Charcot 2020 submission

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

Pender MP,[1] Hodgkinson SJ,[2,3] Broadley S,[4] Lindsey J,[5] Ioannides ZA,[1] Bagert B,[6] Khanna R,[7] Smith C,[7] Gamelin L,[8] Ye W,[8] Willmer J,[8] Bar-Or A[9]

[1]The University of Queensland, Brisbane, Australia; [2]University of New South Wales, Sydney, Australia; [3]Liverpool Hospital, Liverpool, New South Wales, Australia; [4]Griffith University, Southport, Australia; [5]University of Texas Health Science Center at Houston, Houston, TX, USA; [6]Ochsner Health, New Orleans, LA, USA; [7]QIMR Centre for Immunotherapy and Vaccine Development, QIMR Berghofer Medical Research Institute, Brisbane, Australia; [8]Atara Biotherapeutics, South San Francisco, CA, USA; [9]Center for Neuroinflammation and Experimental Therapeutics, and Department of Neurology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA

ABSTRACT:

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

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). In part-1, four cohorts received escalating doses of ATA188 to determine the recommended part-2 dose (RP2D). Patients 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 [Pender MP *et al.* EAN 2020].

As of April 2020, 25 patients 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 and 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 at 6- (n=24) and 12-months (n=23). Six patients met SDI criteria at 6-months and 7 patients at 12-months, which was driven by EDSS in all but 2 patients. At both timepoints, a greater proportion of patients achieved SDI at higher doses. In cohorts-1–4, all patients with SDI at 6-months maintained it through 12-months. OLE data were available for 6 patients; 3 had SDI at 6- and 12-months which was maintained at 15-months.

Preliminary data indicate ATA188 is well tolerated. A greater proportion of patients showed SDI at higher doses. Patients achieving SDI at any timepoint maintained it at future timepoints. Based on these data, part-2 of the study has been initiated using the cohort-3 dose.