Pfizer-sponsored Symposium:

single medication to both treat and prevent migraine: what is the evidence?

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▽ This drug is subject to additional follow-up. It is a priority to report suspected adverse reactions associated with this medicinal product.

This is for healthcare professionals only.

Nurtec ODT 75 mg UAE LPD USPI. Revision date May 2021.

Pfizer | Nurtec® ODT (rimegepant) orally disintegrating tablets 75 mg

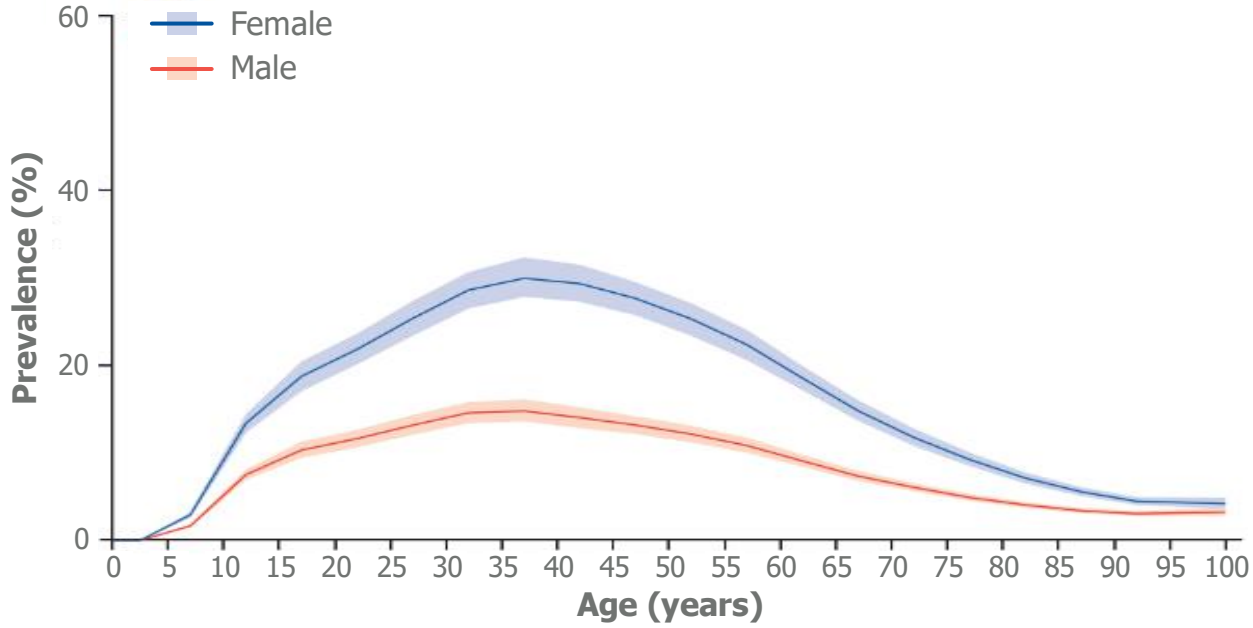
Slides are prepared by the Speaker, Pfizer review is limited to check of adherence to label and local regulations, references have not been checked by Pfizer, Views if any expressed by the Speaker are their own and not necessarily those of Pfizer.

Migraine affects over one billion people worldwide and causes a significant burden[2]

Migraine is the **second highest** cause of global disability in the general population, but **first among women** aged 15–49*[3]

Migraine is **3x** more prevalent in women than men†[4]

Global prevalence of migraine by age and sex (in 2016)[5]



Extracted from GBD. *Lancet Neurol* 2018.[5]

GBD, Global Burden of Disease; MOH, medication overuse headache.
*The level-3 grouping of headache disorders in GBD 2019 includes only specific diseases: migraine and tension-type headache, each with medication overuse headache as a sequela factored in according to the proportion of MOH attributed to it. Expressed as years lived with disability;[3] †Prevalence peaks between the ages of 25 and 55.[4]

2. Ashina M, *et al. Lancet* 2021;397:1485–1495; 3. Steiner TJ, *et al. J Headache Pain* 2020;21:137; 4. Ailani J, *et al. Headache* 2021;61:1021–1039; 5. GBD 2016 Headache Collaborators. *Lancet Neurol* 2018;17:954–976.

Current consensus for acute treatment of migraine[6]

2021 EHF/EAN consensus statement

Acute treatment[6]	
First-line	• NSAIDs + prokinetic antiemetic if necessary
3 consecutive attacks without treatment success	
Second-line	• Triptans (when suboptimal effect, consider combining with fast-active NSAID) • Switch to a different triptan after 3 consecutive attacks without treatment success
Treatment failure of all available options	
Third-line	• Ditans • Gepants

Created from Eigenbrodt A, *et al. Nat Rev Neurol* 2021.[6]

Offer acute medication to all eligible patients who **experience acute migraine attacks** and advise use **early in the headache phase** of the attack, as effectiveness depends on **timely use with the recommended dose**

UAE consensus statement Acute Treatment

The expert panel agreed that the gepants and ditans could be reserved for those who show an inadequate response to **two triptans** or those in whom **triptans are contraindicated**

EAN, European Academy of Neurology; EHF, European Headache Federation; NSAID, non-steroidal anti-inflammatory drug.

6. Eigenbrodt A, *et al. Nat Rev Neurol* 2021;17:501–514.

Current consensus for prevention of migraine[6]

2021 EHF/EAN consensus statement

Preventive treatment*[6]	
First-line	• Beta blockers • Topiramate • Candesartan
Second-line	• Flunarizine • Amitriptyline • Sodium valproate†
Treatment failure of all available options	
Third-line	• Botulinum toxin • CGRPs based therapy

Created from Eigenbrodt A, *et al. Nat Rev Neurol* 2021.[6]

Consider preventive treatment in patients who are adversely **affected by migraine on ≥2 days per month despite optimised acute treatment** or in patients who overuse acute treatment

UAE consensus statement Preventive Treatment

For individuals with migraines who require preventive treatment **CGRP based therapies** should be considered as a **first-line treatment option for migraine prophylaxis**

CGRP, calcitonin gene-related peptide; EAN, European Academy of Neurology; EHF, European Headache Federation; mAb, monoclonal antibody.
*Gepants were not approved for migraine prevention at the time the consensus statement was created; †Sodium valproate is absolutely contraindicated in women of childbearing potential;[6] ‡The EHF updated 2022 guidelines recommend mAbs targeting the CGRP pathway to be included as first-line treatment options in individuals with migraine who require preventive treatment.[7]
6. Eigenbrodt A, *et al. Nat Rev Neurol* 2021;17:501–514; 7. Sacco S, *et al. J Headache Pain* 2022;23:67.

What are some of your patients' treatment goals?

- Rapid and consistent freedom from pain and associated symptoms, especially MBS, without recurrence[4]
- Reduction in headache frequency, intensity and duration[4]
- Minimise need for urgent medical care[4]
- Reduce the overuse of acute medication, which may lead to MOH[4,6]
- Improve quality of life[4]

MBS, most bothersome symptom; MOH, medication overuse headache.

4. Ailani J, *et al. Headache* 2021;61:1021–1039; 6. Eigenbrodt A, *et al. Nat Rev Neurol* 2021;17:501–514.

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Nurtec ODT (rimegepant) orally disintegrating tablets 75 mg

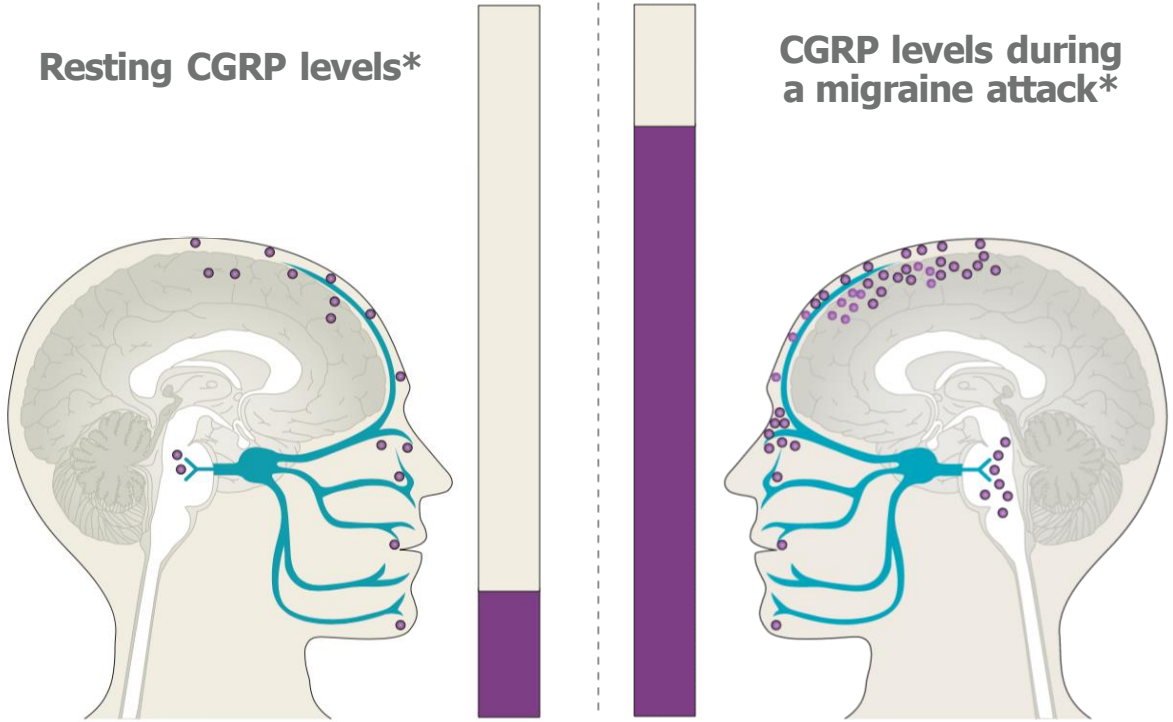
Targeting the CGRP pathway

Pfizer | Nurtec® ODT (rimegepant) orally disintegrating tablets 75 mg

Rimegepant is a small molecule CGRP receptor antagonist[1,8]

CGRP is an important mediator of migraine and a target of migraine treatment[9–11]

Plasma CGRP levels increase during a migraine attack[8–10]



Extracted from Schuster N, Rapoport A. *Nat Rev Neurol* 2016.[10]

CGRP is a pain-signalling neuropeptide and potent vasodilator[8]

- Released from the trigeminal sensory afferents and the spinal trigeminal nucleus[10]

Studies have shown that CGRP:[8,11]

- Plasma levels are elevated during and outside of migraine attacks in people with migraine
- Infusion into people with migraine can trigger a migraine attack

CGRP, calcitonin gene-related peptide.
*CGRP levels in blood and saliva.[10]

1. Nurtec ODT 75 mg UAE LPD USPI. Revision date May 2021. 8. Ho T *et al. Nat Rev Neurol* 2010;6:573–582; 9. Noseda R, Burstein R. *Pain* 2013;154:S44–53; 10. Schuster N, Rapoport A. *Nat Rev Neurol* 2016;12:635–650; 11. Ashina M *et al. Pain* 2000;86:133–138.

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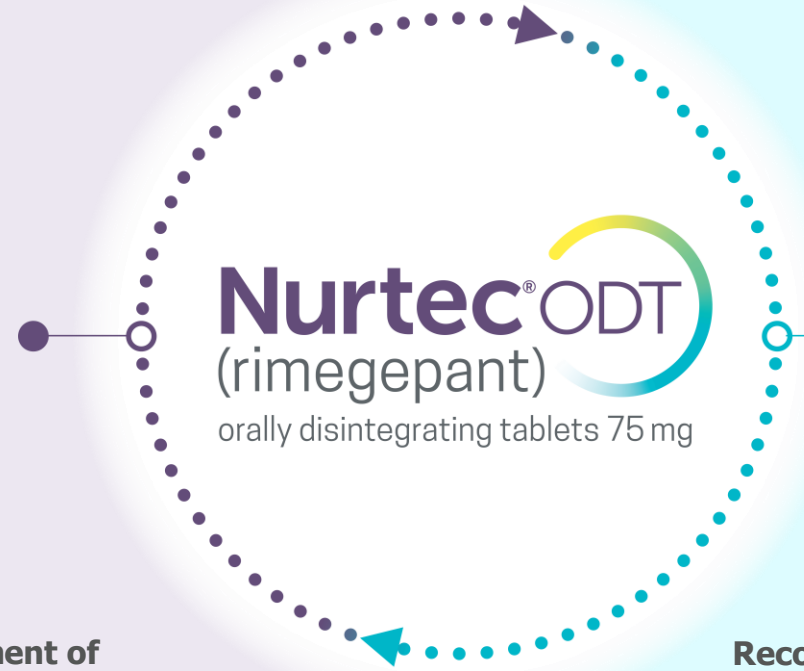
Nurtec® ODT (rimegepant) orally disintegrating tablets 75 mg

Nurtec® is the first and only medication approved to treat migraine and prevent episodic migraine in adults*[1,12]

An orally disintegrating tablet administered under or on the tongue[1]

ACUTE

treatment of migraine with or without aura in adults



PREVENTIVE

treatment of episodic migraine in adults who have at least four migraine attacks per month

Recommended dosage for acute treatment of migraine: 75 mg Nurtec®, as needed, once daily. The maximum dose per day is 75 mg[1]

Recommended dosage for preventive treatment of episodic migraine: 75 mg Nurtec® every other day. The maximum dose per day is 75 mg[1]

*Who have at least four migraine attacks per month.[1]

1. Nurtec ODT 75 mg UAE LPD USPI. Revision date May 2021. 12. Lipton RB, *et al. Practical Neurology* 2021;26.

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Nurtec® ODT (rimegepant) orally disintegrating tablets 75 mg

The evidence behind Nurtec®

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Nurtec® ODT (rimegepant) orally disintegrating tablets 75 mg

Nurtec® was investigated for both acute treatment of migraine and prevention of episodic migraine in adults[13–17]

Pivotal Phase III trials: Acute treatment

PHASE III STUDY 301 (NCT03235479)[13]

Rimegepant 75 mg* *versus* placebo for the acute treatment of migraine with and without aura in adults (N=1162)

PHASE III STUDY 302 (NCT03237845)[13,14]

Rimegepant 75 mg* *versus* placebo for the acute treatment of migraine with and without aura in adults (N=1186)

PHASE III STUDY 303 (NCT03461757)[13,15]

Rimegepant ODT† *versus* placebo for the acute treatment of migraine with and without aura in adults (N=1466)

POST-HOC ANALYSIS OF POOLED DATA[16]

Pooled results from Study 301, Study 302 and Study 303, assessing efficacy in adults with migraine based on triptan treatment experience (N=3507)

Pivotal Phase II/III trials: Preventive treatment

PHASE II/III STUDY 305 (NCT03732638)[13,17]

Rimegepant 75 mg* every other day *versus* placebo for the preventive treatment of migraine in adults (N=695)

Phase II longer-term safety: Acute treatment

PHASE II/III STUDY 201 (NCT03266588)[13]

Open-label long-term safety study of rimegepant 75 mg* for the acute treatment of migraine with and without aura in adults (N=1800)

ODT, orally disintegrating tablet.
*A different oral dosage form of rimegepant that was bioequivalent to **Nurtec®** was used in Study 301, 302, 305 and 201.[#13,14,17] † Lyophilisate /ODT formulation.[15]
[#] The approved form is ODT.

13. Vydura® EPAR. Available at: https://www.ema.europa.eu/en/documents/assessment-report/vydura-epar-public-assessment-report_en.pdf (Last accessed: December 2023); 14. Lipton R, *et al. N Engl J Med* 2019;381:142–149; 15. Croop R, *et al. Lancet* 2019;394:737–745; 16. Lipton RB, *et al. Cephalalgia*. 2023;43(2):03331024221141686; 17. Croop R *et al. Lancet* 2021;397:51–60.

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Nurtec® ODT (rimegepant) orally disintegrating tablets 75 mg

Study 303 assessed the efficacy, safety and tolerability of rimegepant ODT* for the acute treatment of migraine[13,15]

Acute

Phase III, randomised, double-blind, placebo-controlled trial[13,15]

- Included adults aged **≥18 years** with **≥1 year history of migraine**† with or without aura[13,15]
- 1466 participants were **randomly assigned** to rimegepant ODT* (n=732) or placebo (n=734) for **acute attacks** experienced within 45 days of randomisation‡[15]

The majority of patients in Study 303 had migraine without aura, with a mean of 4.6 moderate to severe attacks per month[15]

ICHD-3, The International Classification of Headache Disorders (Third Edition); ODT, orally disintegrating tablet.
* Lyophilisate /ODT formulation;[15] †Migraine according to ICHD-3 criteria;[15] ‡Participants who had not had an attack of moderate or severe pain intensity within 45 days of randomisation were instructed to return unused study medication and the eDiary to the study centre and completed all end of study procedures.[15]
13. Vydura® EPAR. Available at: https://www.ema.europa.eu/en/documents/assessment-report/vydura-epar-public-assessment-report_en.pdf (Last accessed: December 2023); 15. Croop R, *et al. Lancet* 2019;394:737–745.

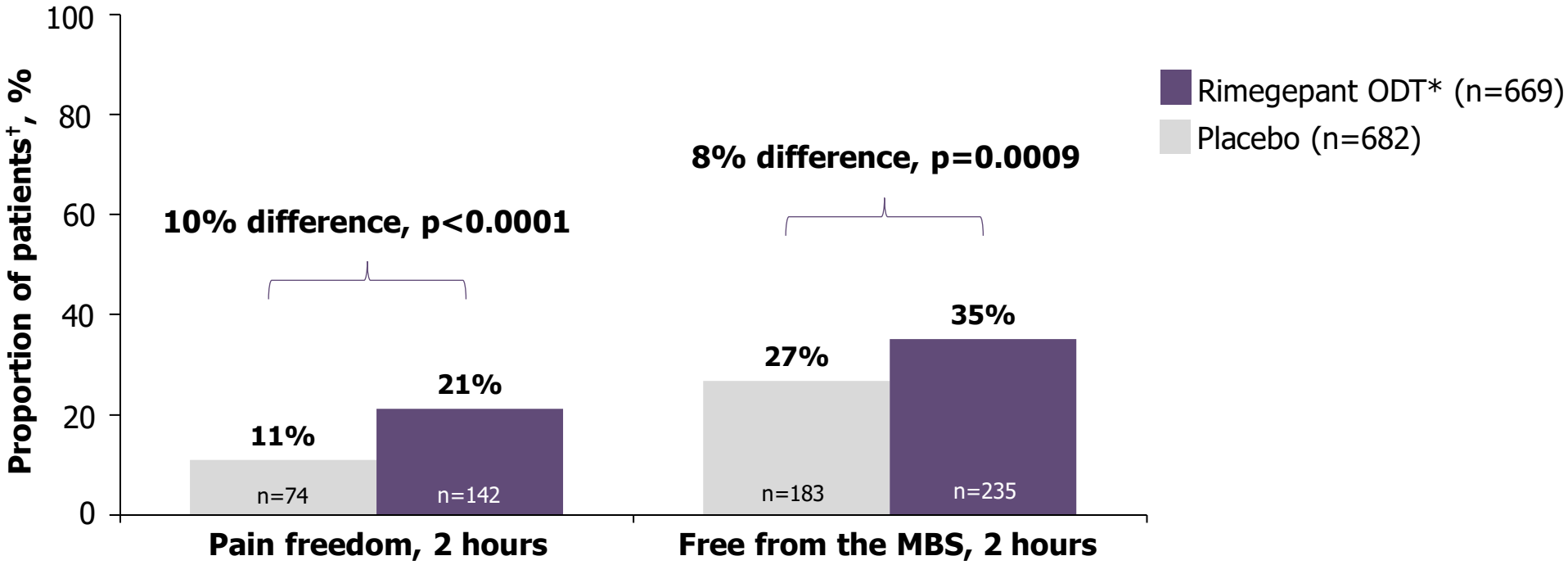
Pfizer

Nurtec® ODT (rimegepant) orally disintegrating tablets 75 mg

Rimegepant ODT* provided pain freedom and freedom from MBS compared with placebo at 2 hours post-dose[13,15]

Acute

COPRIMARY ENDPOINTS



Created from Croop R, *et al. Lancet* 2019.[15]

MBS, most bothersome symptom; ODT, orally disintegrating tablet.
* Lyophilisate /ODT formulation;[15] †Patients using rescue medications at or before the assessment and patients not providing data were classified as treatment failures.[15]
13. Vydura® EPAR. Available at: https://www.ema.europa.eu/en/documents/assessment-report/vydura-epar-public-assessment-report_en.pdf (Last accessed: December 2023); 15. Croop R, *et al. Lancet* 2019;394:737–745.

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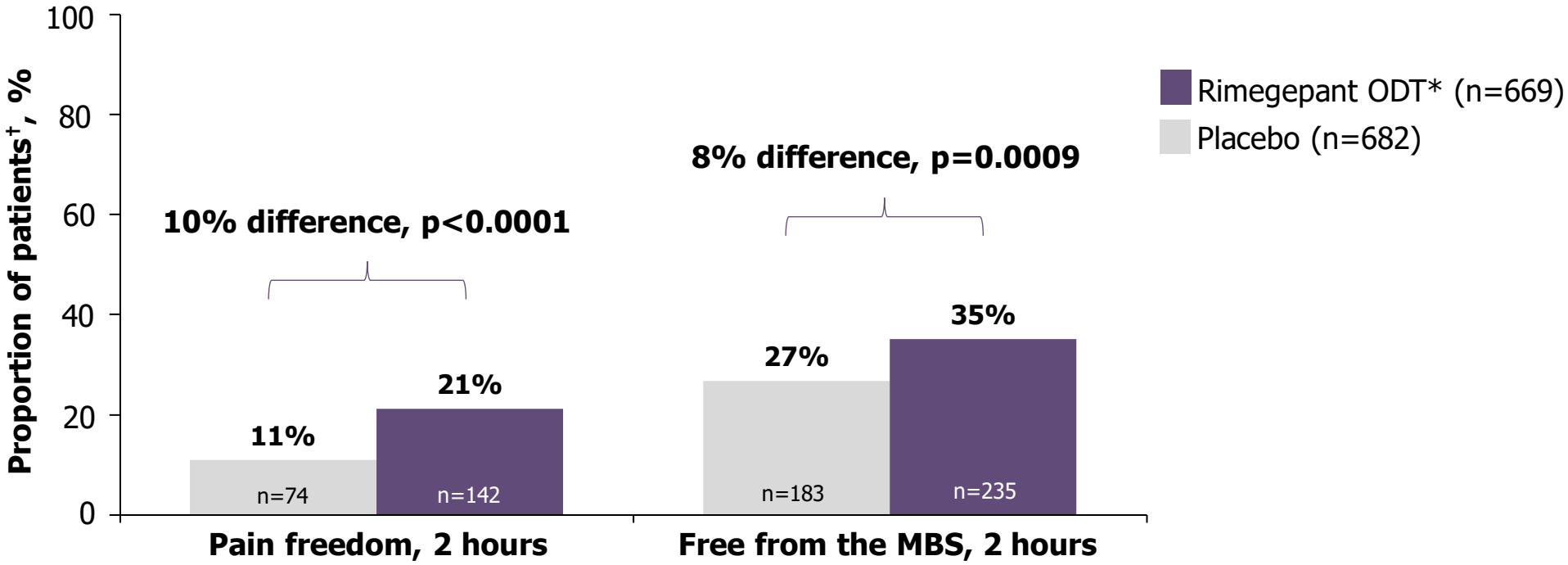

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MBS, most bothersome symptom; ODT, orally disintegrating tablet.
* Lyophilisate /ODT formulation;[15] †Patients using rescue medications at or before the assessment and patients not providing data were classified as treatment failures.[15]
13. Vydura® EPAR. Available at: https://www.ema.europa.eu/en/documents/assessment-report/vydura-epar-public-assessment-report_en.pdf (Last accessed: December 2023); 15. Croop R, *et al. Lancet* 2019;394:737–745.

Pfizer

Nurtec® ODT (rimegepant) orally disintegrating tablets 75 mg

Study 303: All primary and secondary endpoints*[13,15]

Acute

- Rimegepant ODT† was **significantly superior to placebo** in **19 of the 21** secondary efficacy endpoints[15]
- Secondary endpoints were divided into three categories:[15]
  - **Early action (60–90 min)**
  - **2-hour effects**
  - **Durable effects (24–48 h)**

	Rimegepant Events/patients (%)	Placebo Events/patients (%)	Risk difference (95% CI)
Primary endpoints			
Freedom from pain at 2 h postdose	142/669 (21·2)	74/682 (10·9)	10·4 (6·5 to 14·2)
Freedom from most bothersome symptom at 2 h postdose	235/669 (35·1)	183/682 (26·8)	8·3 (3·4 to 13·2)
Secondary endpoints			
Pain relief at 2 h postdose	397/669 (59·3)	295/682 (43·3)	16·1 (10·8 to 21·3)
Ability to function normally at 2 h postdose	255/669 (38·1)	176/682 (25·8)	12·3 (7·4 to 17·2)
Sustained pain relief from 2–24 h postdose	320/669 (47·8)	189/682 (27·7)	20·1 (15·1 to 25·2)
Sustained freedom from most bothersome symptom from 2–24 h postdose	181/669 (27·1)	121/682 (17·7)	9·3 (4·9 to 13·7)
No rescue medication within 24 h postdose	574/669 (85·8)	483/682 (70·8)	15·0 (10·7 to 19·3)
Sustained ability to function normally from 2–24 h postdose	198/669 (29·6)	115/682 (16·9)	12·7 (8·3 to 17·2)
Sustained pain relief from 2–48 h postdose	282/669 (42·2)	172/682 (25·2)	16·9 (12·0 to 21·9)
Sustained freedom from most bothersome symptom from 2–48 h postdose	155/669 (23·2)	112/682 (16·4)	6·7 (2·5 to 11·0)
Sustained ability to function normally from 2–48 h postdose	174/669 (26·0)	105/682 (15·4)	10·6 (6·3 to 14·9)
Freedom from photophobia at 2 h postdose	198/593 (33·4)	150/611 (24·5)	8·8 (3·7 to 13·9)
Ability to function normally at 90 min postdose	202/669 (30·2)	145/682 (21·3)	8·9 (4·3 to 13·6)
Pain relief at 90 min postdose	332/669 (49·6)	254/682 (37·2)	12·4 (7·1 to 17·6)
Sustained freedom from pain from 2–24 h postdose	105/669 (15·7)	38/682 (5·6)	10·1 (6·9 to 13·4)
Freedom from most bothersome symptom at 90 min postdose	183/669 (27·4)	147/682 (21·5)	5·8 (1·2 to 10·4)
Freedom from pain at 90 min postdose	101/669 (15·1)	50/682 (7·3)	7·8 (4·4 to 11·1)
Freedom from phonophobia at 2 h postdose	188/451 (41·7)	135/447 (30·2)	11·5 (5·3 to 17·7)
Sustained freedom from pain from 2–48 h postdose	90/669 (13·5)	37/682 (5·4)	8·0 (4·9 to 11·1)
Pain relief at 60 min postdose	246/669 (36·8)	213/682 (31·2)	5·5 (0·5 to 10·6)
Ability to function normally at 60 min postdose	149/669 (22·3)	108/682 (15·8)	6·4 (2·3 to 10·6)
Freedom from nausea at 2 h postdose	203/397 (51·0)	194/430 (45·2)	5·9 (−0·9 to 12·7)
No pain relapse from 2–48 h postdose	90/142 (63·4)	37/74 (50·0)	13·3 (−0·4 to 27·1)

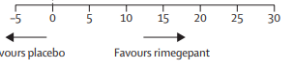

***Figure 3*: Forest plot of primary and secondary endpoints**
All comparisons of rimegepant with placebo were statistically significant in hierarchical testing, except freedom from nausea at 2 h postdose and no pain relapse from 2–48 h postdose. Percentages are Cochran-Mantel-Haenszel estimates.

Extracted from Croop R, *et al. Lancet* 2019.[15]

CI, confidence interval; h, hours; ODT, orally disintegrating tablet.
*To control the type I statistical error rate at 0.05, a hierarchical gatekeeping procedure was applied, with a prespecified sequence of comparisons from the co-primary endpoints through the secondary endpoints in the order listed in the protocol;[15] † Lyophilisate /ODT formulation.[15]

13. Vydura® EPAR. Available at: https://www.ema.europa.eu/en/documents/assessment-report/vydura-epar-public-assessment-report_en.pdf (Last accessed: December 2023); 15. Croop R, *et al. Lancet* 2019;394:737–45.

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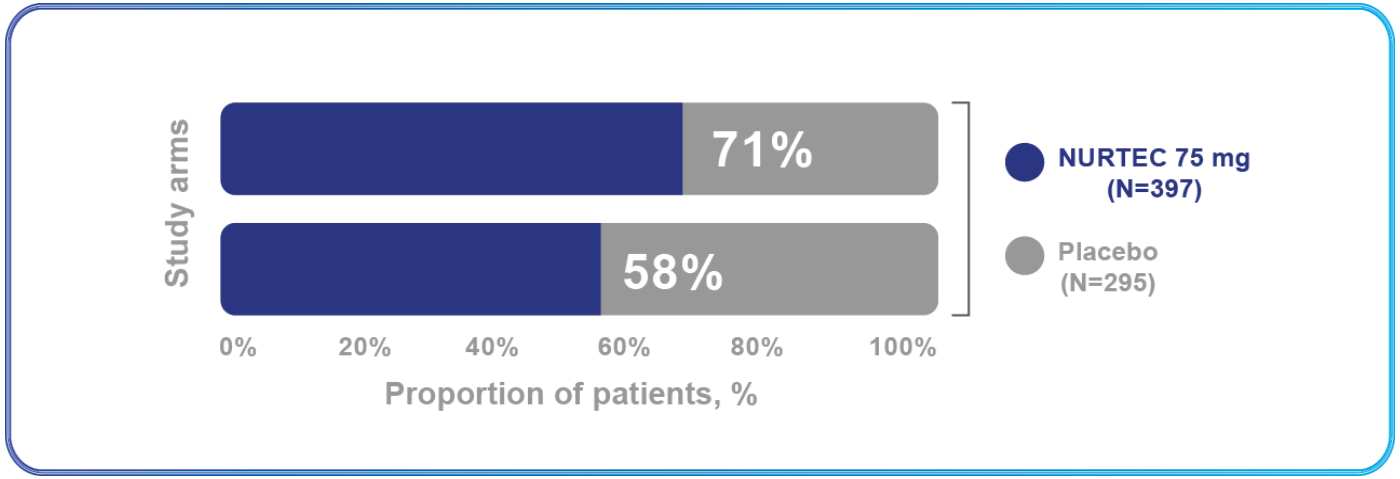
Nurtec® ODT (rimegepant) orally disintegrating tablets 75 mg

Acute

NURTEC Provides Sustained Pain Relief From a Migraine Attack for Up to 48 Hours

Of those patients who achieved pain relief at 2 hours (59%), 71% continued to experience sustained pain relief through 48 hours[2]



86%
of patients on NURTEC did not require rescue medication in the first 24 hours vs 71% with placebo[2]
P<0.0001[3]

71% of patients achieved sustained pain relief vs 58% taking placebo.[2]

The tablet and oral lyophilisate Rimegepant formulations were shown to be bioequivalent and the decision on what formulation to proceed with was based on patient convenience.[4]

REFERENCES
1. VYDURA (rimegepant) [package insert]. Dublin, Ireland: Pzer Incorporated/Biohaven Pharmaceutical Holding Company Ltd; 2022
2. Croop R, Goadsby PJ, Stock DA, et al. Efficacy, safety, and tolerability of rimegepant orally disintegrating tablet for the acute treatment of migraine: a randomised, phase 3, double-blind, placebo-controlled trial. *Lancet*. 2019;394(10200):737-745.
3. Data on File. [BHV3000-303]. Biohaven Pharmaceuticals.
4. European Medicines Agency. Vydura (rimegepant) Assessment Report. 2022. 1-135. https://www.ema.europa.eu/en/documents/assessment-report/vydura-epar-public-assessment-report_en.pdf, Last accessed (November 2023)

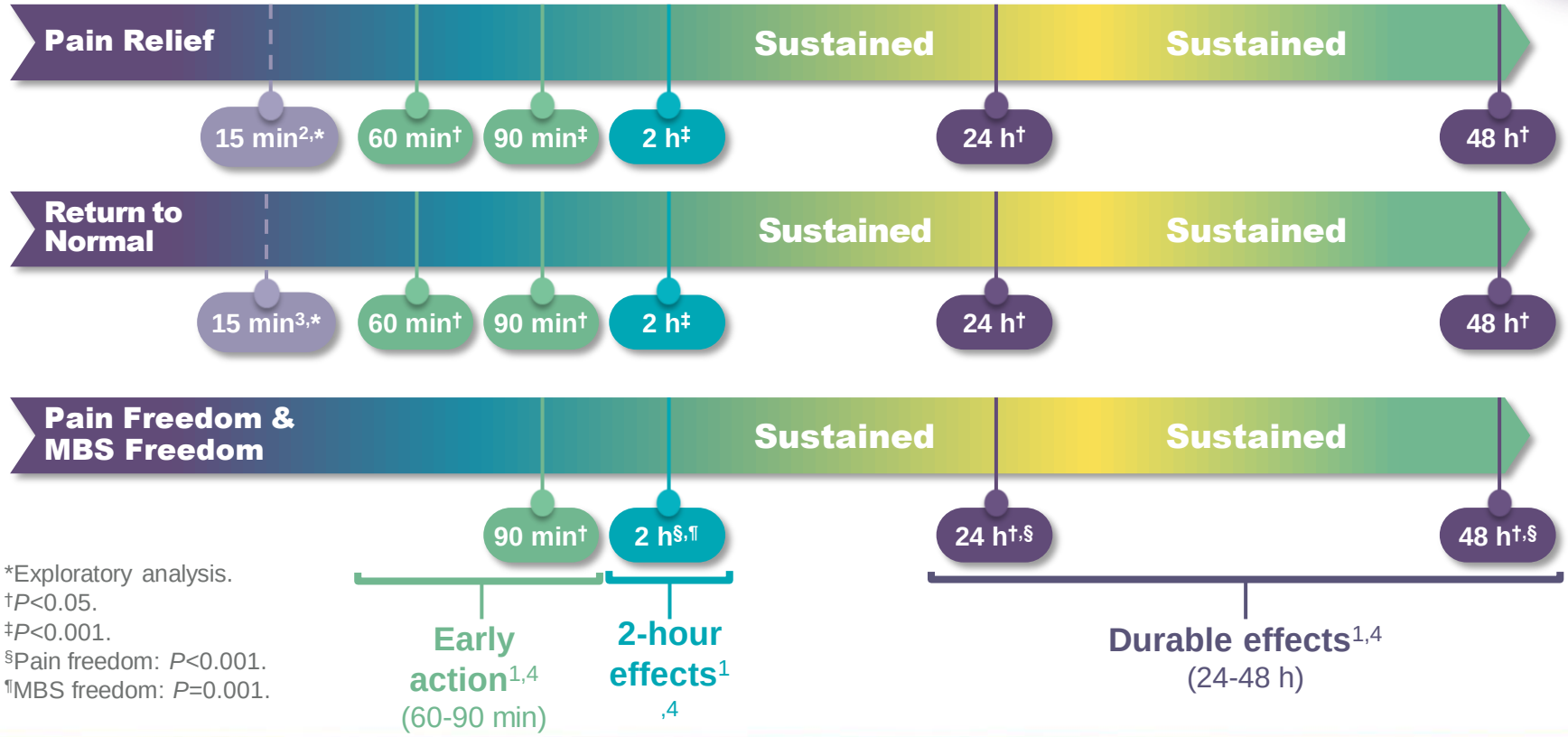
Pfizer

Nurtec® ODT (rimegepant)
orally disintegrating tablets 75 mg

One Dose of Nurtec ODT Works Quickly and Treats Migraine for up to 48 Hours

Acute

ONE DOSE WITHOUT RESCUE MEDICATION



*Exploratory analysis.
†*P*<0.05.
‡*P*<0.001.
§Pain freedom: *P*<0.001.
¶MBS freedom: *P*=0.001.

63% of patients taking Nurtec ODT (rimegepant) who experienced freedom from pain at 2 hours maintained it through 48 hours

63.4% (n=90/142) of patients taking Nurtec ODT vs 50% (n=37/74) of patients taking placebo

1. Croop R et al. *Lancet*. 2019;394(10200):737-745. 2. Data on file. RIM108. Biohaven Pharmaceuticals Inc. 3. Data on file. RIM106. Biohaven Pharmaceuticals Inc. 4 Nurtec ODT, UAE LPD, Revision date May 2021.

Pfizer

Nurtec® ODT (rimegepant) orally disintegrating tablets 75 mg

The most common AEs in either treatment group were nausea, urinary tract infection and dizziness[13,15]

Acute

Summary of AEs†[15]	Rimegepant ODT* n=682	Placebo n=693
Participants with adverse event	90 (13)	73 (11)
AEs, ≥1% in either treatment group		
Nausea	11 (2)	3 (<1)
Urinary tract infection	10 (1)	4 (1)
Dizziness	6 (1)	7 (1)
AEs related to treatment	47 (7)	36 (5)
Serious AEs	0	0

Extracted from Croop R *et al. Lancet* 2019.[15]

One subject in each treatment arm had an ALT or AST >3 x ULN[15]

AE, adverse events; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ODT, orally disintegrating tablet; ULN, upper limit of normal.
* Lyophilisate /ODT formulation;[15] †Data are n (%).[15]
13. Vydura® EPAR. Available at: https://www.ema.europa.eu/en/documents/assessment-report/vydura-epar-public-assessment-report_en.pdf (Last accessed: December 2023); 15. Croop R, *et al. Lancet* 2019;394:737–745.

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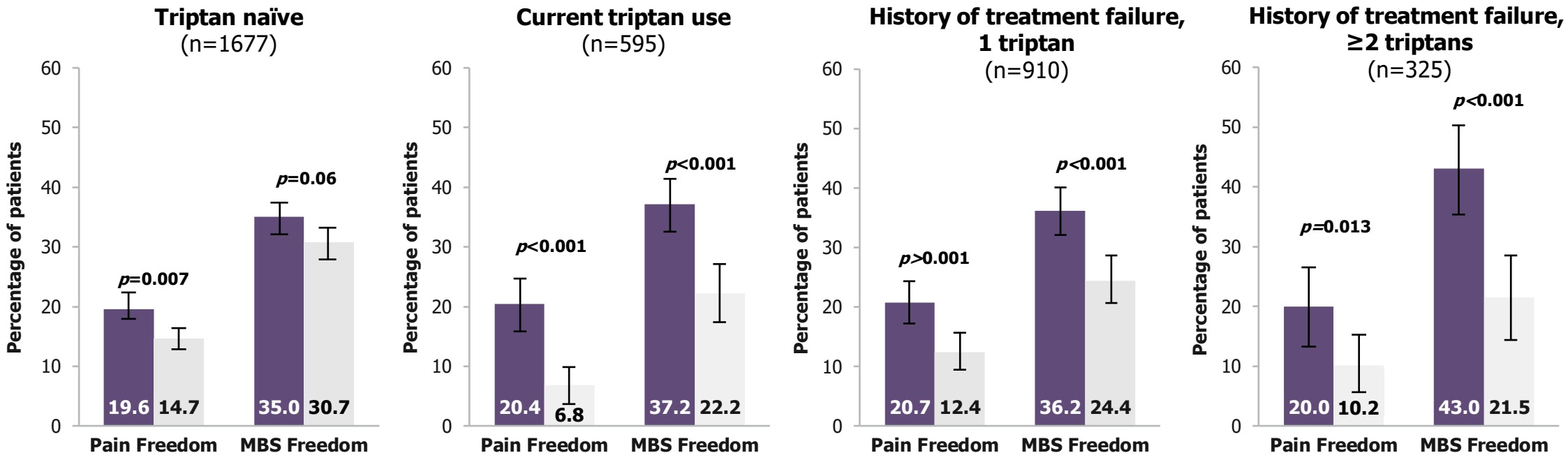
Rimegepant* improved pain and MBS freedom outcomes compared with placebo irrespective of triptan treatment status[16]

Acute

Pain and MBS freedom 2 h post-dose by triptan treatment status in a pooled post-hoc analysis[16]



	Triptan naïve		Current triptan use		History of treatment failure, 1 triptan		History of treatment failure, ≥2 triptans	
Rimegepant*, n=	866	866	285	285	450	450	148	148
Placebo, n=	811	811	310	310	460	460	177	177

Extracted from Lipton RB, *et al. Cephalalgia* 2023.[16]

h, hours; MBS, most bothersome symptom; ODT, orally disintegrating tablet.
*This study evaluated solid oral dosage form of rimegepant that was bioequivalent to the oral lyophilisate was used in Study 301 and Study 302.[#] Study 303 used a ODT formulation.[13–15]
[#] The approved form is ODT.
13. Vydura® EPAR. Available at: https://www.ema.europa.eu/en/documents/assessment-report/vydura-epar-public-assessment-report_en.pdf (Last accessed: December 2023); 14. Lipton RB, *et al. N Engl J Med* 2019;381:142–149; 15. Croop R, *et al. Lancet* 2019;394:737–745; 16. Lipton RB, *et al. Cephalalgia* 2023;43:3331024221141686.

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Study 305 assessed the efficacy and safety of rimegepant 75 mg* for the prevention of episodic migraine[13,17]

Preventive

Phase II/III, randomised, double-blind, placebo-controlled trial[13,17]

- Included adults aged **≥18 years** with **≥1 year history of migraine**,† with or without aura, or **chronic migraine**[13,17]
- After a 4-week observation period, eligible participants were randomised to oral rimegepant* (n=370) or placebo (n=371) **EOD for 12 weeks**‡[13,17]

The majority of patients in Study 305 had migraine without aura, with a mean of 10.1 migraine days per month during the 4-week observation period[13,17]

EOD, every other day; ICHD-3, The International Classification of Headache Disorders (Third Edition); MMDs, monthly migraine days; ODT, orally disintegrating tablet.
*This study evaluated a solid oral dosage form;[17] †Migraine according to ICHD-3 criteria;[17] ‡In efficacy-evaluable participants, 348 assigned rimegepant and 347 assigned placebo.[17]

13.Vydura® EPAR. Available at: https://www.ema.europa.eu/en/documents/assessment-report/vydura-epar-public-assessment-report_en.pdf (Last accessed: December 2023); 17. Croop R, *et al. Lancet* 2021;397:51–60.

Pfizer

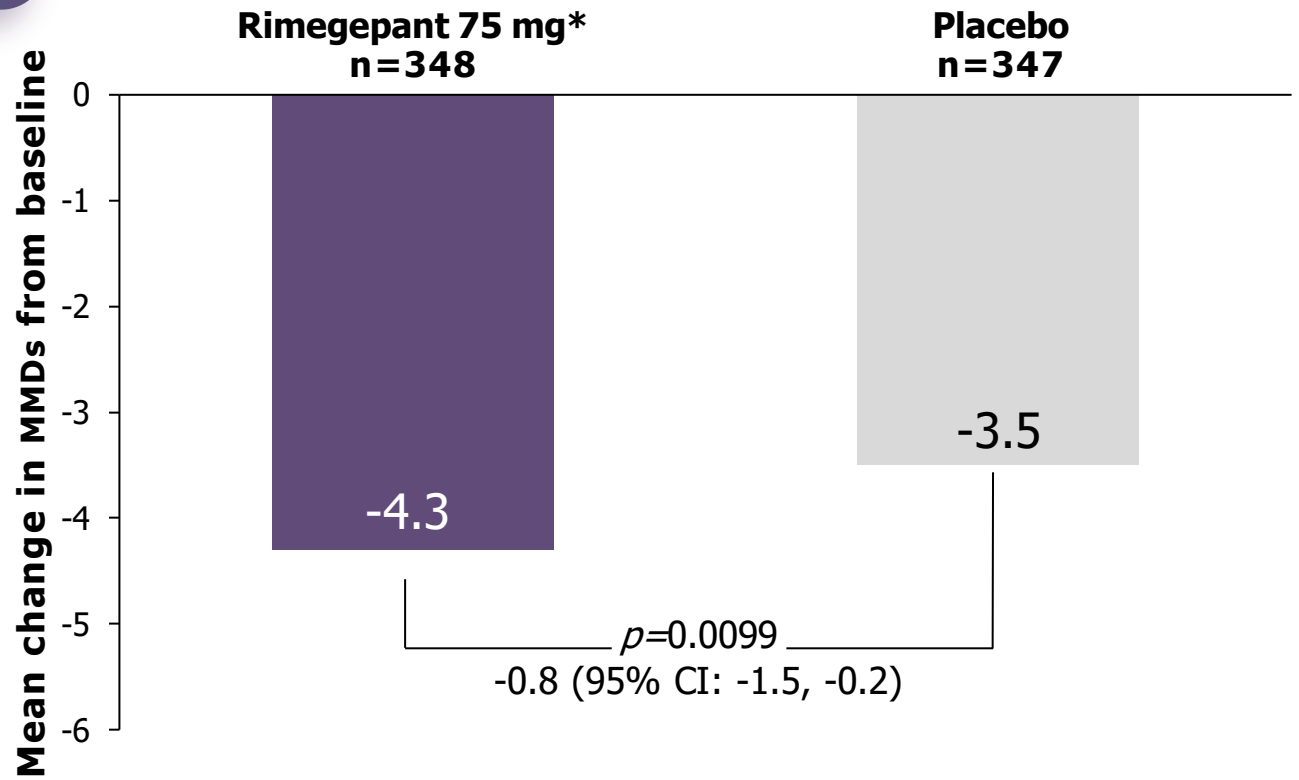
Nurtec® ODT (rimegepant) orally disintegrating tablets 75 mg

Rimegepant 75 mg* provided a significant reduction in MMDs from baseline compared with placebo[13,17]

Preventive

PRIMARY ENDPOINT

Reduction of mean MMDs during weeks 9 to 12[17]



Created from Croop R, *et al. Lancet* 2021.[17]

CI, confidence interval; MMDs, monthly migraine days; ODT, orally disintegrating tablet.
*This study evaluated a solid oral dosage form.[17]

13. Vydura® EPAR. Available at: https://www.ema.europa.eu/en/documents/assessment-report/vydura-epar-public-assessment-report_en.pdf (Last accessed: December 2023); 17. Croop R, *et al. Lancet* 2021;397:51–60.

Pfizer

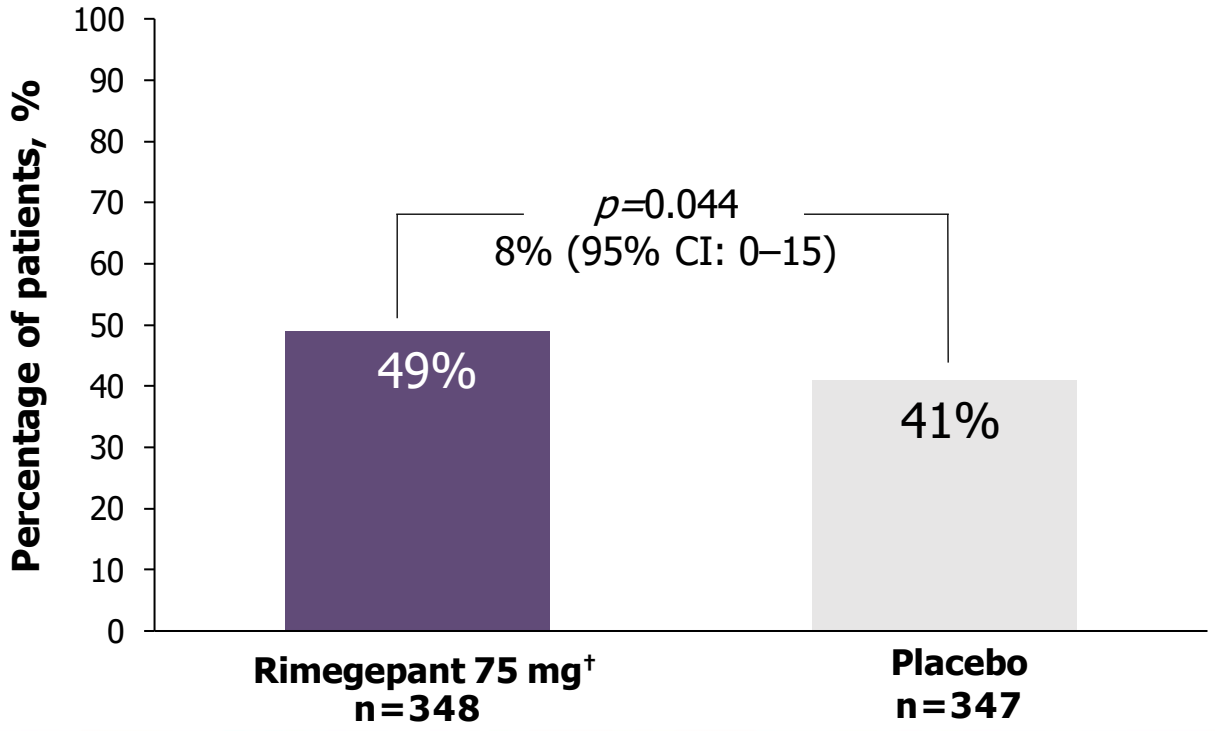
Nurtec® ODT (rimegepant) orally disintegrating tablets 75 mg

Significantly* more patients taking rimegepant 75 mg† had a ≥50% reduction in the mean number of moderate or severe MMDs compared with placebo[13,17]

Preventive

SECONDARY ENDPOINT

≥50% reduction in mean number of moderate or severe MMDs during weeks 9–12[17]



Created from Croop R, *et al. Lancet* 2021.[17]

CI, confidence interval; MMDs, monthly migraine days; ODT, orally disintegrating tablet.
*Significant p-value in hierarchical testing;[17] †This study evaluated a solid oral dosage form.[17]

13. Vydura® EPAR. Available at: https://www.ema.europa.eu/en/documents/assessment-report/vydura-epar-public-assessment-report_en.pdf (Last accessed: December 2023); 17. Croop R *et al. Lancet* 2021;397:51–60.

Pfizer

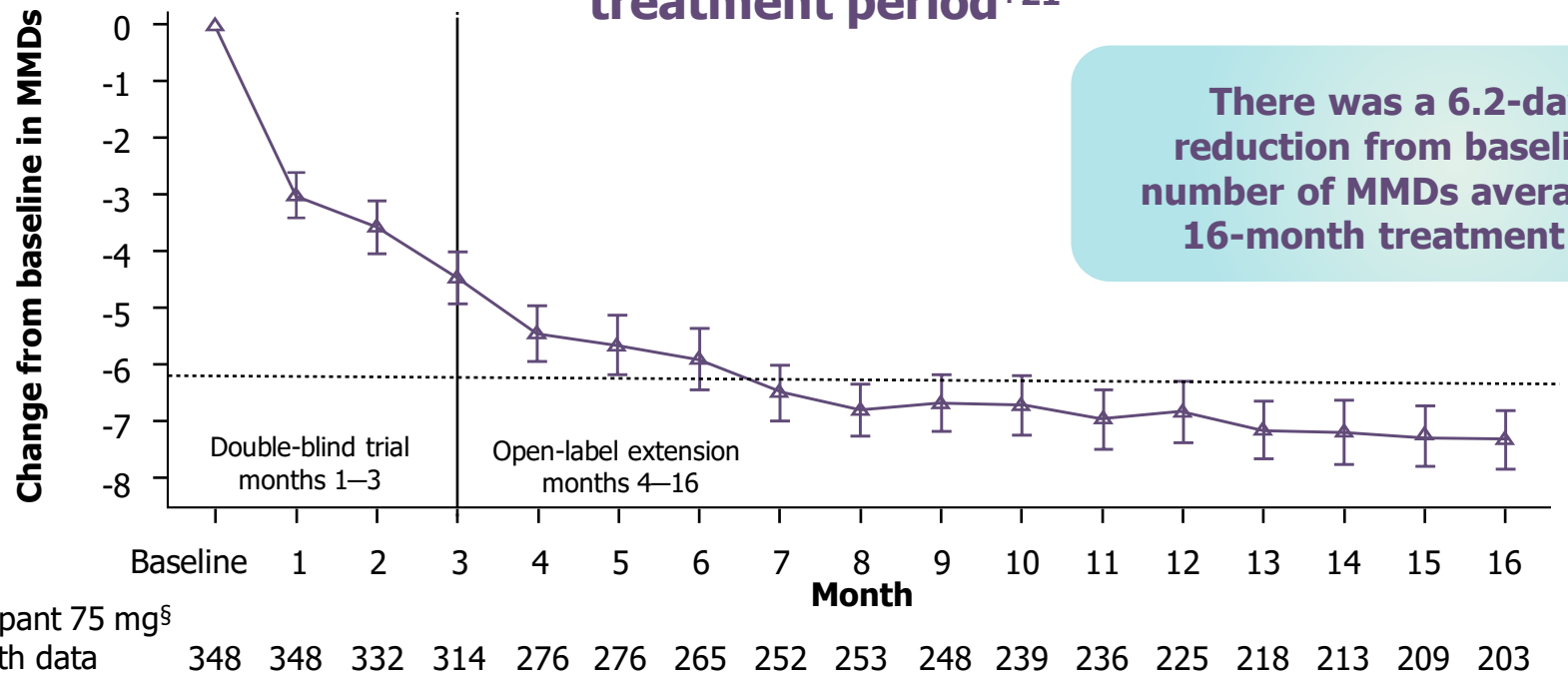
Nurtec® ODT (rimegepant) orally disintegrating tablets 75 mg

Efficacy was sustained for up to 1 year in the open-label study extension period in Study 305*†21

Preventive

OPEN-LABEL EXTENSION

Change in mean number of MMDs during the 16-month treatment period‡21



There was a 6.2-day mean reduction from baseline in the number of MMDs averaged over a 16-month treatment period[21]

Extracted from Vydura SmPC[21]

MMDs, monthly migraine days; ODT, orally disintegrating tablet; SmPC, Summary of Product Characteristics.

*Open-label study extension lasted up to 1 year, patients received rimegepant;[1] †This study evaluated a solid oral dosage form;[17] ‡203 patients in the 12-month open-label extension assigned to rimegepant completed the overall 16-month treatment period;[1] §Every other day plus as needed on non-scheduled dosing days.[1]

21. Vydura® (rimegepant) Summary of Product Characteristics. Available in English at: https://www.ema.europa.eu/en/documents/product-information/vydura-epar-product-information_en.pdf (Last accessed: December 2023). 17. Croop R *et al. Lancet* 2021;397:51–60.

Pfizer

Nurtec® ODT (rimegepant) orally disintegrating tablets 75 mg

The safety and tolerability of rimegepant 75 mg* in Study 305 were comparable to placebo and are consistent with Study 303[13,17]

Preventive

Summary of AEs†‡[17]		
	Rimegepant 75 mg* (n=370)	Placebo (n=371)
Patients with any AE	133 (36)	133 (36)
AEs, ≥2% of patients treated with rimegepant*		
Nasopharyngitis	13 (4)	9 (2)
Nausea	10 (3)	3 (1)
Urinary tract infection	9 (2)	8 (2)
Upper respiratory tract infection	8 (2)	10 (3)
Patients with mild AEs	92 (25)	91 (25)
Patients with moderate AEs	64 (17)	62 (17)
Patients with AEs related to treatment	40 (11)	32 (9)
Serious AEs	3 (1)	4 (1)
Serious AEs related to treatment	0	1 (<1%)
AEs leading to discontinuation	7 (2)	4 (1)

Extracted from Croop R, *et al. Lancet* 2021.[17]

- Liver function tests showed **low rates of increased enzymes** in both treatment groups in Study 305[13,17]
- **Four** (1%) patients who were treated with rimegepant* and two (1%) who were treated with placebo had **ALT or AST >3 X ULN**[13,17]
- One patient in the rimegepant* group (<1%) had **asymptomatic aminotransferase elevations**, with ALT >10 x ULN; ALP and bilirubin levels were always within **normal limits**[13,17]
- One other patient in the rimegepant* group (<1%) had **bilirubin levels >2 x ULN** and was diagnosed with a hereditary liver disorder after genotyping[13,17]

AE, adverse event; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ODT, orally disintegrating tablet; ULN, upper limit of normal.
*This study evaluated a solid oral dosage form;[17] †Safety Analysis Set: Enrolled subjects who received at least one dose of rimegepant;[17] ‡Data are n (%).[17]
13. Vydura® EPAR. Available at: https://www.ema.europa.eu/en/documents/assessment-report/vydura-epar-public-assessment-report_en.pdf (Last accessed: December 2023); 17. Croop R, *et al. Lancet* 2021;397:51–60.

Pfizer | Nurtec® ODT (rimegepant) orally disintegrating tablets 75 mg

BREAKING NEWS

CHALLENGE-MIG TRIAL

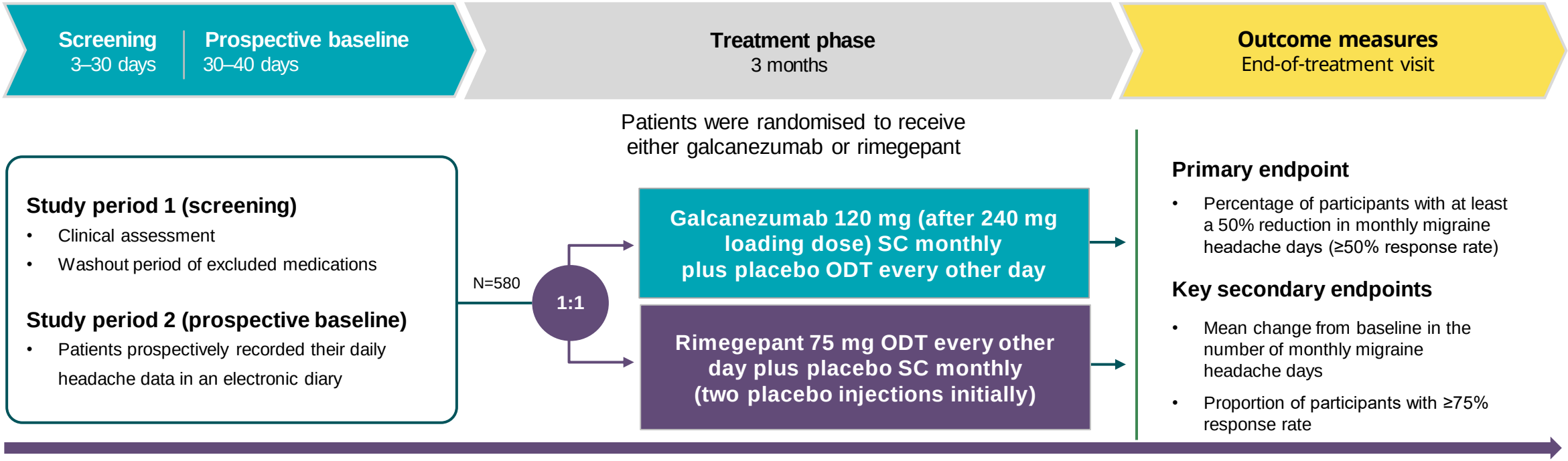
The first and only head-to-head trial of a monoclonal antibody against a gepant

1. Schwedt TJ, *et al. Neurol Ther* 2023. doi: 10.1007/s40120-023-00562-w. [Epub ahead of print]

CHALLENGE-MIG: Phase IV trial for preventive treatment of episodic migraine

Preventive

- This head-to-head study (NCT05127486) was a Phase IV, double-blind, randomised, double-dummy trial of Rimegepant 75 mg ODT vs galcanezumab 120 mg SC for the preventive treatment of episodic migraine



Protocol-specified acute migraine headache medications (paracetamol; nonsteroidal anti-inflammatory drugs; triptans; ergotamine and derivatives; aspirin, caffeine and paracetamol combination; or combinations thereof), as needed, were permitted during all study periods. Gepants, including rimegepant, were not allowed to be used for acute migraine treatment

*Rimegepant is centrally authorised in the EU but not yet marketed in Spain pending pricing and reimbursement approval. ▼Emgality (galcanezumab), Eli Lilly.
ODT, orally disintegrating tablet; SC, subcutaneous.

1. Schwedt TJ, *et al. Neurol Ther* 2023. doi: 10.1007/s40120-023-00562-w. [Epub ahead of print];
2. NCT05127486. Available at https://clinicaltrials.gov/study/NCT05127486. (last accessed November 2023).

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Nurtec® ODT (rimegepant) orally disintegrating tablets 75 mg

CHALLENGE-MIG: efficacy primary endpoint

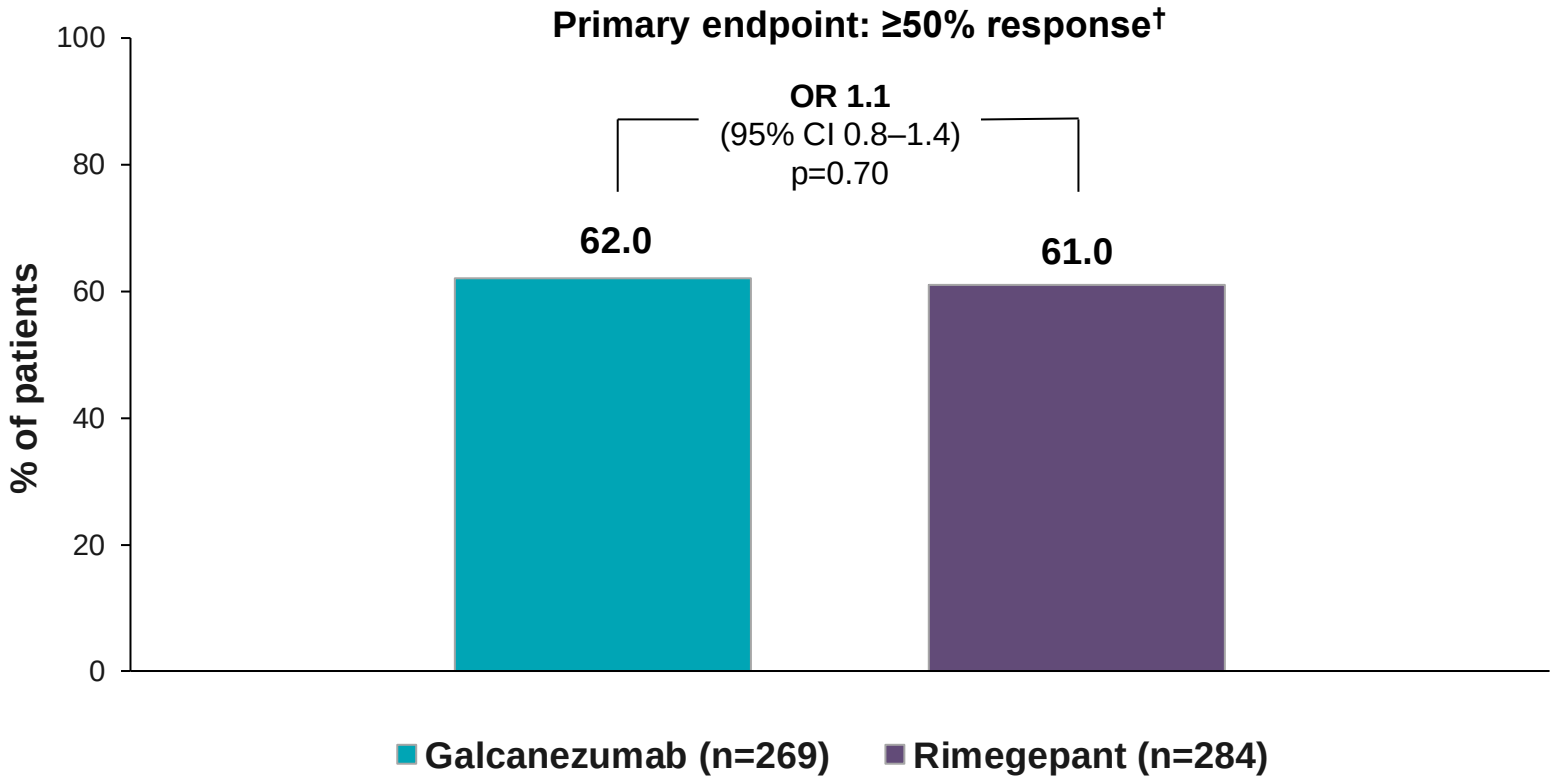
Preventive

Galcanezumab failed to meet its primary endpoint of statistical superiority over Rimegepant

The proportion of participants with at least a 50% reduction in monthly migraine headache days (≥50% response rate) from baseline across 3 months of the double-blind phase was:

- 62.0% in the galcanezumab group
- 61.0% in the rimegepant group

There was no statistically significant difference between groups; odds ratio 1.1 (95% CI 0.8–1.4; p=0.70)



*Rimegepant is centrally authorised in the EU but not yet marketed in Spain pending pricing and reimbursement approval. ▼Emgality (galcanezumab), Eli Lilly.
ODT, orally disintegrating tablet; SC, subcutaneous.

1. Schwedt TJ, *et al. Neurol Ther* 2023. doi: 10.1007/s40120-023-00562-w. [Epub ahead of print];
2. NCT05127486. Available at https://clinicaltrials.gov/study/NCT05127486. (last accessed November 2023).

Pfizer

Nurtec ODT (rimegepant) orally disintegrating tablets 75 mg

Adverse event rates were similar between galcanezumab and rimegepant[18]

Preventive

Variable, n (%)	Galcanezumab* 120 mg (n=287)	Rimegepant† 75 mg (n=293)
Serious adverse events	0	1 (0.3)
Participants with ≥1 TEAE	60 (20.9)	60 (20.5)
Discontinuation from study due to an AE	2 (0.7)	4 (1.4)
TEAEs occurring in ≥3 participants (overall)		
COVID-19	12 (4.2)	5 (1.7)
Nausea	3 (1.0)	4 (1.4)
Fatigue	2 (0.7)	4 (1.4)
Injection-site pain	2 (0.7)	4 (1.4)
Nasopharyngitis	1 (0.3)	5 (1.7)
Influenza	3 (1.0)	2 (0.7)
Anemia	3 (1.0)	1 (0.3)
Migraine	0	4 (1.4)
Sinusitis	1 (0.3)	3 (1.0)
Constipation	3 (1.0)	0
Diarrhea	2 (0.7)	1 (0.3)
Hypertension	1 (0.3)	2 (0.7)
Upper respiratory tract infection	1 (0.3)	2 (0.7)
Vertigo	2 (0.7)	1 (0.3)

Extracted from Schwedt T.J., *et al. Neurol Ther* 2023.[18]

- **One SAE reported:[18]**
  - A **pulmonary embolism** (PE) occurred in a participant receiving rimegepant who had an undisclosed history of PE
  - The participant **recovered and discontinued the study**. The event was considered by the investigator to be related to the blinded study intervention
- **No clinically meaningful differences** between study intervention groups in **vital signs** or **laboratory parameters[18]**

ODT, orally disintegrating tablet; (S)AE, (serious) adverse event; SC, subcutaneous; TEAE, treatment-emergent adverse event.
*Participants received galcanezumab 120 mg and placebo ODT;[18] †Participants received rimegepant 75 mg and SC placebo injection.[18]
18. Schwedt T.J., *et al. Neurol Ther* 2023;1–21.

Pfizer | Nurtec ODT (rimegepant) orally disintegrating tablets 75 mg

Practical aspects of Nurtec® treatment

Pfizer

Nurtec® ODT
(rimegepant)
orally disintegrating tablets 75 mg

Dosing and administration of Nurtec® [1]

Treat acute migraine attacks with or without aura in adults

Take Nurtec® 75 mg, as needed, once daily for migraine

Prevent episodic migraine attacks in adults who have at least four migraine attacks per month

Take Nurtec® 75 mg every other day for preventive treatment of episodic migraine

- Patients place Nurtec® under or on top of their tongue where it dissolves in seconds
- Can be taken with or without meals. No drink or water is needed
- The maximum dose per day is 75 mg
- Another dose of Nurtec® should be avoided within 48 hours when it is concomitantly administered with moderate inhibitors of CYP3A4
- No dose adjustment is required in the elderly, in patients with mild to severe renal impairment, or in patients with mild or moderate hepatic impairment

1. Nurtec ODT 75 mg UAE LPD USPI. Revision date May 2021.

Pfizer

Nurtec® ODT (rimegepant) orally disintegrating tablets 75 mg

Nurtec® for the treatment of acute migraine and prevention of episodic migraine in adults*[1]

Nurtec® is the first dual therapy licensed to **both treat and prevent migraine**, offering patients the flexibility to meet their changing needs[1]

Nurtec® targets CGRP receptors, an important **mediator of migraine**[1,20]

Acute

For the acute treatment of migraine in adults, rimegepant 75 mg† offered **early and sustained efficacy**‡ with acceptable tolerability[15]

Preventive

For episodic migraine prevention in adults, rimegepant 75 mg† was **effective**, with tolerability comparable to placebo[17]

CGRP, calcitonin gene-related peptide; ODT, orally disintegrating tablet.

- Nurtec® is indicated for the acute treatment of migraine with or without aura; and preventive treatment of episodic migraine in adults who have at least four migraine attacks per month;[1] †A solid oral dosage form of rimegepant that was bioequivalent to the oral lyophilisate was used in Study 301, 302, and 305.[#]Study 303 used a ODT formulation;[13–15, 17] ‡Sustained pain relief was for 2–48 hours.[15]

[#]The approved form is ODT.

1. Nurtec ODT 75 mg UAE LPD USPI. Revision date May 2021.; 13. Vydura® EPAR. Available at: https://www.ema.europa.eu/en/documents/assessment-report/vydura-epar-public-assessment-report_en.pdf (Last accessed: December 2023); 14. Lipton R, *et al. N Engl J Med* 2019;381:142–149; 15. Croop R, *et al. Lancet* 2019;394:737–745; 17. Croop R, *et al. Lancet* 2021;397:51–60; 20. Durham P. *N Engl J Med* 2004;350:1073–1075.

Pfizer

Nurtec® ODT (rimegepant) orally disintegrating tablets 75 mg

Important information for the use of Nurtec® in specific populations[1]

Contraindications: Hypersensitivity to the active substance or any of the excipients[1]

Warnings and precautions for use: Hypersensitivity reactions, including serious hypersensitivity, can occur days after administration. If a hypersensitivity reaction occurs, Nurtec® should be discontinued, and appropriate therapy should be initiated[1]

Overuse of any type of medicinal products for headaches can make them worse. If this situation is experienced or suspected, medical advice should be obtained, and treatment should be discontinued. The diagnosis of medication overuse headache should be suspected in patients who have frequent or daily headaches despite (or because of) the regular use of medicinal products for acute headache[1]

Nurtec® is not recommended:[1]

- in patients with severe hepatic impairment
- in patients with end-stage renal disease (CrCl < 15 ml/min)
- for concomitant use with strong inhibitors of CYP3A4
- for concomitant use with strong or moderate inducers of CYP3A4

There are limited data from the use of rimegepant in pregnant women. As a precautionary measure, it is preferable to avoid the use of Nurtec® during pregnancy[1]

Please see the PI for full information on drug interactions and on use in special populations.

CrCl, creatinine clearance; min, minutes; ml, millilitres; PI: Prescribing Information.

1. Nurtec ODT 75 mg UAE LPD USPI. Revision date May 2021.

Nurtec® important safety information[1]

The most common adverse reaction was nausea for acute treatment (2%) and for migraine prophylaxis (2%). Most of the reactions were mild or moderate in severity. Hypersensitivity, including dyspnoea and severe rash, occurred in less than 1% of patients treated.

1. Nurtec ODT 75 mg UAE LPD USPI. Revision date May 2021.

Thank you

Any questions?

Pfizer Breakthroughs that change patients' lives®

Further information is available upon request

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PP-NNT-ARE-0475

Abbreviated Prescribing Information

NURTEC ODT ® ***Abbreviated Prescribing Information***

GENERIC NAME: Rimegepant

PRESENTATION: NURTEC ODT 75 mg orally disintegrating tablets are white to off-white, circular, debossed with the symbol, and supplied in cartons containing a blister pack of 8 orally disintegrating tablets. Each ODT contains 75 mg Rimegepant.

INDICATION(s):

NURTEC ODT is a calcitonin gene-related peptide receptor antagonist indicated for the:

• acute treatment of migraine with or without aura in adults

• preventive treatment of episodic migraine in adults

DOSAGE AND ADMINISTRATION:

• Recommended dosage for acute treatment of migraine: 75 mg taken orally as needed.

• The safety of using more than 18 doses in a 30-day period has not been established.

• Recommended dosage for preventive treatment of episodic migraine: 75 mg taken orally every other day.

• The maximum dose in a 24-hour period is 75 mg.

Pregnancy: Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to NURTEC ODT during pregnancy. For more information, healthcare providers or patients are encouraged to contact: 1-877-366-0324, email nurtecpregnancyregistry@ppd.com, or visit nurtecpregnancyregistry.com.

Risk Summary: There are no adequate data on the developmental risk associated with the use of NURTEC ODT in pregnant women.

Disease-Associated Maternal and/or Embryo/Fetal Risk: Published data have suggested that women with migraine may be at increased risk of preeclampsia and gestational hypertension during pregnancy.

Lactation:

A lactation study was conducted, and the results have established a relative infant dose of less than 1% of the maternal weight-adjusted dose and the milk-to-plasma ratio of 0.20 (see Data). These data support that transfer of Rimegepant into breastmilk is low. There are no data on the effects of Rimegepant on a breastfed infant or on milk production.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for NURTEC ODT and any potential adverse effects on the breastfed.

infant from NURTEC ODT or from the underlying maternal condition.

Pediatric Use:

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use:

In pharmacokinetic studies, no clinically significant pharmacokinetic differences were observed between elderly and younger subjects. Clinical studies of NURTEC ODT did not include enough patients aged 65 and over to determine whether they respond differently from younger patients.

Hepatic Impairment:

No dosage adjustment of NURTEC ODT is required in patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment. Plasma concentrations of Rimegepant were

significantly higher in subjects with severe (Child-Pugh C) hepatic impairment. Avoid use of NURTEC ODT in patients with severe hepatic impairment.

Renal Impairment

No dosage adjustment of NURTEC ODT is required in patients with mild, moderate, or severe renal impairment. NURTEC ODT has not been studied in patients with end-stage renal disease and in patients on dialysis. Avoid use of NURTEC ODT in patients with end-stage renal disease (CLcr < 15 mL/min) [see Clinical Pharmacology (12.3)].

CONTRAINDICATIONS:

• NURTEC ODT is contraindicated in patients with a history of hypersensitivity reaction to Rimegepant, NURTEC ODT, or any of its components. Delayed serious hypersensitivity has occurred.

WARNING AND PRECAUTIONS:

• Hypersensitivity reactions, including dyspnea and rash, have occurred with NURTEC ODT in clinical studies. Hypersensitivity reactions can occur days after administration, and delayed serious hypersensitivity has occurred. If a hypersensitivity reaction occurs, discontinue NURTEC ODT and initiate appropriate therapy.

NURTEC ODT ® ***Abbreviated Prescribing Information***

GENERIC NAME: Rimegepant

PRESENTATION: NURTEC ODT 75 mg orally disintegrating tablets are white to off-white, circular, debossed with the symbol, and supplied in cartons containing a blister pack of 8 orally disintegrating tablets. Each ODT contains 75 mg Rimegepant.

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• preventive treatment of episodic migraine in adults

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• Recommended dosage for preventive treatment of episodic migraine: 75 mg taken orally every other day.
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Pregnancy: Pregnancy Exposure Registry
There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to NURTEC ODT during pregnancy. For more information, healthcare providers or patients are encouraged to contact: 1-877-366-0324, email nurtecpregnancyregistry@ppd.com, or visit nurtecpregnancyregistry.com.
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Disease-Associated Maternal and/or Embryo/Fetal Risk: Published data have suggested that women with migraine may be at increased risk of preeclampsia and gestational hypertension during pregnancy.
Lactation:
A lactation study was conducted, and the results have established a relative infant dose of less than 1% of the maternal weight-adjusted dose and the milk-to-plasma ratio of 0.20 (see Data). These data support that transfer of Rimegepant into breastmilk is low. There are no data on the effects of Rimegepant on a breastfed infant or on milk production.
The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for NURTEC ODT and any potential adverse effects on the breastfed.
infant from NURTEC ODT or from the underlying maternal condition.
Pediatric Use:
Safety and effectiveness in pediatric patients have not been established.
Geriatric Use:
In pharmacokinetic studies, no clinically significant pharmacokinetic differences were observed between elderly and younger subjects. Clinical studies of NURTEC ODT did not include enough patients aged 65 and over to determine whether they respond differently from younger patients.
Hepatic Impairment:
No dosage adjustment of NURTEC ODT is required in patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment. Plasma concentrations of Rimegepant were
significantly higher in subjects with severe (Child-Pugh C) hepatic impairment. Avoid use of NURTEC ODT in patients with severe hepatic impairment.
Renal Impairment
No dosage adjustment of NURTEC ODT is required in patients with mild, moderate, or severe renal impairment. NURTEC ODT has not been studied in patients with end-stage renal disease and in patients on dialysis. Avoid use of NURTEC ODT in patients with end-stage renal disease (CLcr < 15 mL/min) [see Clinical Pharmacology (12.3)].
CONTRAINDICATIONS:
• NURTEC ODT is contraindicated in patients with a history of hypersensitivity reaction to Rimegepant, NURTEC ODT, or any of its components. Delayed serious hypersensitivity has occurred.

WARNING AND PRECAUTIONS:
• Hypersensitivity reactions, including dyspnea and rash, have occurred with NURTEC ODT in clinical studies. Hypersensitivity reactions can occur days after administration, and delayed serious hypersensitivity has occurred. If a hypersensitivity reaction occurs, discontinue NURTEC ODT and initiate appropriate therapy.

DRUG INTERACTIONS:
CYP3A4 Inhibitors:
• Concomitant administration of NURTEC ODT with strong inhibitors of CYP3A4 results in a significant increase in Rimegepant exposure. Avoid concomitant administration of NURTEC ODT with strong inhibitors of CYP3A4.
• Concomitant administration of NURTEC ODT with moderate inhibitors of CYP3A4 may result in increased exposure of Rimegepant. Avoid another dose of NURTEC ODT within 48 hours when it is concomitantly administered with moderate inhibitors of CYP3A4.

CYP3A Inducers:
• Concomitant administration of NURTEC ODT with strong or moderate inducers of CYP3A can result in a significant reduction in Rimegepant exposure, which may lead to loss of efficacy of NURTEC ODT. Avoid concomitant administration of NURTEC ODT with strong or moderate inducers of CYP3A.

P-gp Inhibitors:
• Concomitant administration of NURTEC ODT with potent inhibitors of P-gp (e.g., amiodarone, cyclosporine, lapatinib, quinidine, ranolazine) may result in increased exposure of Rimegepant. Avoid another dose of NURTEC ODT within 48 hours when it is concomitantly administered with potent inhibitors of P-gp.

OVERDOSE:
There is limited clinical experience with NURTEC ODT overdosage. Treatment of an overdose of NURTEC ODT should consist of general supportive measures including monitoring of vital signs and observation of the clinical status of the patient. No specific antidote for the treatment of Rimegepant overdose is available. Rimegepant is unlikely to be significantly removed by dialysis because of high serum protein binding.

ADVERSE REACTION:
Acute Treatment of Migraine: The adverse reaction reported in ≥ 1% of patients treated with NURTEC ODT is nausea.

• The most common adverse reaction in Study 1 was nausea (2% in patients who received NURTEC ODT compared to 0.4% of patients who received placebo).
• Hypersensitivity, including dyspnea and severe rash, occurred in less than 1% of patients treated with NURTEC ODT.

Preventive Treatment of Episodic Migraine: Adverse reactions reported in ≥ 2% for Rimegepant and ≥ 1% higher than placebo are nausea and abdominal pain/dyspepsia.
• The most common adverse reactions (occurring in at least 2% of Rimegepant-treated patients and at a frequency of at least 1% higher than placebo) in Study 2 were nausea (2.7% in patients who received Rimegepant compared with 0.8% of patients who received placebo) and abdominal pain/dyspepsia (2.4% in patients who received Rimegepant compared with 0.8% of patients who received placebo).

PHARMACEUTICAL PRECAUTIONS*: Do not Store NURTEC™ ODT above 30°C.*
PHARMACOKINETICS / PHARMACODYNAMICS (If required per local regulations):
Absorption: Following oral administration of NURTEC ODT, Rimegepant is absorbed with the maximum concentration at 1.5 hours. The absolute oral bioavailability of Rimegepant is approximately 64%.
Effects of Food: Following administration of NURTEC ODT under fed conditions with a high-fat or low-fat meal, Tmax was delayed by approximately 1 to 1.5 hours. A high-fat meal reduced Cmax by 42 to 53% and AUC by 32 to 38%. A low-fat meal reduced Cmax by 36% and AUC by 28%.
Distribution: The steady state volume of distribution of Rimegepant is 120 L. Plasma protein binding of Rimegepant is approximately 96%.
Elimination/Metabolism: Rimegepant is primarily metabolized by CYP3A4 and to a lesser extent by CYP2C9.Rimegepant is the primary form (~77%) with no major metabolites (i.e., > 10%) detected in plasma.
Excretion: The elimination half-life of Rimegepant is approximately 11 hours in healthy subjects. Following oral administration of [14C]-Rimegepant to healthy male subjects, 78% of the total radioactivity was recovered in feces and 24% in urine.
REFERENCE: Nurtec ODT 75 mg LPD USPI Revision date April 2023 in UAE
DATE OF THIS DOCUMENT: 25th March 2024