Outcome measures for Nusinersen efficacy in Adults with Spinal Muscular Atrophy
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Objective:
Evaluate valid outcome measures for adults receiving intrathecal nusinersen for spinal muscular atrophy(SMA)

Background: Nusinersen significantly improves motor function and survival in infants, children and teenagers with SMA, but treatment benefits in adults are uncertain. Given high treatment costs, it is practical and ethical to establish reliable measures of clinical improvement for adult SMA treatment programs

Design/Methods: This is a single-center cohort study of 8 SMA Type 3 patients aged 25-56, with 3 or more SMN2 copies, who received nusinersen over 2-13 months. Of these, 3 were non-ambulatory. Fatigue(PedsQL Fatigue scale), pulmonary function(FVC, FEV1, MEP and MIP), overall function(SMA-Functional Rating Scale(FRS)) and motor function(Functional Motor Score-Expanded (HFMSE), 6-minute walk test(6MWT) and Revised Upper Limb Measure(RULM)) were assessed. Statistical analysis was performed with 2-tailed paired t-tests

Results: Over mean 7 months, 100% adult SMA patients on nusinersen self-reported increased energy and improved exercise tolerance. PedsQL-cognitive improved in 100% non-ambulatory and 0% ambulatory patients. PedsQL-sleep improved in 100% non-ambulatory and 50% ambulatory patients. SMA-FRS and 6MWT showed no clinically meaningful change. HFMSE increased from 33.5 to 35.5(p=0.04, 95% CI =(0.123, 3.877)) and RULM increased from 27.9 to 31.7(p=0.0395, 95% CI=(0.26, 7.46)). FVC and FEV1 improved by 7%, and MEP and MIP improved by 2-3% in 2 non-ambulatory patients over mean 8.5 months

Conclusions: Observations of modest trends in improvement in HFMSE and RULM scores, over a short observation period of 2-13 months, show potential as outcome measures in this population of ambulatory and non-ambulatory type 3 SMA adult patients. Cognitive/sleep PedsQL and pulmonary function tests show promise. More patients are being observed over a longer timeframe. The observations of self-reported improvement suggest that more work is needed to evaluate more clinically meaningful outcome measures, such as additional quality of life questionnaires