Letters

Anti-SARS-CoV-2 monoclonal antibodies for the treatment of active COVID-19 in multiple sclerosis: An observational study

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Dear Editor,

In their short report "*Anti-SARS-CoV-2 monoclonal antibodies for the treatment of active COVID-19 in multiple sclerosis: An observational study*,"[1] Dr. Manzano et al. reported an overall safe and likely helpful profile of neutralizing anti-Spike protein monoclonal-antibody (mAbs) treatment in people with multiple sclerosis (pwMS) with acute coronavirus disease 2019 (COVID-19).

We found similar results in a cohort of 16 pwMS followed at the MS center of University of Genoa IRCCS Policlinico San Martino, who developed COVID-19 between April 2021 and February 2022.

Most of our patients (13/16) were treated before December 2021 using a combination of monoclonal antibodies (casivirimab + imdevimab and bamlanivimab + etesevimab) because the predominant variant of concern (VOC) in our region was delta. The remaining three patients were treated with sotrovimab because the predominant VOC was Omicron.[2] Delta was more than twice as contagious as previous variants and caused more COVID19-hospitalization, especially in people who were not fully vaccinated.[3] With new less virulent VOC (such as Omicron), higher vaccination coverage and higher viral circulation, neutralizing mAbs treatment was prioritized for patients with multiple underlying conditions.

The mean interval time between first positive test and mAbs infusion was 3.5 days (range 1–7), with most patients (11; 69%) treated within 5 days of positivity. Overall, 11 (69%) patients were fully vaccinated according to current recommendations (two doses) at the time of COVID-19. Of note, five vaccinated patients (45%) were under treatment with anti-CD20 agents at the time of vaccination; therefore, it is possible that their humoral response to SARS-CoV-2 vaccines was reduced.[4] The median interval time between the first positive and first negative swab was 12 days (range 5–30), being 10 days (range 5–20) when considering patients treated with mAbs before day 5 from symptoms onset 20 days (range 12–30) for patients treated between Day 5 and Day 10.

In our cohort, 14/16 (87%) patients did not experience COVID-19 progression. Two patients developed dyspnea after mAbs administration which required oxygen support. One of them had also chronic lymphocytic leukemia (CLL), for which she was under treatment with bendamustine and rituximab. On hospital admission, she was neutropenic, had fever, and modest reduction of saturation in ambient air (92%). She received empirical antibiotic treatment for febrile neutropenia, 1 day of oxygen therapy, no specific anti-SARS-CoV-2 antivirals was needed, and she was discharged after 7 days and resolution of neutropenia. The other patient was 84 years old and suffered from arterial hypertension; she refused hospital admission and was successfully treated at home with low-level oxygen support and steroid treatment. No patient was admitted to the intensive care unit (ICU) or died.

Overall, treatment with mAbs was well tolerated. No serious adverse events (SAEs) or infusion-related reactions occurred. Two patients reported temporary clinical worsening of neurological symptoms (without evidence of relapses or magnetic resonance imaging (MRI) activity) after the infusion, with a spontaneous return to normal functioning within 3 days. A causal correlation between the reported symptomatology and mAbs infusion could not be established.

In line with previous findings,[1,5] our limited experience highlights the negative effect of advanced age, high disability, and comorbidities. Our results confirm and strengthen those of Manzano et al.,[1] showing potential clinical benefit of early testing for SARS-CoV-2 infection coupled with prompt intervention with neutralizing mAbs, which led to a low incidence of COVID-19-related hospitalization or death and appeared to be safe and well tolerated in pwMS who develop symptomatic COVID-19.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Matilde Inglese

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References

1. Manzano GS, Rice DR, Klawiter EC, et al. Anti-SARS-CoV-2 monoclonal antibodies for the treatment of active COVID-19 in multiple sclerosis: An observational study. *Mult Scler* 2022; 28(7): 1146–1150.
2. Takashita E, Kinoshita N, Yamayoshi S, et al. Efficacy of antibodies and antiviral drugs against Covid-19 omicron variant. *N Engl J Med* 2022; 386(10): 995–998.
3. Shiehzadegan S, Alaghemand N, Fox M, et al. Analysis of the delta variant B.1.617.2 COVID-19. *Clin Pract* 2021; 11(4): 778–784.
4. Sormani MP, Inglese M, Schiavetti I, et al. Effect of SARS-CoV-2 mRNA vaccination in MS patients treated with disease modifying therapies. *Ebiomedicine* 2021; 72: 103581.
5. Sormani MP, Schiavetti I, Carmisciano L, et al. COVID-19 severity in multiple sclerosis: Putting data into context. *Neurol Neuroimmunol Neuroinflamm* 2021; 9(1): e1105.

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Confronting a misnomer about the SDMT: A David and Goliath story

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The recent report in MSJ by Wojcik et al.,[1] presents a novel and exciting approach to understanding the progression of cognitive impairment in multiple sclerosis (MS). Cognitive tests were administered to a longitudinal sample of 1073 patients across a (mean) 4.5-year span; the order in which different cognitive domains become impaired was evaluated. Using validated, widely accepted and consensus-based test measures to estimate the sequence of domains in which impairment arises, the authors concluded that processing speed preceded all other cognitive impairments. These results could have critically important implications for the development of targeted treatments and may suggest that forestalling decline in one identified domain precludes decline in additional domains.

The problem is that the authors' interpretation hinges on a misnomer: that the Symbol Digit Modalities Test (SDMT) primarily measures processing speed. In addition to processing speed, lexical access speed, as well as verbal and nonverbal memory, jointly and uniquely contribute to SDMT performance, according to a recent study by Sandry et al.[2] In 661 MS patients, high sensitivity of the SDMT was attributed to its ability to capture heterogeneous cognitive profiles. In addition, recent work by Arnett et al.[3] revealed contributions of rudimentary oral motor speech and visual acuity to performance on the SDMT. The SDMT is best considered a cognitive screener sensitive to