RESEARCH LETTER

SARS-CoV-2 Antibodies in Adult Patients With Multiple Sclerosis in the Amsterdam MS Cohort

Various cohorts of patients with multiple sclerosis (MS) and COVID-19 have been described. So far, limited information is available regarding severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies in patients with MS. The objective of this study was to test for SARS-CoV-2 antibodies in a large MS cohort to evaluate asymptomatic infections and immunological responses to COVID-19.

Methods | This is a prospective cohort study conducted at the MS Center Amsterdam in Amsterdam, the Netherlands. On July 31, 2020, all adult patients with a current diagnosis of MS who had visited the MS Center Amsterdam in the past 2 years were invited to participate. The database was closed on December 18, 2020. The study was approved by the Medical Ethical Committee of the VU University Medical Center, and all patients provided written informed consent. The STROBE reporting guideline was followed.

Blood samples were drawn for SARS-CoV-2 antibody measurements with a total antibody assay with 98.1% sensitivity and 99.5% specificity.[1] Signals were quantified as normalized optical density (nOD) units, ranging from low (0.1-1.0 nOD) to high (>1.0 nOD). In the week following blood sampling, patients filled in digital questionnaires regarding their characteristics, current MS complaints, and COVID-19 symptoms. Other MS-specific data were retrieved from the medical files. Groups were compared with the Mann-Whitney *U* test (for continuous data) or the Pearson χ^2 test (categorical data). The level of significance was set at .05, and SPSS version 26.0 (IBM) was used for data analysis.

Results | A total of 1778 patients were contacted, and 546 patients were included (mean [SD] age, 46.9 [12.1] years; 388 women [71.1%]). Additional baseline characteristics are described in the **Table**. In 64 patients (11.7%), SARS-CoV-2 antibodies were detected. Thirty-five patients experienced COVID-19, as established by polymerase chain reaction (PCR) testing (**Figure**, A). Of the patients positive by PCR, 4 (11%) tested negative for SARS-CoV-2 antibodies.

Nine patients who were antibody positive (14%) did not experience any symptoms suggestive of COVID-19. The most frequently reported symptom in those positive for SARS-CoV-2 antibodies was a loss of taste and/or smell (30 of 64 patients [47%]), while only 14 of 482 patients (2.9%) without SARS-CoV-2 antibodies reported these symptoms. To our knowledge, there were no COVID-19 fatalities in this MS population.

Of all 546 patients, 405 (74.2%) were receiving disease-modifying therapy. In these, SARS-CoV-2 antibodies were less prevalent in patients using injectable drugs (interferon β and glatiramer acetate) than patients with other treatments (3 of 69 [4%] vs 44 of 336 [13.1%]; $P = .04$).

The median SARS-CoV-2 antibody response in patients treated with ocrelizumab was lower in comparison with other patients (0.2 [interquartile range, 0.1-0.4] nOD vs 2.5 [interquartile range, 0.6-2.5] nOD; $P < .001$; Figure, B). All patients taking ocrelizumab were B-cell depleted, as measured at a median (range) of 2.5 (0-41) days before the antibody response was measured. None of these patients experienced hypogammaglobulinemia at that time.

Discussion | In this study, we found a lower SARS-CoV-2 antibody response in patients with MS who were depleted of B cells. Case reports[2-4] have described patients with MS and neuromyelitis optica treated with anti-CD20 therapies who did not develop detectable SARS-CoV-2 antibodies after PCR-confirmed COVID-19. Furthermore, in a retrospective cohort,[5] SARS-CoV-2 antibodies were less prevalent in patients with MS and suspected COVID-19 who were treated with ocrelizumab.

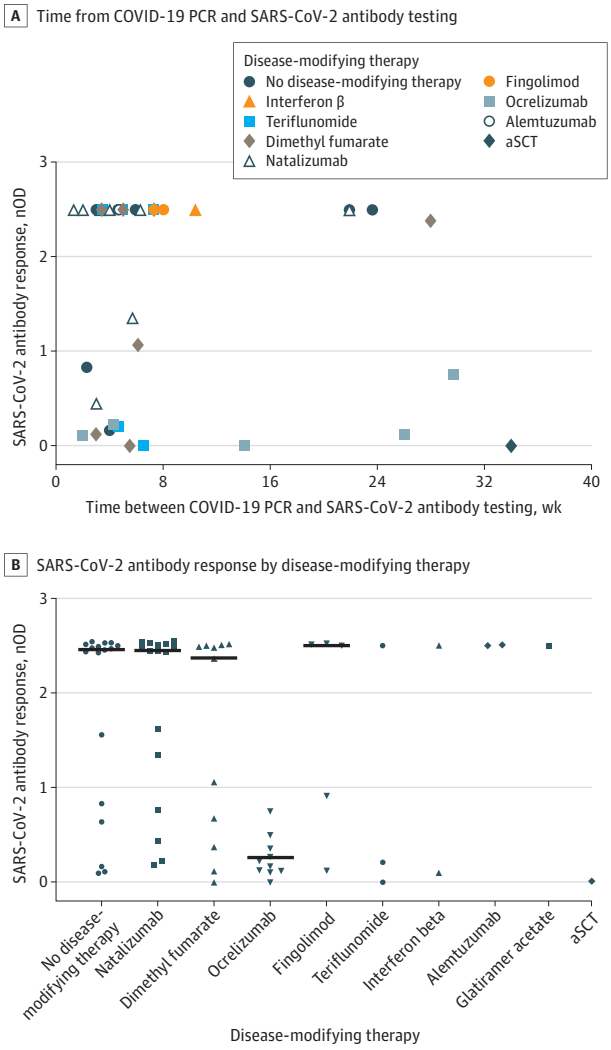
Table. Baseline and COVID-19 Characteristics

Characteristic	Patients, No. (%)		
	Total (N = 546)	SARS-CoV-2 antibody positive (n = 64)	SARS-CoV-2 antibody negative (n = 482)
Age, mean (SD), y	46.9 (12.1)	46.3 (12.6)	46.9 (12.1)
Women	388 (71.1)	43 (67.2)	345 (71.6)
Men	158 (28.9)	21 (32.8)	137 (28.4)
Weight, mean (SD), kg[a]	75.4 (25.1)	74.2 (12.7)	75.6 (26.4)
Years since diagnosis, median (interquartile range)	12 (6-18)	11 (5-21)	12 (6-17)
SARS-CoV-2 polymerase chain reaction test performed, No.	148	38	110
Positive	35 (23.6)	31 (82.6)	4 (3.6)
Negative	113 (76.4)	7 (18.4)	106 (96.4)

Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a] Not all answers were complete.

Figure. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Antibody Response in Patients With Multiple Sclerosis With Positive Results on Polymerase Chain Reaction (PCR) and Antibody Testing



A, Time between the positive PCR (at month 0) and the SARS-CoV-2 total antibody test. In 4 patients, no SARS-CoV-2 antibodies could be detected. None were lymphopenic (<1000 cells per microliter; to convert to cells × 10^9 per liter, multiply by 0.001) in testing in the 2 months prior to the start of COVID-19 complaints. The patient taking ocrelizumab was B-cell depleted prior to COVID-19 and had received 4 cycles of ocrelizumab. B, SARS-CoV-2 antibody response in patients with positive results on PCR and/or antibody testing who were receiving different disease-modifying therapies. The maximum response that could be measured was 2.5 normalized optical density (nOD) units, with a cutoff of 0.1 for seropositivity. The 2 patients treated with alemtuzumab received their last course 43 and 29 months prior to SARS-CoV-2 antibody sampling, respectively. One patient with an autologous stem cell transplant (aSCT) was treated 10 months prior to SARS-CoV-2 antibody sampling.

This cohort study showed that 14% of patients with MS and COVID-19 were asymptomatic for COVID-19, which is comparable with a reported 17% in the general population.[6] Because patients may have been more willing to participate in this study after experiencing symptoms fitting COVID-19, the percentage of patients who were asymptomatic might be an underrepresentation.

A limitation of our study is the relatively low percentage of patients who were SARS-CoV-2 positive. Still, we were able to show a lower antibody response in patients depleted of B cells.

Conclusions | In conclusion, our data imply that B-cell depletion could influence SARS-CoV-2 antibody production in patients with MS. This holds important consequences for humoral immunity after COVID-19 infection and possibly vaccination.

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Accepted for Publication: March 19, 2021.

Published Online: April 30, 2021. doi:10.1001/jamaneurol.2021.1364

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Statistical analysis: van Kempen, Strijbis.
Obtained funding: van Kempen, Killestein.
Administrative, technical, or material support: van Kempen, Strijbis, Al, Steenhuis.
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Conflict of Interest Disclosures: Dr van Kempen reports a grant from Dutch MS Research Foundation (grant 20-005 PP) during the conduct of the study. Dr Uitdehaag reports personal fees from Biogen Idec, Genzyme, Merck Serono, Novartis, Roche, and Teva consultancy fees outside the submitted work. Dr Rispens reports grants from Netherlands Organisation for Health Research and Development (ZonMw) during the conduct of the study. Dr Killestein reports a grant from Dutch MS Research Foundation (grant 20-005 PP) during the conduct of the study; personal fees from Biogen, Genzyme, Merck, Novartis, and Roche; and grants from Teva, Biogen, Genzyme, Merck, Novartis, and Roche, outside the submitted work. No other disclosures were reported.

Funding/Support: We are very grateful to the Dutch MS Research Foundation for fully funding this study (grant 20-005 PP).

Role of the Funder/Sponsor: The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Additional Contributions: We thank the patients for participating in this study. Furthermore, we thank Birgit Lissenberg-Witte, PhD, Amsterdam UMC, for statistical contributions; Gert-Jan Wolbink, PhD, Amsterdam Rheumatology and Immunology Center, Jean-Luc Murk, PhD, Elizabeth Tweesteden Hospital, and Floor Loonstra, MD, Amsterdam UMC, for help in the study design; Samantha Noteboom, MSc, Brigit de Jong, PhD, and Bob van Oosten, PhD, Amsterdam UMC, for help with data collection; and Gerard van Mierlo, MSc, and Rivka

de Jongh, MSc, Sanquin Research, for performing SARS-CoV-2 antibody testing. This study is affiliated with the Dutch Target to B! Consortium on COVID-19 in Autoimmune Diseases (www.target-to-b.nl). We acknowledge the support of our colleagues in the Dutch Target to B! Consortium on COVID-19 in Autoimmune Diseases: Filip Eftimov, PhD, Taco Kuijpers, PhD, Luuk Wieske, PhD, Sander Tas, PhD, and Koos van Dam, MD, Amsterdam UMC; Marieke van Ham, PhD, Sanquin Research; and Laura Boekel, MD, Rheumatology and Immunology Center. These individuals were not compensated.

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