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Title: Durability of Immune Response to COVID-19 Vaccines in MS Patients on B-Cell Depleting Therapy

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Introduction: B-lymphocyte depleting therapies are commonly used for MS. Small studies have shown that individuals who are B-cell depleted (BCD) do not mount a robust antibody (Ab) response at 30 days post-SARS-CoV-2 vaccination, while T-cell response is largely spared. How this translates into longer lasting immunity is poorly characterized.
Objectives: Characterize long-term immune responses to SARS-CoV-2 vaccines in subjects with treated and untreated MS.
Aims: Quantify Spike and Receptor binding domain (RBD) Abs, vaccine specific T-cells, and functional T-cell response in MS subjects pre-, 2-3 weeks post-, and 6 months post- vaccine series.
Methods: Data was collected from subjects with MS at one or more of the above time points. Donors with evidence of prior infection were excluded. Spike and RBD Abs were quantified by enzyme-linked immunoassays. Vaccine specific T-cells were identified by expression of activation-induced markers following stimulation with peptide pools spanning the entire spike protein.
Results: 111 subjects were enrolled: 63% were BCD (ofatumumab [n=7], ocrelizumab [n=43], rituximab [n=20]), 37% were on alternative therapies or untreated. In preliminary analysis of 48 samples, Ab titers increased following vaccination in all subjects. Two weeks post-vaccination mean titers of BCD subjects (Spike 1546.1, RBD 699.3) were lower than those not BCD (Spike 11920.81, RBD 3093.2). The difference was significant (p=0.002) for Spike Ab titers and near significant (p=0.017) for RBD Ab titers. By six months, both groups' titers had dropped and neither Spike Ab (p=0.101) nor RBD Ab titers (p=0.104) were different between groups. There was no trend towards a difference amongst the BCD agents in Spike Ab levels at 2 weeks post-vaccination, although the one sample from a subject on ofatumumab obtained 6 months post vaccination had Spike Ab titers of 1322 (versus a mean of 54 and 375 in rituximab and ocrelizumab, respectively).A robust CD4+ predominant T-cell response was induced in both BCD and non-BCD subjects. Percentage of Spike-specific CD4 T-cells was similar between the two groups at 2 weeks (p=0.097) and 6 months (p=0.734) post-vaccination. Data on cytokine production following antigen exposure is pending.
Conclusions: B-cell depleting therapy alters the initial strength and the kinetics of the humoral vaccine response, but long-term humoral immunity may not be significantly impaired. The cellular response remains intact and endures.
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