Preliminary Experience With Sodium Phenylbutyrate and Taurursodiol in a United States Expanded Access Program

Poster #123

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BACKGROUND

- The largest single-product amyotrophic lateral sclerosis (ALS) Expanded Access Program (EAP) in the United States to date was initiated by Amylyx in May 2022 to provide preapproval access to sodium phenylbutyrate and taurursodiol (PB&TURSO) to people living with ALS (PLWALS) alongside the ongoing phase 3 PHOENIX trial
- The US EAP enrolled participants >36 months from symptom onset who were otherwise not eligible for any therapeutic ALS clinical trial. Thus, these eligibility criteria led to enrollment of a population of participants not included in the Amylyx CENTAUR or PHOENIX ALS trials (**Table 1**)

TABLE 1. KEY ELIGIBILITY CRITERIA FOR US EAP, CENTAUR, AND PHOENIX

US EAP	CENTAUR	PHOENIX
▪ Diagnosed with ALS	▪ Clinically definite ALS	▪ Clinically definite or probable ALS
▪ >36 mo from symptom onset	▪ ≤18 mo from symptom onset	▪ <24 mo from symptom onset
▪ Excluded if required invasive mechanical ventilation	▪ SVC >60%	▪ SVC ≥55%
▪ Excluded if eligible for any therapeutic ALS clinical trial at site	▪ N/A	▪ N/A

SVC, slow vital capacity; N/A, not applicable.

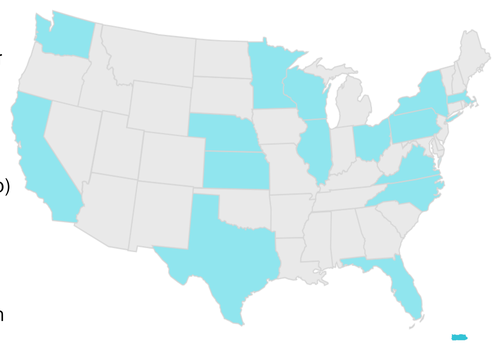
OBJECTIVE AND METHODS

- To describe preliminary PB&TURSO safety findings from the US EAP
- Demographics, adverse events (AEs), and discontinuation rates were summarized using descriptive statistics. Categorical variables were summarized by counts and percentages of participants in corresponding categories

RESULTS

FIGURE 1. US EAP SITES

- Cleveland Clinic
- Columbia University Medical Center
- Duke ALS Clinic
- Healey & AMG Center for ALS Research at MGH
- Hispanic Alliance for Research & Translational Research (Puerto Rico)
- Holy Cross Health-Fort Lauderdale
- Mayo Clinic
- Northwestern University
- Nova Southeastern University
- Providence St. Luke's Rehabilitation Medical Center



- Swedish Neuroscience Institute
- Somnos Clinical Research/Neurology Associates
- Texas Tech University Health Sciences Center El Paso
- The Kaiser Permanente Medical Group
- Thomas Jefferson University
- University of Florida-Gainesville
- University of Kansas
- University of Pennsylvania
- University of Southern California
- University of Washington School of Medicine
- University of Wisconsin
- Virginia Commonwealth University

RESULTS

- One hundred ninety-four participants were enrolled in 22 sites (**Figure 1**). Participants had mean (SD) age of 61.3 (11.8) (**Table 2**)
- Participants enrolled over the span of 5 months from May to September 2022. Upon approval of PB&TURSO by the US Food and Drug Administration in September 2022, US EAP participants could then choose to transition to commercial product

TABLE 2. PARTICIPANT DEMOGRAPHICS

	US EAP (N=194)	CENTAUR PB&TURSO[b] (N=89)
Age, y		
Mean (SD)	61.3 (11.8)	57.9 (10.6)
Median	63.0	60.0
Min, Max	28, 91	31, 79
Sex, n (%)		
Male	123 (63)	61 (68.5)
Female	71 (37)	28 (31.5)
Race, n (%)		
White	173 (89)	84 (94.4)
Black or African American	7 (4)	2 (2.2)
Asian	7 (4)	2 (2.2)
Not reported[a]	3 (2)	0 (0)
Other	4 (2)	0 (0)
Unknown	0 (0)	1 (1.1)
Ethnicity, n (%)		
Hispanic or Latino	27 (14)	6 (6.7)
Not Hispanic or Latino	164 (85)	83 (93.3)
Not reported[a]	3 (1.5)	0 (0)

[a]Not reported due to confidentiality regulations. [b]Data from the 24-week randomized phase CENTAUR PB&TURSO group are provided for reference purposes only. No head-to-head comparisons should be made.

- Median exposure to PB&TURSO in the EAP was approximately 5 months (**Table 3**), 72 out of 194 (37%) of participants received >6 months of treatment exposure
  - Majority of participants (86.1%) did not reduce treatment dose

TABLE 3. TREATMENT EXPOSURE IN THE US EAP AND CENTAUR TRIAL

	US EAP (N=194)	CENTAUR PB&TURSO[a] (N=89)
Exposure, patient months		
Mean (SD)	4.74 (2.26)	4.53 (1.81)
Median	5.01	5.50
Min, Max	0.13, 8.55	0.13, 7.27

[a]Data from the 24-week randomized phase CENTAUR PB&TURSO group are provided for reference purposes only. No head-to-head comparisons should be made.

- The safety and tolerability of PB&TURSO in the EAP was consistent with the PB&TURSO arm from the phase 2 CENTAUR trial. In the US EAP, 19% of participants discontinued due to an AE; diarrhea was the most common AE (**Table 4**)

TABLE 4. SAFETY EVENTS FROM THE US EAP AND CENTAUR TRIAL

	US EAP (N=194)	CENTAUR PB&TURSO[a] (N=89)
Participants with ≥1 AE, n (%)	122 (63)	86 (97)
Participants with ≥1 SAE, n (%)	21 (11)	11 (12)
Discontinuation due to AE, n (%)	37 (19)	18 (20)
AEs reported in ≥5% of participants		
Diarrhea	53 (27)	19 (21)
Nausea	12 (6)	16 (18)
Constipation	11 (6)	12 (14)
Abdominal discomfort	7 (4)	5 (6)
Fatigue	12 (6)	7 (8)
Dizziness	10 (5)	9 (10)
Fall	13 (7)	25 (28)

[a]Data from the 24-week randomized phase CENTAUR PB&TURSO group are provided for reference purposes only. No head-to-head comparisons should be made.

CONCLUSIONS

Learnings for the Community About Implementing EAPs

- The PB&TURSO US EAP was successfully implemented alongside the phase 3 PHOENIX trial, enrolling 194 participants across 22 sites over the span of 5 months
  - Planning EAPs alongside pivotal trials provides the opportunity for access to investigational therapies for people ineligible for clinical trials and can also provide data in a broader, real-world population
  - Community and site feedback was essential in designing and implementing the EAP

Learnings About PB&TURSO Safety

- PB&TURSO was generally well tolerated with an acceptable safety profile in this broader and relatively more advanced population of PLWALS
- Despite differences in study populations, the safety and tolerability of PB&TURSO in the EAP was consistent with the PB&TURSO arm from the phase 2 CENTAUR trial

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Disclosures

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