from MBS (**Figure 2**), pain relief (**Figure 3**), and return to normal function (**Figure 4**).

Table 1: Demographics and clinical characteristics

	Rimegepant n=666	Placebo n=674
Age, mean (SD), y	37.8 (10.15)	37.7 (10.70)
Gender, n (%)		
Female	525 (78.8)	563 (83.5)
Male	141 (21.2)	111 (16.5)
Country, n (%)		
China	537 (80.6)	537 (79.7)
South Korea	129 (19.4)	137 (20.3)
BMI, mean (SD), kg/m^2	23.00 (3.578)[a]	22.99 (3.399)
Migraine history, n (%)		
Primary migraine type		
Without aura	596 (89.5)	606 (89.9)
With aura	70 (10.5)	68 (10.1)
Number of moderate or severe attacks/mo		
Mean (SD)	3.66 (1.406)	3.62 (1.382)
Median (minimum, maximum)	3.30 (2.0, 8.0)	3.30 (2.0, 8.0)
Average duration of attack untreated, h		
Mean (SD)	19.76 (15.587)	20.28 (15.492)
Median (minimum, maximum)	12.50 (4.0, 72.0)	16.00 (3.5, 72.0)
Historical/typical MBS, n (%)		
Nausea	362 (54.4)	367 (54.5)
Phonophobia	179 (26.9)	175 (26.0)
Photophobia	125 (18.8)	131 (19.4)
Missing	0	1 (0.1)

Modified intent-to-treat population.
[a] n=665.
BMI=body mass index; MBS=most bothersome symptom

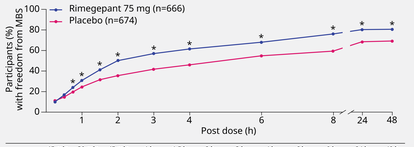
Figure 1: Participants with freedom from pain through 48 h post dose



	15 min	30 min	45 min	1 h	1.5 h	2 h	3 h	4 h	6 h	8 h	24 h	48 h
Rimegepant (n=666), n (%)	5 (0.8)	7 (1.1)	22 (3.3)	40 (6.0)	82 (12.3)	132 (19.8)	193 (29.0)	248 (37.2)	320 (48.0)	404 (60.7)	485 (72.8)	524 (78.7)
Placebo (n=674), n (%)	10 (1.5)	7 (1.0)	15 (2.2)	30 (4.5)	48 (7.1)	72 (10.7)	101 (15.0)	137 (20.3)	208 (30.9)	283 (42.0)	408 (60.5)	449 (66.6)
Risk difference (95% CI)	−0.7 (−1.9, 0.4)	0.0 (−1.1, 1.1)	1.0 (−0.7, 2.8)	2.4 (−0.1, 4.8)	5.2 (2.1, 8.4)	8.2 (5.4, 13.0)	14.0 (9.6, 18.3)	16.9 (13.1, 21.6)	17.1 (12.0, 22.3)	18.7 (13.4, 23.9)	12.3 (7.4, 17.1)	11.9 (7.3, 16.5)
P value	0.2057	0.9702	0.2419	0.0597	0.0012	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

*P<0.05. Except for 2 h, all P values unadjusted, nominal.

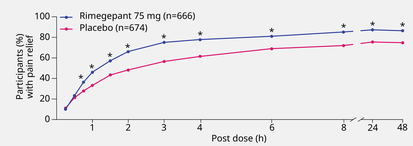
Figure 2: Participants with freedom from MBS through 48 h post dose



	15 min	30 min	45 min	1 h	1.5 h	2 h	3 h	4 h	6 h	8 h	24 h	48 h
Rimegepant (n=666), n (%)	68 (10.2)	112 (16.8)	161 (24.2)	207 (31.1)	276 (41.4)	336 (50.5)	382 (57.4)	412 (61.9)	490 (73.6)	535 (79.5)	539 (80.9)	541 (81.2)
Placebo (n=674), n (%)	70 (10.4)	100 (14.8)	142 (19.9)	167 (24.8)	214 (31.8)	261 (38.8)	284 (42.1)	313 (46.4)	373 (55.2)	460 (69.0)	465 (69.6)	470 (69.7)
Risk difference (95% CI)	−0.1 (−3.9, 3.5)	2.1 (−1.6, 6.0)	4.5 (0.4, 8.6)	6.4 (1.6, 11.3)	9.9 (4.8, 14.9)	14.8 (9.4, 20.0)	15.4 (10.2, 20.7)	15.5 (10.2, 20.7)	13.3 (8.2, 18.4)	16.8 (11.9, 21.7)	11.9 (7.4, 16.4)	11.4 (7.0, 15.9)
P value	0.8809	0.2586	0.0421	0.0066	0.0002	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

*P<0.05. Except for 2 h, all P values unadjusted, nominal.
MBS=most bothersome symptom

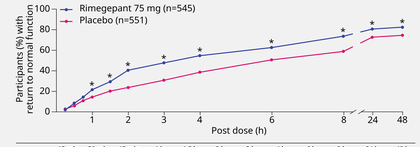
Figure 3: Participants with pain relief through 48 h post dose



	15 min	30 min	45 min	1 h	1.5 h	2 h	3 h	4 h	6 h	8 h	24 h	48 h
Rimegepant (n=666), n (%)	47 (10.1)	166 (25.6)	243 (36.5)	309 (46.4)	383 (57.5)	443 (66.5)	502 (75.4)	521 (78.2)	542 (81.4)	570 (85.6)	584 (87.7)	578 (86.8)
Placebo (n=674), n (%)	75 (11.1)	144 (21.4)	188 (27.9)	225 (33.4)	293 (43.5)	327 (48.5)	383 (56.8)	407 (60.4)	467 (69.3)	487 (72.3)	511 (75.8)	506 (75.1)
Risk difference (95% CI)	−1.0 (−4.5, 2.3)	2.1 (−2.3, 5.6)	8.5 (3.7, 13.7)	13.2 (8.1, 18.4)	14.1 (8.8, 19.4)	18.1 (13.0, 23.1)	18.6 (13.6, 23.5)	16.8 (11.6, 21.3)	11.9 (7.4, 16.4)	13.3 (9.1, 17.6)	11.8 (7.9, 15.7)	11.6 (7.5, 15.6)
P value	0.5533	0.3457	0.0006	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

*P<0.05. Except for 2 h, all P values unadjusted, nominal.

Figure 4: Participants with return to normal function through 48 h post dose



	15 min	30 min	45 min	1 h	1.5 h	2 h	3 h	4 h	6 h	8 h	24 h	48 h
Rimegepant (n=545), n (%)	11 (2.0)	46 (8.4)	79 (14.5)	118 (21.7)	161 (29.5)	222 (40.7)	261 (47.9)	299 (54.9)	342 (62.8)	403 (73.9)	441 (80.9)	451 (82.8)
Placebo (n=551), n (%)	15 (2.7)	33 (6.0)	61 (11.1)	80 (14.5)	112 (20.3)	131 (23.8)	170 (30.9)	215 (39.1)	265 (48.1)	325 (59.0)	402 (73.0)	412 (74.8)
Risk difference (95% CI)	−0.7 (−2.5, 1.1)	2.3 (−0.6, 5.5)	3.5 (−0.7, 7.2)	7.1 (2.5, 11.7)	9.1 (4.0, 14.2)	16.9 (11.4, 22.3)	17.0 (11.3, 22.7)	16.2 (10.3, 22.0)	11.9 (6.1, 17.8)	15.1 (9.5, 20.6)	8.0 (3.1, 12.8)	8.0 (3.3, 12.8)
P value	0.4579	0.1134	0.1032	0.0023	0.0005	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.0013	0.0009

*P<0.05. Except for 2 h, all P values unadjusted, nominal. Assessed among participants with any level of functional disability at time of dosing.

CONCLUSIONS

- Rimegepant 75 mg demonstrated efficacy for the acute treatment of migraine in adults living in China or South Korea.
- Benefits over placebo were first evident at 45–90 min post dose (depending on the endpoint) and were evident at all subsequent timepoints through 48 h post dose.

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DISCLOSURES

SY: No conflicts of interest. **B-KK:** Personal compensation for serving on a scientific advisory board or as speaker for Allergan Korea, GSK Korea, Lundbeck Korea, Pfizer Korea, Teva Korea, and SK-Pharma. **YS, YL, YZ, ZL and QZ:** Employees of Pfizer and may hold stock/stock options in Pfizer.

ACKNOWLEDGMENTS

This study was sponsored by Biohaven which was acquired by Pfizer in October 2022. Medical writing support was provided by Kim Russell, PhD, of Engage Scientific Solutions and was funded by Pfizer.

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Presented at the 66th American Headache Society (AHS) Annual Scientific Meeting, June 13–16, 2024, San Diego, CA, USA