Nusinersen in Infants Who Initiate Treatment in a Presymptomatic Stage of Spinal Muscular Atrophy (SMA): Interim Efficacy and Safety Results From the Phase 2 NURTURE Study

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Objective: To present interim results from the ongoing NURTURE study (NCT02386553) examining efficacy/safety of intrathecal nusinersen, initiated prior to symptom onset, in infants most likely to develop SMA Type I/II.

Background: Nusinersen is the first approved treatment for SMA, supported by safety and meaningful efficacy in multiple clinical trials of affected populations across a broad spectrum of SMA severity.

Design/Methods:
Enrolled infants were age ≤6 weeks at first dose, clinically presymptomatic, and genetically diagnosed with SMA with 2 or 3 *SMN2* copies. The primary endpoint is time to death or respiratory intervention (≥6 hours/day continuously for ≥7 days or tracheostomy). The data cutoff date was May 15, 2018.

Results: Twenty-five infants (2 copies *SMN2*, n=15; 3 copies, n=10) were enrolled. Median (range) age at last visit was 26.0 (14.0–34.3) months. All infants were alive and none required permanent ventilation including tracheostomy. Four infants (4/15 with 2 *SMN2* copies; 0/10 with 3 *SMN2* copies) required respiratory intervention, meeting the primary endpoint; all 4 initiated respiratory support during an acute, reversible illness. All (25/25) participants achieved the WHO motor milestone sitting without support and 22/25 (88%) achieved walking with assistance; 17/22 (77%) were walking alone. All infants had the ability to suck and swallow at their last observed visit. Plasma pNF-H levels rapidly declined during the loading phase of nusinersen and then stabilized. AEs were reported in all 25 infants; most (20/25; 80%) had AEs mild/moderate in severity; 9 had serious AEs. AEs of 6 infants were possibly related to study drug that resolved despite continued treatment, with the exception of one participant with proteinuria that was ongoing at data cutoff. No new safety concerns were identified.

Conclusions:
These data demonstrate continued benefit to infants who initiated nusinersen in the presymptomatic stage of SMA and emphasize the value of early treatment.
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