P254

The CONFIDENCE Study: Impact of Timing, Headache Severity and Functional Impairment at Intake of Rimegepant on Pain Relief, Return to Function and Treatment Satisfaction

Karin Hygge Blakeman[1], Alexandre Urani[2], Giorgio Lambru[3], Richard B Lipton[4], Peter J Goadsby[5], Patricia Pozo-Rosich[6], Todd J. Schwedt[7], Kristina M Fanning[8], Lucy Abraham[9]

[1]Pfizer AB, Stockholm, Sweden; [2]Aptar Digital Health, Paris, France; [3]The Headache and Facial Pain Service, Guy's and St. Thomas' NHS Foundation Trust, London, UK; [4]Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, NY, USA; [5]NIHR King's Clinical Research Facility, King's College Hospital/SLaM Biomedical Research Centre, King's College London, UK, and King Abdullah University of Science and Technology, Thuwal, Saudi Arabia; [6]Headache and Neurological Pain Research Group, Vall d'Hebron Research Institute, Universitat Autònoma de Barcelona, Barcelona, Spain; [7]Mayo Clinic, Scottsdale, AZ, USA; [8]MIST Research, Wilmington, NC, USA; [9]Pfizer R&D UK Ltd., Tadworth, Surrey, UK

INTRODUCTION

- Rimegepant is an oral calcitonin gene-related peptide (CGRP) receptor antagonist approved for the acute treatment of migraine and the preventive treatment of episodic migraine in many countries.[1,2]
- Although clinical trials have demonstrated the efficacy of rimegepant for the acute treatment of migraine, there remains a lack of real-life evidence collected over multiple attacks to guide optimal timing of rimegepant intake.[3]
- An observational study in Italy (GAINER; NCT05903027) found rimegepant taken within 1 h of pain onset was positively associated with achievement of pain freedom 2 h post treatment.[4]
- The recently completed prospective, observational, CONFIDENCE study (NCT06467370) evaluated the effectiveness of rimegepant for the acute treatment of migraine over multiple attacks, including in participants using preventive therapy.
  - This exploratory analysis of CONFIDENCE investigated the effect of rimegepant intake timing (in relation to attack progression, duration since the attack started, headache intensity, and functional impairment at time of treatment) on outcomes.

METHODS

STUDY DESIGN

- CONFIDENCE was an observational study of real-world rimegepant users recruited in the Migraine Buddy app®.[5]
  - All participants were in the United States.
  - Participants used rimegepant prescribed to them for the acute treatment of migraine. No study medication was provided.
- The CONFIDENCE study comprised screening and baseline questionnaires, a 28-day observation period where participants completed a daily diary (describing the occurrence and nature of any migraine attacks, any treatments taken, and the effectiveness of treatment), and a study completion questionnaire.

PARTICIPANTS

Key enrollment criteria

- Age ≥18 years.
- 3 to 14 headache days in the last 30 days.
- Rimegepant prescription for the acute treatment of migraine and plan to use rimegepant to treat a migraine attack during the next 30 days.
- Not using rimegepant as preventive treatment.
- Stable preventive treatment was permitted except concomitant onabotulinumtoxinA with any anti-CGRP monoclonal antibody.
- No diagnoses of cluster headache, post-traumatic headache, new daily persistent headache, hemicrania continua, or chronic daily headache.

Analyses

- The daily diary captured treatment outcomes following rimegepant use for the acute treatment of migraine, including the achievement of:
  - Meaningful pain relief, as determined by the participant, within 2 h of treatment.
  - Meaningful improvement in function, as determined by the participant, within 2 h of treatment.
  - Participant-reported "satisfaction" or "extreme satisfaction" (from a 7-point scale) with rimegepant treatment of the attack (further termed overall treatment satisfaction).
- In this analysis, linear by linear associations and Pearson's chi-squared test were used to evaluate how these outcomes were influenced by:
  - How far the attack had progressed before rimegepant was taken.
  - Time since the attack started before rimegepant was taken.
  - How intense the participant's headache pain was at the time when rimegepant was taken.
  - How much the participant's functional ability was affected by migraine symptoms at the time when rimegepant was taken.

RESULTS

PARTICIPANTS

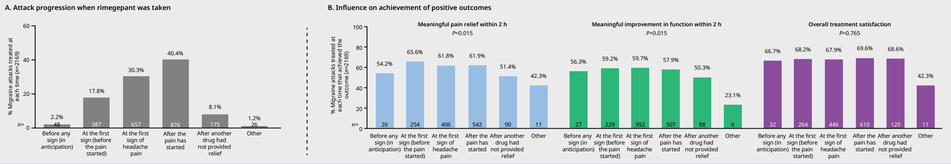
- 416 participants reported ≥1 rimegepant-treated migraine attack during the CONFIDENCE study.
- Participants had a mean age of 39.6 (SD 10.9) years, 86.1% were female, and 90.4% were White (**Table**).
- Median headache days in the past 30 days was 8 (interquartile range: 5–10).
- 89.9% had a Disability Assessment Score (MIDAS) indicating moderate or severe disability.
- 84.1% used an indicated migraine preventive therapy, most commonly a calcitonin gene-related peptide monoclonal antibody (CGRP mAb; 33.9%) or onabotulinumtoxin A (33.7%).

Table 1: Demographics and clinical characteristics

Demographic	Participants with ≥1 rimegepant-treatment migraine attack *N*=416
Age, mean (SD), y	39.6 (10.9)
Female gender, *n* (%)	358 (86.1)
White race, *n* (%)	376 (90.4)
BMI, mean (SD), kg/m^2	30.0 (7.6)
Headache days/month, median (IQR)	8 (5–10)
MIDAS classification, *n* (%)	
None to mild disability (score 0–10)	42 (10.1)
Moderate to severe disability (score ≥11)	374 (89.9)
Use of indicated migraine preventive therapy, *n* (%)[a]	
Any	350 (84.1)
CGRP mAb	141 (33.9)
OnabotulinumtoxinA	140 (33.7)
Anticonvulsant	41 (9.9)
Antidepressant	40 (9.6)
Atogepant	40 (9.6)
Beta-blocker	28 (6.7)
Angiotensin blocker	1 (0.2)
Calcium channel blocker	3 (0.7)

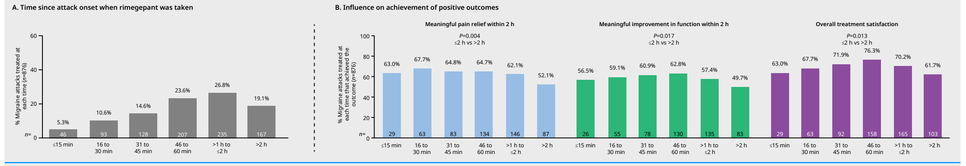
[a] Participants could use >1 type of preventive medication.
BMI=body mass index; CGRP=calcitonin gene-related peptide; IQR=interquartile range; mAb=monoclonal antibody; MIDAS=Migraine Disability Assessment Score

Figure 1: Rimegepant-treated migraine attacks achieving positive outcomes by attack progression at treatment



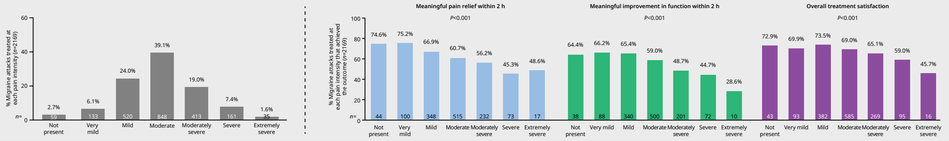
All rimegepant-treated attacks presented by progression at the time of treatment are shown. Includes attacks treated "before any sign of the migraine attack, but in anticipation of one starting (ahead of a known trigger)", "at the first sign of the migraine attack (before the pain started)", "at the first sign of headache pain", "after the pain has started", "after another drug had not provided enough relief", and "other". (*A*) *n* (base of bar) and % (plotted) of attacks treated at each time; (*B*) *n* (base of bar) and % (plotted) of attacks treated at each time that achieved the outcome stated. Statistical testing is based on linear-by-linear associations.

Figure 2: Rimegepant-treated migraine attacks achieving positive outcomes by time between attack onset and treatment



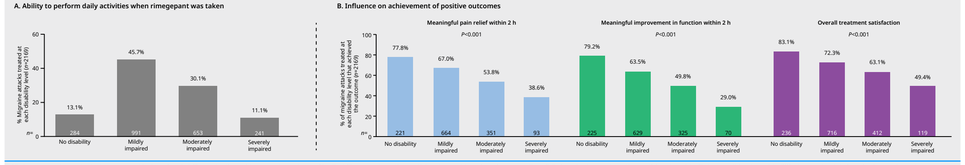
Rimegepant-treated attacks treated "after the pain had started" presented by time since attack onset are shown. (*A*) *n* (base of bar) and % (plotted) of attacks treated at each time since the attack onset; (*B*) *n* (base of bar) and % (plotted) of attacks treated at each time that achieved the outcome stated. Statistical testing is based on Pearson's chi-squared tests.

Figure 3: Rimegepant-treated migraine attacks achieving positive outcomes by headache intensity at treatment



All rimegepant-treated attacks presented by headache pain intensity at the time of treatment are shown. (*A*) *n* (base of bar) and % (plotted) of attacks treated at each headache intensity; (*B*) *n* (base of bar) and % (plotted) of attacks treated at each intensity that achieved the outcome stated. Statistical testing is based on linear-by-linear associations.

Figure 4: Rimegepant-treated migraine attacks achieving positive outcomes by functional ability at treatment



All rimegepant-treated attacks presented by functional ability at the time of treatment are shown. No disability was where the participant was able to function normally; mildly impaired was where the participant could still do everything but with difficulty; moderately impaired was where the participant was not able to do some things; severely impaired was where the participant was unable to do all or most things, and where best rest might be necessary. (*A*) *n* (base of bar) and % (plotted) of attacks treated at each level of ability; (*B*) *n* (base of bar) and % (plotted) of attacks treated at each ability that achieved the outcome stated. Statistical testing is based on linear-by-linear associations.

CONCLUSIONS

- Findings from this observational study complement clinical trial data to demonstrate the effectiveness of rimegepant for the acute treatment of migraine.[3]
- Findings additionally suggest treatment early in an attack, at lower pain and disability levels, can further increase the possibility of positive outcomes.

ATTACK PROGRESSION AT THE TIME OF TREATMENT VS OUTCOME

- 2169 migraine attacks were treated with rimegepant during the study; in most, rimegepant was taken "after the pain had started" (*n*=876 [40.4%]) or "at the first sign of headache pain" (*n*=657 [30.3%]; **Figure 1A**).
- Meaningful pain relief within 2 h of rimegepant treatment and meaningful improvement in function within 2 h of rimegepant treatment were achieved in a higher proportion of attacks where rimegepant was taken early in an attack ie, "at the first sign of the migraine attack (before the pain started)", "at the first sign of headache pain", or "after the pain has started" (linear-by-linear associations, *P*<0.05; **Figure 1B**).

TIME SINCE ATTACK ONSET VS OUTCOME

- Of the 876 attacks where rimegepant was taken "after the pain had started", most were treated >1 h but ≤2 h after the attack had started (*n*=235 [26.8%]), or between 46 and 60 min after the attack started (*n*=207 [23.6%]; **Figure 2A**).
- Meaningful pain relief within 2 h of rimegepant treatment, meaningful improvement in function within 2 h of rimegepant treatment, and overall treatment satisfaction were all achieved in a higher proportion of attacks where rimegepant was taken in the first 2 h of an attack (binary comparison by Pearson's chi-squared test ≤2 h vs >2 h after the attack started; *P*<0.05; **Figure 2B**).

HEADACHE INTENSITY AT THE TIME OF TREATMENT VS OUTCOME

- Among all 2169 rimegepant-treated migraine attacks, most were treated when headache pain was of moderate (*n*=848 [39.1%]) or mild (*n*=520 [24.0%]) intensity (**Figure 3A**).
- Meaningful pain relief within 2 h of rimegepant treatment, meaningful improvement in function within 2 h of rimegepant treatment, and overall treatment satisfaction were all achieved in a higher proportion of attacks where rimegepant was taken at a lower headache intensity (linear-by-linear associations, all *P*<0.001; **Figure 3B**).

FUNCTIONAL ABILITY IMPAIRMENT AT THE TIME OF TREATMENT VS OUTCOME

- Most of the 2169 rimegepant-treated migraine attacks were treated when the participant's functional ability was mildly impaired (can still do everything but with difficulty; *n*=991 [45.7%]) or moderately impaired (unable to do some things; *n*=653 [30.1%]; **Figure 4A**).
- Meaningful pain relief within 2 h of rimegepant treatment, meaningful improvement in function within 2 h of rimegepant treatment, and overall treatment satisfaction were all achieved in a higher proportion of attacks where rimegepant was taken at a lower level of functional disability (linear-by-linear associations, all *P*<0.001; **Figure 4B**).

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DISCLOSURES

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