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

Alexandra Akrivaki[1], Viktor Gotzamanis[1], Christina. Ikonomidou[2], Aikaterini Kardiakou[1], Athanasios Akalestos[3], Ioanna Charitaki[4], Evangelos Sfikas[1], Dimitra Tzavella[1], Athanasios Tsibonakis[1], Evangelos Terpos[4], Nikolaos Fakas[1]

[1] Multiple Sclerosis Unit, Neurology Department, 401 General Military Hospital of Athens, Athens, Greece
[2] Affidea Laboratories, Kallithea, Athens, Greece
[3] Roche Diagnostics (Hellas) SA, Athens, Greece
[4] Department of Clinical Therapeutics, School of Medicine, National and Kapodistrian University of Athens, "Alexandra" General Hospital, Athens, Greece

Introduction-Objectives

- 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).
- The objective of this study is to investigate the effect of DMTs on serological immune response 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.

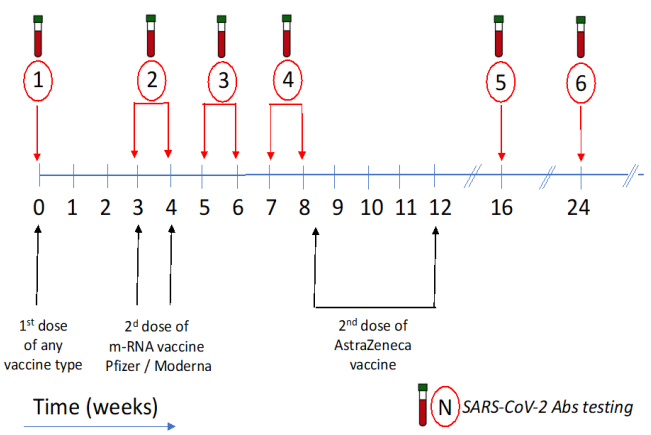


Figure 1. Study design

Characteristics	HC (N=258)	pwMS (N= 260)	p-value
Age-Mean (SD) (Min-Max)	46.94 (11.9) (20-70)	45.08 (11.5) (19-73)	0.07
Female sex – no. (%)	166 (64.3)	172 (66.2)	0.665
BMI- no. (%)			0.764
<18.5 Kg/m²	8 (3.1)	9 (3.5)	
18.5-24.9 Kg/m²	131 (50.8)	141 (54.2)	
25-29.9 Kg/m²	81 (31.4)	79 (30.4)	
≥30 Kg/m²	38 (14.7)	31 (11.9)	
Vaccine Type (%)			0.976
Vector	27 (10.5)	27 (10.4)	
mRNAs	231 (89.5)	233 (89.6)	
Pre Vaccination Seropositivity	6 (2.03)	8 (3.07)	0.598

Table 1. Demographics of Healthy Controls (HC) and pwMS

Characteristics	pwMS (N= 260)
Comorbidities - no. (%)	
None or 1	241 (92.7)
MS Disease Duration - no. (%)	
<10 yr	140 (53.8)
10-19 yr	80 (30.8)
≥20 yr	40 (15.4)
MS Phenotype - no. (%)	
Relapsing Remitting	196 (75.4)
Primary Progressive	28 (10.8)
Secondary Progressive	36 (13.8)
EDSS - no. (%)	
0-3	191 (73.5)
3.5-6	38 (14.6)
≥6.5	31 (11.9)
MS Treatment - no. (%)	
None	34 (13.1)
IMDs	132 (50.8)
S1Ps	39 (15)
IRT	19 (7.3)
AntiCD20s	36 (13.8)
Number of Previous DMTs - no. (%)	
0-1	184 (70.8)
2-3	60 (23.1)
≥4	16 (6.2)

Table 2. Characteristics of pwMS
Footnote: EDSS=Expanded Disability Status Scale, DMTs=Disease Modifying Treatments, IMDs=Immunomodulatory Drugs, IRTs=Immune Reconstitution Therapies, S1Ps=Sphingosine-1-Phosphate modulators

Results

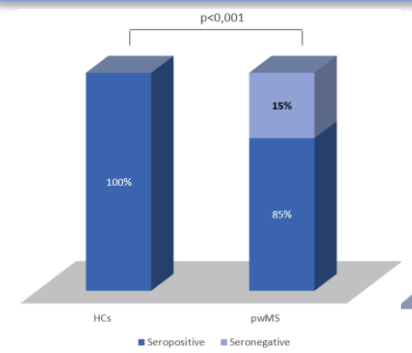
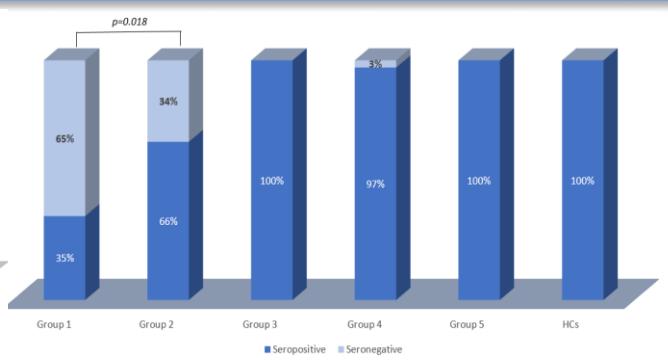


Figure 2. Post-vaccination rates of seroconversion



Groups		
Group 1	anti-CD20s n=36	Ocrelizumab Rituximab Ofatumumab
Group 2	S1Ps n=39	Fingolimod Ponesimod Ozanimod Siponimod
Group 3	IRTs n=19	Cladribine Alemtuzumab
Group 4	IMDs n=132	Interferon-β Glatiramer acetate Teriflunomide Dimethyl-fumarate Natalizumab other
Group 5	no therapy n=34	

Figure 3. Post-vaccination rates of seroconversion in different treatment groups Differences between Group 1 and Group 2 and all other Groups are statistically significant (all *p<0.001)*

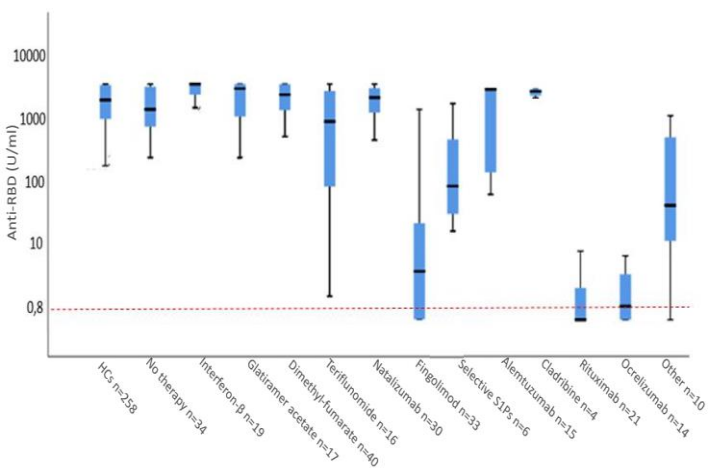


Figure 4. Post-vaccination anti-RBD titers in pwMS under treatment with different DMTs

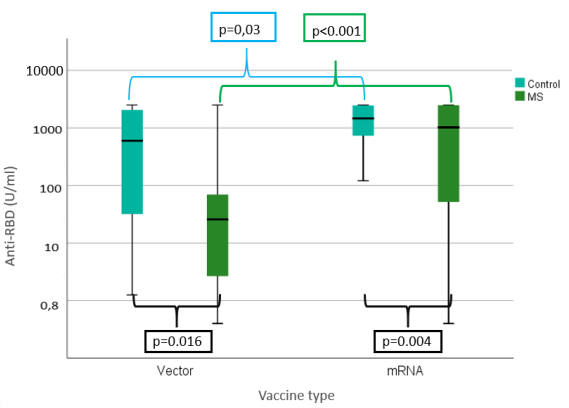


Figure 5. Differences in anti-RBD titers between vaccine types in HCs and pwMS. p-value from Mann-Whitney test with Bonferroni corrections for multiple comparison

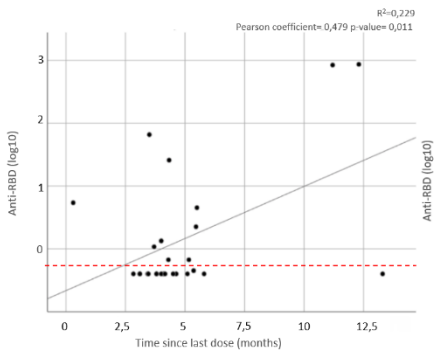


Figure 6. Significant association between anti-RBD titer 4-weeks post-vaccination and time since last anti-CD20 infusion at the time of vaccination in pwMS under treatment with anti-CD20

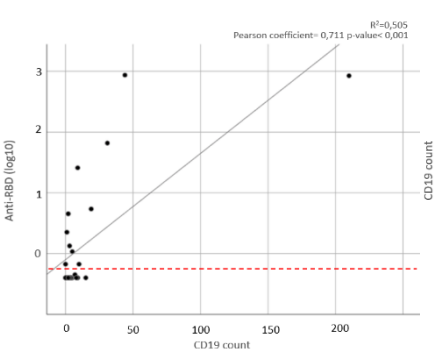


Figure 7. Significant association between anti-RBD titer 4-weeks post vaccination and CD19⁺ B-cells absolute count at the time of vaccination in pwMS under treatment with anti-CD20

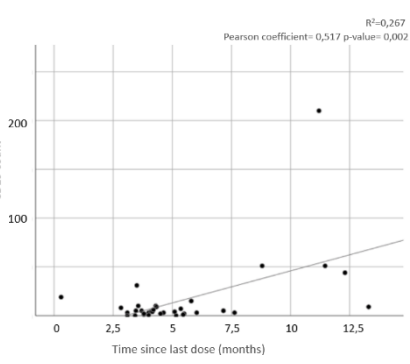


Figure 8. Significant association between CD19⁺ B-cells absolute count and time since anti-CD20 infusion at the time of first dose of vaccination

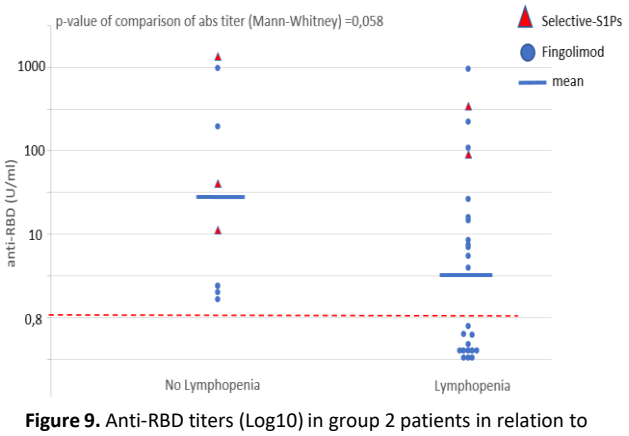


Figure 9. Anti-RBD titers (Log10) in group 2 patients in relation to lymphopenia (<1000/μL) at the time of vaccination. Different colors and shapes represent fingolimod and selective-S1Ps.

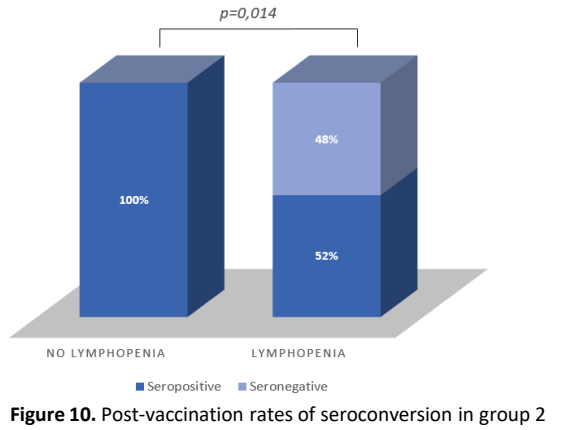


Figure 10. Post-vaccination rates of seroconversion in group 2 patients in relation to lymphopenia (<1000/μL) at the time of vaccination

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.