O-011 - PHASE 2/3 TRIAL TO ASSESS THE SAFETY AND EFFICACY OF LENTI-D HEMATOPOIETIC STEM CELL GENE THERAPY FOR CEREBRAL ADRENOLEUKODYSTROPHY

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OBJECTIVE: Cerebral adrenoleukodystrophy (CALD) is characterized by inflammatory demyelination leading to progressive loss of neurologic function and death. Early diagnosis and treatment are key in ensuring optimal long-term outcomes. ***METHODS:*** Lenti-D Drug Product (DP) is an investigational gene therapy for the treatment of CALD. Boys with CALD (≤17 years) enrolled in an open-label phase 2/3 study of the safety and efficacy of Lenti-D DP underwent full myeloablation with busulfan and cyclophosphamide followed by infusion of autologous CD34+ cells transduced with elivaldogene tavalentivec (Lenti-D) lentiviral vector. The primary efficacy endpoint is the proportion of patients who are alive and free of major functional disabilities (MFD) at Month 24. The primary safety endpoint is the proportion of patients who experience either acute (≥Grade 2) or chronic graft-versus-host disease (GVHD) by Month 24. Additional assessments include engraftment failure, and changes in neurologic function score and Loes score. ***RESULTS:*** As of April 2018, 29 patients received Lenti-D DP (median follow-up 34 months, min-max, 0.4-54.0). Of the 17 patients who reached 24 months of follow-up, 15 (88%) remain alive and MFD-free with evidence of disease stabilization. One patient succumbed to disease progression; another was withdrawn from the trial due to neuroimaging changes with no changes in neurological functioning noted. None of the other 12 patients have 24 months of follow-up (median follow-up 4.2 months, min-max, 0.4-11.7). One was withdrawn due to neuroimaging changes with no changes in neurological functioning noted and 11 remain in the study with no evidence of MFDs at last follow-up. No graft failure, GVHD, or transplant-related mortality were reported. There was no evidence of replication competent lentivirus or insertional oncogenesis. Most adverse events were consistent with myeloablative conditioning. ***CONCLUSION:*** These data suggest that Lenti-D DP stabilizes neurologic disease progression and appears to be a promising gene therapy for CALD.