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Efficacy and Safety of Symbravo® (MoSEIC™ meloxicam and rizatriptan) in Participants With Migraine Experiencing an Inadequate Response to Oral CGRP Inhibitors: Topline Results From the EMERGE Trial

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Disclosures: Richard B. Lipton, M.D.

Role	Company
Consultant	Allergan/Abbvie, Amgen, Axson, Axsome, BDSI, Biohaven, Clexio, Cool Tech, Eli Lilly, Genentech, GlaxoSmithKline, Grifols, Linpharma, Lundbeck, Merck, Pfizer, Satsuma, Shiratronics, Teva, Vedanta
Scientific Advisory/Data Safety Monitoring board	Allergan/Abbvie, Biohaven, Eli Lilly, Lundbeck
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Introduction/aim

- Available acute treatment options do not fully meet the needs of all patients with migraine[1,2]
- Oral calcitonin gene-related peptide (CGRP) inhibitors (gepants) are a newer class of medication approved for the acute treatment of migraine that addresses some but not all patient needs[3-6]
- Combination acute treatment with an NSAID and triptan provides a multi-mechanistic approach for patients who do not respond well to monotherapy
- Symbravo® (MoSEIC™ meloxicam and rizatriptan [mMR]) is a recently approved acute treatment for migraine which combines rapidly absorbed MoSEIC™ meloxicam with rizatriptan to target multiple pathophysiological pathways of migraine[7,8]
- The EMERGE study evaluated the efficacy and safety of mMR in participants who were undergoing treatment with a gepant for ≥1 month and experiencing an inadequate response to the gepant

1. Morton BA, et al. 2021. https://headachemigraine.org/wp-content/ uploads/CHAMP-Survey-Brief-2.pdf. **2.** Bigal M, et al. Headache. 2007;47(4):475-9. **3.** Younis S, et al. Handb Clin Neurol. 2024;199:51-66. **4.** Dodick DW, et al. N Engl J Med. 2019;381(23):2230-2241. **5.** Croop R, et al. Lancet. 2019;394(10200):737-745. **6.** Lipton RB, et al. Lancet Neurol. 2023;22(3):209-217. **7.** Symbravo PI. New York, NY: Axsome Therapeutics, Inc.; 2025. **8.** O'Gorman C, et al. Poster presented at: American Headache Society Virtual Annual Scientific Meeting; June 3-6 2021. MoSEIC, Molecular Solubility Enhanced Inclusion Complex

EMERGE: Study Design

- Phase 3, open-label study of mMR for the acute treatment of migraine in adults experiencing an inadequate response to a gepant

Open-label treatment period

Enrollment:
N=96

→ mMR (for up to 8 weeks for **next 4 migraine attacks**)

Primary Efficacy Endpoint vs gepants

- Change in mTOQ-4 total score from pre-trial gepant treatment period (baseline) to mMR treatment period (Visit 4/end of study)

Co-primary Efficacy Endpoints

- Headache pain relief at Hour 2*
- Absence of MBS† at Hour 2*

*By migraine episode, without the use of rescue medication.
†Most bothersome symptom was photophobia, phonophobia, or nausea.
CGRP, calcitonin gene-related peptide; MBS, most bothersome symptom; mMR, MoSEIC™ meloxicam and rizatriptan.

EMERGE: Key Eligibility Criteria

Inclusion	Exclusion
• ≥18 years old • ICHD-3 migraine • Treated ≥4 migraines w/oral CGRP inhibitor, with inadequate response, ie ≤7 on mTOQ-4[1] ○ 1 or 0 on Item 2 (After taking your migraine medication, are you pain free within 2 hours for most attacks?)	• Adverse reaction or intolerance to NSAIDs, acetaminophen, or triptans • >8 migraines per month prior to screening • Chronic daily headache 1 year prior to screening • Cardiovascular disease/uncontrolled hypertension

1. Lipton RB et al., Cephalalgia. 2009 Jul;29(7):751-9.

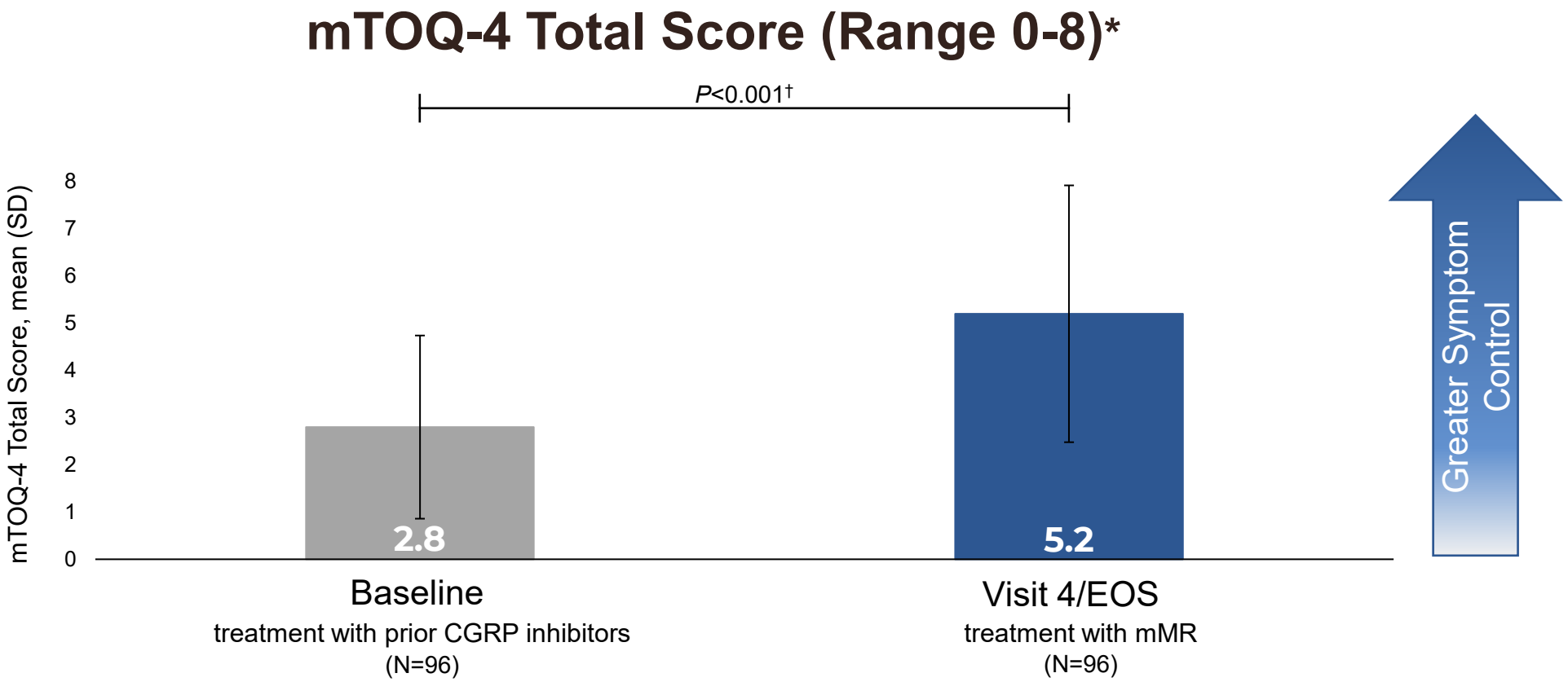
EMERGE: Baseline Characteristics

Characteristics, mITT population*	mMR (N=96)
Age, mean (SD)	43.2 (12.49)
Female sex, n (%)	84 (87.5)
Race, n (%)	
White	72 (75.0)
Other†	24 (25.0)
Years since migraine diagnosis, mean (SD)	19.2 (13.5)
Frequency of migraines (monthly average for past 3 months), mean (SD)	5.6 (1.8)
Typical most bothersome symptom, n (%)	
Nausea	29 (30.2)
Sensitivity to light	46 (47.9)
Sensitivity to sound	21 (21.9)
Number of mMR doses taken, median (min, max)	4 (1, 5)

- 100 participants were enrolled, 96 received ≥1 dose of study medication and 90 completed the study

*mITT population: all subjects who took a dose of study drug to treat a migraine and provided at least 1 post-baseline efficacy evaluation.
†Other race groups: American Indian or Alaska native (n=1); Asian (n=6), Black/African American: (n=15); multiple (n=1); other (n=1).
CGRP, calcitonin gene-related peptide; mMR, MoSEIC™ meloxicam and rizatriptan; SD, standard deviation.

Greater Migraine Treatment Response with mMR Compared to Oral CGRPs

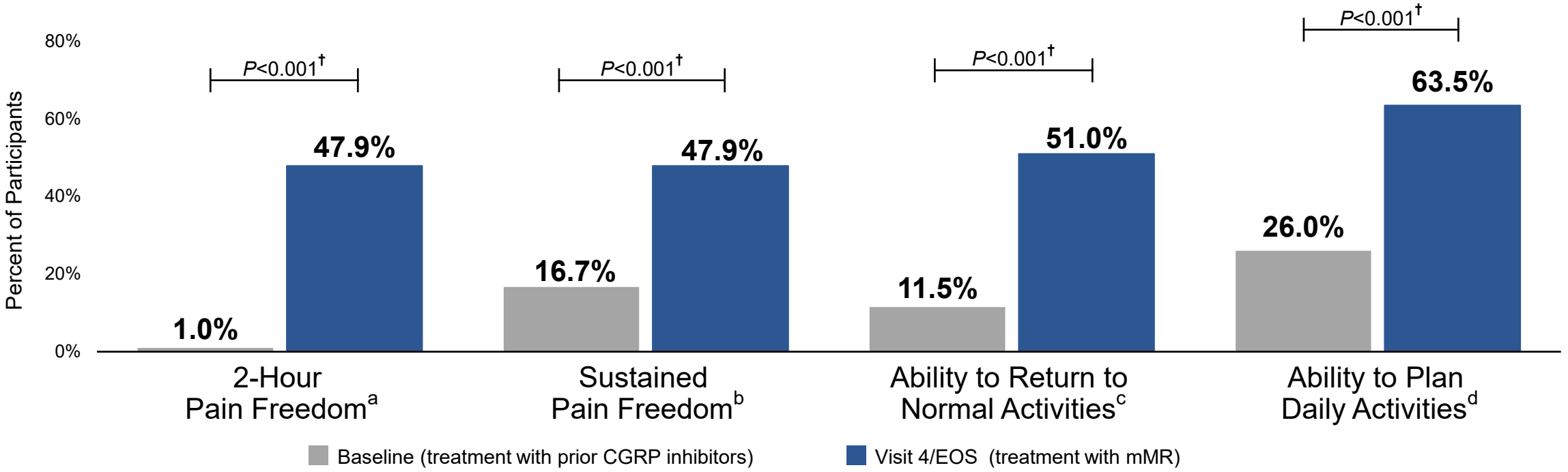


- mMR demonstrated significantly greater migraine treatment response score compared to baseline scores on oral CGRP inhibitors

*mTOQ-4 Total Score change from baseline to Visit 4/EOS. †T-test was used to test the null hypothesis of mean change equal to 0. P value is nominal.
CGRP, calcitonin gene-related peptide; EOS, end of study; mMR, MoSEIC™ meloxicam and rizatriptan; mTOQ-4, Migraine Treatment Optimization Questionnaire, 4-item.

More Participants Achieved Response (Item score = 2) in Each mTOQ-4 Individual Item* With mMR

Individual mTOQ-4 Item Scores



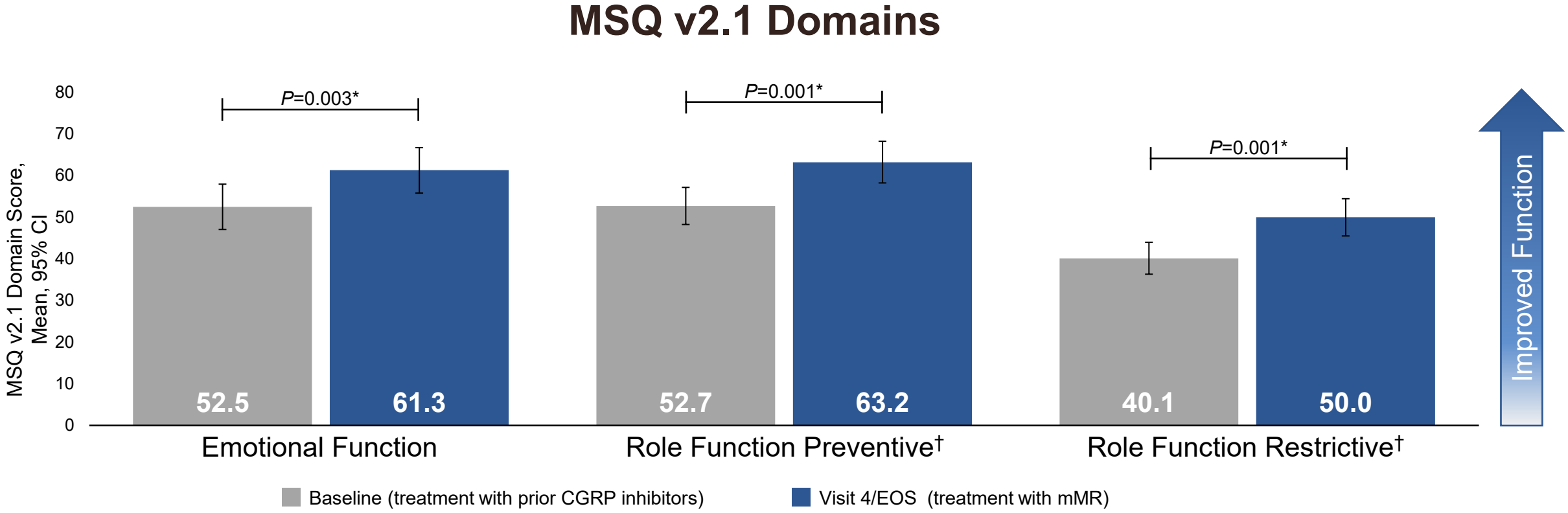
- Significantly more mMR patients experienced response compared to oral CGRP inhibitors

[a]mTOQ-4 Item 2: *"After taking your migraine medication, are you pain free within 2 hours for most attacks?"*; [b]mTOQ-4 Item 3: *"Does one dose of your migraine medication usually relieve your headache and keep it away for at least 24 hours?"*; [c]mTOQ-4 Item 1: *"Are you able to quickly return to your normal activities (ie, work, family, leisure, social activities) after taking your migraine medication?"*; [d]mTOQ-4 Item 4: *"Are you comfortable enough with your migraine medication to be able to plan your daily activities?"*

*Reported half the time or more. †T-test was used to test the null hypothesis of mean change equal to 0. All P values are nominal.

CGRP, calcitonin gene-related peptide; EOS, end of study; mTOQ-4, Migraine Treatment Optimization Questionnaire, 4-item.

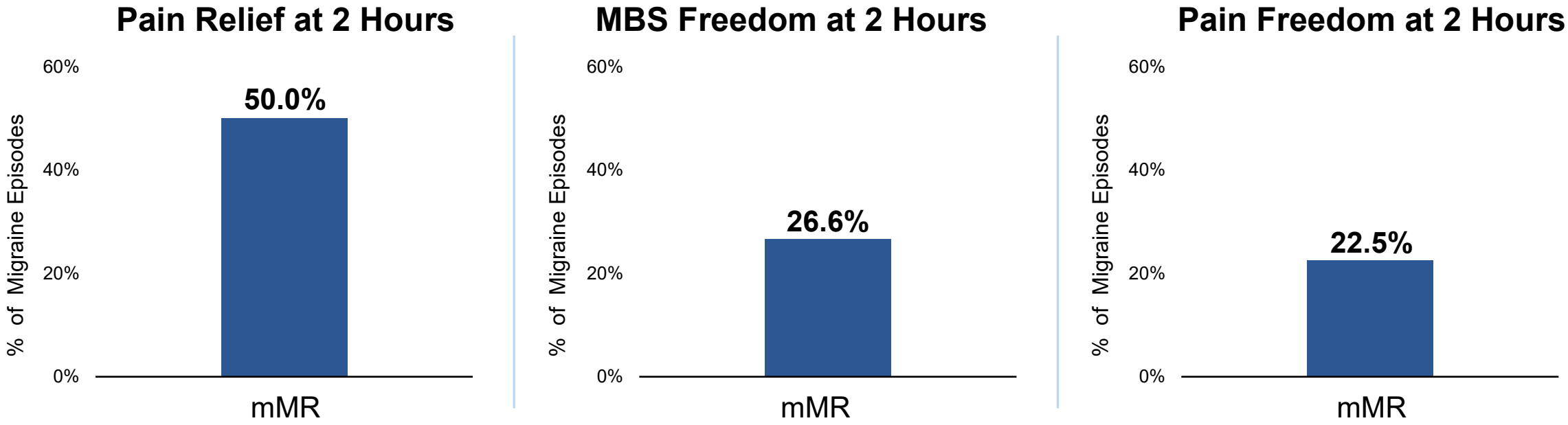
Significant Improvement in Overall QoL and Daily Functioning with mMR



- mMR treatment resulted in improvement in overall QoL and daily functioning compared to oral CGRP inhibitors

*T-test was used to test the null hypothesis of mean change equal to 0. All P values are nominal.
†Role function preventive domain: how migraines prevent social/work activities. Role function restrictive: how migraines restrict social/work activities.
EOS, end of study; mMR, MoSEIC™ meloxicam and rizatriptan; MSQ, Migraine-Specific Quality of Life Questionnaire; QoL, quality of life.

High Rates of Pain Relief & MBS Freedom at 2 Hours With mMR

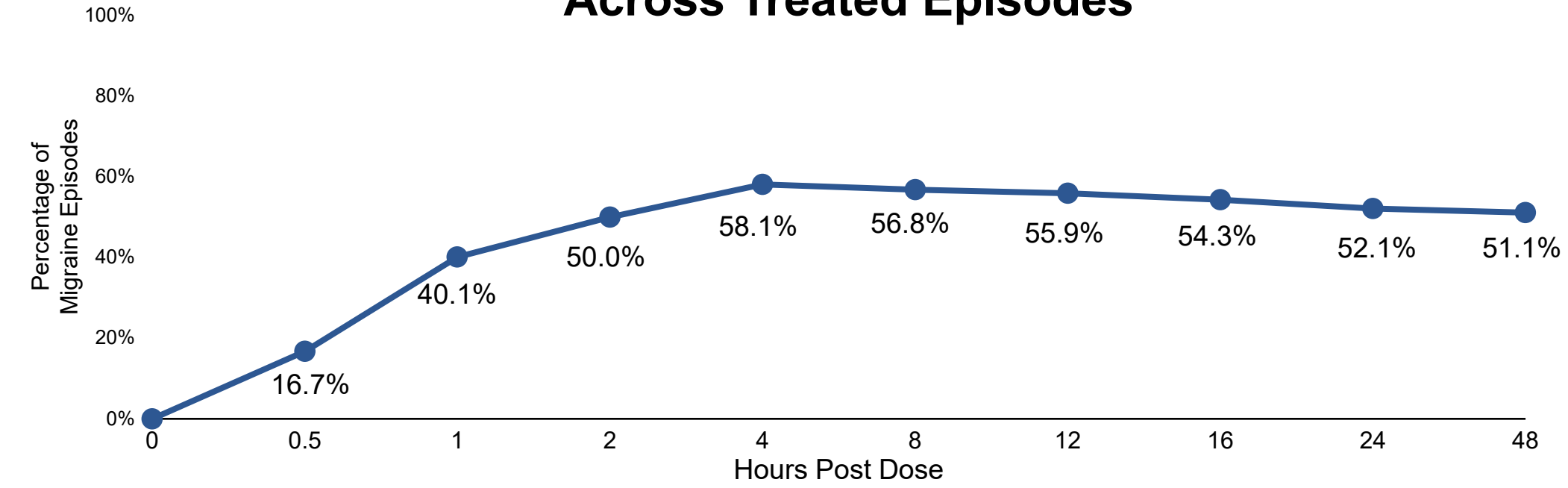


- Pain relief, freedom from MBS, and pain freedom at 2 hours after dosing with mMR was achieved for 50.0%, 26.6%, and 22.5% of migraine attacks, respectively

MBS, most bothersome symptom (nausea, photophobia, or phonophobia); mMR, MoSEIC™ meloxicam and rizatriptan.

Rapid Onset and Sustained Pain Relief With mMR

Change in Pain Relief Rates Over Time* Across Treated Episodes



# of episodes	(365)	(364)	(364)	(363)	(361)	(358)	(359)	(359)	(358)

- Pain relief was experienced in 16.7% of attacks as early as 30 minutes after dosing with mMR

*Headache pain relief at each timepoint was defined as pain intensity less than that at baseline and without the use of rescue medication. Percentage of migraine episodes with headache pain relief is calculated as the percentage of migraine episodes with headache pain relief out of the number of all migraine episodes (except for number of missing on each time point).

Safety and Tolerability

Adverse Events Occurring in ≥2% of Subjects*

Adverse Event	mMR (N=96)
Any TEAE	19 (19.8%)
Fatigue	3 (3.1)
Nausea	3 (3.1)
Vomiting	2 (2.1)
Muscle tightness	2 (2.1)
Dizziness	2 (2.1)

- mMR was well tolerated with a safety profile consistent with prior studies
- The most commonly reported adverse events (≥2% of patients) were fatigue, nausea, vomiting, muscle tightness, and dizziness

*Safety population included all participants who received at least 1 dose of the study drug.
AE, adverse event; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Conclusion

- In the EMERGE trial in participants experiencing an inadequate response to gepants, treatment with mMR was associated with significant improvements in migraine treatment response
  - Higher rates of rapid and sustained relief and improved functional recovery, as assessed by the mTOQ-4, and improved quality of life were also observed
- Headache pain relief following treatment with mMR was reported in 50% of all migraine attacks 2 hours post-dose, reached a maximum at 4 hours, and was sustained over 48 hours
- Limitations of the study include its open-label, pre-post design without the inclusion of a contemporaneous control group
- These results extend upon the findings from the prior phase 3 studies of mMR, providing additional evidence for its efficacy across a range of migraine patient populations with varying pain intensities and inadequate responses to a broader range of acute treatments