P0226 - Phase I study of ATA188, an off-the-shelf, allogeneic Epstein-Barr virus-targeted T-cell immunotherapy for progressive forms of multiple sclerosis (ID 1635)

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Abstract

Background

 Epstein-Barr virus (EBV) is a necessary risk factor for the development of multiple sclerosis (MS) [Abrahamyan S et al. JNNP 2020; Pakpoor J et al. Mult Scler 2012]. Early experience with autologous EBV-specific T-cell adoptive immunotherapy proved safe and may offer clinical benefit [Pender MP et al. JCI Insight 2018].

Objectives

 This Phase I study evaluated the safety and potential efficacy of off-the-shelf, allogeneic EBV-targeted T-cell therapy (ATA188) in adults with progressive forms of MS (NCT03283826).

Methods

 In part 1, four cohorts received escalating doses of ATA188 to determine the recommended part 2 dose (RP2D). Patients (pts) were followed for 1-year and given the option to participate in a 4-year open label extension (OLE) at the RP2D (cohort 3 dose). In addition to safety, sustained disability improvement (SDI) was assessed, defined as improvement in Expanded Disability Status Scale (EDSS) or Timed 25-Foot Walk (T25FW) at ≥2 consecutive time points [Pender MP et al. EAN 2020; LB130]. Other measures evaluated include Fatigue Severity Scale (FSS), 12-item MS Walking Scale (MSWS-12), MS Impact Scale-29 (physical; MSIS-29), and whole brain volume (via magnetic resonance imaging [MRI]). As of August 2020, we expect 12-month (m) data for all 4 cohorts, which marks the end of the dose finding portion of this study, will be available for presentation.

Results

 As of April 2020, 25 pts had received ≥1 dose of ATA188. No grade >3 events, dose-limiting toxicities, cytokine release syndrome, graft vs host disease, or infusion reactions were observed. Two treatment-emergent serious adverse events were reported: muscle spasticity (grade 2; not treatment related) and MS relapse (grade 3; possibly treatment related). Efficacy endpoints were assessed in cohorts 1–4 (n=24) at 6m and in cohorts 1–3 (n=17) at 12m. Six pts met SDI criteria at 6m and 5 pts met it at 12m, which was driven by EDSS in all but 2 pts at both 6 and 12m. At both timepoints, a higher proportion of pts showed SDI with increasing dose. In cohorts 1–3, all pts with SDI at 6m maintained it through 12m. Pts with SDI (vs those without) tended to have greater improvements in FSS, MSWS-12, and MSIS-29 (physical) scores, as well as less reduction in whole brain volume on MRI, from baseline to 12m. As of June 2020, OLE data from the 15m timepoint were available for 4 pts; 3 had SDI at 6m and 12m which was maintained at 15m.
Conclusions

Preliminary data indicate ATA188 is well tolerated. A higher proportion of pts showed sustained disability improvement (SDI) with increasing dose. Pts who achieved SDI at any timepoint maintained it at all future timepoints and tended to show improvements in fatigue, physical function, and MRI whole brain volume at 12m. Based on these data, part 2 of the study (randomized placebo-controlled portion) has been initiated using the cohort 3 dose.