Characterization of the Enrolled Population in the Phase 3 PHOENIX Trial in Amyotrophic Lateral Sclerosis: Preliminary Results

Leonard van den Berg,[1] Lahar Mehta,[2] Ryan Miller,[2] Suzanne Bijl,[3] Feifan Zhang,[2] Sabrina Paganoni[4,5]

[1]Department of Neurology, UMC Utrecht Brain Center, University Medical Center Utrecht, Utrecht, the Netherlands; [2]Amylyx Pharmaceuticals, Inc., Cambridge, MA, USA; [3]Amylyx Pharmaceuticals EMEA B.V., Amsterdam, the Netherlands; [4]Sean M. Healey and AMG Center for ALS & the Neurological Clinical Research Institute, Massachusetts General Hospital, Boston, MA, USA; [5]Department of Physical Medicine and Rehabilitation, Harvard Medical School, Boston, MA, USA

Poster
218

AMYLYX

BACKGROUND

- AMX0035, an oral, fixed-dose combination of sodium phenylbutyrate (PB) and ursodoxicoltaurine (TURSO, also known as taurursodiol), is hypothesized to reduce neuronal death by simultaneously mitigating endoplasmic reticulum stress and mitochondrial dysfunction, which are 2 key pathways of ALS pathogenesis[1-5]
- PB&TURSO significantly slowed functional decline and prolonged survival duration compared with placebo in adults with definite amyotrophic lateral sclerosis (ALS; revised El Escorial criteria[6]), symptom onset ≤18 months, and baseline slow vital capacity >60% in the phase 2 CENTAUR trial[7-9]
- The global phase 3 PHOENIX trial (NCT05021536; EudraCT 2021-000250-26) was designed to assess the efficacy and safety of PB&TURSO in a larger population of people living with ALS

OBJECTIVE

- To report a preliminary profile of baseline characteristics for participants in PHOENIX conducted as of February 2, 2023, upon completion of trial enrollment

METHODS

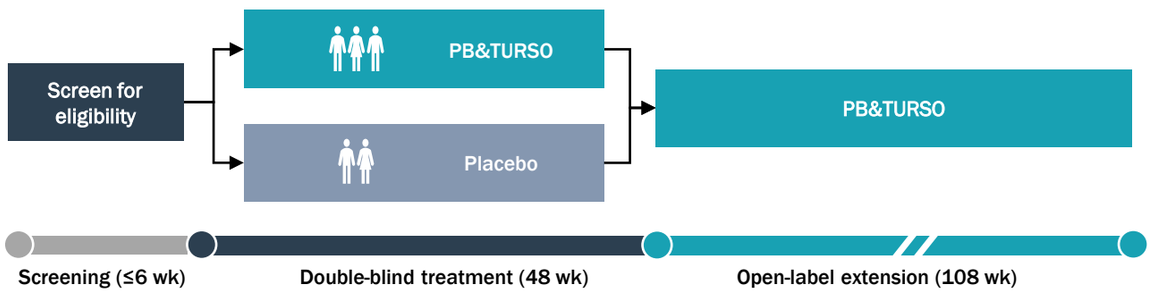
- Participants were enrolled from 69 sites, including members of the Treatment Research Initiative to Cure ALS (TRICALS) and Northeast ALS Consortium (NEALS)
- PHOENIX incorporated broader eligibility criteria than the CENTAUR trial (**Table 1**)
- Eligible participants were randomized in a 3:2 ratio to receive PB&TURSO or matching placebo by mouth or feeding tube for 48 weeks (**Figure 1**)
  - Continuation of a stable dosing regimen of riluzole and/or edaravone was permitted
- Demographics and baseline disease characteristics were summarized using appropriate descriptive statistics

Table 1. Comparative Key Eligibility Criteria in PHOENIX and CENTAUR

Parameter	Criterion for Study Inclusion	
	PHOENIX	CENTAUR[7]
Clinical ALS diagnosis (revised El Escorial criteria[6])	Clinically definite or clinically probable	Clinically definite
Time since ALS symptom onset, mo	<24	≤18
Screening SVC, percentage of predicted normal	≥55	>60

ALS, amyotrophic lateral sclerosis; mo, months; SVC, slow vital capacity.

Figure 1. PHOENIX Study Design



PB, sodium phenylbutyrate; PB&TURSO, sodium phenylbutyrate and ursodoxicoltaurine; TURSO, ursodoxicoltaurine; wk, weeks.

Acknowledgements
The authors would like to thank the PHOENIX trial participants and their families and caregivers, as well as the Treatment Research Initiative to Cure ALS and Northeast ALS Consortium. Funding support was provided by Amylyx Pharmaceuticals, Inc.

Disclosures
LvdB and SP are members of the steering committee for this study. LM, RM, SB, and FZ have stock option ownership of and are employees of Amylyx Pharmaceuticals, Inc.

References
1. Rodrigues CM, Steer CJ. *Expert Opin Investig Drugs*. 2001;10(7):1243-1253. 2. Rodrigues CM, et al. *Biochemistry*. 2003;42(10):3070-3080. 3. Manfredi G, Kawamata H. *Neurobiol Dis*. 2016;90:35-42. 4. Walker AK, Atkin JD. *IUBMB Life*. 2011;63(9):754-763. 5. Kiernan MC, et al. *Nat Rev Neurol*. 2021;17(2):104-118. 6. Brooks BR, et al. *Amyotroph Lateral Scler Other Motor Neuron Disord*. 2000;1(5):293-299. 7. Paganoni S, et al. *N Engl J Med*. 2020;383(10):919-930. 8. Paganoni S, et al. *Muscle Nerve*. 2022;66(2):136-141. 9. Paganoni S, et al. *Muscle Nerve*. 2022;66(2):136-141. Supplement.

Presented at ENCALS 2023; July 12-14, 2023; Barcelona, Spain

RESULTS

- A total of 664 participants were enrolled from Europe (n=552) and the United States (n=112) (**Figure 2**)
- Baseline characteristics of the overall population are summarized in **Table 2**

Figure 2. Geographic Distribution of Participants in the PHOENIX Trial

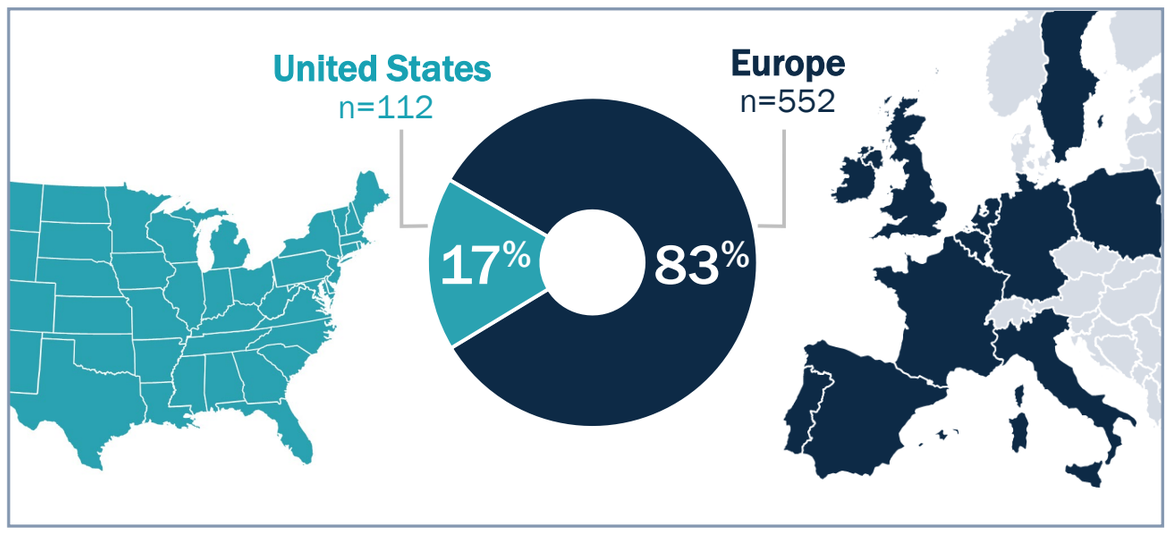


Table 2. Baseline Characteristics of the Overall PHOENIX and CENTAUR Trial Populations

Characteristic[a]	PHOENIX (N=664)	CENTAUR (N=137)
Sex, n (%)		
Male	411 (62)	93 (68)
Female	253 (38)	44 (32)
Race, n (%)		
White	554 (83)	130 (95)
Asian	9 (1)	3 (2)
Black	6 (1)	3 (2)
American Indian or Alaska Native	1 (<1)	0
Other	5 (1)	0
Unknown	2 (<1)	1 (<1)
Not reported	87 (13)	0
Age, y	59.5 ± 10.81	57.7 ± 9.60
BMI[b], kg/m^2	25.3 ± 4.32	26.7 ± 4.92
SVC[b], percent predicted normal	82.8 ± 17.73	83.1 ± 17.93
Time since ALS symptom onset, mo	14.4 ± 5.30	13.5 ± 3.75
Time since ALS diagnosis, mo	5.6 ± 4.52	6.1 ± 3.28
Bulbar onset, n (%)	148 (22)	36 (26)
Riluzole and/or edaravone use, n (%)	612 (92)	106 (77)
Riluzole	611 (92)	98 (72)
Edaravone	20 (3)	47 (34)
ALSFRS-R total score[b], points	36.7 ± 6.06	36.0 ± 5.52
ALSAQ-40 total score[c], points	51.4 ± 27.11	N/A[d]

[a]Plus-minus values are means ± SD.
[b]At the time of this preliminary analysis, data for these baseline characteristics were available for 662 participants in PHOENIX.
[c]At the time of this preliminary analysis, data for this baseline characteristic were available for 641 participants in PHOENIX.
[d]ALSAQ-40 total score was not assessed in CENTAUR.
ALS, amyotrophic lateral sclerosis; ALSAQ-40, Amyotrophic Lateral Sclerosis Assessment Questionnaire (40 items); ALSFRS-R, Amyotrophic Lateral Sclerosis Functional Rating Scale–Revised; BMI, body mass index; mo, months; N/A, not applicable; SVC, slow vital capacity, y, years.

CONCLUSIONS

- Summary baseline characteristics from the PHOENIX trial are presented; however, these data are preliminary and subject to updates upon final database lock
- Top-line data are anticipated in mid-2024

AMX0035 is an investigational drug in the EU and UK and not approved for use in ALS.