Combined Efficacy and Safety of AXS-07 (MoSEIC™ Meloxicam and Rizatriptan) in Two Phase 3 Clinical Trials

Stewart Tepper,[1] Richard B. Lipton,[2] Angad Chhabra,[3] Caroline Streicher,[3] Gregory Parks,[4] Herriot Tabuteau[3]

[1]New England Institute for Neurology and Headache, Stamford, CT, USA; [2]Albert Einstein College of Medicine, Bronx, NY, USA; [3]Axsome Therapeutics, New York, NY, USA; 4Formerly of Axsome Therapeutics, New York, NY, USA.

Key Question

What is the pooled efficacy and safety profile of AXS-07 (MoSEIC™ meloxicam and rizatriptan) in the acute treatment of migraine headache across two phase 3 clinical studies?

Conclusions

- Based on pooled data from 2 randomized placebo-controlled trials (MOMENTUM and INTERCEPT):
  - AXS-07 was effective for the acute treatment of migraine
  - AXS-07 was generally safe and well tolerated

References

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Disclosures

ST, RBL are consultants to Axsome Therapeutics.

AC, CS, GP, and HT are full-time employees of Axsome Therapeutics and may hold stock or stock options.

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Background

Better Acute Treatments of Migraine Are Needed

- All patients with migraine require acute treatment[1]
- Current treatments are suboptimal, as approximately 70% of people with migraine are not fully satisfied with current treatment[2]
- Suboptimal acute treatment of migraine is associated with an increased risk of medication overuse, progression to chronicity, and poor treatment outcomes[3,4]
- There is a substantial unmet need for new acute treatments that provide rapid, sustained response for patients with migraine

AXS-07 Uses a Multi-Mechanistic Approach to Treat Migraine

- AXS-07 is a novel, oral, rapidly absorbed, multi-mechanistic investigational medicine, consisting of MoSEIC™ meloxicam and rizatriptan (**Supplementary Figure 1**)
- Meloxicam is a cyclooxygenase-2 (COX-2) preferential non-steroidal anti-inflammatory drug and rizatriptan is a 5-$HT_{1B/1D}$ agonist
- In AXS-07, meloxicam is enabled by the proprietary MoSEIC™ technology, which results in rapid absorption while maintaining a long half-life

AXS-07 Demonstrated Efficacy in Clinical Trials

- MOMENTUM (NCT0389600, **Supplementary Information**):
  - AXS-07 improved clinical outcomes in patients with a history of inadequate response to acute migraine treatment compared with placebo, MoSEIC™ meloxicam, and rizatriptan.[5,6]
- INTERCEPT (NCT04163185, **Supplementary Information**):
  - AXS-07 resulted in rapid, substantial, and sustained pain relief as an early treatment of migraine.[7]
- MOVEMENT (NCT04068051):
  - AXS-07 consistently improved clinical outcomes across multiple headache episodes and was well tolerated in long-term episodic treatment of acute migraine[8]

Methods

Study Design

- MOMENTUM and INTERCEPT were randomized, double-blind, multicenter, active- (MOMENTUM) and placebo- (MOMENTUM and INTERCEPT) controlled trials in participants with migraine
- In MOMENTUM, 1594 participants were randomized (2:2:2:1) to take a single dose of AXS-07, 20 mg MoSEIC™ meloxicam, 10 mg rizatriptan, or placebo to treat a single migraine attack of moderate or severe intensity[5,6]
  - In INTERCEPT, 302 participants were randomized (1:1) to take a single dose of AXS-07 or placebo at the earliest onset of migraine pain[7]

Participants

- Key inclusion criteria:
  - Adults (male or female) aged 18 to 65 years
  - Established diagnosis (≥1 year) of migraine with or without aura
  - 2 to 8 migraines per month on average
  - **For MOMENTUM only**, history of inadequate response as assessed by a score of ≤7 on the Migraine Treatment Optimization Questionnaire (mTOQ-4)
- Key exclusion criteria:
  - Cluster headaches, tension headaches, or other types of migraines
  - Chronic daily headache (≥15 non-migraine headache days per month)
  - History of significant cardiovascular disease
  - Uncontrolled hypertension

Outcomes

- Co-primary endpoints for both studies were pain freedom at hour 2 post dose and freedom from most bothersome symptom (MBS) at hour 2 post dose.
- AXS-07 results from the 2 studies, MOMENTUM and INTERCEPT, compared with placebo were pooled for the present analysis.

Results

Demographics and Baseline Characteristics

- Demographics and baseline characteristics were generally balanced between treatment groups; rates of characteristics associated with poor treatment outcomes were high (**Table 1**)

Table 1. Baseline Characteristics (ITT Population)

Characteristics	AXS-07 Pooled (N = 560)	Placebo Pooled (N = 344)
Participants of MOMENTUM, n	428	209
Participants of INTERCEPT, n	132	135
Age, years, mean (SD)	41.3 (11.51)	41.0 (11.29)
Sex, female, n (%)	459 (82.0)	292 (84.9)
Race, n (%)		
White	450 (80.4)	263 (76.5)
Black or African American	88 (15.7)	61 (17.7)
Asian	9 (1.6)	11 (3.2)
Other	13 (2.3)	9 (2.6)
Allodynia, n (%)		
Yes (ASC-12 ≥3)	438 (78.2)	246 (71.5)
No (ASC-12 <3)	122 (21.8)	98 (28.5)
Migraine pain, n (%)		
1 – mild	132 (23.6)	135 (39.2)
2 – moderate	244 (43.6)	121 (35.2)
3 – severe	184 (32.9)	88 (25.6)
Nausea, n (%)	244 (43.6)	159 (46.2)
Depression, n (%)	78 (13.9)	51 (14.8)
Obese (BMI ≥30 kg/m^2), n (%)	239 (42.7)	145 (42.2)

ASC-12, 12-item Allodynia symptom Checklist; BMI, body mass index; ITT, intent-to-treat; SD, standard deviation.

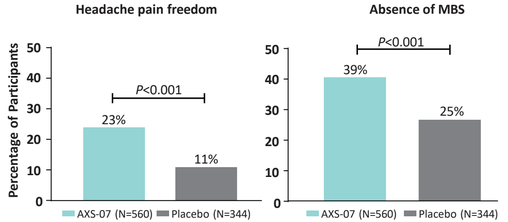
Efficacy

- The percentage of participants with headache pain freedom at Hour 2 was significantly higher with AXS-07 compared with placebo (*P*<0.001) (**Figure 1A**)
- Absence of MBS (nausea, photophobia, or phonophobia) at Hour 2 was achieved by a significantly greater percentage of participants taking AXS-07 versus placebo (*P*<0.001) (**Figure 1B**)
- In the AXS-07 group, 60.5% of participants experienced headache pain relief 2 hours after dosing, compared with 39.5% in the placebo group (*P*<0.001)

Efficacy

- The percentage of participants achieving 24-hour and 48-hour sustained pain freedom was significantly greater in the AXS-07 group compared with the placebo group; the between-group difference was 10.6% and 9.9 %, respectively (both *P*<0.001) (**Figures 2A** and **2B**)
- Participants receiving AXS-07 had reduced rescue medication use through 24 hours compared with placebo (*P*<0.001) (**Figure 3**)
- More participants receiving AXS-07 returned to normal functioning than those taking placebo, starting at 1 hour after dosing and maintained at every timepoint thereafter (*P*<0.05 or *P*<0.001) (**Figure 4**)

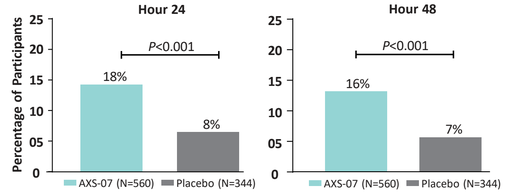
Figure 1. Headache Pain Freedom and Absence of MBS at Hour 2



- AXS-07 effectively reduced headache pain and MBS at Hour 2

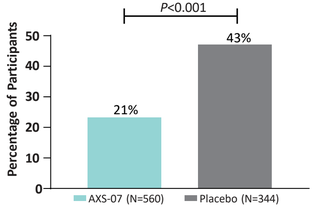
MBS=most bothersome symptom

Figure 2. Sustained Pain Freedom



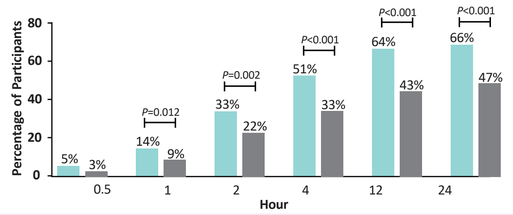
- AXS-07 improved 24-hour and 48-hour sustained pain freedom

Figure 3. Rescue Medication Use in the First 24 Hours Post-dose



- AXS-07 effectively reduced the usage of rescue medication

Figure 4. Percentage of Participants Able to Perform Normal Activity Over Time



- AXS-07 promoted the resumption of normal activity

Safety

- Treatment-emergent adverse events (TEAEs) were experienced by 12.7% of participants taking AXS-07 compared with 6.6% of participants on placebo (**Table 2**)
- The most frequently reported TEAEs in the AXS-07 and placebo groups were nausea, somnolence, and dizziness (**Table 2**)

Table 2. Most Frequently Reported TEAEs (Safety Population)

Participants, n (%)	AXS-07 Pooled (N = 581)	Placebo Pooled (N = 361)
At least 1 TEAE	74 (12.7)	24 (6.6)
Nausea	14 (2.4)	9 (2.5)
Somnolence	12 (2.1)	4 (1.1)
Dizziness	11 (1.9)	4 (1.1)

TEAE, treatment-emergent adverse event.