

Supplementary Online Content

Title: Effect of sodium phenylbutyrate and taurursodiol on plasma concentrations of neuroinflammatory biomarkers in amyotrophic lateral sclerosis: results from the CENTAUR trial

Authors: Robert Bowser,^{1,2} Jiyang An,^{1,2} Lahar Mehta,³ Junliang Chen,³ Jamie Timmons,³ Merit Cudkowicz,⁴ Sabrina Paganoni^{4,5}

Author affiliations: ¹Departments of Neurology and Translational Neuroscience, Barrow Neurological Institute, Phoenix, AZ, USA; ²nVector, Inc., Phoenix, AZ, USA; ³Amylyx Pharmaceuticals, Inc., Cambridge, Massachusetts, USA; ⁴Sean M. Healey and AMG Center for ALS & the Neurological Clinical Research Institute, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA; ⁵Spaulding Rehabilitation Hospital, Harvard Medical School, Boston, Massachusetts, USA

Supplemental Table 1 Baseline characteristics in the neuroinflammatory biomarkers analysis population*

Characteristic	PB and TURSO (n=81)	Placebo (n=45)
Male, n (%)	56 (69.1)	29 (64.4)
White, n (%)	76 (93.8)	43 (95.6)
Mean (SD) age, y	57.3 (10.41)	57.3 (7.71)
Bulbar onset, n (%)	24 (29.6)	10 (22.2)
Riluzole or edaravone use, n (%)	56 (69.1)	39 (86.7)
Riluzole	53 (65.4)	34 (75.6)
Edaravone	21 (25.9)	22 (48.9)
Both	18 (22.2)	17 (37.8)
Mean (SD) prebaseline ALSFRS-R slope, points/mo [†]	0.95 (0.431)	0.90 (0.552)
Mean (SD) SVC, percent predicted normal	84.7 (17.99)	84.6 (15.69)
Mean (SD) ALSFRS-R total score, points [‡]	35.8 (5.76)	36.8 (5.02)
Bulbar score	9.6 (2.36)	9.9 (2.66)
Fine-motor score	8.0 (2.68)	8.2 (2.49)
Gross-motor score	7.5 (2.81)	7.6 (2.65)
Breathing score	10.6 (1.95)	11.0 (1.84)
Mean (SD) upper-limb ATLAS score, percent predicted normal [§]	55.3 (24.84)	53.3 (24.96)
Mean (SD) lower-limb ATLAS score, percent predicted normal [§]	57.2 (25.47)	58.2 (25.96)
Mean (SD) total ATLAS score, percent predicted normal [§]	56.9 (20.61)	55.4 (20.71)
Mean (SD) duration since ALS symptom onset, mo	13.4 (3.92)	13.6 (3.57)
Mean (SD) duration since ALS diagnosis, mo	5.9 (3.44)	6.4 (3.18)
Mean (SD) BMI, kg/m ²	27.0 (4.53)	26.5 (5.99)

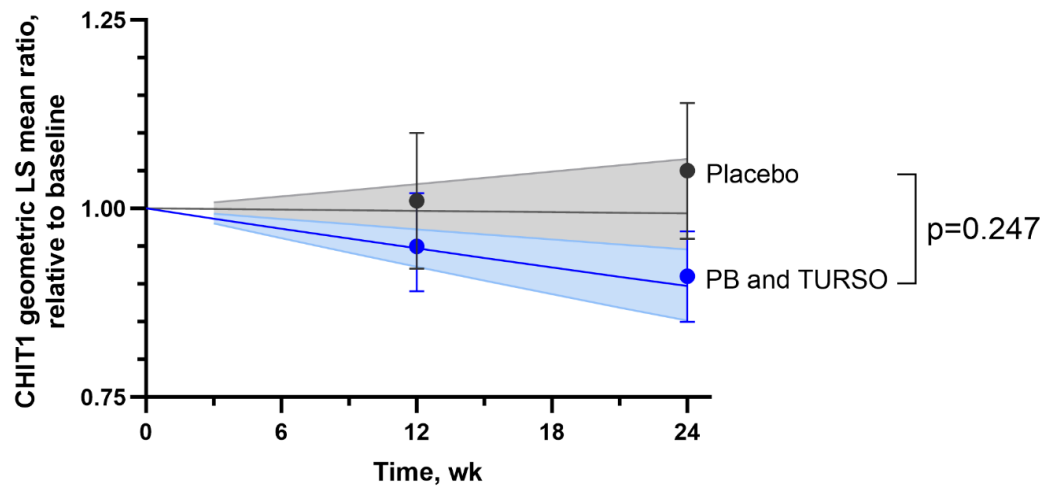
*Consisted of participants within the modified intent-to-treat population with ≥ 1 postbaseline plasma sample collected over the 24-week randomised phase duration. The modified intent-to-treat population consisted of participants who received ≥ 1 dose of study medication and had ≥ 1 postbaseline ALSFRS-R assessment (N=135; PB and TURSO, n=87; placebo, n=48).

[†]Defined as the rate of change in ALSFRS-R total score from symptom onset to trial baseline.

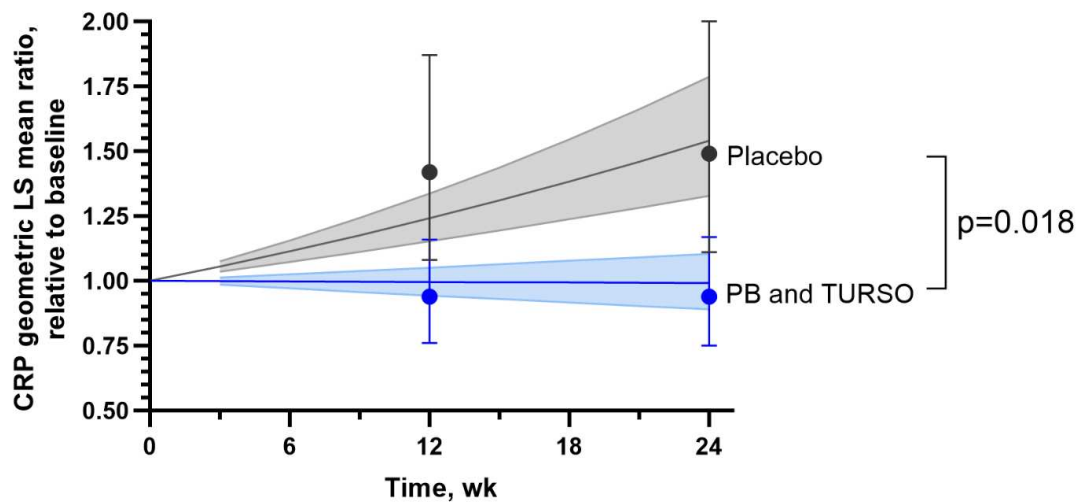
[‡]The ALSFRS-R measures 12 items in 4 subdomains of function, each scored on a scale from 0–4, with higher scores indicating better function (maximum total score, 48 points; maximum score for each subdomain, 12 points).¹

[§]ATLAS values are standardised to the percentage of the predicted normal value based on sex, age, weight and height.²

ALS, amyotrophic lateral sclerosis; ALSFRS-R, Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised; ATLAS, Accurate Test of Limb Isometric Strength; BMI, body mass index; PB and TURSO, sodium phenylbutyrate and taurursodiol; SD, standard deviation; SVC, slow vital capacity.



Supplemental Figure 1 Change in CHIT1 plasma concentration relative to baseline over 24 weeks. Log10-transformed CHIT1 concentration measurements³ were analysed using a random-slope, shared-baseline, linear mixed-effects model adjusted for age and ALSFRS-R slope interacting with time (colored lines, with shading reflecting SEs). Geometric mean ratios (solid dots) and 95% CIs (bars) from an MMRM model without linear trend assumption are shown at weeks 12 and 24. ALSFRS-R, Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised; CHIT1, chitinase 1; LS, least squares; MMRM, mixed model for repeated measures; PB and TURSO, sodium phenylbutyrate and taurursodiol.



Supplemental Figure 2 Change in CRP plasma concentration relative to baseline over 24 weeks. Log10-transformed CRP concentration measurements³ were analysed using a random-slope, shared-baseline, linear mixed-effects model adjusted for age and ALSFRS-R slope interacting with time (colored lines, with shading reflecting SEs). Geometric mean ratios (solid dots) and 95% CIs (bars) from an MMRM model without linear trend assumption are shown at weeks 12 and 24. ALSFRS-R, Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised; CRP, C reactive protein; LS, least squares; MMRM, mixed model for repeated measures; PB and TURSO, sodium phenylbutyrate and taurursodiol.

References

1. Cedarbaum JM, Stambler N, Malta E, *et al.* The ALSFRS-R: a revised ALS functional rating scale that incorporates assessments of respiratory function. *J Neurol Sci.* 1999;**169**:13-21. doi:10.1016/s0022-510x(99)00210-5
2. Andres PL, English R, Mendoza M, *et al.* Developing normalized strength scores for neuromuscular research. *Muscle Nerve.* 2013;**47**:177-82. doi:10.1002/mus.23516
3. Vu L, An J, Kovalik T, Gendron T, Petrucelli L, Bowser R. Cross-sectional and longitudinal measures of chitinase proteins in amyotrophic lateral sclerosis and expression of CHI3L1 in activated astrocytes. *J Neurol Neurosurg Psychiatry.* 2020;**91**:350-8. doi:10.1136/jnnp-2019-321916