MSMilan2023
9th Joint ECTRIMS-ACTRIMS Meeting
11–13 October 2023 | Milan, Italy

Abstract Number: [1625]

Abstract Title: Efficacy of Ofatumumab on Microglial Activity and Brain Iron in Patients With Relapsing Forms of Multiple Sclerosis: Results From a 9-Month Study

Abstract Category: Imaging and non-imaging biomarkers - 27 - MRI & PET

Preferred Presentation Type: Oral or poster presentation

Tarun Singhal*[1, 2], Ferdinand Schweser[3], Steven Vaquerano[2], John Hunter Ficke[2], Preksha Kukreja[2], Hong Pan[1, 2], Eero Rissanen[1, 2], Kelsey Carter[2], Gauruv Bose[1, 2], Kristin Galetta[1, 2], Bonnie Glanz[1, 2], Jonathan Zurawski[1, 2], Steven Cicero[2], Maria K. Houtchens[1, 2], Christopher Severson[1, 2], Shipra Dubey[1, 2], Bo Yeun Yang[1, 2], Rohit Bakshi[1, 2], Tanuja Chitnis[1, 2], Brandon Brown[4], Ibolya Boer[5], Howard Weiner[1, 2]

[1]Harvard Medical School, Boston, MA, United States, [2]Department of Neurology, Brigham and Women's Hospital, Boston, MA, United States, [3]Department of Neurology, Jacobs School of Medicine & Biomedical Sciences, University of Buffalo, Buffalo Neuroimaging Analysis Center, Buffalo, NY, United States, [4]Novartis Pharmaceutical Corporation, East Hanover, NJ, United States, [5]Novartis Pharma AG, Basel, Switzerland

Introduction:
Potential impact of ofatumumab on microglial activation and its association with peripheral B-cell depletion, serum biomarkers, and brain iron changes in multiple sclerosis (MS) are unknown. It is important to study the effect of anti-CD20 therapies on the innate immune system to understand their role in limiting disease progression in MS.
Objectives/Aims:
To determine the effect of ofatumumab on microglial activation and brain iron, using [F-18]PBR06 PET and quantitative susceptibility mapping (QSM) in patients with MS, in relation to peripheral B-cell depletion, serum biomarker measurement and changes in clinical impairment, longitudinally over 9 months.
Methods:
An open-label, single-centre, observational study was conducted in 10 patients with active relapsing MS. The following evaluations were performed at baseline, and at Week 1 and Months 1, 3 and 9 after ofatumumab initiation, in the first 5 patients (mean age, 40.2±12 years, median EDSS, 3.0): [F-18]PBR06 PET scans, peripheral CD-19+ counts, MRI (including QSM), clinical evaluations, serum neurofilament light chain (NfL) and glial fibrillary acid protein (GFAP) levels. Statistical parametric mapping (SPM) analysis was performed to assess the reduction in PET and QSM signal, analysed at Month 9 versus baseline. Normal-appearing white matter (NAWM), cortical grey matter (CoGM), and thalamic (Th) regions of interest (ROI) in standard atlas space were interrogated for peak cluster T-values corresponding to $P<0.05$.
Results:
At 9 months following ofatumumab initiation, voxel-clusters with significantly decreased PET uptake were observed in the CoGM ($P<0.01$) versus baseline. There were no clusters of significantly reduced PET uptake detectable in NAWM or Th-ROIs. Clusters of decreased QSM signal, representing decreased brain iron, were also seen in CoGM and NAWM ($P<0.01$). Serum NfL, but not serum GFAP, was significantly lower at 9 months ($P<0.05$). CD-19+ B cells were reduced significantly after 1 week of treatment initiation. EDSS and T25FW remained stable but hospital anxiety and depression scores (HADS-D and HADS-A) were significantly decreased at 9 months (both $P<0.05$).
Conclusion:
Ofatumumab treatment was associated with decreased cortical grey matter microglial activation, decreased brain iron and reduced NfL levels at 9 months and was preceded by peripheral CD19+ cell

depletion. The relationship between changes in cortical microglial activation, brain iron and serum NfL, in response to ofatumumab, warrants further investigation.

Disclosures: The study was supported by Novartis Pharma AG, Switzerland.
Tarun Singhal has received research support from Novartis Pharmaceuticals and Genzyme-Sanofi, consulting fees from Novartis pharmaceuticals and Genentech, speaking fee from Tiziana Life Sciences, and research funding from Nancy Davis Foundation's "Race to Erase MS" program, Ann Romney Center for Neurologic Diseases, Harvard Neuro-Discovery Center, National Multiple Sclerosis Society, Department of Defense, and Water Cove Charitable Foundation. Ferdinand Schweser: nothing to disclose. Steven Vaquerano: nothing to disclose. John Hunter Ficke: nothing to disclose. Preksha Kukreja: nothing to disclose. Hong Pan: nothing to disclose. Eero Rissanen has received fellowship grant from the Sigrid Jusélius Foundation and research grant from the Sakari Alhopuro Foundation. Kelsey Carter: nothing to disclose. Gauruv Bose: nothing to disclose. Kristin Galetta: nothing to disclose. Bonnie Glanz: nothing to disclose. Jonathan Zurawski: nothing to disclose. Steven Cicero: nothing to disclose. Maria K Houtchens: nothing to disclose. Christopher Severson: nothing to disclose. Shipra Dubey: nothing to disclose. Bo Yeun Yang: nothing to disclose. Rohit Bakshi has received consulting fees from Bristol-Myers Squibb and EMD Serono and research support from Bristol-Myers Squibb, EMD Serono, and Novartis. Tanuja Chitnis has received compensation for consulting from Biogen, Novartis Pharmaceuticals, Roche Genentech and Sanofi Genzyme. She has received research support from the National Institutes of Health, National MS Society, US Department of Defense, Sumaira Foundation, Brainstorm Cell Therapeutics, EMD Serono, I-Mab Biopharma, Mallinckrodt ARD, Novartis Pharmaceuticals, Octave Bioscience, Roche Genentech and Tiziana Life Sciences. Disclosures do not conflict with the work being presented. Brandon Brown and Ibolya Boer are employees of Novartis. Howard Weiner has received research support from Cure Alzheimer's Fund, EMD Serono, Inc., Genentech, Inc., National Institutes of Health, National Multiple Sclerosis Society, Sanofi Genzyme, and Verily Life Sciences. He has received payment for consulting from Genentech, Inc, IM Therapeutics, I-MAB Biopharma, MedDay Pharmaceuticals, Tiziana Life Sciences, and vTv Therapeutics.

Travel / Abstract Grant Application and Young Scientific Investigators' Session: I will not apply for Travel Grant or Young Scientific Investigators' Session

Which one would you like to apply to:

Date of Birth: