ECTRIMS 2022
38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis
27th Annual RIMS Conference
26 – 28 October 2022
Amsterdam, The Netherlands

P713

Preserved T cell but attenuated antibody response in MS patients on Fingolimod and Ocrelizumab following 2nd and 3rd SARS-CoV-2mRNA vaccine

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Introduction: Immunosuppressed patients may not mount an adequate immune response to 2 doses of SARS-CoV-2 mRNA vaccine and are eligible to receive a 3rddose. There is limited knowledge about T cell responses specifically in patients with multiple sclerosis (MS) who receive 3 doses of vaccine.
Objectives & Aims: To assess the SARS-CoV-2 spike antibody responses and T cell responses in MS patients on high efficacy immunotherapies and healthy controls (HC) who received 2 and 3 doses of SARS-CoV-2 mRNA vaccines.
Methods: This is a study of patients with MS, aged 18-65, on fingolimod (FIN) and ocrelizumab (OCR) for at least 3 months prior to 1 stmRNA SARS-CoV-2 vaccine dose (BNT162b2 or mRNA-1273) and a cohort of HC. Blood samples were collected after 2nd(2-vax) and 3rd(3-vax) dose of mRNA vaccine. The proportion of patients and HC who exhibited seroconversion, demonstrating serum SARS-CoV-2 spike antibody levels >0.4 U/ml,was determined. T cell responses were examined in a subgroup of patients with MS and HC after 2-vax and 3-vax by flow cytometry.
Results: The proportion of patients who seroconverted after 2-vax was 8/33 (24.2%) in the OCR group, 5/7 (71.4%) in the FIN group, and 29/29 (100%) in the HC group (Fisher's exact test,P=5.7*10^{-11}). After 3-vax, 9/21 (40.9%) patients in the OCR group seroconverted as compared to 19/21 (90.5%) in the FIN group, and 7/7 (100%) in the HC group (Fisher's exact test for difference,P=0.0003). There was SARS-CoV-2 peptide reactive CD4+ and CD8+ T cell activation across all 3 groups (OCR 2-vax n=10, FIN 2-vax n=6, HC 2-vax n=8, OCR 3-vax n=9, FIN 3-vax n=10, HC 3-vax n=5) as compared to unstimulated condition after 2-vax and 3-vax (Mixed effects analysis,P<0.0001). There was an increase in the percentage of SARS-CoV-2 peptide reactive CD4+ T cells in HC and OCR group but not in FINgroupafter 2-vax and 3-vax. There was anincrease in the percentage ofIFNγandTNFαproducing CD4+ and CD8+ T cells in FIN group as compared to HC and OCR group after 2-vax and 3-vax.TNFαproducing central memory CD4+ T cells were increased in OCR group after 2-vax andIFNγandTNFαproducing effector memory and terminally differentiated effector memory CD4+ T cells were increased in FIN group after 2-vax and 3-vax as compared to HC.
Conclusions: MS patients on ocrelizumab and fingolimod had decreased spike antibody responses, but preserved T cell responses compared to HCs after SARS-CoV-2 mRNA vaccination.
Disclosure: Shrishti Saxena- no disclosures
Sarah Conway- no disclosures
Clare Baecher-Allan- has received research support from the National MS Society
Rajesh Krishnan- no disclosures
Maria Houtchens- has received consulting income from Biogen, Novartis, Roche Genetech, Genzyme, EMD Serono. She has also received research support from Biogen, Roche Genentech, Novartis and Genzyme
Bonnie Glanz- has received research support fromVerily Life Sciences and Merck Serono
Mariann Polgar-Turcsanyi - no disclosures
Gauruv Bose-has received a postdoctoral fellowship from the MS Society of Canada
Rohit Bakshi-has received consulting fees from Bristol-Myers Squibb and EMD Serono and research support from Bristol-Myers Squibb, EMD Serono, and Novartis
Shamik Bhattacharyya- has received research support from NIH and Alexion Pharmaceuticals; consulting from Alexion Pharmaceuticals and Teladoc Health, publishing honorarium from UpToDate
Kristin Galetta- has received consulting money from GlaxoSmithKline
Tamara Kaplan-has received consulting and advisory board fees from Roche-Genentech, Novartis, and Bristol Myers Squibb
Christopher Severson-has consulted for Biogen, Novartis,Genentech, and Genzyme, and hasreceived grant support from the NMSS
Tarun Singhal- has received research support from Novartis Pharmaceuticals and Genzyme-Sanofi, and consulting fees from Novartis pharmaceuticals.
Lynn Stazzone- no disclosures
Jonathan Zurawski- has received research support from Novartis Pharmaceuticals and the Race to Erase MS Foundation
Taylor J. Saraceno- has received compensation for consulting from the Cumming Foundation and research support from Tiziana Life Sciences and I-Mab Biopharma (paid to the institution)
Anu Paul- no disclosures
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, MedDay Pharmaceuticals, Tiziana Life Sciences and vTv Therapeutics
Brian Healy-has received research support from Analysis Group, Celgene (Bristol-Myers Squibb), Verily Life Sciences, Merck-Serono, Novartis and Genzyme
Tanuja Chitnis- has received compensation for consulting from Banner Life Sciences, Biogen, Bristol Myers Squibb, 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,Bristol Myers Squibb, EMD Serono, I-Mab Biopharma, Mallinckrodt ARD, Novartis Pharmaceuticals, Octave Bioscience, Roche Genentech, Sanofi Genzyme, and Tiziana Life Sciences (paid to the institution)