CENTAUR

Functional and Long-Term Survival Benefit of AMX0035 in ALS

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The CENTAUR Trial Was an ALS Community Collaboration

NEALS Northeast Amyotrophic Lateral Sclerosis Consortium

NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

BARROW Neurological Institute

ALS ASSOCIATION

alsFINDINGaCURE

AMYLYX

CENTAUR Randomized Phase and Open-Label Extension (OLE)[1,2]

Randomized, Double-Blind Trial

Open-Label Extension

Outcomes

- Safety
- ALSFRS-R
- ATLIS
- pNF-H
- SVC
- Time to death, tracheostomy, PAV +/- any hospitalization*

Outcomes

- Safety
- ALSFRS-R
- Survival
- ATLIS
- SVC
- Time to death, tracheostomy, PAV +/- any hospitalization*

All-cause mortality analysis incorporated all randomized participants (not just those that went into OLE)

*Permanent assisted ventilation defined as >22 hours daily for >7 days. ALSFRS-R, Amyotrophic Lateral Sclerosis Functional Rating Scale–Revised; ATLIS, Accurate Test of Limb Isometric Strength; pNF-H, phosphorylated axonal neurofilament H subunit; SVC, slow vital capacity; PAV, permanent assisted ventilation.

1. Paganoni S, et al. N Engl J Med. 2020;383:919-930. 2. Data on File. Amylyx Pharmaceuticals.

CENTAUR Randomized Phase and Open-Label Extension (OLE)[1,2]

CENTAUR

Randomized, Double-Blind Trial

Open-Label Extension

Key Inclusion Criteria

- Definite ALS, El Escorial criteria
- <18 months from symptom onset
- SVC >60%
- Riluzole and edaravone use allowed

Key Inclusion Criteria

- Completion of all visits in randomized trial on study drug
- Enrollment within 28 days of week 24 visit in randomized trial
- Tracheostomy or initiation of PAV during randomized trial did not preclude eligibility
- Riluzole and edaravone use allowed

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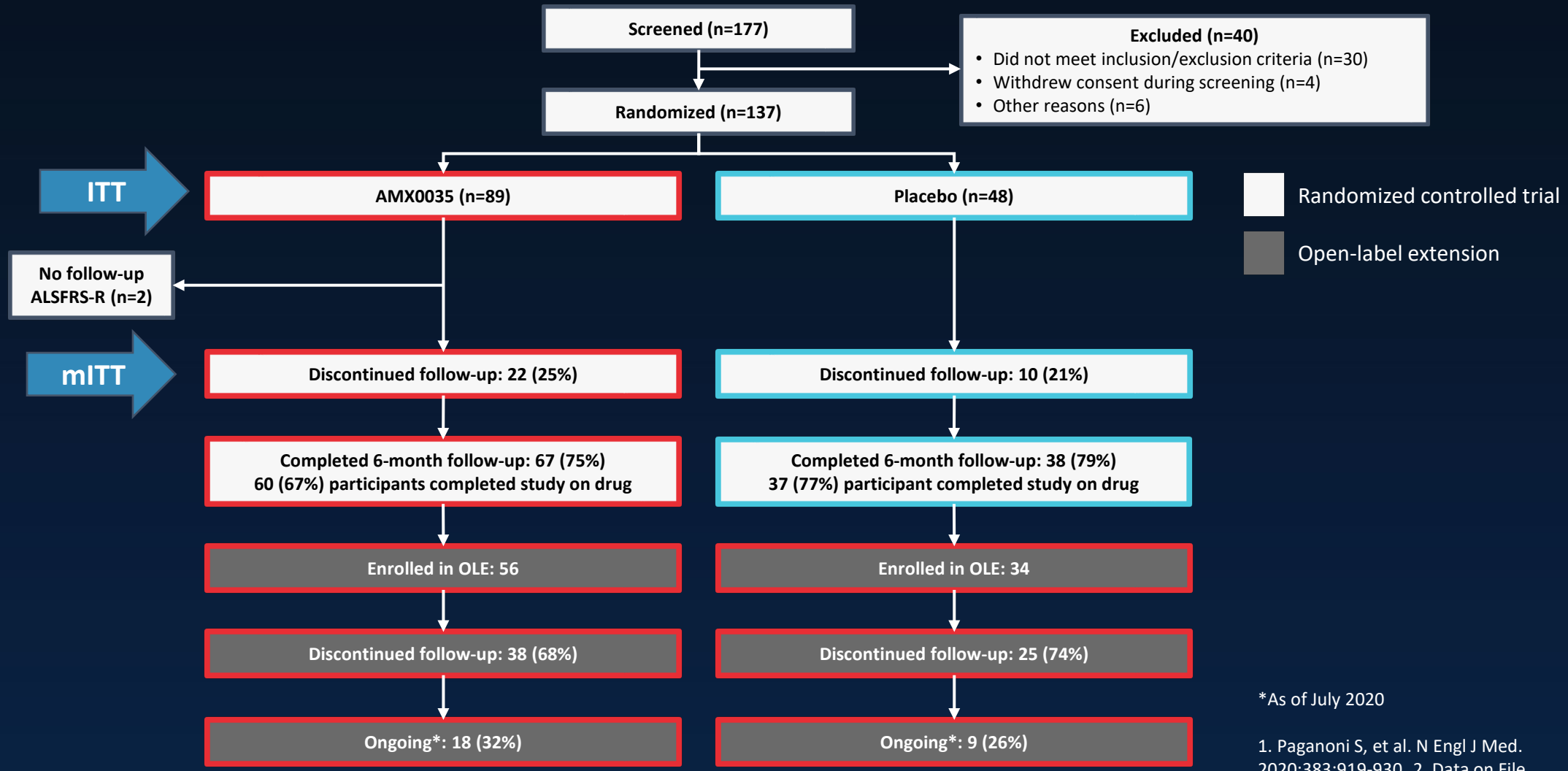
Participant Disposition and Baseline Characteristics

Participant Disposition[1,2]



*As of July 2020

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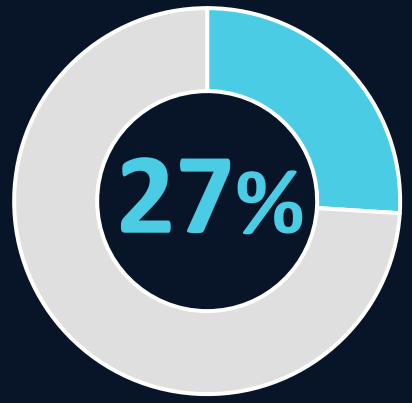
Characteristics of Study Participants

Overall,
137
participants with ALS
enrolled in the study

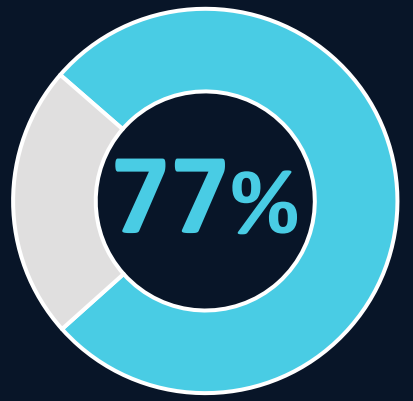
Average age:
57

13.5 months
since symptom
onset

and
6 months
since diagnosis



Bulbar onset



On riluzole or edaravone or both

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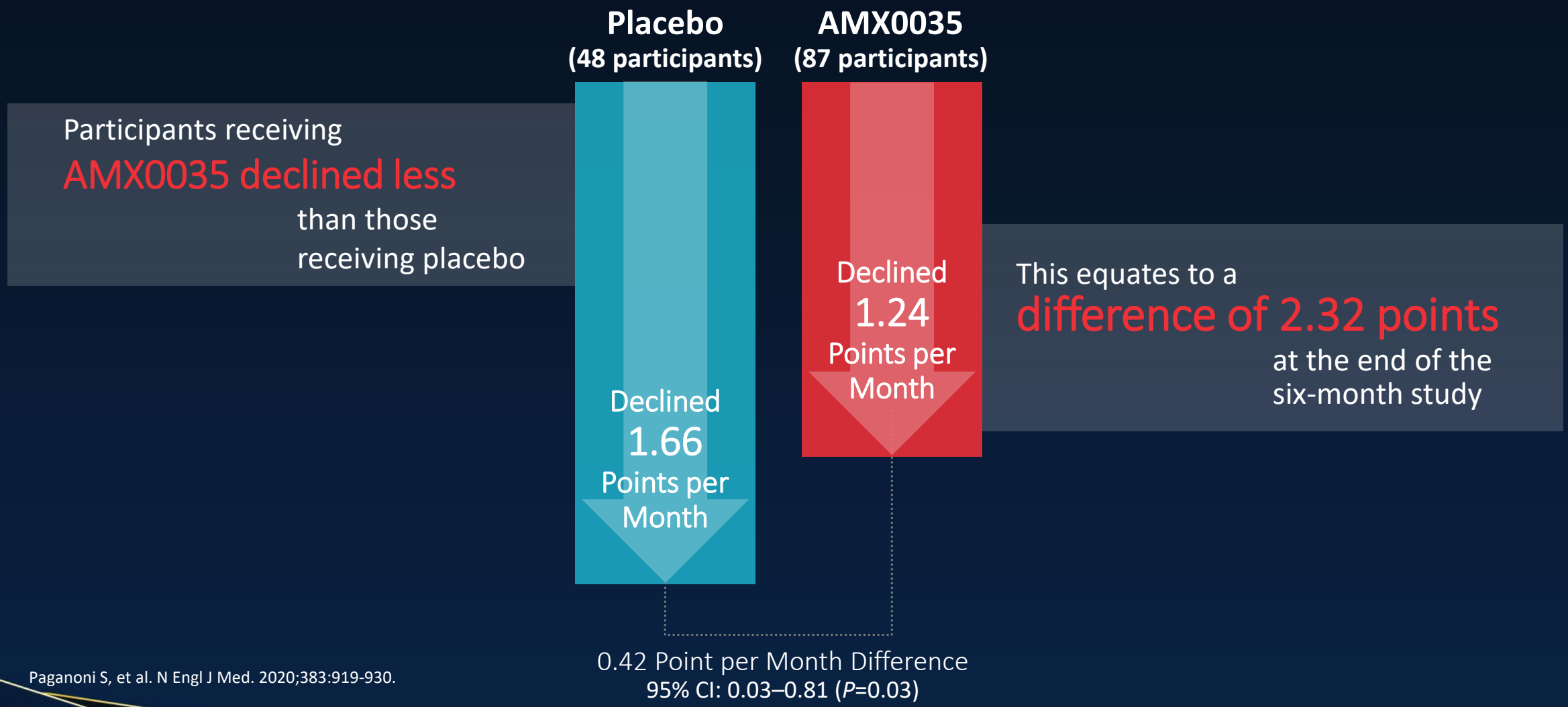
CENTAUR Primary and Secondary Outcomes

Treatment With AMX0035 Significantly Slowed the Rate of Decline in ALSFRS-R Total Score (mITT)



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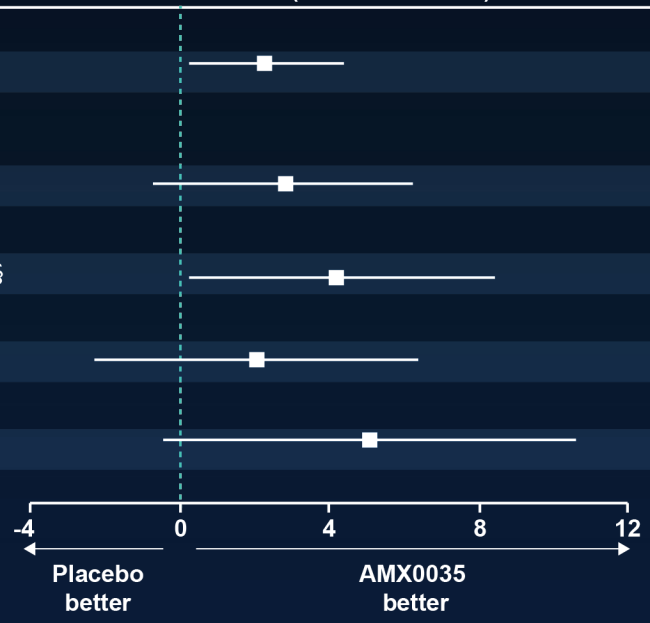
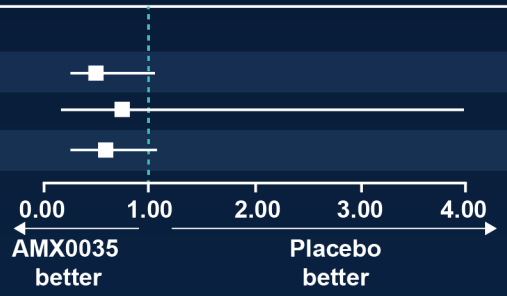
Outcome Summary (mITT)

		Shared Baseline Estimate (SE)	LS* Mean (SE) Placebo (n=48)	LS* Mean (SE) AMX0035 (n=87)	LS* Difference (SE), Active Minus Placebo [95% CI†]	P Value
Primary						
ALSFRS-R total score	Week 24 score	35.92 (0.50)	26.73 (0.98)	29.06 (0.78)	2.32 (1.09) [0.18, 4.47]	0.03
	Change per month		-1.66 (0.16)	-1.24 (0.12)	0.42 (0.20) [0.03, 0.81]	
Secondary (Clinical) **- PPN**						
ATLIS total score§	Week 24 score	55.80 (1.80)	36.26 (2.22)	39.08 (1.99)	2.82 (1.77) [-0.67, 6.31]	0.11
	Change per month		-3.54 (0.26)	-3.03 (0.19)	0.51 (0.32) [-0.12, 1.14]	
ATLIS upper extremity score§	Week 24 score	53.42 (2.15)	32.36 (2.59)	36.63 (2.32)	4.27 (2.09) [0.16, 8.38]	0.04
	Change per month		-3.81 (0.31)	-3.04 (0.23)	0.77 (0.38) [0.03, 1.52]	
ATLIS lower extremity score§	Week 24 score	57.64 (2.21)	39.09 (2.66)	41.17 (2.37)	2.09 (2.20) [-2.23, 6.41]	0.34
	Change per month		-3.36 (0.33)	-2.98 (0.24)	0.38 (0.40) [-0.40, 1.16]	
SVC	Week 24 score	83.28 (1.54)	61.06 (2.81)	66.17 (2.33)	5.11 (2.87) [-0.54, 10.76]	0.08
	Change per month		-4.03 (0.42)	-3.10 (0.31)	0.93 (0.52) [-0.10, 1.95]	



	Estimated Percentage (SE) of Event Placebo (n=48)	Estimated Percentage (SE) of Event AMX0035 (n=87)	Hazard Ratio, Active vs. Placebo [95% CI]
Event			
Death, tracheostomy, or hospitalization	33.1 (6.9)	19.3 (4.2)	0.53 [0.27, 1.05]
Death or tracheostomy	4.4 (3.0)	2.8 (1.7)	0.63 [0.11, 3.92]
Hospitalization	29.7 (6.6)	17.5 (4.1)	0.54 [0.27, 1.12]



*LS denotes a mean or difference adjusted for terms in the model . †Unadjusted 95% CIs. §Number of participants (placebo/active) represented at week 24: 32/55 for total ATLIS, 32/55 for upper ATLIS, and 33/56 for lower ATLIS. ALSFRS-R denotes Amyotrophic Lateral Sclerosis Functional Rating Scale Revised, ATLIS Accurate Test of Limb Isometric Strength, LS least squares, mITT modified intent-to-treat, PPN percentage of predicted normal, SVC slow vital capacity.

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CENTAUR Safety Outcomes

Safety Outcomes

- **Serious Adverse Events** were more frequent in the placebo group compared with the AMX0035 group, predominantly resulting from a higher incidence of respiratory events in the placebo group (8% vs. 3% in the AMX0035 group)
  - 1% AMX0035 group and 6% placebo group discontinued therapy due to serious AEs (all considered unrelated to study drug)

- Nearly all participants (AMX0035, 97%; placebo, 96%) reported one or more **Treatment-Emergent Adverse Events (TEAEs)** during the trial
  - 19% AMX0035 group and 8% placebo group discontinued therapy due to TEAEs
  - GI events in the AMX0035 group were reported most frequently in the first 3 weeks, decreasing to less than placebo group for the remainder of the study

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Overall Survival Analysis of All Participants in CENTAUR

Statistical Methods Overview: Overall Survival

- The vital status (all-cause death only) of every participant randomized in CENTAUR was successfully determined for all but two (135/137) in July 2020

- Vital status for participants who withdrew, were lost to follow-up, or did not enroll in the OLE was determined by OmniTrace via search of public records

Survival Analysis

AMX0035 exposure

- This analysis compares 2 groups – those **originally randomized to AMX0035** and **originally randomized to placebo** in CENTAUR
  - The majority (92%) of eligible participants from CENTAUR enrolled in the OLE
    - Most of the originally randomized to placebo participants in this analysis received some exposure to AMX0035

Median AMX0035 exposure duration

- **Original AMX0035:** 8.8 months
- **Original Placebo:** 1.9 months

AMX0035 Demonstrates Long-Term Survival Benefit

Risk of death was **44% lower** over the duration of follow-up among those originally randomized to AMX0035 compared to placebo

- HR 0.56 (95% CI: 0.34-0.92), *P*=0.02

6.5 month
longer median survival in the group originally randomized to AMX0035

Median survival is the time at which 50% of participants have died.
Data on File. Amylyx Pharmaceuticals.

Impact of death-equivalent events and concomitant ALS meds on outcome

- Similar rates of death-equivalent events (tracheostomy or PAV) were seen in the 2 groups

- Results of sensitivity analyses accounting for concomitant riluzole, edaravone, or both at baseline are consistent with the primary analysis – suggesting that the benefit of AMX0035 was independent of baseline concomitant medication use

Data on File. Amylyx Pharmaceuticals.

Summary

- **AMX0035 treatment is associated with:**
  - **Functional benefit:** significant slowing of ALSFRS-R decline over 24 weeks
  - **Long-term survival benefit:** 6.5 month longer median survival in the group originally randomized to AMX0035

Next Steps

- Full overall survival results are under peer review
- Additional analyses (OLE functional outcomes and safety) and sub analyses (CENTAUR and OLE) are ongoing

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Thank you!