Efficacy of Symbravo® (MoSEIC™ Meloxicam and Rizatriptan) by Baseline Migraine-Associated Disability: Post-hoc Analysis of the INTERCEPT Trial

American Headache Society (AHS)
67th Annual Scientific Meeting
June 19–22, 2025
Minneapolis, MN, USA

Stewart J. Tepper[1], Angad Chhabra[2], Todd Grinnell[2], Graham M.L. Eglit[2], Herriot Tabuteau[2]
[1]New England Institute for Neurology and Headache, Stamford, CT, USA; [2]Axsome Therapeutics, Inc., New York, NY, USA

Key Objective

To evaluate the effect of Symbravo® (MoSEIC™ meloxicam and rizatriptan [mMR]) among adult patients with differing levels of migraine-related disability at baseline

Introduction

- Migraine is a neurologic disorder characterized by recurrent attacks of pulsating, throbbing head pain, often with nausea, vomiting, autonomic symptoms, and multiple comorbidities[1]
- In a recent survey, the majority of patients with migraine reported that they are dissatisfied with their current migraine treatment[2]
- A novel fixed-dose combination of 20 mg MoSEIC™ meloxicam and 10 mg rizatriptan (mMR) was approved by the US Food and Drug Administration (FDA) in January 2025 for the acute treatment of migraine, based on data from the MOMENTUM (NCT03896009)[3,4] and INTERCEPT (NCT04163185)[5] phase 3 trials
- In INTERCEPT, participants treated their migraine early while pain was mild, and mMR significantly improved the percentage achieving freedom from migraine pain and their most bothersome symptom (MBS) at 2 hours post dose
  - The difference in percentage of participants treated with mMR able to return to normal function was numerically superior to placebo at 2 hours, reaching significance at later timepoints
- In this post-hoc analysis of INTERCEPT, participants were stratified by baseline migraine disability assessment (MIDAS) score category, and efficacy endpoints were compared between mMR and placebo within each category

Plain Language Summary

- A new treatment called Symbravo® was recently approved by the FDA for the acute treatment of migraine
- In clinical trials, participants who took Symbravo® were more likely to have headache pain relief and relief from their most bothersome symptom within 2 hours, compared with participants who took placebo
- In this study, participants from the same clinical trial were divided into groups based on their history of migraine disability, and it was found that those who had a history of more severe migraine disability had greater improvement with Symbravo® treatment than those with a history of less migraine disability

Methods

- INTERCEPT was a phase 3, multicenter, randomized, placebo-controlled study
- The study included adults with an average of 2–8 migraine attacks per month over the prior 3 months
- Participants were randomized 1:1 to 1 oral dose of mMR or placebo taken as soon as possible after the onset of migraine pain, while pain was mild
- Baseline functional disability for current migraine symptoms was recorded by the participant on a scale of 0–3 prior to taking mMR or placebo
- The MIDAS questionnaire was used at baseline to assess migraine disability over the past 3 months; participants were categorized post-hoc by baseline MIDAS score:
  - Little or no disability (MIDAS score ≤5)
  - Mild disability (MIDAS score 6–10)
  - Moderate disability (MIDAS score 11–20)
  - Severe disability (MIDAS score ≥21)
- The co-primary endpoints were headache pain freedom and freedom from patient-identified MBS, both at 2 hours post dose
- Treatment and placebo groups were compared in each MIDAS category using chi-square tests. In the event of expected cell counts ≤5, Fisher's exact test was used instead
- Absolute risk reduction effect sizes with 95% CI are reported

Limitations

- Interpretation is limited by the post-hoc nature of these analyses and the small sample size and resultant underpowered nature of the analysis
  - The sample size of the little or no disability category was particularly small, and caution is warranted in interpretation of that category
- Although the MIDAS scores used to categorize participants based on historical disease disability most frequently indicated severe disability, participants reported low levels of functional disability during the attacks treated in INTERCEPT, likely due to the instruction to treat early in the attack when pain was mild

Results

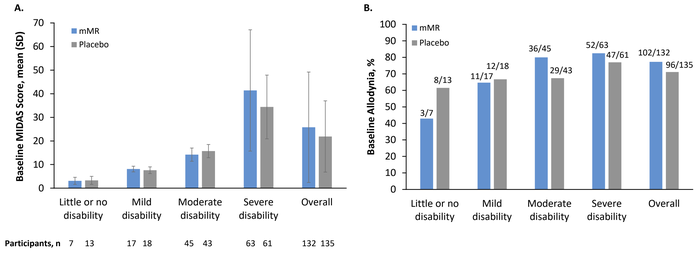
Participant Baseline Characteristics

Table. Demographics and Baseline Characteristics Across MIDAS Categories

	Little or no disability		Mild disability		Moderate disability		Severe disability		Overall	
	mMR (n=7)	Placebo (n=13)	mMR (n=17)	Placebo (n=18)	mMR (n=45)	Placebo (n=43)	mMR (n=63)	Placebo (n=61)	mMR (n=132)	Placebo (n=135)
Age, y, mean (SD)	41.6 (10.4)	40.2 (8.7)	37.4 (11.9)	42.6 (11.8)	42.2 (11.7)	39.3 (10.9)	42.4 (11.4)	42.6 (10.6)	41.6 (11.5)	41.4 (10.7)
Female, n (%)	7 (100)	11 (84.6)	14 (82.4)	17 (94.4)	36 (80.0)	34 (79.1)	56 (88.9)	53 (86.9)	113 (85.6)	115 (85.2)
Race, n (%)										
White	4 (57.1)	11 (84.6)	16 (94.1)	17 (94.4)	38 (84.4)	34 (79.1)	55 (87.3)	47 (77.0)	113 (85.6)	109 (80.7)
Black	3 (42.9)	0	1 (5.9)	1 (5.6)	6 (13.3)	8 (18.6)	6 (9.5)	7 (11.5)	16 (12.1)	16 (11.9)
Asian	0	2 (15.4)	0	0	0	0	1 (1.6)	5 (8.2)	1 (0.8)	7 (5.2)
Other	0	0	0	0	1 (2.2)	1 (2.3)	1 (1.6)	2 (3.3)	2 (1.5)	3 (2.2)
MIDAS score, median (range)	3 (1–5)	4 (0–5)	8 (6–10)	7 (6–10)	13 (11–20)	16 (11–20)	33 (21–166)	30 (21–79)	19 (1–166)	19 (0–79)
Duration of illness, y, mean (SD)	12.7 (9.8)	14.2 (10.4)	11.6 (8.2)	20.9 (12.5)	19.3 (11.7)	14.0 (9.7)	21.0 (12.7)	20.6 (13.3)	18.7 (12.1)	17.9 (12.2)
Typical monthly migraine frequency, mean (SD)	4.4 (2.0)	3.9 (1.4)	4.3 (2.0)	3.8 (1.7)	4.1 (1.4)	4.6 (1.4)	5.1 (1.8)	4.8 (1.6)	4.6 (1.8)	4.5 (1.6)
Nausea at baseline, n (%)	3 (42.9)	3 (23.1)	5 (29.4)	8 (44.4)	14 (31.1)	20 (46.5)	27 (42.9)	28 (45.9)	49 (37.1)	59 (43.7)
Morning migraine (onset before 10 a.m.), n (%)	4 (57.1)	8 (61.5)	9 (52.9)	5 (27.8)	20 (44.4)	15 (34.9)	22 (34.9)	23 (37.7)	55 (41.7)	51 (37.8)
Depression at baseline, n (%)	0	0	0	5 (27.8)	6 (13.3)	9 (20.9)	19 (30.2)	7 (11.5)	25 (18.9)	21 (15.6)
Obesity (BMI ≥30 kg/m^2), n (%)	3 (42.9)	2 (15.4)	6 (35.3)	2 (11.1)	23 (51.1)	23 (53.5)	22 (34.9)	25 (41.0)	54 (40.9)	52 (38.5)

BMI, body mass index; MIDAS, migraine disability assessment.

Figure 1. Mean Baseline MIDAS Score Across Categories (A) and Percent With Allodynia at Baseline (B)



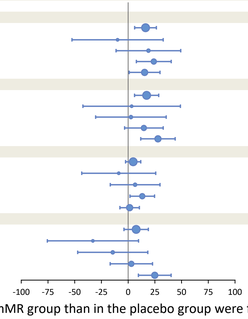
- A total of 132 participants received mMR (mean age 41.6 years, 85.6% women) and 135 received placebo (mean age 41.4 years, 85.2% women; **Table**)
- Mean (SD) baseline functional disability scores were 1.3 (0.67) in the mMR group and 1.3 (0.77) in the placebo group, indicating relatively mild current disability prior to treatment
- Participant demographic characteristics were relatively similar across baseline MIDAS categories (**Table, Figure 1**)
  - Participants in the little or no disability category had the highest level of dissimilarity between the treatment and placebo groups, likely due to small sample size (n=7 and n=13, respectively)

MIDAS, migraine disability assessment; mMR, 20 mg MoSEIC™ meloxicam and 10 mg rizatriptan.

Treatment Outcomes by Baseline MIDAS Category

Figure 2. Treatment Outcomes 1–2 Hours Post Dose

	mMR n/N (%)	Placebo n/N (%)	Absolute Risk Reduction (95% CI)	*P* Value
Pain freedom at 2 hours				
Total	43/132 (32.6)	22/135 (16.3)	16.3 (6.1, 26.4)	0.002
Little or no disability	2/7 (28.6)	5/13 (38.5)	-9.9 (-52.5, 32.8)	1.000
Mild disability	7/17 (41.2)	4/18 (22.2)	19.0 (-11.3, 49.2)	0.227
Moderate disability	15/45 (33.3)	4/43 (9.3)	24.0 (7.7, 40.3)	0.006
Severe disability	19/63 (30.2)	9/61 (14.8)	15.4 (1.0, 29.8)	0.040
Freedom from MBS at 2 hours				
Total	58/132 (43.9)	36/135 (26.7)	17.3 (6.0, 28.6)	0.003
Little or no disability	4/7 (57.1)	7/13 (53.8)	3.3 (-42.3, 48.9)	1.000
Mild disability	8/17 (47.1)	8/18 (44.4)	2.6 (-30.4, 35.6)	0.877
Moderate disability	15/45 (33.3)	8/43 (18.6)	14.7 (-3.3, 32.8)	0.116
Severe disability	31/63 (49.2)	13/61 (21.3)	27.9 (11.8, 44.0)	0.001
Pain freedom at 1 hour				
Total	16/132 (12.1)	10/135 (7.4)	4.7 (-2.4, 11.8)	0.194
Little or no disability	1/7 (14.3)	3/13 (23.1)	-8.8 (-43.4, 25.8)	1.000
Mild disability	3/17 (17.6)	2/18 (11.1)	6.5 (-16.7, 29.8)	0.658
Moderate disability	7/45 (15.6)	1/43 (2.3)	13.2 (1.7, 24.7)	0.031
Severe disability	5/63 (7.9)	4/61 (6.6)	1.4 (-7.7, 10.5)	0.767
Functional ability at 2 hours				
Total	51/132 (38.6)	42/135 (31.1)	7.5 (-3.9, 18.9)	0.197
Little or no disability	2/7 (28.6)	8/13 (61.5)	-33.0 (-75.6, 9.7)	0.350
Mild disability	7/17 (41.2)	10/18 (55.6)	-14.4 (-47.2, 18.4)	0.395
Moderate disability	16/45 (35.6)	14/43 (32.6)	3.0 (-16.8, 22.8)	0.767
Severe disability	26/63 (41.3)	10/61 (16.4)	24.9 (9.6, 40.2)	0.002

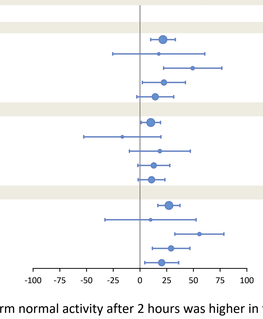


- A greater percentage of participants in the mMR group than in the placebo group were free from pain at Hour 2 in the mild disability, moderate disability, and severe disability categories, though not in the little or no disability category, likely due to a high placebo response (**Figure 2**)
- The percentage of participants free from their MBS at Hour 2 was higher in the mMR group than the placebo group across MIDAS categories, and this effect was greater in the more severe MIDAS categories
  - The percentage was nominally significantly greater with mMR than placebo in the severe disability category
- Pain freedom at Hour 1 was more common in those receiving mMR than placebo in the mild disability, moderate disability, and severe disability categories, and was nominally statistically significant in the moderate disability category

Size of circle represents population size. MBS, most bothersome symptom; mMR, MoSEIC™ meloxicam and rizatriptan.

Figure 3. Treatment Outcomes 24 Hours Post Dose

	mMR n/N (%)	Placebo n/N (%)	Absolute Risk Reduction (95% CI)	*P* Value
Pain freedom at 24 hours				
Total	91/132 (68.9)	64/135 (47.4)	21.5 (10.0, 33.1)	<0.001
Little or no disability	5/7 (71.4)	7/13 (53.8)	17.6 (-25.5, 60.6)	0.642
Mild disability	15/17 (88.2)	7/18 (38.9)	49.3 (22.1, 76.6)	0.003
Moderate disability	31/45 (68.9)	20/43 (46.5)	22.4 (2.2, 42.5)	0.034
Severe disability	40/63 (63.5)	30/61 (49.2)	14.3 (-3.0, 31.6)	0.108
Sustained pain freedom 2–24 hours				
Total	30/132 (22.7)	17/135 (12.6)	10.1 (1.1, 19.2)	0.030
Little or no disability	1/7 (14.3)	4/13 (30.8)	-16.5 (-52.6, 19.6)	0.613
Mild disability	6/17 (35.3)	3/18 (16.7)	18.6 (-9.9, 47.1)	0.264
Moderate disability	10/45 (22.2)	4/43 (9.3)	12.9 (-2.0, 27.9)	0.098
Severe disability	13/63 (20.6)	6/61 (9.8)	10.8 (-1.7, 23.3)	0.095
Avoidance of rescue medication at 24 hours				
Total	20/132 (15.2)	57/135 (42.2)	27.1 (37.4, 16.7)	<0.001
Little or no disability	2/7 (28.6)	5/13 (38.5)	9.9 (-32.8, 52.5)	1.000
Mild disability	0/17 (0.0)	10/18 (55.6)	55.6 (32.6, 78.5)	<0.001
Moderate disability	5/44 (11.4)	17/42 (40.5)	29.1 (11.6, 46.7)	0.002
Severe disability	13/63 (20.6)	25/61 (41.0)	20.3 (4.5, 36.2)	0.014



- The percentage of participants able to perform normal activity after 2 hours was higher in the mMR group than the placebo group in the moderate and severe disability categories, while it was higher in the placebo group in the lower severity categories
- After 24 hours, pain freedom continued to be more common in the mMR group versus the placebo group, with a slightly larger effect in mild and moderate disability categories (**Figure 3**)
- The percentage of participants experiencing sustained freedom from pain between Hours 2 and 24 post dose was larger in the mMR group versus the placebo group for the mild, moderate, and severe disability categories
- The percentage of participants who did not use rescue medication within 24 hours was greater in the mMR group versus the placebo group, with a slightly larger effect in the mild and moderate disability categories

Size of circle represents population size. mMR, MoSEIC™ meloxicam and rizatriptan.

Conclusions

- Early treatment of migraine, when pain was still mild, with a fixed-dose combination of 20 mg MoSEIC™ meloxicam and 10 mg rizatriptan (Symbravo®), improved migraine pain, MBS, and avoidance of rescue medication use compared with placebo
- While improvements occurred across baseline historical disability categories, treatment effects were more pronounced in participants with greater disability at baseline for freedom from MBS and return to normal function
  - This may reflect a floor effect for return to normal function in the INTERCEPT study, whereby those with minimal disability, treated early while pain was still mild, had limited opportunity to improve with treatment
  - This may also reflect a higher placebo response in the milder severity categories
- At later timepoints, participants with mild disability exhibited a somewhat greater response, which may indicate that early intervention prevented progression of migraine
  - Future analyses may assess the impact of treatment with mMR on migraine progression

References

1. Minagé G. *P T*. 2008;33:404-416. 2. Lipton RB, Stewart WF. *Headache*. 1999;39:S20-S26. 3. Jones A, et al. *Neurology*. 2020;95(4). 4. O'Gorman C, et al. *Headache*. 2021;61:1-178. 5. Jones A, et al. *Headache*. 2021;61:1-178.

Acknowledgments

Axsome Therapeutics funded and conducted the study. The authors would like to express their appreciation to the study participants and their families as well as the investigators and site personnel. Under the direction of the authors, Hayley White, PhD, of Envision Ignite, an Envision Medical Communications agency, a part of Envision Pharma Group, provided medical writing, editorial, and formatting support, which was funded by Axsome Therapeutics.

QR Code

Scan the QR code at the top of this poster or access https://www.axsomemedicalaffairs.com/congress-presentations/AHS2025 to view or download a PDF of this poster or access additional information and other Axsome Therapeutics presentations at AHS 2025.

Disclosures

Stewart J. Tepper has received grants/research support from AbbVie, Aeon, Amgen, Annovis, Axsome, Cassava, Cognition, Eli Lilly, Inhibikase, Ipsen, Lundbeck, Merz, Neurolief, Pfizer, PrecisionMed, Revance, Scilex, Suven, and UCB. He has consulted and/or served as advisor to AbbVie, Aeon, AlphaSights, Amgen, Aruene/eNeura, Atheneum, Axsome Therapeutics, Becker Pharmaceutical Consulting, Catch Therapeutics, ClearView Healthcare Partners, Click Therapeutics, CoolTech, CRG, Decision Resources, Defined Health, DRG, Dr. Reddy's, Eli Lilly, ExpertConnect, FCB Health, Fenix, Gilmartin Capital, GLG, Guidepoint Global, Health Advances, Health Science Communications, HMP Communications, Impel, Initiator Pharma, InteractiveForums, IQVIA, Keyquest, Ki Health Partners, Krog and Partners, Lundbeck, M3 Global Research, Magellan Health, Magnolia Innovation, Miravo Healthcare, MJH Holdings, NeuroFront Therapeutics, Neurolief, Nocira, Novartis, Pain Insights, Inc, Palion Medical, Perfood, Pfizer, Pulmatrix, Putnam Associates, P Value Communications, Rehaler, SAI MedPartners, Satsuma, Scilex, Slingshot Insights, Spheric Global Insights, Strategy Inc, Synapse Medical Communication, System Analytic, Taylor and Francis, Tegus, Teva, Theranica, Third Bridge, Tonix, Trinity Partners, Unity HA, Vial, and XOC. He has received salary from Dartmouth-Hitchcock Medical Center, Thomas Jefferson University, and Ki Health Partners. He serves on the Speakers' Bureau for AbbVie, Dr. Reddy's, Eli Lilly, Lundbeck, Pfizer, Scilex, and Teva and has received continuing medical education (CME) honoraria from the American Academy of Neurology, American Headache Society, Annenberg Center for Health Sciences, Catamount Medical Education, Diamond Education Foundation, Forefront Collaborative, Haymarket Medical Education, HMP Global, Medical Education Speakers Network, Medical Learning Institute Peerview, Migraine Association of Ireland, Miller Medical Education, National Association for Continuing Education, North American Center for CME, The Ohio State University, Physicians' Education Resource, PlatformQ Education, Primed, Vindico Medical Education, and WebMD/Medscape. **Angad Chhabra**, **Todd Grinnell**, **Graham Eglit**, and **Herriot Tabuteau** are full-time employees of Axsome Therapeutics, Inc.

axsome