Efficacy and Safety of AXS-07 (MoSEIC™ Meloxicam/Rizatriptan) in the Acute Treatment of Migraine: Results from the MOMENTUM Phase 3 Trial

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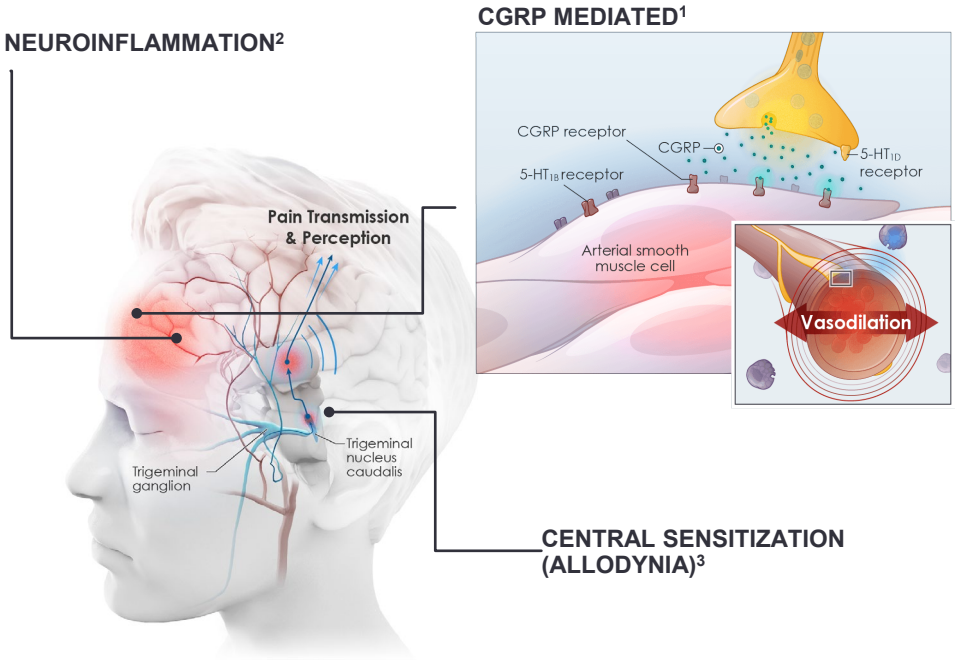
Disclosures: COG, AJ, and HT are full-time employees of Axsome Therapeutics

AXS-07 (MoSEIC™ Meloxicam/Rizatriptan): Multi-Mechanistic Treatment for Migraine

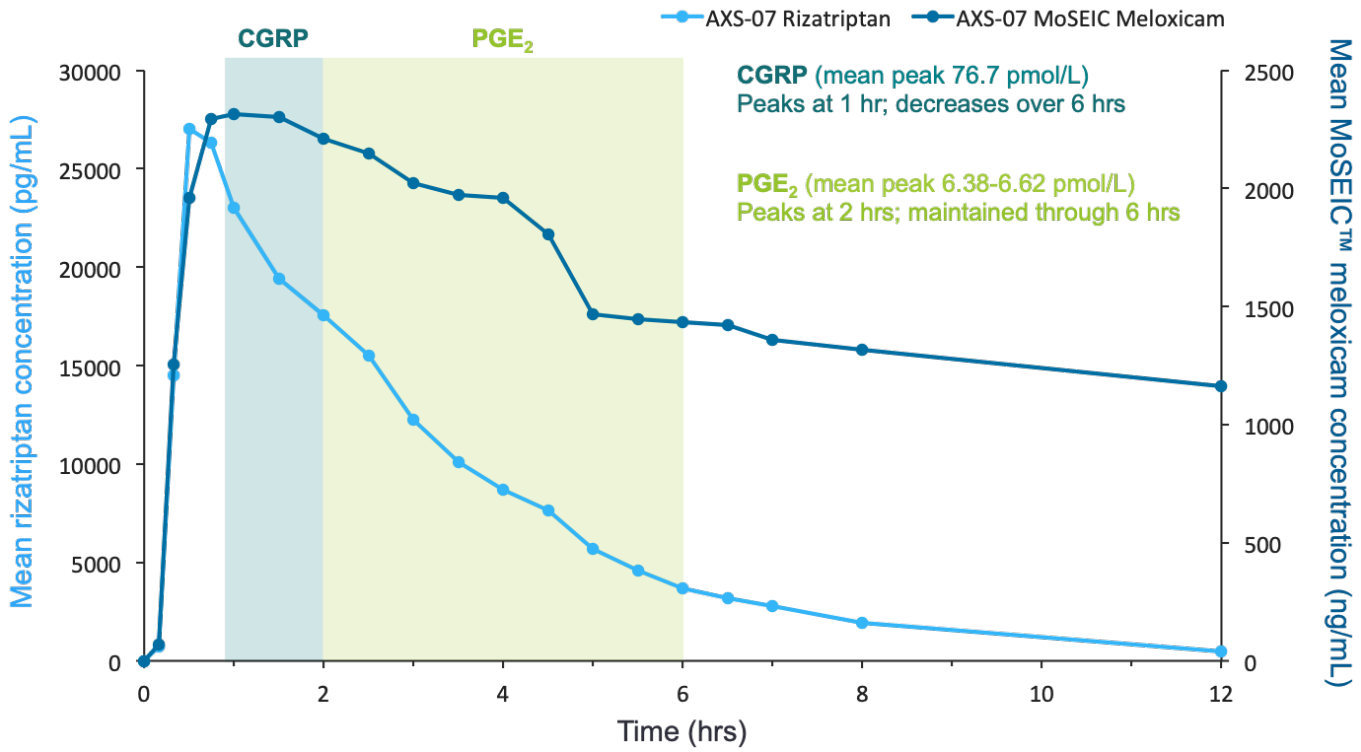


Migraine Process	AXS-07 Mechanism / Action	AXS-07 Component
CGRP Mediated	✓ Inhibition of CGRP release ✓ Reversal of CGRP-mediated vasodilation	Rizatriptan
Neuroinflammation	✓ Cyclooxygenase inhibition ✓ PGE_2 synthesis inhibition	MoSEIC™ meloxicam
Pain Signal Transmission	✓ Decrease passage of pain signals to trigeminal nucleus caudalis	Rizatriptan
Central Sensitization	✓ Reversal of central sensitization	MoSEIC™ meloxicam

[1]Geppetti et al. *J Headache Pain*. 2012; 13:103–111.
[2]Changes measured in migraine patients. COX-2 data from Li et al. *Med Sci Monit*. 2017 Jan 3;23:24-28. PGE_2 data from Sarchielli et al. *Cephalalgia*. 2000 Dec;20(10):907-18.
[3]Change measured in migraine patient. Data from Burstein et al. *Brain*. 2000;123 (Pt 8):1703-9.

Temporal Alignment:
AXS-07 PK versus CGRP and PGE_2 Increases

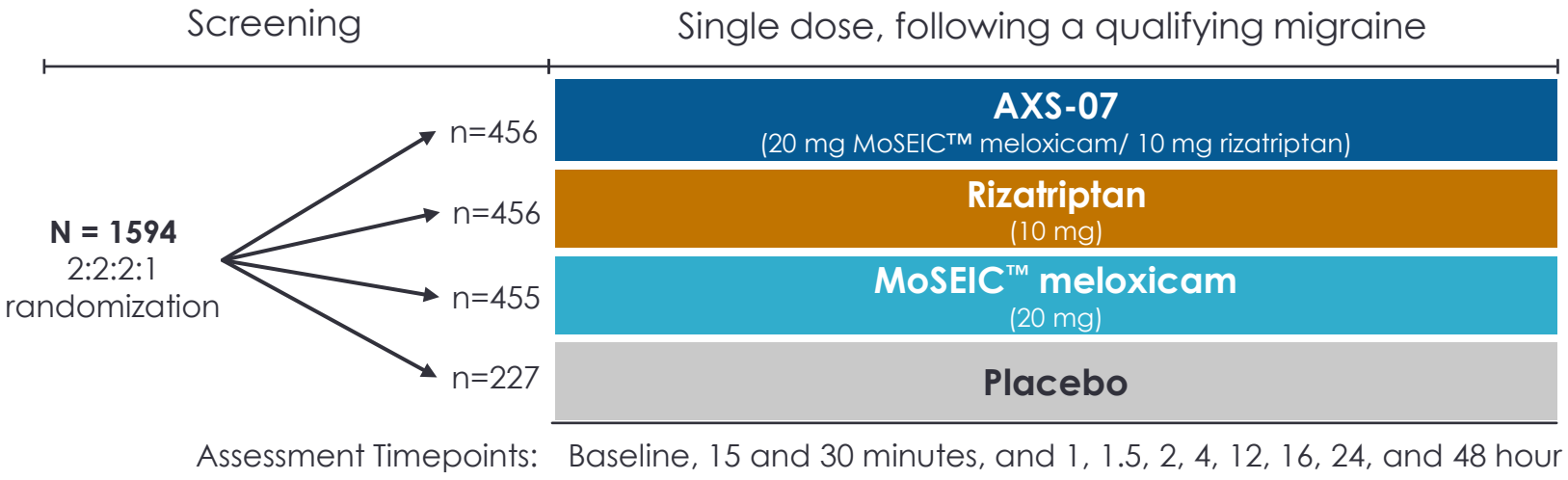
Temporal Alignment of AXS-07 Pharmacokinetics and CGRP and PGE_2 Increases During Migraine Attacks in Human Subjects



Sarchielli et al. *Cephalalgia*. 2000;20:907-18.
Abbreviations: CGRP, Calcitonin gene-related peptide; PGE_2, Prostaglandin E2.

MOMENTUM Phase 3 Trial:
Design Summary

MOMENTUM: Maximizing **O**utco**ME**s i**N** **T**reating ac**U**te **M**igraine
Phase 3 study of AXS-07 for the acute treatment of migraine in adults with history of inadequate response to prior treatment



- **Co-Primary Endpoints (AXS-07 vs placebo)**
  - Pain Freedom at 2 hours
  - Freedom from MBS at 2 hours
- **Key Secondary Endpoint (AXS-07 vs rizatriptan and MoSEIC™ meloxicam)**
  - Superiority of AXS-07 to individual components (component contribution) based on sustained pain freedom 2-24 hours after dosing

MOMENTUM Phase 3 Trial: Key Entry Criteria

Inclusion Criteria

- Male or female, 18 to 65 years of age, inclusive
- Established diagnosis (at least 1 year) of migraine with or without aura as defined by the ICHD-3 criteria
- An average 2 to 8 moderate to severe migraines per month, on average
- History of inadequate response as assessed by a score of ≤ 7 on the mTOQ-4

Exclusion Criteria

- Cluster headaches or other types of migraines
- Chronic daily headache (≥15 non-migraine headache days per month)
- History of significant cardiovascular disease
- Uncontrolled hypertension

Abbreviations: ICHD-3 = International Classification of Headache Disorder, 3rd Edition; mTOQ-4 = Migraine Treatment Optimization Questionnaire.

MOMENTUM Baseline Characteristics: Difficult-to-Treat Migraine

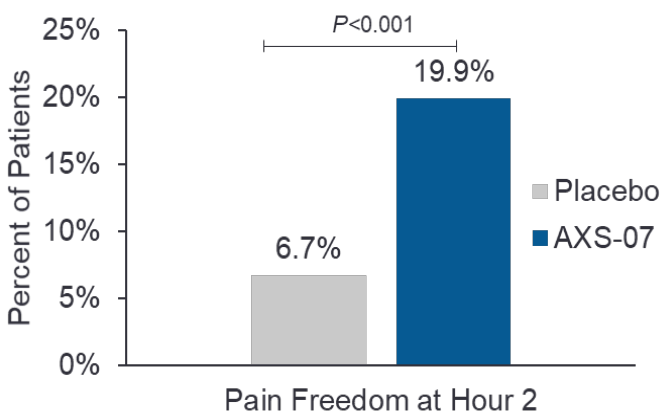
	AXS-07 (20 mg MoSEIC MIx / 10 mg Riz)	Rizatriptan (10 mg)	MoSEIC Meloxicam (20 mg)	Placebo
	n=428	n=419	n=421	n=209
Age, years	41.2 (11.52)	41.4 (10.68)	41.0 (12.07)	40.8 (11.47)
Female gender, n (%)	346 (80.8%)	353 (84.2%)	355 (84.3%)	177 (84.7%)
Race, n (%)				
White	337 (78.7%)	320 (76.4%)	324 (77.0%)	154 (73.7%)
Black or African American	73 (17.1%)	83 (19.8%)	86 (20.4%)	47 (22.5%)
Asian	10 (2.3%)	6 (1.4%)	9 (2.1%)	5 (2.4%)
Prior triptan use, n (%)	171 (40.0%)	163 (38.9%)	147 (34.9%)	73 (34.9%)
Total mTOQ-4 Score, mean (SD)	3.5 (2.17)	3.6 (2.25)	3.8 (2.14)	3.6 (2.19)
Presence of Allodynia, n (%)	336 (78.5%)	305 (72.8%)	322 (76.5%)	150 (71.8%)
Severe Pain Intensity, n (%)	184 (43.0%)	155 (37.0%)	181 (43.0%)	88 (42.1%)
Obese (>30mg/kg^2), n (%)	184 (43.0%)	197 (47.0%)	174 (41.3%)	90 (43.1%)
Morning Migraine, n (%)	162 (36.7%)	158 (36.4%)	159 (36.7%)	76 (34.9%)

Abbreviations: BMI = body mass index, MIx = meloxicam; mTOQ-4 = Migraine Treatment Optimization Questionnaire; Riz = rizatriptan

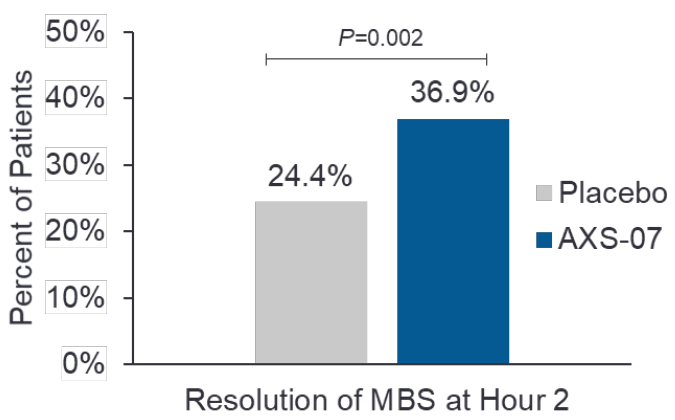
- Enrolled patients exhibited a high rate of characteristics associated with poor treatment outcomes
- Overall, demographics and baseline characteristics were consistent across treatment groups

AXS-07 Achieved Co-Primary Endpoints:
Pain and MBS Improvement

Pain Freedom at 2 hour vs. Placebo

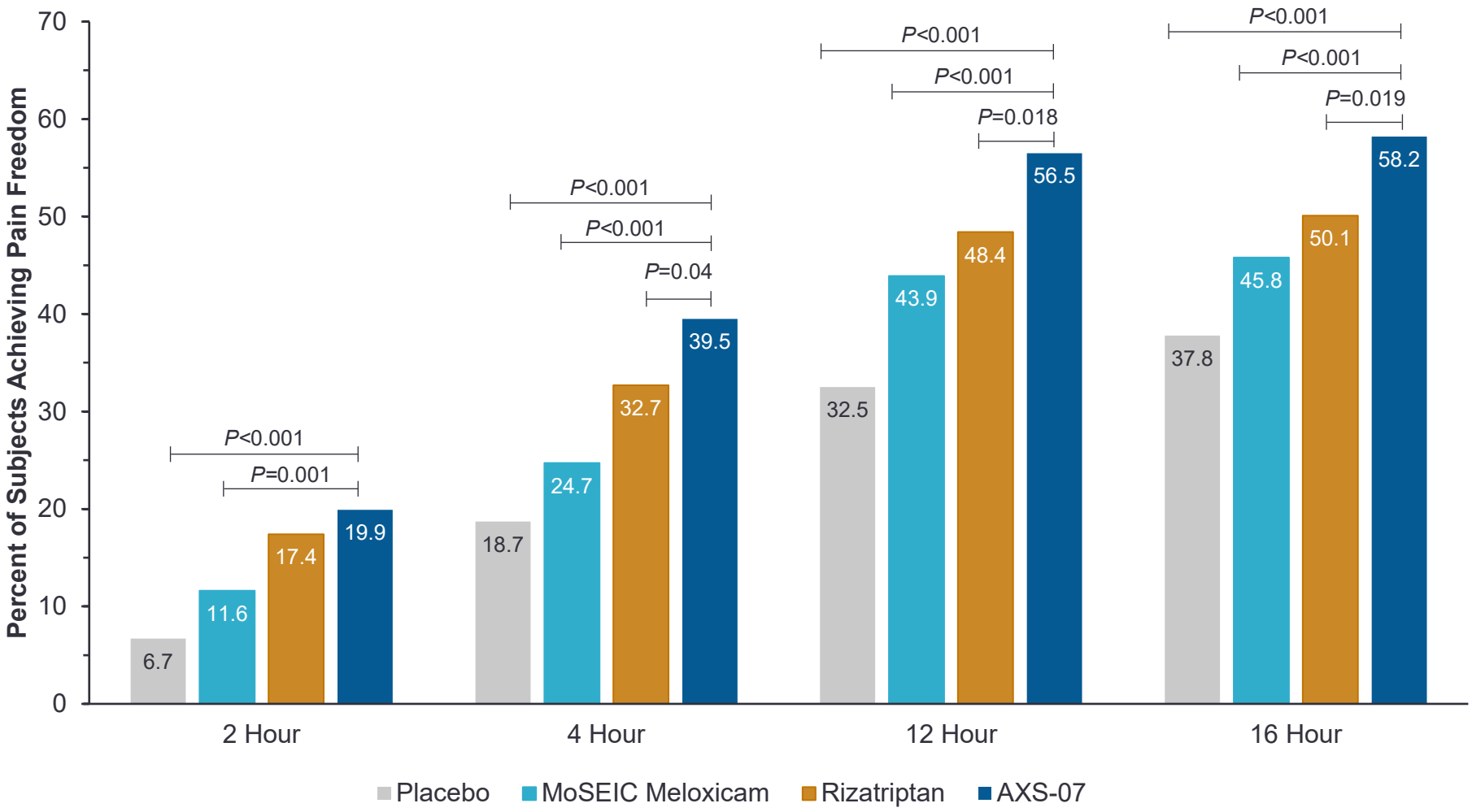


MBS Freedom at 2 hours vs. Placebo

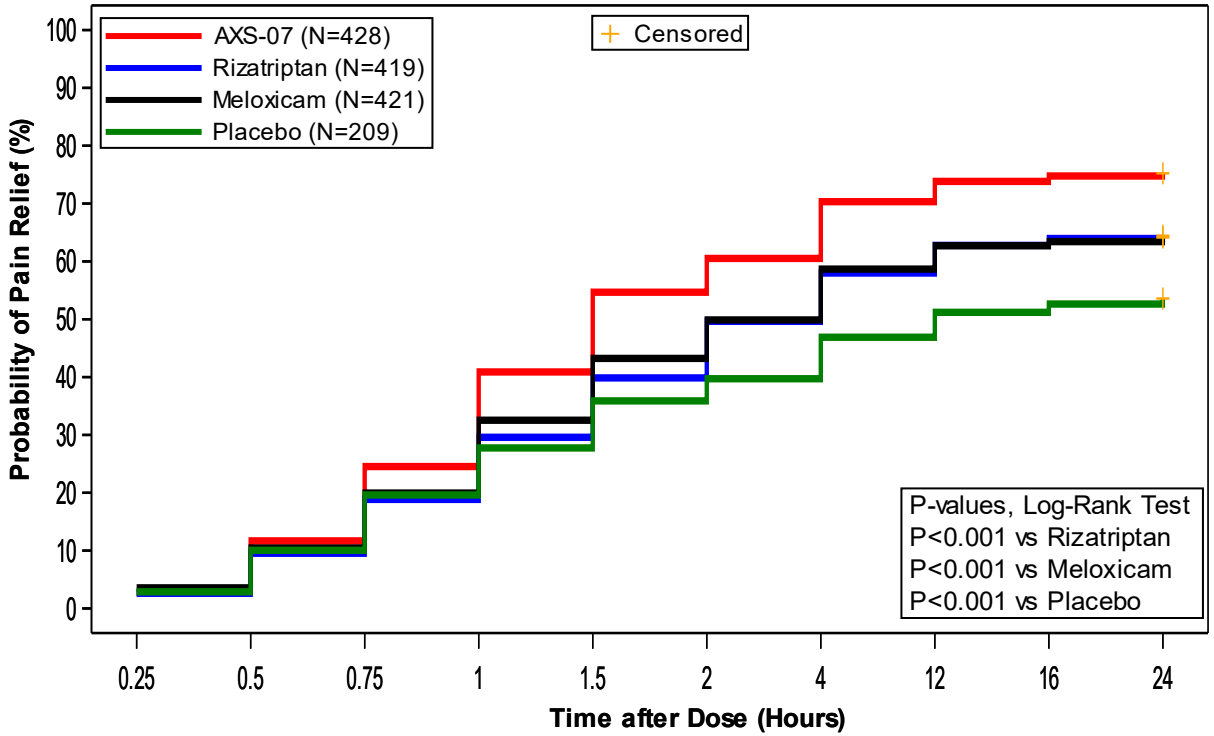


Endpoints	AXS-07 (n=428)	Placebo (n=209)	Difference	*P*-Value
Co-Primary Endpoint 1: *Pain Freedom 2 Hours after Dose, %*	19.9%	6.7%	-13.2%	<0.001
Co-Primary Endpoint 2: *Absence of Most Bothersome Symptom 2 Hours after Dose, %*	36.9%	24.4%	-12.5%	0.002

Pain Freedom Rates Over Time:
Significant Improvements in Pain Freedom

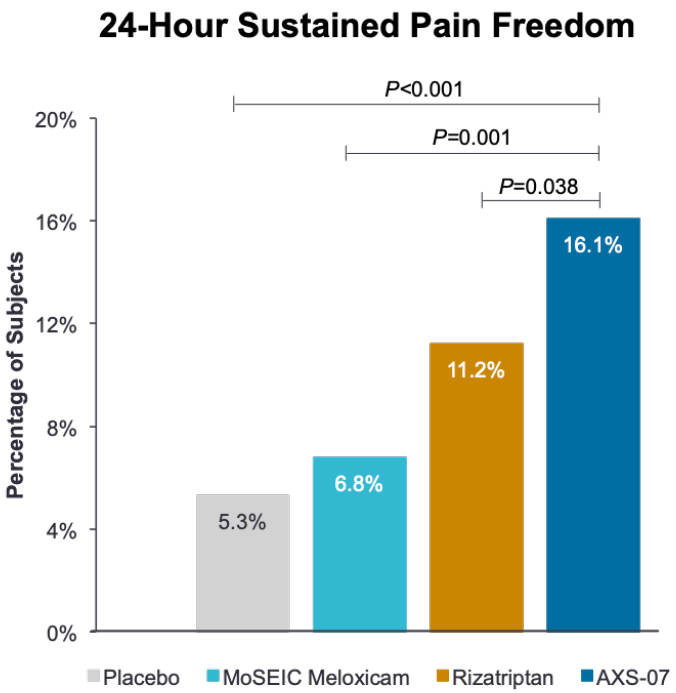


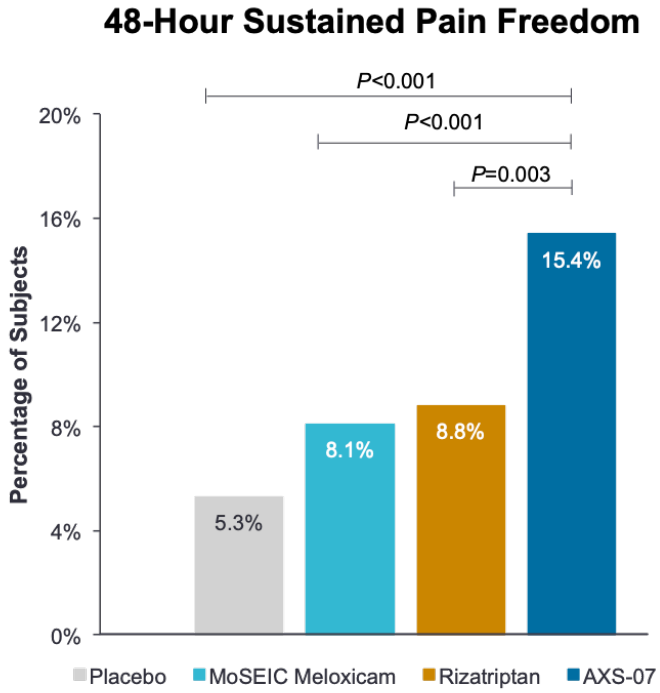
Rapid Relief of Migraine Pain:
Time to Pain Relief



- Probability of achieving pain relief with AXS-07 was greater than with rizatriptan within 30 minutes after dosing, resulting in a median time to pain relief that was nearly 3x faster for AXS-07 compared to rizatriptan (1.5 vs. 4.0 hours, p<0.001)

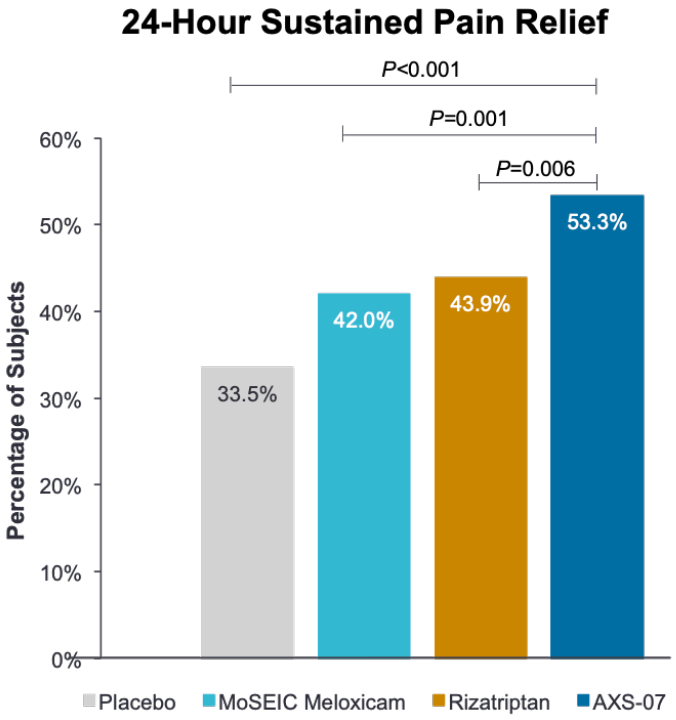
Sustained Pain Freedom Greater with AXS-07

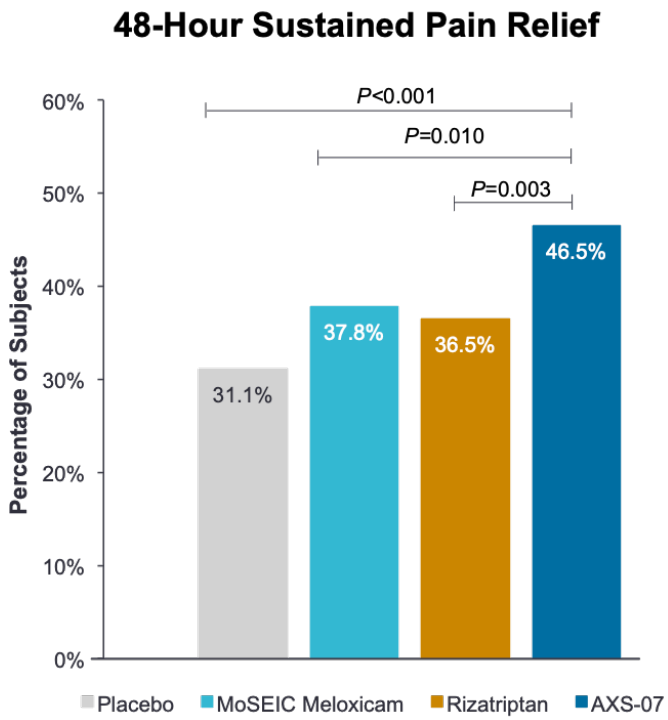




- 77% of patients treated with AXS-07 who achieved migraine pain freedom at Hour 2 maintained it through Hour 48

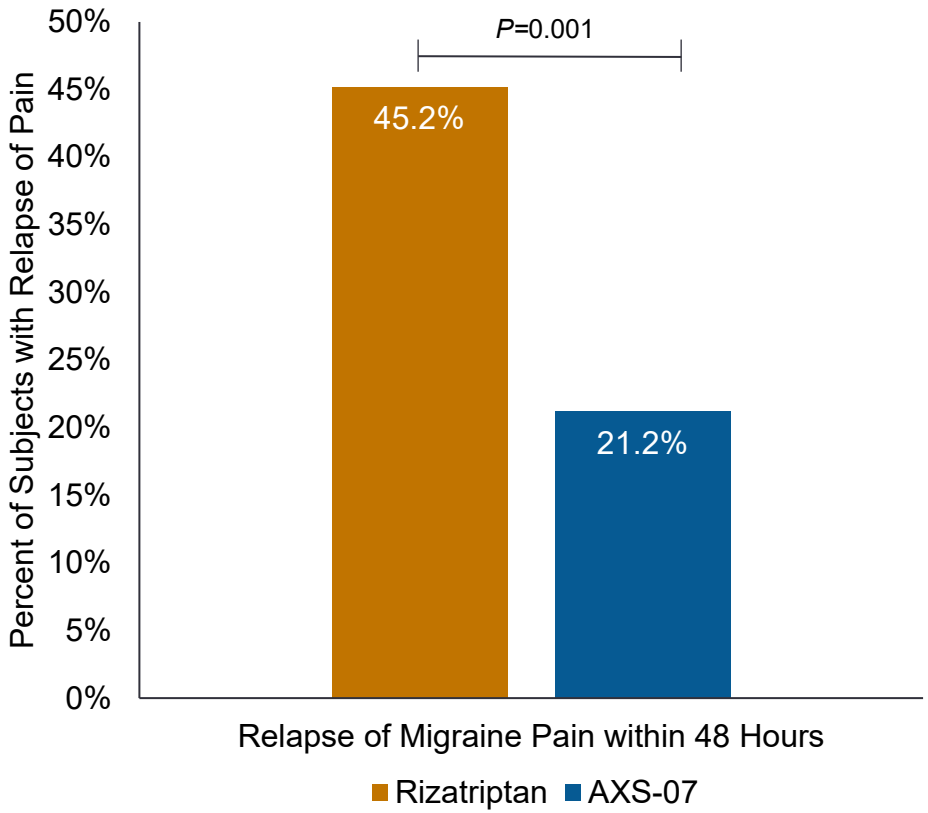
Sustained Pain Relief Greater with AXS-07





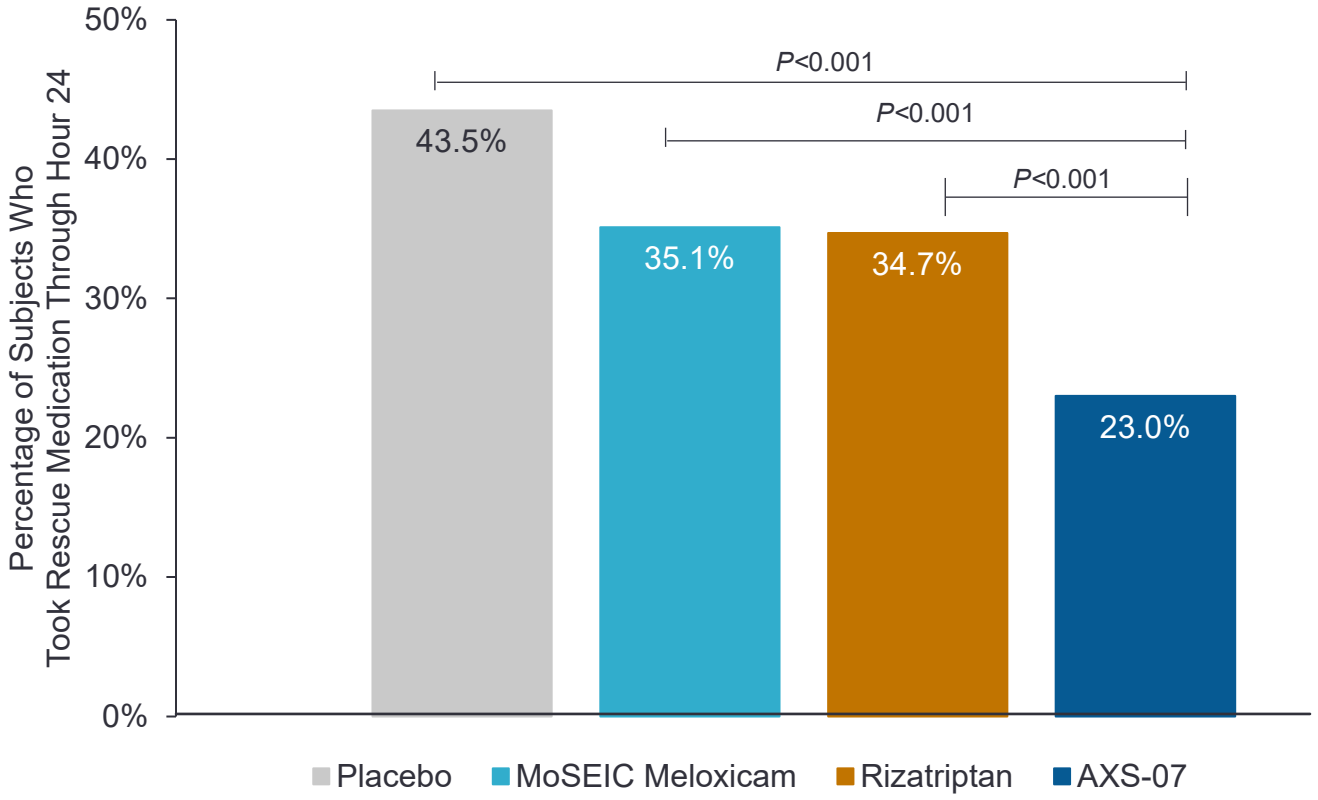
- A significantly greater percentage of patients who achieved relief of migraine pain at Hour 2 with AXS-07 maintained it through Hour 48 as compared to active and placebo controls

Pain Relapse Significantly Reduced with AXS-07



- AXS-07 reduced pain relapse by more than 50% compared to rizatriptan over 48 hours after dosing

Rescue Medication Use Significantly Reduced with AXS-07



- Rescue medication was required by 50% more rizatriptan patients and nearly 90% more placebo patients as compared to AXS-07

Multiple Efficacy-Related Endpoints: AXS-07 Superiority Over Rizatriptan

	Results*		
Clinically Significant Endpoint	**AXS-07**	**Rizatriptan**	**P-value**
Time to Pain Relief (probability of relief greater with AXS-07 starting at 30 mins, median times shown)	1.5 hours	4.0 hours	<0.001
24-hour Sustained Pain Relief	53.3%	43.9%	0.006
48-hour Sustained Pain Relief	46.5%	36.5%	0.003
24-hour Sustained Pain Freedom	16.1%	11.2%	0.038
48-hour Sustained Pain Freedom	15.4%	8.8%	0.003
Pain Relapse	21.2%	45.2%	0.001
Rescue Medication Use within 24 hours	23.0%	34.7%	<0.001
PGI-C (Very Much/Much Improved at 2 hours)	47.3%	41.1%	0.022
Return to Normal Functioning at 24 hours	63.8%	56.1%	0.027

*Presented as percent of patients responding, except time to pain relief which is presented as median time.
Abbreviations: PGI-C = patient global impression of change.

- AXS-07 demonstrated superiority over rizatriptan on multiple endpoints after a single dose

Safety of AXS-07:
Adverse Events Occurring in ≥2% of Subjects

	AXS-07 (N = 441)	Rizatriptan (N = 434)	Meloxicam (N = 433)	Placebo (N = 218)
Any Treatment-Emergent AE	**49 (11.1%)**	**67 (15.4%)**	**50 (11.5%)**	**13 (6.0%)**
Nausea	12 (2.7%)	21 (4.8%)	14 (3.2%)	8 (3.7%)
Dizziness	7 (1.6%)	9 (2.1%)	5 (1.2%)	5 (1.2%)
Somnolence	6 (1.4%)	9 (2.1%)	10 (2.3%)	6 (1.4%)

Data presented as number of subjects (% of subjects)

- AXS-07 was generally safe and well tolerated in this trial
- One serious adverse event in the AXS-07 arm which was not treatment related

MOMENTUM Phase 3 Trial Results: Conclusions

- AXS-07 resulted in rapid, substantial, and sustained pain relief compared to rizatriptan, MoSEIC™ meloxicam, and placebo in patients with a history of inadequate response to prior acute migraine treatments
- Low placebo response for pain freedom at 2 hours (6.7%) is consistent with the difficult-to-treat patient population enrolled in the trial
- Time to pain relief was nearly 3x faster for AXS-07 compared to rizatriptan, with a greater probability of achieving pain relief within 30 minutes after dosing
- The effects of AXS-07 were durable as demonstrated by significantly greater rates of sustained pain freedom, and significantly lower rates of pain relapse as compared to rizatriptan
- The efficacy benefits of AXS-07 translated into significantly less use of rescue medication, and greater rates of functional improvement as compared to rizatriptan and placebo
- AXS-07 was generally safe and well tolerated with low rates of adverse events
- The greater efficacy of AXS-07 observed in this trial indicate that AXS-07 may represent a superior treatment choice, especially for patients with more difficult-to-treat migraine