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LETTER TO THE EDITOR

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Is monoclonal antibody administration necessary in all vaccinated patients with breakthrough COVID-19 infections?

Anti-SARS-CoV-2 monoclonal antibodies have reduced viral shedding, time to symptom resolution, and admission to hospital for COVID-19 in patients with risk factors for severe disease.[1,2] Almost all evidence was provided by studies in unvaccinated patients. In the last few months, a massive vaccination campaign has been implemented in Italy. Monoclonal antibodies are nowadays increasingly used in vaccinated people with breakthrough COVID-19 infections; their clinical efficacy in this patient population has been recently reported from one group in the United States.[3,4]

We retrospectively reviewed the data of all patients to whom treatment with monoclonal antibodies was offered at the Infectious Diseases Unit of Santa Maria della Misericordia Hospital, Rovigo, Italy, from September 1, 2021, to January 15, 2022; the Delta variant of SARS-CoV-2 predominated until mid-December 2021 when the Omicron variant became predominant. Vaccinated and unvaccinated nonhospitalised patients with mild to moderate COVID-19, at high risk of progressing to severe disease were screened at home by general practitioners and included in an online regional portal. Eligibility and enrollment were made by a dedicated Infectious Diseases specialist. One hundred twenty-two vaccinated patients were offered monoclonal antibodies treatment. Patients who had received a minimum two doses of mRNA vaccines (Spikevax Moderna, Comirnaty Pfizer-BioNTech) or one or two doses of adenovirus vector vaccines (Janssen Johnson & Johnson, Vaxzevria AstraZeneca) were considered fully vaccinated; some patients could have received a third vaccine dose. 4/122 patients were excluded because they had not completed the vaccine cycle or received one dose of Janssen Johnson & Johnson vaccine over 6 months earlier).

The mean age of the remaining 118 patients (64 males) was 66.4 (26–96) years. Eight-one patients had received Pfizer vaccine, 23 AstraZeneca, 13 Moderna, and 5 Janssen Johnson & Johnson. In 102 patients vaccinated with two doses, the mean time between infection diagnosis and last dose was 151.6 (27–273) days. The 16 patients vaccinated with three doses developed the disease after a mean time of 60 (23–121) days from the third dose. The prevalent comorbidities increasing severe COVID-19 disease risk, were age >65 years (69 patients, 58.4%), body mass index ≥30 (36, 30.5%), cardiovascular or cerebro-vascular diseases (42, 35.6%), chronic obstructive pulmonary disease and other chronic lung diseases (19, 16%), uncontrolled diabetes mellitus (14, 11.8%), immunocompromised status (11, 9.3%), chronic kidney disease (7, 5.9%), neurodegenerative diseases (4.3, 3%).

Fifty-eight patients (Group A, including four immunocompromised patients) were treated with monoclonal antibodies and 60 (Group B, including seven immunocompromised) refused the treatment. The mean age of Group A was 67.4 (30–96) and of group B 65.4 (26–88) years. Among treated patients, bamlanivimab/etesivamb (30) and casirivimab/imdevimab (27) were the most used monoclonal antibody combinations. All monoclonal antibodies were infused within 10 days (mean 4.3 days; range 1–9) from symptom onset.

In 48 patients (30 vaccinated with two doses, one with three doses in Group A; 16 vaccinated with two doses, one with three doses in Group B) serum levels of IgG anti-SARS COV-2 S-RBD (Maglumi 2000 plus CLIA assay, Snibe Diagnostics) were measured (at the time of monoclonal antibody infusion for group A patients or the day after refusal for Group B). A level >1 KBAU/L was considered positive. Forty-four patients were positive (the four negative patients being all in Group A). Mean antibody levels were 3055.1 KBAU/L (<1–25 000 KBAU/L) in Group A and 4239.2 (12.1–25 000 KBAU/L) in Group B.

The degree of medical comorbidity was assessed using the Monoclonal Antibody Screening Score (MASS) for the risk of severe COVID-19 outcomes.[5,6] The results are reported in Table 1.

All patients were contacted by telephone at least 28 days after COVID-19 diagnosis to assess their health status; none had died or had been hospitalized for severe disease (defined as need for oxygen supplementation or intensive care unit admission). Five patients (three treated with monoclonal antibodies, two untreated) had been hospitalized for unrelated diseases.

In the REGN-COV 2 trial, pre-existence of either IgA anti-S1, IgG anti-S1, or IgG anti-nucleocapsid protein was associated with lower baseline viral loads, and exogenously provided antibodies had substantial benefit only in antibody-negative patients.[1] Even though the role of antispike receptor binding domain antibodies in preventing severe COVID-19 disease in vaccinated individuals is not well defined, the results in our small cohort (in whom no deaths or hospitalizations for the severe disease were observed in patients untreated with monoclonal antibodies) suggest that these patients are generally protected by a severe course. Measurement of antispike protein antibodies could guide the administration of monoclonals to vaccinated patients; reserving the treatment for antibody-negative patients would also considerably reduce costs.

TABLE 1

MASS* score	Group A—number of patients (monoclonal antibody treatment)	Group B—number of patients (no monoclonal antibody treatment)
0	11	8
1	4	4
2	10	17
3	7	9
4	11	9
5	10	2
6	4	3
7	0	2
≥8	1	6

Note: MASS score assigns a score to each criterion linked to a major risk of severe COVID-19 disease: age ≥ 65 (2 points), BMI ≥ 35 (1 point), diabetes mellitus (2 points), chronic kidney disease (3 points), cardiovascular disease in a patient ≥55 years (2 points), chronic respiratory disease in a patient ≥55 years (2 points), hypertension in a patient ≥55 years (1 point), and immunocompromised status (3 points).

Abbreviations: BMI, body mass index; MASS, Monoclonal Antibody Screening Score.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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