Interim Analysis of CONFIDENCE: A Prospective Observational Study With Acute Treatment of Rimegepant ODT on Consistency, Satisfaction, and Tolerability of Treatment in the Real World

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

[1]Pfizer R&D UK Ltd., Tadworth, Surrey, UK; [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, New York, NY, USA; [5]NIHR King's Clinical Research Facility, King's College Hospital/ SLaM Biomedical Research Centre, King's College London, UK, and University of California, Los Angeles, CA, USA; [6]Headache and Neurological Pain Research Group, Vall d'Hebron Research Institute, Universitat Autònoma de Barcelona and Vall d'Hebron University Hospital, Barcelona, Spain; [7]Mayo Clinic, Scottsdale, AZ, USA; [8]Pfizer Inc, New York, NY, USA; [9]Pfizer AB, Stockholm, Sweden

BACKGROUND

- Rimegepant 75 mg orally disintegrating tablet (ODT) is the only small molecule calcitonin gene-related peptide (CGRP) receptor antagonist approved for the acute treatment of migraine and prevention of episodic migraine in adults.[1]
  - Approval for acute migraine treatment was based on findings from a phase 3 randomized trial (NCT03461757) that demonstrated efficacy of rimegepant with higher proportion of patients achieving freedom from pain and the most bothersome symptom vs placebo at 2 h post dose.[2]
- CONFIDENCE, is a prospective, real-world observational study in the United States, evaluating the effectiveness of rimegepant 75 mg ODT for the acute treatment of migraine in adults (NCT06467370).

OBJECTIVE

- To present findings from CONFIDENCE, investigating real-world effectiveness of rimegepant 75 mg ODT in an (1) interim analysis of adults using rimegepant for the acute treatment of migraine over multiple attacks and a (2) subgroup analysis of participants receiving rimegepant who were already using an anti-CGRP monoclonal antibody (mAb) for migraine prevention.

METHODS

- CONFIDENCE utilized a bespoke interface of the Migraine Buddy® mobile app to collect data. The app is a widely used tool for tracking headache symptoms, triggers, and treatment outcomes.[3]
  - Participants were recruited in the United States from among the existing Migraine Buddy app users.
- Recruitment was conducted in 2 phases to reach a predefined sample size (n=156) in each of the subpopulations of interest: participants with migraine (1) on any prophylaxis or none and (2) on background prophylaxis of anti-CGRP mAbs.
- Eligible participants with migraine (female and male, aged ≥18 years) included those who had 3–14 headache days within the last 30 days, received a prescription for rimegepant 75 mg ODT for acute treatment, and planned to treat attacks in the next 30 days with rimegepant.
  - Participants were excluded if they were using rimegepant for preventive treatment; received concomitant treatment with onabotulinumtoxinA with any of the anti-CGRP mAbs; participating in a migraine-related clinical trial; or were diagnosed with cluster, post-traumatic, or new daily persistent headache, hemicrania continua, or secondary headache disorders.
- Participants completed a baseline survey capturing demographics and clinical characteristics; a 28-day daily diary that assessed occurrence of attacks, time to meaningful pain relief or restoration of function, and treatment satisfaction; and a questionnaire at study completion.
- Effectiveness was evaluated for each attack using the daily diary and across the entire study using a recall-based survey at the end of the study.
- Analysis and outcomes are listed in **Table 1**.
- The study was conducted in accordance with legal and regulatory requirements following generally accepted research practices.[4,5]

Table 1: Outcomes and analyses

Outcomes

1. Time to meaningful pain relief or meaningful functional improvement (<1, >1–2, >2–4, or >4 h, or no relief/improvement)[a]

- Defined as time after rimegepant intake when participants experienced reduced pain or improved function that they considered meaningful

2. Treatment satisfaction with rimegepant across different domains (pain reduction, attack duration, speed of action, cognitive symptoms, and overall)

- Measured using a 7-point rating scale ranging from extremely satisfied to extremely dissatisfied

Analysis

Interim analysis

- Population level consistency
  - Proportion of all rimegepant-treated attacks achieving meaningful pain relief and meaningful functional improvement within 2 h post dose
- Conducted mid-study using data collected between July and September 2024 including all participants who used rimegepant to treat ≥1 attack, with or without concomitant prophylaxis

Subgroup analysis

- Proportion of participants using rimegepant with preventive anti-CGRP mAb who achieved a response rate of ≥66.7% for the first 10 rimegepant-treated attacks for each specific outcome
- Conducted at the end of study using data collected between July 2024 and March 2025

All data were summarized using descriptive statistics.
[a] To determine functional improvement, participants rated their ability to perform daily activities using the functional disability scale.
CGRP=calcitonin gene-related peptide; mAb=monoclonal antibody

RESULTS

INTERIM ANALYSIS

- Of 146 eligible participants, (mean age: 40 years), most were female (92.5%), White (93.8%), overweight/obese (76.7%), and using preventive treatment (65.1%) at baseline (**Table 2**).
- Mean (SD) headache days was 7.4 (3.0) in the past 30 days and 87.0% had a Migraine Disability Assessment score ≥11, indicating moderate to severe disability (**Table 2**).
- Overall, 142 participants had ≥1 recorded rimegepant-treated attack. The median number (interquartile range) of rimegepant-treated attacks per individual was 5 (3–6).
  - Of 1054 total migraine attacks recorded by participants, rimegepant was used to treat 706 (67.0%) attacks.

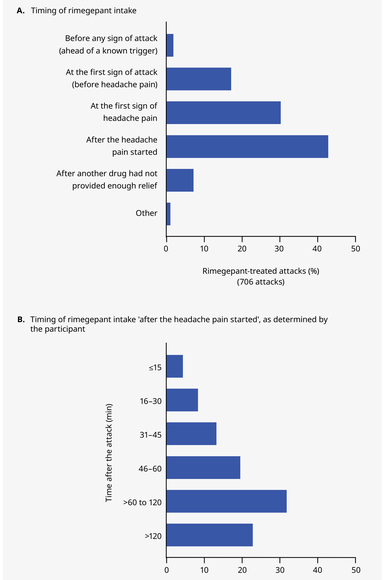
Table 2: Baseline demographics and clinical characteristics of participants

	Interim analysis Rimegepant 75 mg ODT *N*=146
Age, mean (SD), y	40.1 (11.1)
Sex, *n* (%)	
Female	135 (92.5)
Male	11 (7.5)
Race, *n* (%)[a]	
White	137 (93.8)
Black or African American	3 (2.1)
Asian	3 (2.1)
American Indian or Alaska Native	3 (2.1)
Native Hawaiian or Other Pacific Islander	1 (0.7)
BMI category, *n* (%)	
Underweight	2 (1.4)
Normal	32 (21.9)
Overweight	41 (28.1)
Obese	71 (48.6)
Headache days, mean (SD), days	7.4 (3.0)
MIDAS score, median (IQR)	33.5 (16.8, 50.3)
MIDAS migraine disability grade, *n* (%)	
Little to mild	19 (13.0)
Moderate to severe	127 (87.0)
Any preventive medication, *n* (%)	95 (65.1)
Oral[b]	54 (56.8)
Anticonvulsant	20 (37.0)
Atogepant	17 (31.5)
Antidepressant	15 (27.8)
Injectable[b]	59 (62.1)
Fremanezumab	20 (33.9)
Galcanezumab	19 (32.2)
Erenumab	14 (23.7)

[a] Participants could select ≥1 race.
[b] The 3 most common medications are shown.
BMI=body mass index; CGRP=calcitonin gene-related peptide; IQR=interquartile range; MIDAS=Migraine Disability Assessment; ODT=orally disintegrating tablet

- Rimegepant was taken after the start of the attack (including 'at the first sign of headache pain', 'after the headache pain started', and 'after another drug had not provided enough relief') in 80.0% (565/706) of treated attacks (**Figure 1A**).
  - Of 302 attacks reported to have been treated with rimegepant 'after the headache pain started', treatment was taken within 2 h of onset in 77.2% (233/302) of attacks (**Figure 1B**).
- Of all rimegepant-treated attacks, the proportion achieving meaningful pain relief and meaningful functional improvement within 2 h was 58.6% and 56.4%, respectively (**Figure 2A**).
- Most participants were satisfied or extremely satisfied with rimegepant treatment across all domains (overall, 67.3%), including headache pain relief (68.3%), attack duration (65.0%), speed of action (63.2%), and cognitive symptoms (62.7%) (**Figure 2B**).

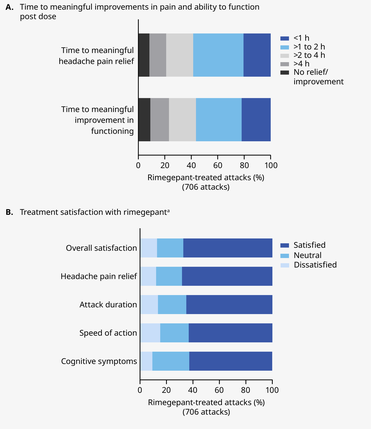
Figure 1: Timing of rimegepant 75 mg ODT intake (interim analysis)



ODT=orally disintegrating tablet

- Meaningful pain relief was achieved within 2 h post dose for the first (63.4%, 90/142), second (58.4%, 80/137), and third (59.3%, 70/118) rimegepant-treated attacks.
- Meaningful return to function was achieved within 2 h post dose for the first (60.6%, 86/142), second (59.1%, 81/137), and third (54.2%, 64/118) rimegepant-treated attacks.

Figure 2: Time to improvement in pain relief and functioning and treatment satisfaction (interim analysis)



[a] For each rimegepant-treated attack, participants were asked how satisfied they were with rimegepant for reducing headache pain and the duration of their migraine attack, how quickly it worked to treat the attack, and treating cognitive symptoms of the attack (eg, brain fog, ability to think clearly); and how satisfied they were overall with rimegepant for treating the attack.

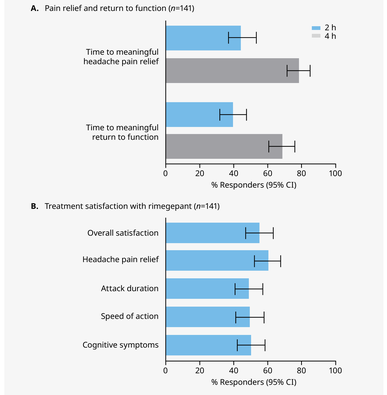
SUBGROUP ANALYSIS

- Of 141 participants on preventive anti-CGRP mAb (mean age: 40 years) who used rimegepant to treat ≥1 attack, with evaluable data, most were female (83.7%), White (92.2%), overweight/obese (71.6%), and had moderate to severe migraine-related disability (84.4%).
- Among participants with ≥1 rimegepant-treated attack, the first 10 treated attacks were analyzed. The proportion of participants who achieved a treatment response of ≥66.7% for the first up to 10 rimegepant-treated attacks is shown in **Figure 3**.
  - Meaningful pain relief was achieved in 44.7% and 78.7% of participants within 2 h and 4 h post dose, respectively (**Figure 3A**).
  - Meaningful return to function was achieved in 39.7% and 68.8% of participants within 2 h and 4 h post dose, respectively (**Figure 3A**).
  - Many participants were satisfied or extremely satisfied with rimegepant treatment across all domains (55.3%), including headache pain relief (60.3%), attack duration (48.9%), speed of action (49.6%), and cognitive symptoms (50.4%) (**Figure 3B**).

CONCLUSIONS

- **Interim analysis:** Meaningful pain relief and restoration of function occurred within 2 h of rimegepant treatment for most of the attacks, with high levels of population consistency across multiple attacks and high treatment satisfaction across different domains.
- **Subgroup analysis:** Many participants using rimegepant with preventive anti-CGRP mAb reported meaningful pain relief and return to function, with high treatment satisfaction particularly in terms of pain relief and overall satisfaction.
- **Overall:** Participants treating migraine attacks with rimegepant, regardless of concomitant preventive anti-CGRP mAb use, reported meaningful pain relief and return to function, and high treatment satisfaction.

Figure 3: Effectiveness of rimegepant for acute migraine treatment in participants on background preventive anti-CGRP mAb (subgroup analysis)



CGRP=calcitonin gene-related peptide; mAb=monoclonal antibody

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DISCLOSURES

AU: Employee of Aptar Digital Health, which was a paid consultant to Pfizer to conduct the study. **GL:** Advisory boards: AbbVie, Dr Reddy's Laboratories, Eli Lilly, Lundbeck, Novartis, Pfizer, TEVA. **RBL:** Editorial board: Neurology, Cephalalgia (not paid); senior advisor: Headache (not paid); research support: National Headache Foundation, NIH, Marx Foundation, US FDA; research grants: Allergan/AbbVie, Amgen, Novartis; reviewer: NIA, NINDS; consultant/advisory board/honoraria: AEON, Allergan/AbbVie, Amgen, Biodelivery Sciences International, Biohaven, CoolTech LLC, Dr Reddy's Laboratories, electroCore, Eli Lilly, GlaxoSmithKline, Impel Neuropharma, Lundbeck Manistee, Merck, Novartis, Satsuma, Teva, Vedanta; royalties: Informa, Wolff's Headache (8th ed), stock options: Axon, Biohaven, CoolTech, Manistee. **PJG:** Consultant: AbbVie, Aeon Biopharma, Aurene, CoolTech LLC, Dr Reddy's, Eli Lilly, Epalex, Kallyope, Lnpharma, Lundbeck, Orion Pharma, Pfizer, PureTech Health LLC, Satsuma, Shiratronics, Teva Pharmaceuticals, Vial; advisor: Gerson Lehrman Group, Guidepoint, SAI Med Partners, Vector Metric; fees for educational materials: CME Outfitters, WebMD; publishing royalties/fees: Massachusetts Medical Society, Oxford University Press, UptoDate, Wolters Kluwer. **PP-R:** Consultant/speaker: AbbVie, Dr. Reddy's, Eli Lilly, Lundbeck, Medscape, Novartis, Organon, Pfizer, Teva Pharmaceuticals; research grants: AbbVie, AGAUR, EraNet Neuron, FEDER RIS3CAT, Instituto Investigación Carlos III, MICINN, Novartis, Teva Pharmaceuticals; clinical trial funding: AbbVie, Amgen, Eli Lilly, Lundbeck, Novartis, Pfizer, Teva Pharmaceuticals; Honorary Secretary of the International Headache Society; editorial board: Revista de Neurologia; associate editor: Cephalalgia, Neurologia; founder of www.midolordecabeza.org. **TJS:** Consultant: AbbVie, Allergan, Amgen, Axsome, Collegium, Eli Lilly, Linpharma, Lundbeck, Salvia, Satsuma, Scilex, Theranica; royalties: UpToDate; stock options: Allevalux, Aural Analytics, Nocira; institution received research grants on his behalf: American Heart Association, Flinn Foundation, Henry Jackson Foundation, National Headache Foundation, NIH, Patient Centered Outcomes Research Institute, Pfizer, Spark Neuro, US Department of Defense. **LA, BG, FD, KHB:** Employees of and own stock/options in Pfizer.

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