Number Needed to Treat (NNT) in Spinal Muscular Atrophy Type 1 (SMA1) with AVXS-101 Relative to Nusinersen

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**Objective:** To assess the NNT to prevent death and use of permanent assisted ventilation, and improve motor function, with onasemnogene abeparvovec (AVXS-101) compared with nusinersen in SMA1 patients.

**Background:** SMA1 is a rapidly progressing neurologic disease that causes loss of motor and respiratory function. Until recently, SMA1 patients faced a poor prognosis with no approved treatments for their condition. Currently, nusinersen is the only FDA-approved SMA treatment; however, treatment with AVXS-101, a new gene-replacement therapy candidate, has recently demonstrated unprecedented survival and motor function in a phase 1 clinical trial.

**Design/Methods:** Patients with SMA1 were treated with AVXS-101 (NCT02122952; cohort 2; N=12; up to 24 months) or nusinersen (NCT02193074; N=80; up to 13 months). NNT with AVXS-101 compared with nusinersen was assessed for survival and event-free survival (absence of death and permanent assisted ventilation) at last visit, and for motor function (≥4-point increase in CHOP-INTEND score from baseline) at last visit and at a median of 9 months. The NNT to prevent 1 death, 1 event (death or use of permanent assisted ventilation), or for 1 patient to improve motor function relative to nusinersen was calculated as the reciprocal of the difference between AVXS-101 and nusinersen in event rates or motor function achievement rates.

**Results:** Mean age at first dose was 3.4 (0.9–7.9) and 5.3 (1.7–7.9) months in the AVXS-101 and nusinersen trials, respectively. NNT analyses suggested that treating 6.2 patients with AVXS-101 instead of nusinersen would prevent 1 more death; treating 2.6 patients with AVXS-101 versus nusinersen would prevent 1 more event; and treating 3.5 patients with AVXS-101 versus nusinersen would allow 1 more patient to improve motor function.

**Conclusions:** Efficacy in preventing death and use of permanent assisted ventilation, and improving motor function, is much higher with AVXS-101 versus nusinersen.