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Long-Term Efficacy and Safety of Inotersen for Hereditary Transthyretin Amyloidosis: NEURO-TTR Open-Label Extension 2-Year Update (S27.008)

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Abstract

Objective: To provide an update on the long-term efficacy and safety of inotersen, an antisense oligonucleotide inhibitor of transthyretin protein production, in patients with hereditary transthyretin amyloidosis (hATTR) with polyneuropathy.

Background: Patients with hATTR, a rare protein misfolding disorder, experience progressive and debilitating polyneuropathy. A randomized, controlled phase 3 trial (NEURO-TTR; NCT01737398) demonstrated efficacy and safety of inotersen treatment in patients with hATTR polyneuropathy (Benson 2018 *NEJM*).

Design/Methods: Patients who completed NEURO-TTR were eligible to enroll in the ongoing open-label extension (OLE) study (NCT02175004). Assessments included modified Neuropathy Impairment Score +7 neurophysiologic tests composite score (mNIS+7), Norfolk Quality of Life–Diabetic Neuropathy questionnaire total score (Norfolk QoL-DN), and adverse events.

Results: Of 139 patients who completed NEURO-TTR, 135 (97.1%) enrolled in the OLE. As of 9/15/17, 134 patients had received ≥1 dose of inotersen. Patients were predominantly white (93.3%) and male (69.4%), and 88/134 (65.7%) had both polyneuropathy and cardiac involvement. At OLE baseline, 83/134 (61.9%) patients were ambulatory without assistance, 47/134 (35.1%) required walking aid(s), and 4/134 (3.0%) were unable to walk. Patients who initiated inotersen in the OLE demonstrated slowing of neurologic disease progression by mNIS+7 and Norfolk QoL-DN within 6 months, and patients who had received inotersen for 27 months (15 months in NEURO-TTR + 12 months in the OLE) continued to show benefit. Greater benefit in mNIS+7 and Norfolk QoL-DN was observed in patients treated earlier with inotersen. There was no evidence of increased risk for grade 4 thrombocytopenia or severe renal events with increased duration of exposure, and no new safety concerns have been identified. This presentation will be updated with data from 2 years of follow-up in the OLE.

Conclusions: In the OLE, inotersen treatment slowed hATTR polyneuropathy progression, with greater stabilization observed in patients who initiated inotersen earlier.

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