

NurOwn® Phase 2 ALS Trial: ALSFRS-R Improvement is Reflected in Subscale Domains

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Objective:

To evaluate the contribution of the four ALSFRS-R domains to the overall ALSFRS-R efficacy outcome in the NurOwn® U.S, Phase 2 ALS multicenter double-blind placebo-controlled trial (NCT02017912).

Background:

MSC-NTF cells (NurOwn®) are autologous bone-marrow derived mesenchymal stem cells (MSC) induced to secrete high levels of neurotrophic factors (NTFs). MSC-NTF cells were evaluated for safety and efficacy.

Design/Methods:

48 ALS participants were randomized 3:1 (active: placebo) and followed for 6-months post-transplantation. Responder analyses compared the treated to placebo groups in the following outcomes: ≥ 1.5 points/month improvement in ALSFRS-R total score; and ≥ 0.375 points/month (25% of 1.5) improvements in each of the four subscales measuring the bulbar, gross motor, breathing, and fine motor domains.

Results:

The trial met its primary safety endpoint. A higher percentage of study participants achieved ≥ 1.5 points/month improvement in the treated group at all time points, was significantly higher in the treated group at 4-weeks (one-sided, $p=0.02$) and 12-weeks (one-sided, $p=0.08$), and was more evident in the subgroup that excluded slow progressors (pre-treatment change ALSFRS-R ≥ -2).

The percentage of responders (≥ 0.375 points/month improvement) in the ALSFRS-R bulbar domain (excluding slow progressors) was significantly higher in the treated group at 4-weeks (47% vs 0, one-sided, $p=0.08$), 8-weeks (47% vs 0, $p=0.08$), 12-week (40% vs 0, $p=0.09$), 16-weeks (47% vs 0, one-sided, $p=0.06$), and 24-weeks (40% vs 0, one-sided, $p=0.09$).

The percentage of responders (≥ 0.375 points/month improvement) in the ALSFRS-R fine motor domain (excluding slow progressors) was significantly higher in the treated group at 2-weeks (87% vs 40%, one-sided, $p=0.07$).

A higher number of participants in the treated group demonstrated ≥ 0.375 points/month improvement in gross motor and breathing domains, although these did not reach statistical significance.

Conclusions:

The observed improvements following MSC-NTF transplantation are reflected in all four ALSFRS-R domains, particularly in the bulbar and fine motor subscales.