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Abstract Title: Durability of Immune Response to COVID-19 Vaccines in Persons with MS on B-cell Depleting Therapy

Abstract Category: Therapy - 33 - Immunomodulation/Immunosuppression

Preferred Presentation Type: Oral or poster presentation

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Introduction:

Therapeutic agents for MS that work through B-cell depletion (BCD) are highly effective and widely used. Up to 30 days post-COVID-19 mRNA vaccination, persons with MS (PwMS) with few circulating B-cells do not mount a robust antibody (Ab) response, despite T-cell response being largely spared. How this translates into longer lasting immunity is poorly understood.

Objectives/Aims:
Prospectively characterize long-term anti-SARS-CoV-2 immune responses in PwMS, including antibody levels and T-cell subsets.

Methods:

Clinical data and blood samples were collected from PwMS at one or more of the following time points: pre-, <1 month post-, 1-6 months, and >6 months post-mRNA vaccine series. Donors testing positive for anti-Nucleocapsid Abs or with history of clinical COVID-19 infection were excluded from analysis. Anti-Spike (S) and anti-Receptor binding domain (RBD) Abs were quantified by enzyme-linked immunoassays and vaccine specific T-cells were identified by expression of activation-induced markers following stimulation with peptide pools spanning the spike protein. Comparison between groups was performed on log-transformed data using an ordinary one-way ANOVA corrected for multiple comparisons by Sidak's test.

Results:

Data from 123 PwMS were analyzed: 45% on BCD [ofatumumab (7%), ocrelizumab (53%), rituximab (40%)]. The remainder were on other immunotherapies or untreated.

With non-BCD therapies, anti-S and anti-RBD Abs were detectable within one month and declined with time. Those on BCD did not induce a robust humoral response and had significantly lower S- and RBD-titers at <1mo ($p = <0.0001$, $p<0.0001$) and 1-6mos ($p=0.0002$, $p<0.0001$) as well as lower anti-S Abs at >6mos ($p=0.0305$) post vaccination compared to non-BCD patients.

There was no difference in Ab levels between those on rituximab and ocrelizumab; comparison with ofatumumab was limited by sample size. Patients on BCD and non-BCD therapies have similar levels of CD4 and CD8 S-specific T cells at <1mo ($p=0.9784$, $p>0.9999$), 1-6mo ($p=0.8120$, $p=0.9973$), and

>6 mo (p=0.7977, p>0.9999) post-vaccination. The memory phenotype of these S-specific cells was similar between the two groups at all times evaluated; however, at >6mo post vaccination, patients on BCD had a lower frequency of S-specific Tfh than those on non-BCD therapies (p=0.0124).

Conclusion:

BCD therapy diminishes the already short-lasting humoral response to the SARS-CoV-2 mRNA vaccine. The cellular response is robustly induced and maintained. Analysis of collected post booster data is pending.

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