Correlation between clinical and biomarker data in ATA188-treated progressive MS

Short title: CDI and MRI in PMS-treated ATA188

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Introduction: ATA188 is associated with disability improvement in progressive MS (PMS); however, the relationship with neurodegenerative and tissue integrity markers on magnetic resonance imaging (MRI) remains unclear.

Aim: Investigate the relationship between confirmed disability improvement (CDI, from the Expanded Disability Status Scale [EDSS]) and longitudinal changes in MRI atrophy measures and normalized magnetization transfer ratio (nMTR) in patients with ATA188-treated PMS.

Methods: Retrospective analysis included patients with PMS treated in a 12-month open-label study with an open-label extension (OLE) portion. Images were analyzed between treatment onset and last available follow-up during the OLE (average 24.9±8.8 months). Percentage brain volume change (PBVC), percentage ventricular volume change (PVVC), and thalamic volume change (TVC) were assessed on MRI. nMTR evolution was measured within baseline unenhancing T2 lesions.

Results: 9/24 patients achieved sustained disability improvement (SDI) in the initial 12-months or the OLE; in 7/9, SDI was driven by EDSS (CDI). Most recent data showed 5/5 patients with CDI remaining in the OLE maintained improvement (median 27.5-months [range, 23.8–36.7]). Safety was consistent with previous reports. At 12-months, patients achieving SDI (vs not) had significantly less enlargement of ventricular volume (PVVC; p=0.019) but similar PBVC and TVC. Similar trends were observed in patients achieving CDI (vs not). Longitudinal MRI analyses including OLE data showed that patients achieving CDI (vs not) had significantly higher nMTR over time (β=0.14, p=0.005), suggesting increased myelin density. PBVC in patients achieving CDI (vs not) showed less decrease over time (β=0.34, p=0.037). There was a trend for less ventricular volume enlargement over time (PVVC); TVC did not differ by CDI status.

Conclusions: Five patients achieving CDI maintained improvement out to 39-months. CDI was associated with less severe brain atrophy at 12-months and increasing nMTR over time, suggesting that brain structural changes persist and may underlie the CDI associated with ATA188.

Disclosures:

Samantha Noteboom: supported by research grants from Atara Biotherapeutics, Merck, and Biogen.

Douglas Arnold: reports consulting fees from Albert Charitable Trust, Alexion Pharma, Biogen, Celgene, Frequency Therapeutics, Genentech, Med-Ex Learning, Merck, Novartis, Population Council, Receptos, Roche, and Sanofi-Aventis, grants from Biogen, Immunotec, and Novartis, and an equity interest in NeuroRx.

Amit Bar-Or: received consulting fees and is a speaker in meetings sponsored by Janssen/Actelion, Atara Biotherapeutics, Biogen Idec, Celgene/Receptos, Roche/Genentech, MAPI, Medimmune, Merck/EMD Serono, Novartis, and Sanofi-Genzyme. He has received grant support from Janssen/Actelion, Atara Biotherapeutics, Biogen Idec, Celgene/Receptos, Roche/Genentech, MAPI, Medimmune, Merck/EMD Serono, Novartis, and Sanofi-Genzyme.

Michael P. Pender: reports grants from MS Queensland, a research grant from Atara Biotherapeutics, clinical trial support from Atara Biotherapeutics, personal consulting fees from Atara Biotherapeutics, travel support from Atara Biotherapeutics, and membership of the Scientific Advisory Board of Atara Biotherapeutics.

Suzanne Hodgkinson: reports clinical trial support from Atara Biotherapeutics and honoraria for advisory boards from Biogen, Novartis, Merck, Roche and Sanofi.

Simon Broadley: reports clinical trial support through Griffith University from Atara Biotherapeutics and has received travel sponsorship to attend international scientific meetings, speaker's honoraria, and fees for advisory board attendance from Bayer-Schering, Biogen Idec, Merck, Novartis, Sanofi-Genzyme, and TEVA.

John W. Lindsey: received personal compensation for speaking or consulting for EMD Serono, Celgene, Mapi Pharmaceuticals, Banner Life Sciences, TG Therapeutics, Genentech, and Genzyme, is participating in clinical trials funded by Genentech, Biogen, Atara Biotherapeutics, EMD Serono, and AbbVie, and has received research funding from the National Multiple Sclerosis Society and Genentech.

Zara A. Ioannides: reports grants from MS Queensland and clinical trial support from Atara Biotherapeutics.

Bridget Bagert: received grant support from Ochsner Health, the National Multiple Sclerosis Society, and the Multiple Sclerosis Foundation. She participates in clinical trials supported by Atara Biotherapeutics, Genentech, Abbvie, Biogen, Sanofi-Genzyme, and GW Pharmaceuticals.

Jonathan Willmer, Laurence Gamelin, Wei Ye and Emily Liu: employees and stockholders of Atara.

Menno M. Schoonheim: serves on the editorial board of Neurology and Frontiers in Neurology, receives research support from the Dutch MS Research Foundation, Eurostars-EUREKA, ARSEP, Amsterdam Neuroscience, MAGNIMS and ZonMW and has served as a consultant for or received research support from Atara Biotherapeutics, Biogen, Celgene/Bristol Meyers Squibb, Genzyme, MedDay, and Merck.

This study is sponsored and funded by Atara Biotherapeutics. Medical writing assistance was provided by Tricia Brown, MS, MBA from AMICULUM Ltd, funded by Atara Biotherapeutics.

This abstract was originally submitted to ECTRIMS 2022.