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# Time to First Report of Rimegepant Efficacy for the Acute Treatment of Migraine in Adults Living in China or South Korea

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## BACKGROUND

- Rapid onset of efficacy is important for the acute treatment of migraine.[1-3]
  - Patients want rapid and complete freedom from pain and migraine-related symptoms, especially the most bothersome symptom (MBS), and their ability to function restored.
- 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 exploratory endpoints assessed the time to first report of efficacy of rimegepant in adults living in China or South Korea.

## METHODS

### STUDY DESIGN

- Data were from a phase 3, double-blind study conducted in China and South Korea (NCT04574362) of single-dose rimegepant 75 mg or placebo for the acute treatment of migraine.[8]
- Eligibility criteria included aged ≥18 y with ≥1-y 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, and 8 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).
- Exploratory endpoints, up to 8 h post dose, included:
  - Time to first report of freedom from pain. Freedom from pain was assessed as pain intensity = none.
  - Time to first report of freedom from MBS. Freedom from MBS was assessed as the absence of the participant's MBS.
  - Time to first report of pain relief. Pain relief was assessed as pain intensity = none or mild.
  - Time to first report of return to normal function. 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.
- Median time-to-event analyses were based on the method of Brookmeyer and Crowley for the 95% CI and log rank P values.
- Kaplan–Meier survival analyses were used to visualize the time-to-event endpoints through 8 h post dose.
  - Actual times were used for censoring and clinical events of interest.
  - Participants were censored at their first use of rescue medication or last reported data point if lost to follow-up.
  - Participants who did not have the clinical event of interest by 8 h post dose were censored at 496 min.

## 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.
- Across all endpoints, first report of efficacy was earlier for rimegepant vs placebo (**Table 2**).
  - Median time to first report of pain freedom was 347.7 min for rimegepant and 468.6 min for placebo (nominal P<0.0001).
  - Median time to first report of freedom from MBS was 118.8 min for rimegepant and 224.8 min for placebo (nominal P<0.0001).
  - Median time to first report of pain relief was 85.0 min for rimegepant and 91.1 min for placebo (nominal P<0.0001).
  - Median time to first report of return to normal function was 346.3 min for rimegepant and 465.4 min for placebo (nominal P=0.0002).
- The benefits of rimegepant compared with placebo were evident through 8 h post dose for freedom from pain (**Figure 1A**), freedom from MBS (**Figure 1B**), pain relief (**Figure 1C**), and return to normal function (**Figure 1D**).

**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 | | |
| Primary migraine type, n (%) | | |
| 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) |

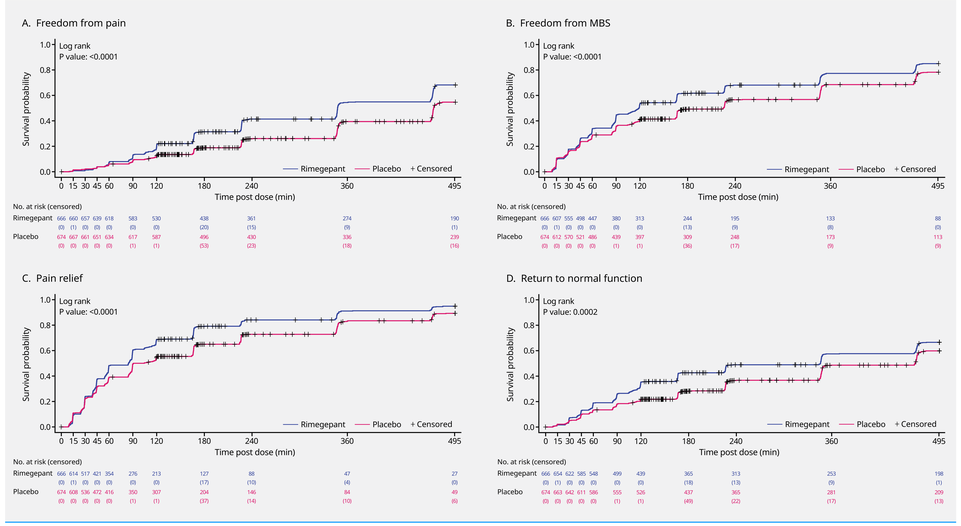
Modified intent-to-treat population.
[a] n=665.
BMI=body mass index; MBS=most bothersome symptom

**Table 2: Time to first report of efficacy endpoints**

| | Rimegepant n=666 | Placebo n=674 | Log rank P value |
|---|---|---|---|
| Time to freedom from pain, min | | | |
| Median | 347.7 | 468.6 | <0.0001 |
| 95% CI | 347.0–351.1 | 467.5–476.4 | |
| Time to freedom from MBS, min | | | |
| Median | 118.8 | 224.8 | <0.0001 |
| 95% CI | 107.2–120.9 | 167.1–227.1 | |
| Time to pain relief, min | | | |
| Median | 85.0 | 91.1 | <0.0001 |
| 95% CI | 59.9–89.3 | 89.8–119.7 | |
| Time to return to normal function, min | | | |
| Median | 346.3 | 465.4 | 0.0002 |
| 95% CI | 226.9–347.5 | 348.5–467.4 | |

Modified intent-to-treat population.
95% CI is based on the method of Brookmeyer and Crowley.
All P values are nominal.
MBS=most bothersome symptom

**Figure 1: Kaplan–Meier survival plots of time to first report of (A) freedom from pain, (B) freedom from MBS, (C) pain relief, and (D) return to normal function through 8 h post dose**




Modified intent-to-treat population.
Survival probability is the probability of having the endpoint. Analyses used actual times of censoring and clinical event of interest.
The number of participants at risk is the number with pain score moderate or severe, with presence of MBS, or with functional disability (according to the respective analysis) just prior to the start of the specified interval and who had not been censored prior to the interval.
The number of participants with an event is the number with pain score none, with absence of MBS, with pain score none or mild, or with normal functioning (according to the respective analysis) for the first time during the specified interval.
The number of participants censored is the number who had pain, had their MBS, had moderate or severe pain, or had non-normal functioning (according to the respective analysis) or were lost to follow-up during the specified interval.
Participants who did not have the respective event by 495 min post dose were censored at 496 min. Survival estimates calculated using the Kaplan–Meier product limit method.
MBS=most bothersome symptom

## CONCLUSION

- For the acute treatment of migraine in adults living in China or South Korea, first report of efficacy was earlier for rimegepant 75 mg compared with placebo, with benefits evident through 8 h post dose.

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### DISCLOSURES
**SY:** No conflicts of interest. **YS, YL, YZ, ZL, QZ:** Employees of Pfizer and may hold stock/stock options in Pfizer.

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