Ph1 OLE and imaging data for ATA188, an allogeneic EBV-targeted MS immunotherapy

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Mounting evidence suggests Epstein-Barr virus (EBV) is a necessary risk factor for development of multiple sclerosis (MS) [Abrahamyan *JNNP* 2020]. Earlier autologous EBV-specific T-cell therapy proved safe, with possible clinical benefit [Pender *JCI Insight* 2018; Ioannides *Front Neurol* 2021]. Here we evaluate the safety and potential efficacy of ATA188 in adults with progressive MS in an ongoing open-label extension (OLE) study, including an imaging biomarker: magnetization transfer ratio (MTR).

In part 1 of this 2-part Phase I/II study, 4 cohorts received escalating doses of ATA188. Patients were followed for 1 year and optional 4-year OLE. Sustained disability improvement (SDI; including expanded disability status scale [EDSS] and timed 25-foot walk) and safety were measured [Pender MP EAN 2020]. An exploratory endpoint, change from baseline in MTR, was assessed.

Twenty-five patients received ≥1 dose of ATA188. No grade >3 adverse events (AE), dose-limiting toxicities, cytokine release syndrome, graft-vs-host disease, or infusion-related reactions were observed. Two treatment-emergent serious AEs were previously reported (muscle spasticity [grade-2; not treatment-related]; MS relapse [grade-3; possibly treatment-related]) and, as of April 2021, 1 was reported in the OLE (fall; grade-2; not treatment-related).

Efficacy was evaluated in 24 patients in the initial 12-month period and, as of April 2021, in 18 patients in the OLE (followed for up to 33 months). Nine patients met SDI criteria either in the initial 12-month period (n=7) or in the OLE (n=2); of these, 7 had sustained EDSS improvement. Of the 8 patients who achieved SDI and entered the OLE, all but 1 patient maintained SDI through subsequent timepoints. Patients with sustained EDSS improvement (vs non-improvers) had greater increases in MTR signal (unenhancing T2 lesions and normal-appearing brain tissue) at 12 months, which may suggest remyelination. Phase 2 of this study, EMBOLD (NCT03283826), is ongoing and currently enrolling.

DISCLOSURES

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