Efficacy of Celecoxib Oral Solution in Participants With Insufficient Response to Triptans for the Acute Treatment of Migraine: Pooled Results From a Post-hoc Analysis of 2 Phase 3 Randomized Clinical Trials

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Background

- Sumatriptan and other serotonin 5-$HT_{1B/1D}$ receptor agonist (triptans) have been associated with insufficient efficacy, recurrence within 24 hours after the first dose, and a high rate of treatment-emergent adverse events[1]
- Specifically, in adults with migraine who take a medication in the triptan class:
  - 2-hour pain freedom occurs in 30% to 40% of treated patients[2]
  - Headache recurs in as many as 40% who report pain freedom at 2 hours postdose[2]
  - Up to 52% experience treatment-emergent adverse events[1]
- When a second drug in the triptan class is prescribed, migraine pain and disability typically do not improve[3]
- For those who have an insufficient response to triptans, the best option is often to switch to another class of medications[3]
- Celecoxib 120 mg oral solution (Elyxyb™) is a liquid formulation of the cyclooxygenase-2-selective nonsteroidal anti-inflammatory drug in a unique drug delivery system
- The Self-Micro-Emulsifying Drug Delivery System (SMEDDS) increases solubility, dissolution rate, and bioavailability and achieves a T_{max} of 42 minutes[4] by:
  - Overcoming the hydrophobic properties of celecoxib[5]
  - Forming a nanometer-sized microemulsion for enhanced bioavailability[4]
  - Increasing intestinal wall permeability[6]
  - Minimizing the effects of gastroparesis associated with migraine[7]
- Celecoxib 120 mg oral solution has demonstrated efficacy in the acute treatment of migraine in 2 randomized, double-blind, placebo-controlled clinical trials (NCT03006276; NCT03009019)[8,9]

Objective

- The objective of this analysis was to compare the efficacy of celecoxib oral solution with placebo in participants based on their historical response to triptans

Methods

Conduct

- This post hoc analysis was based on pooled data from 2 independent, 2-period, randomized, double-blind, placebo-controlled, multicenter, phase 3 trials comparing celecoxib 120 mg oral solution with placebo in the acute treatment of migraine[8,9]

Population

- Participants were adults aged 18 to 75 years (inclusive)
- Participants had a 12-month history of episodic migraine and 2 to 8 migraine attacks per month, 14 or fewer headache days per month, no medication overuse, and 48 hours of headache-free time between migraine attacks

Statistical analysis

- Efficacy was analyzed in the first double-blind treatment period of both trials among participants who reported using a triptan as the primary medication for migraine on the trial case report form
- An insufficient response to triptans was defined based on 2 self-reported criteria:
  - Headache not reduced at all or only slightly reduced at 2 hours postdose (insufficient response)
  - Headache absent at 2 hours postdose but always or sometimes recurred within 24 hours (recurrence)
- Participants satisfying either criterion were defined as triptan insufficient responders; those not satisfying either criterion were defined as triptan responders
- Triptan insufficient response status was computed in each trial before being pooled and merged with a matching pooled analysis sample from the clinical study report (CSR)
- Because some triptan responders were not included in the CSR-matching population, and vice versa, the sample of triptan insufficient responders analyzed for 2-hour pain freedom was smaller than the CSR-matching sample or the triptan insufficient responders sample separately; these missing participants are reported.
- Odds ratios (OR) for achieving 2-hour pain freedom and differences between the subgroups were obtained from logistic regression models

Results

Participants

- Demographics were comparable in participants reporting a history of triptan use (Table 1)
- Among those treated with celecoxib 120 mg oral solution, 48.6% (89/186) of triptan insufficient responders had a history of insufficient response, and 53.0% (97/186) had a history of recurrence; 3 participants met criteria for and were counted in both subgroups

Table 1. Demographics of Participants With a History of Triptan Use

	Celecoxib 120 mg Oral Solution N=138		Placebo N=125	
	Insufficient responders n=99	Responders n=39	Insufficient responders n=84	Responders n=41
Age, years, mean (SD)	43.2 (12.9)	43.2 (12.1)	43.2 (12.6)	42.6 (12.7)
Sex, n (%)				
Female	90 (90.9)	36 (92.3)	74 (88.1)	35 (85.4)
Male	9 (9.1)	3 (7.7)	10 (11.9)	6 (14.6)
Race, n (%)				
White	82 (82.8)	33 (84.6)	74 (88.1)	37 (90.2)
Black or African American	15 (15.2)	5 (12.8)	9 (10.7)	3 (7.3)
Other[a]	2 (2.0)	1 (2.6)	1 (1.2)	1 (2.4)

SD=standard deviation

[a]Includes participants who self-identified as Asian, Native Hawaiian or Other Pacific Islander, and Other.

Efficacy

- Among triptan insufficient responders (Figure 1), celecoxib 120 mg oral solution was more effective than placebo for 2-hour pain freedom (33.3% vs 14.3%); the odds of achieving pain freedom were 200% greater with celecoxib 120 mg oral solution than with placebo (OR=3.0, p=0.0036)
- Among triptan responders, 2-hour pain freedom was also higher for celecoxib oral solution than placebo (33.3% vs 14.6%); the odds of achieving 2-hour pain freedom were 192% greater with celecoxib oral solution than with placebo (OR=2.92, p=0.0548)
- There was no difference in the odds of achieving 2-hour pain freedom between the subgroups (OR=1.03, p=0.9666) — consistent with the CSR-matching sample
- Treatment effects were similar in the insufficient response and recurrence subgroups (Figure 2)
- In the recurrence subgroup, 100% of celecoxib-treated participants with 2-hour pain freedom maintained pain freedom for 24 hours

Figure 1. Pain Freedom at 2 Hours Postdose in Triptan Insufficient Responders and Triptan Responders

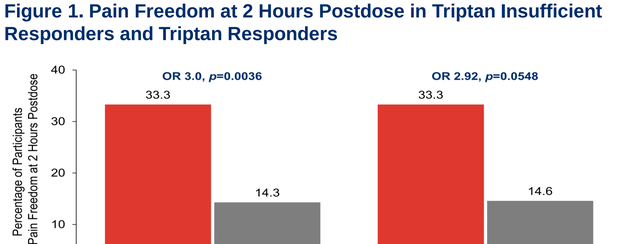
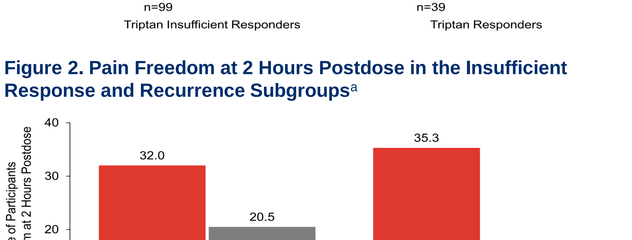


Figure 2. Pain Freedom at 2 Hours Postdose in the Insufficient Response and Recurrence Subgroups[a]



[a]Subgroups too small for statistical comparison.

Conclusions

- **Celecoxib 120 mg oral solution was more likely than placebo to provide 2-hour pain freedom regardless of participants' historical response to triptans; in triptan responders, the numerical superiority of celecoxib oral solution was nonsignificant due to the small sample size.**
- **Celecoxib 120 mg oral solution provides clinical benefits in adults who do not respond to drugs in the triptan class.**
- **Celecoxib 120 mg oral solution may be a useful alternative to oral triptans.**

Disclosures: RBL, SJT, and DS have received honoraria for research support and/or consulting from Scilex Holding Company, which owns the rights to celecoxib oral solution; EC and DL are employed by Scilex Holding Company.

References: 1. *Cochrane Database Syst Rev*. 2012;(2):CD008615; 2. *Cephalalgia*. 2023;43(2):3331024221143773; 3. *Headache*. 2014;54(7):1120-30; 4. *Clin Drug Investig*. 2017;37(10):937-946; 5. *Int Sch Res Notices*. 2014;2014:964051; 6. *Front Pharmacol*. 2019;10:459; 7. *Cephalalgia*. 2013;33(6):408-415; 8. *Headache*. 2020;60:58-70; 9. *J Pain Res*. 2021;14:2529-2542.