DECLINE IN SLOW VITAL CAPACITY PREDICTS RESPIRATORY INSUFFICIENCY, USE OF ASSISTED VENTILATION, TRACHEOSTOMY, OR DEATH
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BACKGROUND
Death and disability in ALS are strongly related to respiratory failure, most often assessed in clinical settings by measuring vital capacity. Vital capacity, assessed either using Forced Vital Capacity (FVC) or Slow Vital Capacity (SVC) is thus an important outcome measure for clinical trials. Transient, a selective fast skeletal muscle atrophy model, showed a statistically significant reduction of the decline in percent predicted SVC over 12 weeks in mice treated with transients compared to mice receiving placebo.

OBSERVATIONS
To investigate the natural history of SVC decline, to determine what demographic variables impact decline of SVC and how changes in SVC predict function and other clinically meaningful events in patients with ALS.

METHODS
All 469 patients randomized to placebo in the EMPOWER clinical trial were included with a maximum duration of follow-up of 1.5 years.

RESULTS
The rate of decline of SVC was estimated using a repeated measures mixed model and adjusting for baseline SVC Pearson Product Moment correlation coefficient (r) was used to evaluate the strength of association between the decline in SVC and other continuous clinical outcomes variables Cox proportional hazards regression was used to model the time to clinical event variables from the Month 6 visit to the end of the follow-up period using the slope of SVC change from baseline to the Month 6 visit as an explanatory variable, adjusting for baseline characteristics and ALSFRS-R score. The respiratory clinical outcomes included the earlier time to death or:
1) time to decline in any of the three questions of the respiration subdomain of ALSFRS-R
2) time to the first onset of respiratory insufficiency
3) time to tracheostomy
All cause mortality was evaluated as well.

CONCLUSIONS
The rate of decline of SVC in ALS is consistent among the three data sets evaluated.

2. From the EM-POWER data set, age and baseline ALSFRS-R had a significant interaction with rate of decline of SVC.

3. The change in SVC strongly predicts meaningful clinical events, including respiratory failure or death in ALS.

FIGURE 1: RATE OF DECLINE IN SVC IS SIMILAR IN THREE LARGE DATA SETS

FIGURE 2: PROBABILITY OF RESPIRATORY FAILURE-FREE SURVIVAL PREDICTED BY SLOPE OF SVC CHANGE*