Responder and Subgroup Analyses for FORTITUDE-ALS, a Phase 2 Trial of Reldesemtiv in Patients with ALS

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BACKGROUND
- FORTITUDE-ALS is a randomized, double-blind, phase 2 study of the fast skeletal muscle troponin activator reldesemtiv, enrolled patients with ALS to placebo or 1 of 3 dose groups.
- The impact of riluzole use/non-use and edaravone use/non-use was evaluated.

METHODS
FORTITUDE-ALS study
- Key inclusion/exclusion criteria:
  - 5 years and over the age of 50
  - Diagnosis of ALS for 6 months to 12 years
  - Upright SVC ≥ 60% predicted for age, height, and sex at screening

FORTITUDE-ALS secondary analyses
- All reldesemtiv groups were combined and change from baseline to Week 12 was compared with placebo.
- The impact of riluzole use/non-use and riluzole use/non-use was evaluated.
- The impact of edaravone on SVC, ALSFRS-R, and HHD was examined in the placebo group.
- Outcomes were evaluated by geographic regions, which were defined as North America, Europe, and Australia.

RESULTS
Patients
- No significant differences were observed between the 4 treatment groups at baseline (Table 1).
- Over half of patients (56.5%) were taking riluzole alone, 4.2% were taking edaravone alone, and 20.8% were taking both.

Effects of geographic location on treatment with reldesemtiv
- The impact of riluzole on SVC, ALSFRS-R, and HHD was generally similar regardless of geographic region, though the small number of patients in Europe showed significantly better SVC with reldesemtiv compared with placebo (Figure 3, Table 2).

CONCLUSIONS
- FORTITUDE-ALS showed an effect of reldesemtiv over 12 weeks in patients with ALS, whether or not patients were taking edaravone and/or riluzole.
- Should these effects of reldesemtiv be confirmed in a phase 3 trial, reldesemtiv will likely be useful with other approved agents.
- Geographic location did not influence outcomes with reldesemtiv in the EU, the slower decline in SVC on reldesemtiv versus placebo achieved statistical significance (p < 0.01).
- A responder analysis did not improve our understanding of the impact of reldesemtiv in ALS.