NurOwn® Phase 2 ALS study: ALSFRS-R subscale responder analysis

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Objective

To evaluate the contribution of the four ALSFRS-R subscales to the overall ALSFRS-R efficacy outcomes in the NurOwn® U.S. Phase 2 ALS multicenter, double-blind, placebo-controlled trial

* www.ClinicalTrials.gov identifier NCT02017912

ALSFRS-R subscale slopes decline at different rates and by region of onset

J.M. Cedarbaum et al. / Journal of the Neurological Sciences 169 (1999) 13–21

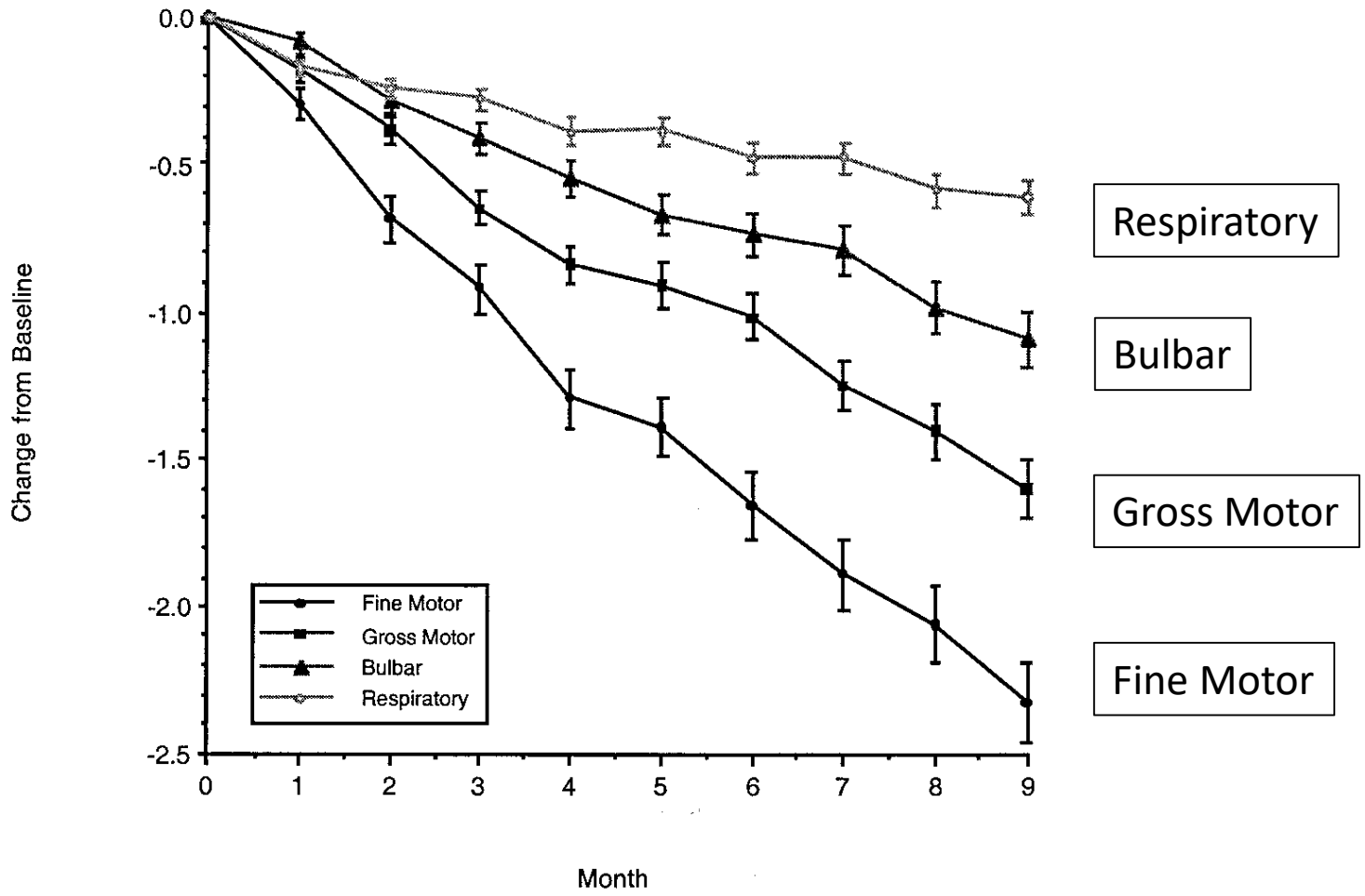
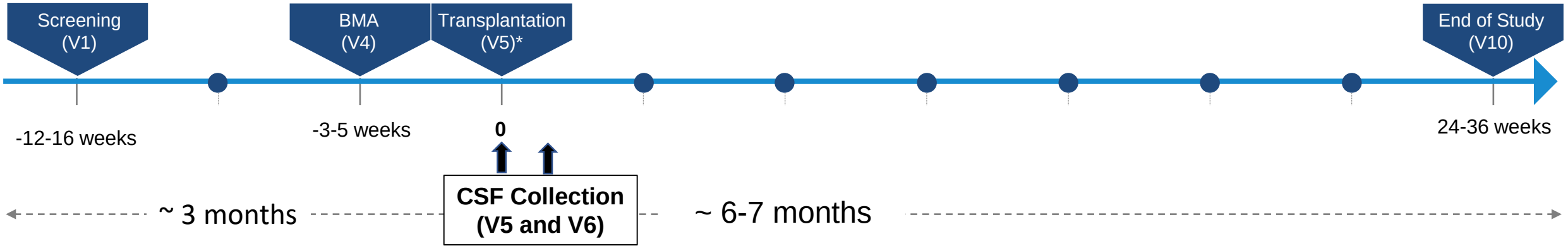


Fig. 1. Cross-sectional mean (±SEM) change from baseline to 9 months for each of the four factors of the ALSFRS-R.

NurOwn® Phase 2 Study Met Primary Safety Outcomes



Study Design
- 48 participants (16 per site)
- Randomized 3:1
- Blinded to allocation

- **No deaths or treatment related SAEs**
- **No drop outs related to SAEs**
- **Most common adverse events transient and mild/moderate severity and procedure related**

Efficacy
- **ALSFRS-R**
- SVC

*IT 125M cells/4 ml and IM (R biceps and R triceps)

BMA*: Bone Marrow Aspirations*

● *Monthly visits*

Phase 2 Subgroups: (>= or < 1 point/month decline pre-treatment*)

Group	MSC-NTF	Placebo
Overall population	36	12
Rapid progressors	15	6
Slow progressors	21	6

*Prespecified

ALSFRS-R Total Score and Subscale Responder Definitions

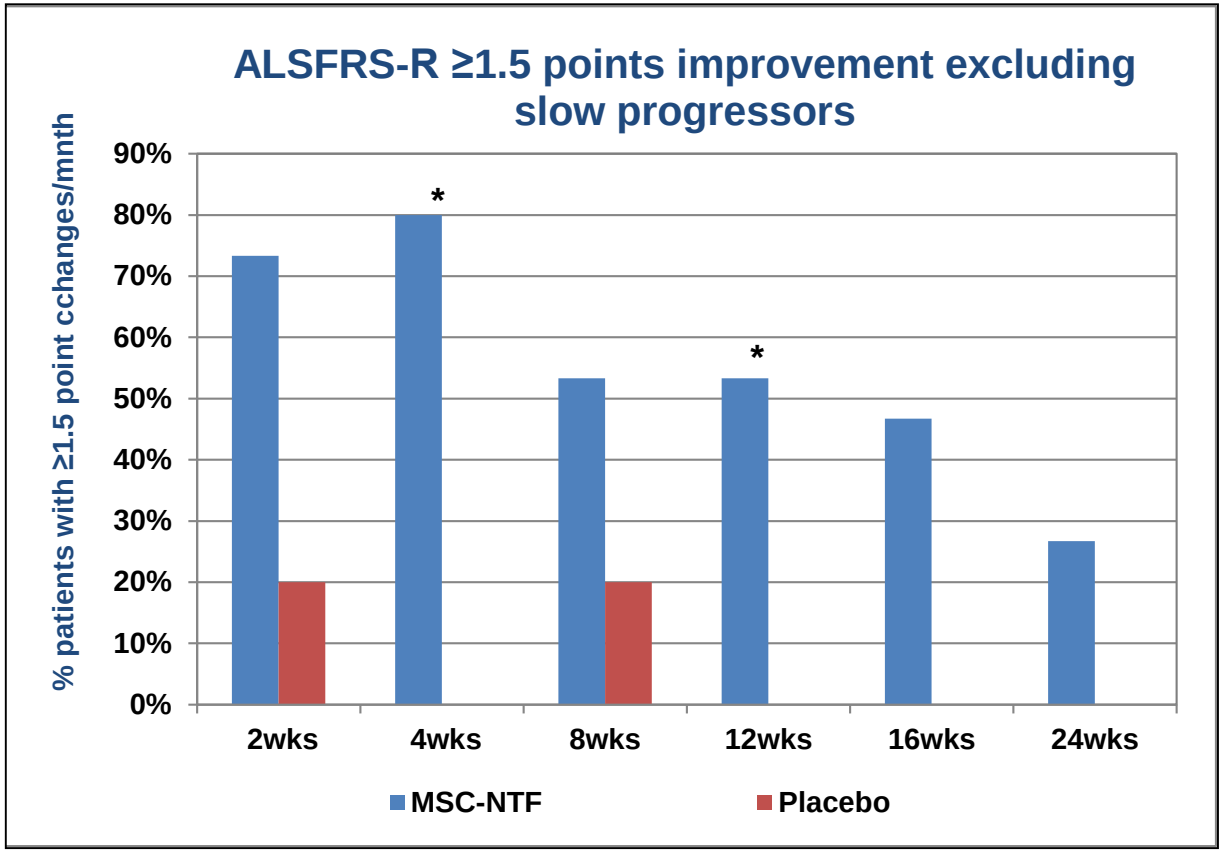
- ≥ 1.5* points/month improvement in ALSFRS-R total score (slope)
- ≥ 0.375* points/month for each of the subscales improvement (25% of 1.5 point/month improvement in total score)
    - Bulbar
    - Gross Motor
    - Fine Motor
    - Breathing

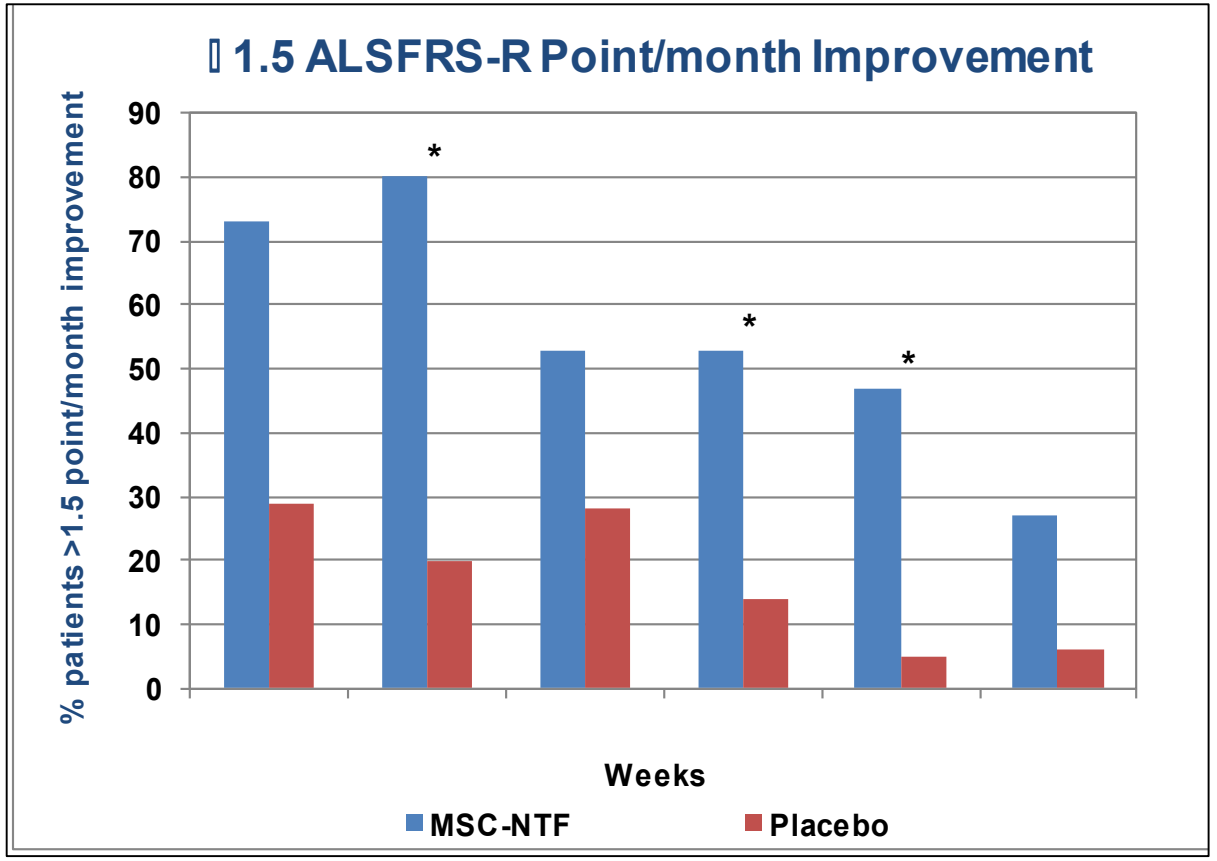
***Post hoc**

Responder Analysis:

≥1.5 points/month improvement (Rapid Progressors)
Comparison of Phase 2 Placebo and Historical Placebo Groups

Phase 2 Placebo Group n=6	ProACT Placebo Group n= 103**

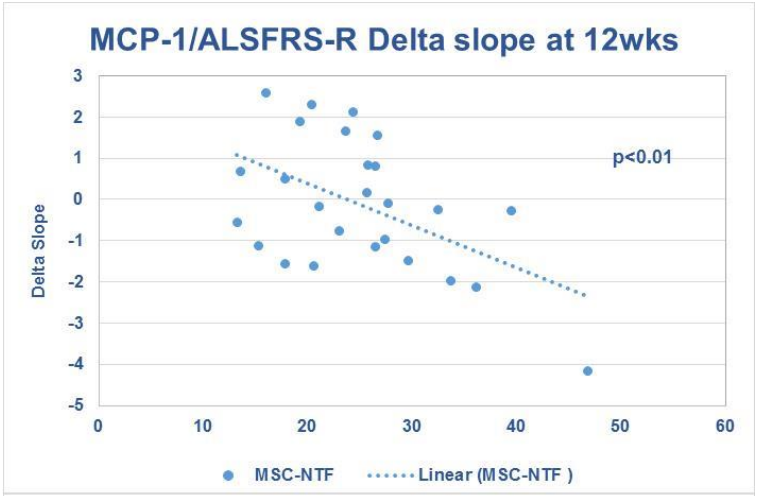




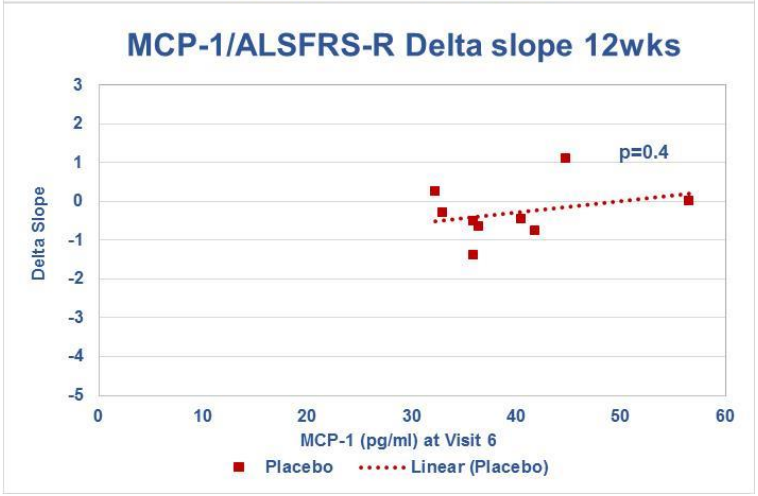
**Matched rapid progressor placebo group by inclusion/exclusion criteria

* p<0.05 (two-sided Fisher's exact test)

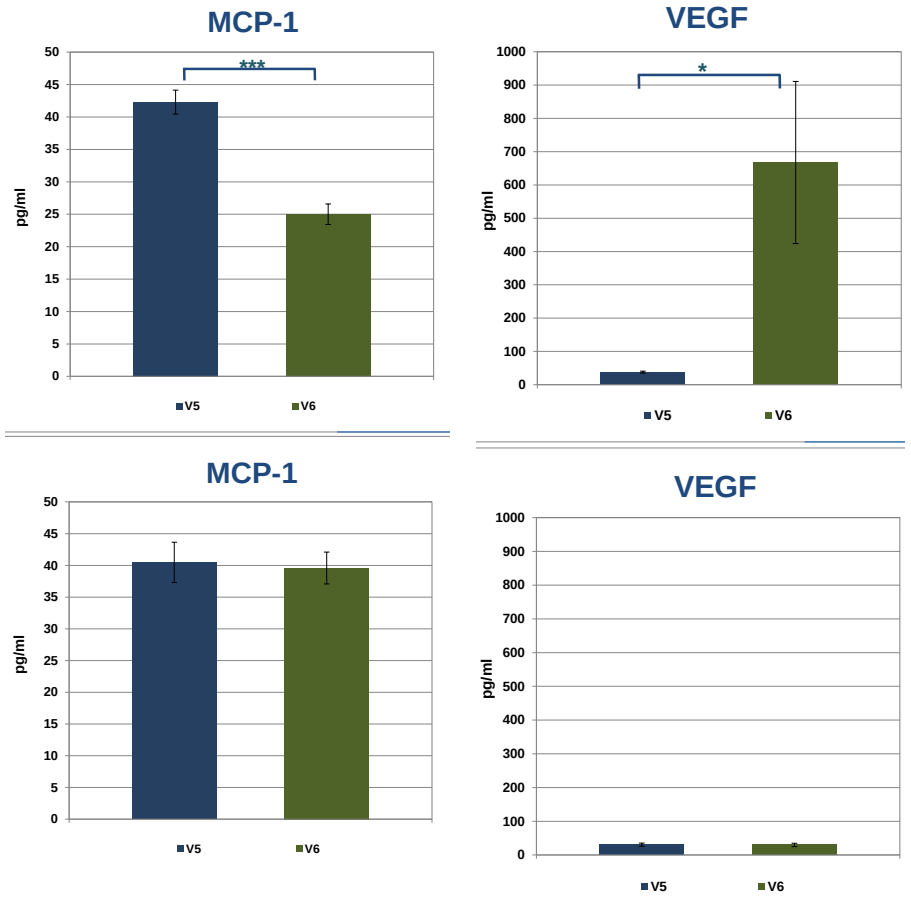
MCP-1 reduction correlates with ALSFRS-R slope improvement



NurOwn ®



Placebo

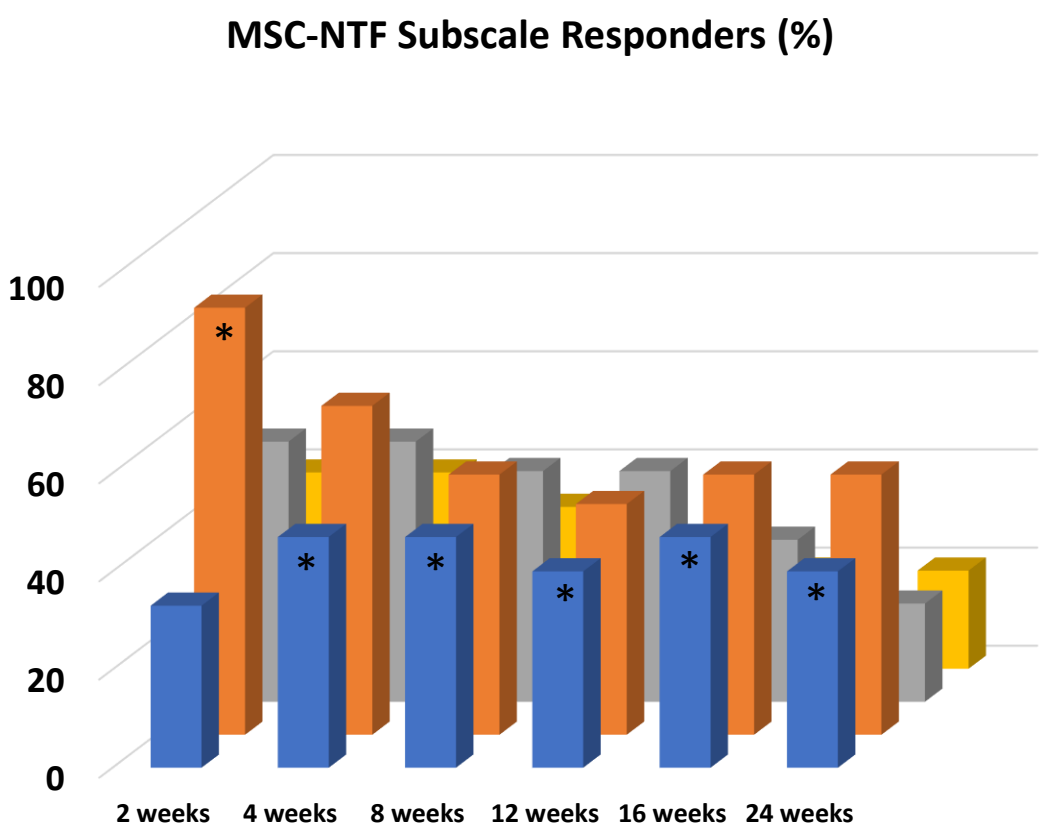


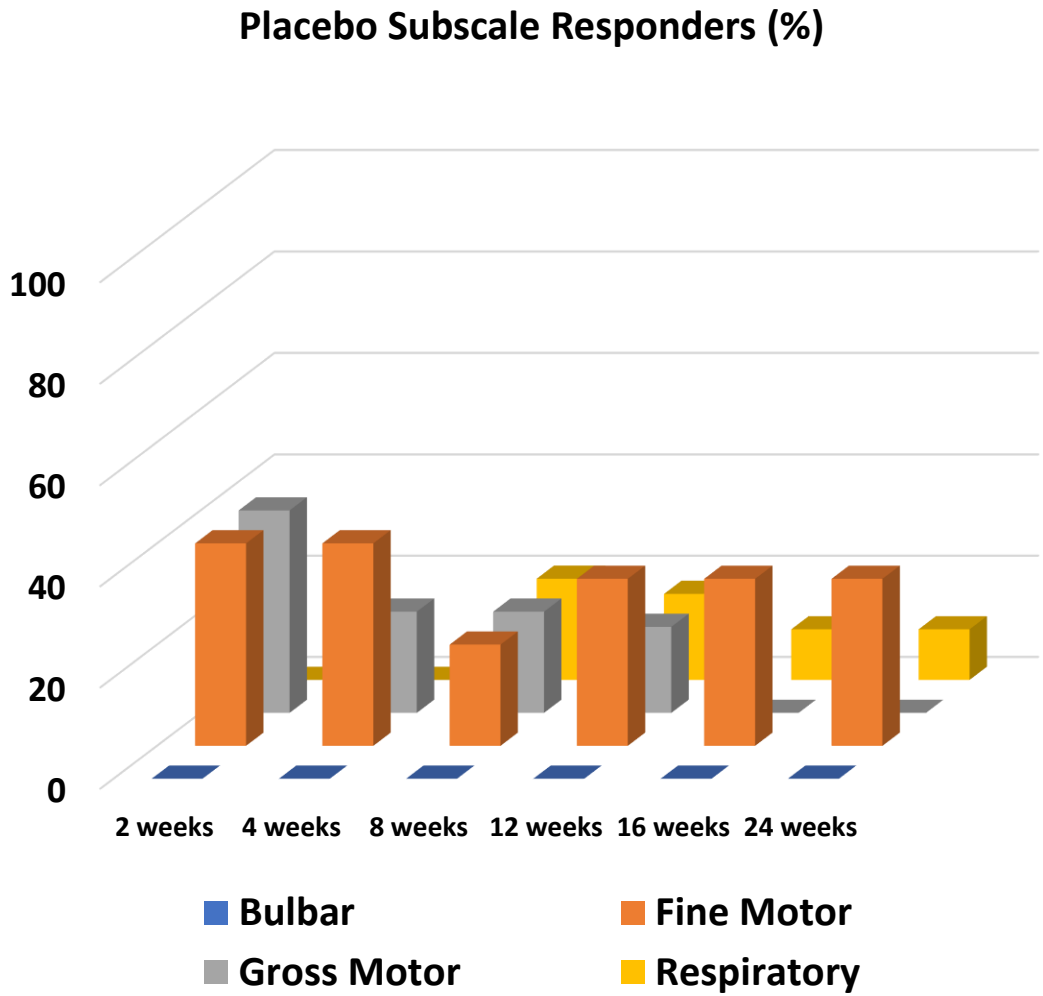
Mean ± SEM
* p< 0.05 ** p<0.01 *** p< 0.001

Pre transplantation

Post transplantation

Subscale responder analysis: ≥ 0.375 point/month improvement (rapid progressors)





* p<0.10: treated vs. placebo

Conclusions

- Evaluation of ALSFRS-R subscale outcomes is important to fully understand the impact of NurOwn® in ALS
- In the NurOwn® single dose phase 2 study, ALSFRS-R improvement in the rapid progressor subgroup is reflected in all four subscales, particularly in the bulbar and fine motor subscales
- A Phase 3 multicenter repeat dose placebo controlled study* is currently underway at 6 US medical centers to confirm and extend these observations

* www.ClinicalTrials.gov identifier NCT03280056