Adaptive B-cell and T-cell responses to SARS-CoV-2 vaccination in patients with Multiple Sclerosis on disease modifying immunotherapy

Anna Tomczak, MS[1], Julia Sumera, BA[1], Yamuna Joseph, MD[1], Danwei Wu, MD[1], Jamie McDonald, MD MS[1], Neda Sattarnezhad, MD[1], Lucas Kipp, MD[1], Christopher Lock, MD, PhD[1], May Han, MD[1], Jeffrey Dunn, MD[1]

[1] Stanford Multiple Sclerosis Center, Division of Neuroimmunology, Department of Neurology and Neurological Sciences, Stanford University, Stanford, CA, United States

Introduction

- Immunomodulatory therapies prescribed for patients with Multiple Sclerosis (MS) have been associated with decreased or absent anti-SARS-CoV-2 immunoglobulin production following COVID-19 vaccination.[1,2]
- While disease modifying treatments (DMTs) are deemed to have an acceptable safety profile during the COVID-19 pandemic, anti-CD20 therapy has been associated with increased risk of severe COVID-19 infection.[3]
- The risk of attenuated immunogenicity to COVID-19 vaccines may differ according to DMT class and mechanism of action. [4]
- Antibody testing does not assess the post-vaccination cellular immune response by which T cell immunity may contribute to human immunity.
- We investigated humoral and cell-mediated responses to SARS-CoV-2 vaccination in patients with MS on DMTs, including anti-CD20 and S1P therapies.

Methods

- Using the Stanford Research Repository database, we identified 79 MS patients – based on the 2017 McDonald Criteria[5] and ICD10 code- who were on a stable DMT regimen for MS and were tested for humoral and cellular reactivity against the SARS-CoV-2 spike protein post-COVID vaccination.
- B-cell and T-cell responses were tested using SARS-CoV-2-IgG and SARS-CoV-2 Interferon Gamma Release Assay (IGRA), respectively.[2]
- The following groups were analyzed: patients on anti-CD20 therapy (ocrelizumab, ofatumumab, rituximab) (n=37), patients on S1P modulators (fingolimod, Siponimod, ozanimod) (n=16), and patients off DMT or on other MS therapies (interferon beta-1a, dimethyl fumarate, diroximel fumarate, glatiramer acetate, natalizumab, and alemtuzumab) (n=26).
- Differences among groups were assessed using Chi-Square Test for categorical variables and T-test test for continuous variables. Results significant if p<0.05.
- All vaccinated patients were assessed between 4 weeks and 10 months after receiving at least one dose of the COVID-19 vaccine. Assessments were completed between December 2020 and February 2022.

Results

	Anti-CD20	S1P modulators	Other or off DMT
Subjects (n=79)	37	16	26
Gender (%)			
Female	25 (67.6)	14 (87.5)	23 (85.2)
Age (years) (SD)	48.0 (14.7)	48.30 (13.0)	51.6 (11.6)
Diagnosis (%)			
CIS	-	-	3 (11.5)
PPMS	6 (16.2)	-	1 (3.8)
RRMS	26 (70.3)	14 (87.5)	18 (69.2)
SPMS	5 (13.5)	2 (12.5)	3 (11.5)
TM			1 (3.8)
Disease duration (years) (SD)	10.36 (6.2)	11.09 (6.83)	14.6 (10.4)
Race (%)			
Asian	8 (21.6)	1 (6.2)	1 (3.8)
Black	1 (2.7)	1 (6.2)	-
White	22 (59.5)	12 (75.6)	22 (84.6)
Other	5 (13.5)	1 (6.2)	3 (11.5)
Unknown	1 (2.7)	1 (6.2)	-
Ethnicity (%)			
Hispanic/Latino	2 (5.4)	1 (6.2)	3 (11.5)
Non-Hispanic	35 (94.6)	13 (81.2)	23 (88.5)
Unknown	-	2 (12.5)	-
Type of Vaccine (%)			
mRNA	36 (97.3)	16 (100.0)	24 (92.3)
Viral Vector	1 (2.7)	-	2 (7.7)
Fully Vaccinated (%)			
CD19 count (SD)#	33.55 (58.3)	-	290.0 (182.5)
ALC (SD)&	1268 (509.0)	545.5 (597.5)	2299.3 (1928.7)
IgG and IGRA response (%)$			
IgG and IGRA response	8 (21.6)	1 (6.2)	25 (96.2)
IgG response only	-	2 (12.5)	-
IGRA response only	26 (70.3)	2 (12.5)	1 (3.8)
No response	3 (8.1)	11 (68.8)	-

Table 1: Baseline demographic and clinical characteristics according to DMT. SD: Standard Deviation, CIS: Clinically Isolated Syndrome, PPMS: Primary progressive MS, SPMS: Secondary progressive MS, RRMS: Relapsing-remitting MS, TM: Transverse Myelitis, ALC: Absolute Lymphocyte Count
#There was a statistically significant difference in CD19 count between the 3 groups (p = 0.001)
&There was a statistically significant difference in ALC between the 3 groups (p < 0.001)
$There was a statistically significant difference in SARS-CoV-2-IgG and SARS-CoV-2 IGRA response between the 3 groups (p < 0.001).

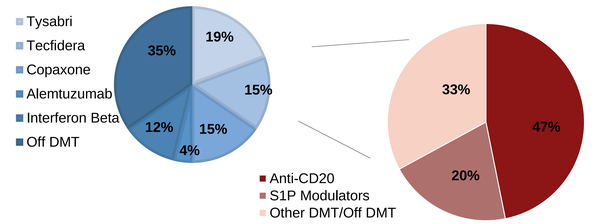

Figure 1: Types of disease modifying treatment (DMT) used by MS patients at the time of vaccination.

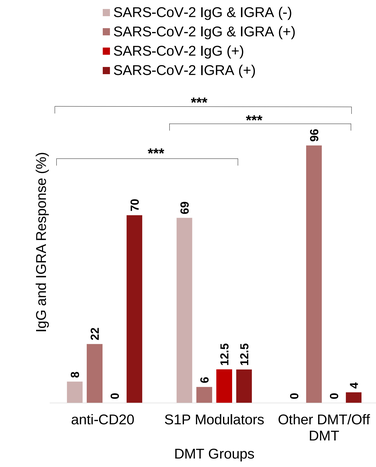

Figure 2: Vaccine response according to DMT.
*** p<0.001

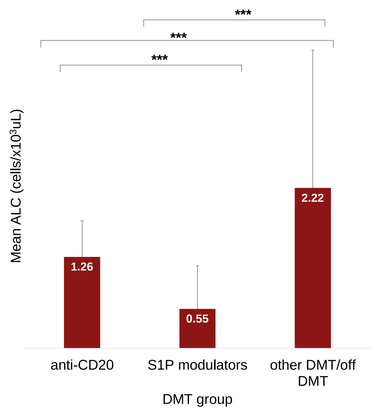

Figure 4: Mean ALC according to DMT.
***p<0.001

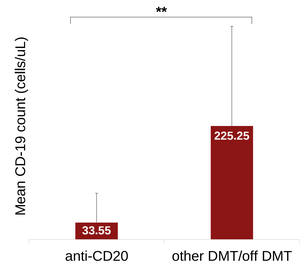

Figure 3: Mean CD-19 count according to DMT.
** p<0.01

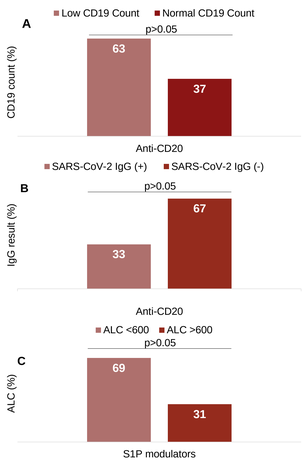

Figure 5: A) CD19 Counts in Patients on anti-CD20 Therapy. B) SARS-CoV-2 IgG Result after Delayed Infusions (>4 months). C) ALC within Patients on S1P modulators with No Immune Response.

Conclusions

- Treatment with anti-CD20 therapy and S1P modulator therapy was associated with attenuated immune response to COVID-19 vaccination
- Treatment with anti-CD20 therapy was associated with attenuated humoral response (IgG) but preserved cellular T cell response to vaccination
- Treatment with S1P modulators yielded absence of both humoral and cellular response to vaccination
- MS patients treated with other assessed DMT classes including interferon beta, glatiramer, fumarates and natalizumab showed measurable humoral and cellular response to COVID vaccination
- MS patients off DMT showed measurable B cell and T cell response to COVID vaccination
- Clinical correlation with the results of SARS-CoV-IgG and SARS-CoV-2 IGRA is not established
- Possible confounding effects of natural asymptomatic or unconfirmed COVID infection are not assessed in this study

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Disclosures

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Correspondence:
jeffdunn@stanford.edu
atomc96@Stanford.edu

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