Humoral immune response to COVID-19 Vaccines in patients with MS on different DMTs

Short title: COVID-19 vaccination in patients with MS

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Background: As global vaccination campaign against SARS-CoV-2 continues, uncertainties remain over vaccine efficacy in people with Multiple Sclerosis (pwMS) on different Disease Modifying Therapies (DMTs).

Objectives: To investigate the effect of DMTs on serological immune response to SARS-CoV-2 vaccines in pwMS.

Methods: We recruited 260 pwMS older than 18 years, being scheduled to receive any approved SARS-CoV-2 vaccine and similar number of healthy volunteers. Receptor-binding domain (RBD) antibodies (Anti-SARS-CoV-2-S) where quantitatively measured to evaluate humoral immune response, 4-weeks post-vaccination. Pre-vaccination test was performed to all participants and those detected positive were excluded.

Results: Patients categorized in the following treatment groups: group 1: anti-CD20s, n=36 (ocrelizumab 14, rituximab 21, ofatumumab 1), group 2: S1Ps, n=39 (fingolimod 33, ponesimod 3, ozanimod 2, siponimod 1), group 3: Immune Reconstitution Therapies, n=19 (cladribine 4, alemtuzumab 15), group 4: Immunomodulatory drugs, n=132 (interferon-β 19, glatiramer acetate 17, teriflunomide 16, dimethyl-fumarate 40, natalizumab 30, other 10), group 5: no therapy, n=34. Overall, 85% of pwMS and 100% of controls developed an antibody titer >0.8 U/ml, which was considered seropositive. Patients in groups 1 and 2 presented significantly lower positivity rates compared to those in other groups (35% and 66%, respectively vs 100%, *p<0.001)*, with a significantly lower mean titer. In group 1, time since last dose was positively correlated with antibody titer *(p<0.001)* as well as $CD19^+$ absolute count *(p=0.002)*. In group 2, patients with lymphopenia presented poorer response rate to vaccination (52% vs 100%, *p=0.014*).

Conclusions: pwMS without therapy or on DMTs other than anti-CD20s and S1Ps develop adequate humoral immune response against SARS-CoV-2, similar to healthy controls. Absolute $CD19^+$ cell count and presence of lymphopenia at time of vaccination, seem to have prognostic value for immune response in pwMS treated with anti-CD20s and S1Ps, respectively, with possible clinical implication in view of anamnestic vaccine shot.

Conflicts of interest

N. Fakas has received compensation for consultation, speech honoraria and travel support from Novartis, Genzyme, Teva, Merck, Biogen, Celgene, Roche, Sanofi, Actelion and Receptos
The rest authors declare no conflict of interest

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Study population

All MS patients included in the study are being followed in Multiple Sclerosis Unit, Neurology Department, 401 General Military Hospital of Athens
Department of Clinical Therapeutics, School of Medicine, National & Kapodistrian University of Athens, “Alexandra” General Hospital, provided data on healthy controls (Health Care Workers) and performed matching with pwMS

Institutional Review Board

This study was approved by both Ethics Committees of the 401 General Military Hospital of Athens (Ref No 5/9-4-2021) and “Alexandra” General Hospital (Ref No 15/23-12-2020) and was conducted according to the guidelines of the Declaration of Helsinki. Written informed consent was obtained from all subjects involved in the study.