Anti-SARS-CoV-2 Monoclonal Antibodies in Solid-organ Transplant Patients

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To the editor:

Solid-organ transplant (SOT) patients are at high risk of developing severe coronavirus disease-19 (COVID-19). Neutralizing monoclonal antibodies that bind to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein prevent viral attachment to ACE2 receptor. When administered to immunocompetent patients in the early phase of infection, they reduce the risk of hospitalization and improved symptoms resolution.[1,2] Similar data were reported in a real-life study that included 69 immunosuppressed patients.[3] However, the proportion of SOT patients and their specific outcome were not reported. Dhand et al reported encouraging results in SOT patients given bamlanivimab monotherapy or casirivimab/imdevimab without a control group.[4,5] Herein, we compared the outcome of SOT patients who were given monoclonal antibodies to an historical control group. According to French law (Loi Jardé), anonymous retrospective studies do not require Institutional Review Board approval. In France, the use of monoclonal antibodies was approved on February 25, 2021 for immunosuppressed patients with positive SARS-CoV-2 nasopharyngeal RT-PCR, having symptoms for <6 d, and not requiring oxygen. Between March 19, 2020 and April 15, 2021, 90 SOT patients with COVID-19 were referred to our center. At admission, 4 were asymptomatic, 23 patients required oxygen, and 15 patients were symptomatic for >5 d. Hence, 48 patients met the criteria for receiving monoclonal antibodies. All patients were hospitalized. Sixteen SOT patients (12 kidney, 1 simultaneous kidney-pancreas, 1 combined kidney-liver, and 2 heart-transplant patients) that presented after February 25, 2021 were offered monoclonal antibodies, while the 32 remaining patients that presented before this date were considered as a control group (Table 1). Five patients were given bamlanivimab monotherapy (700 mg), 9 patients received the combination treatment (700 mg of bamlanivimab and 1400 mg of etesevimab), and 2 patients have received the combination of casirivimab and imdevimab (1200 mg/1200 mg). No infusion reaction was observed. The mean time between first symptoms and admission was similar in both groups. After a follow-up of 39 (10–74) d after the injection of monoclonal antibodies, none of these 16 patients developed a severe respiratory illness defined by the need for high oxygen support, while 15 of the 32 control patients developed a severe respiratory illness (46.9%, P = 0.007), requiring high flow nasal oxygen (n = 7) or orotracheal intubation (n = 8). After exclusion from the control group patients having a C-reactive protein >100 ng/mL (maximal level observed in the treated group) (n = 6), severe respiratory illness rate remained significantly higher in patients non-treated with monoclonal antibodies (11 of 26 [42%] versus 0%, P = 0.003). Three patients from the control group deceased during follow-up. As initially requested by the French Authorities, patients given monoclonal antibodies were hospitalized. All, but one, were discharged on day 3. The latter required oxygen, was given dexamethasone and discharged on day 11. None of them required readmission. At admission and during follow-up, no key mutations associated to reduced treatment activity, including K417N/T, E484K, and N501Y, were detected by single-molecule real-time sequencing (PacBio) of SARS-CoV-2 Spike gene. However, bamlanivimab monotherapy is not recommended anymore. Despite small and relatively heterogenous groups, our retrospective study shows that neutralizing anti-SARS-CoV-2 monoclonal antibodies can prevent acute respiratory failure in SOT patients and can be safely applied.

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A.D.B. managed the patients, collected the data, and designed the study. O.M. managed the patients, collected the data, and reviewed the article. C.V. did the virological work-up. S.F. managed the patients and reviewed the article. J.I. did the virological work-up and reviewed the article. N.K. designed the study and wrote the article.

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TABLE 1.

Comparison between solid-organ-transplant patients who were given or not monoclonal antibodies

	Patients who received monoclonal antibodies (N = 16)	Patients who did not receive monoclonal antibodies (N = 32)	*P*
Age (y)	54 ± 14	59 ± 13	0.26
Age ≥ 55 y	50%	65.6%	0.36
Gender—male/female	10/6	20/12	>0.99
Transplanted organ			0.46
Heart	2	3	
Kidney	11	26	
Liver	0	2	
Kidney-pancreas	1	1	
Kidney-liver	1	0	
Number of transplantations	1.2 ± 0.42	1.1 ± 0.36	0.58
Body mass index (Kg/m^2)	27.3 ± 4.3	27.5 ± 5.2	0.89
Diabetes (%)	18.75%	31.2%	0.49
Cardiovascular disease (%)	37.5%	50%	0.54
Hypertension (%)	68.75%	77.5%	0.14
Tobacco use (%)	31.25%	15.6%	0.27
Pulmonary comorbidities	25%	28%	>0.99
Immunosuppression at admission			
Calcineurin inhibitors (%)	87.5%	87.5%	>0.99
Tacrolimus (%)	81.25%	87.5%	0.67
Second signal inhibitors (%)	12.5%	6.15%	0.59
Mycophenolic acid (%)	75%	81.2%	0.71
mTOR inhibitors (%)	18.75%	18.75%	>0.99
Steroids (%)	87.5%	93.75%	0.59
Biologic parameters at admission			
C-reactive protein (mg/L)	17 (1–100)	38 (1–205)	0.02
Ferritin level (ng/mL)	750 ± 863	804 ± 859	0.76
Neutrophils count (/mm^3)	4869 ± 3080	6250 ± 599	0.63
Lymphocytes count (/mm^3)	1106 ± 423	969 ± 655	0.17
Platelets count (10^3/mm^3)	182 ± 48	183 ± 87	0.46
Serum creatinine level (μmol/L)	169 ± 89	178 ± 115	0.90
Oxygen saturation (%)	97.7 ± 1.8	97.5 ± 1.5	0.88
Treatment			
Anti-viral therapy	0 (0%)	0 (0%)	>0.99
Hydroxychloroquine	0 (0%)	2/32 (6.25%)	0.54
Dexamethasone	1/16 (6.25%)	18/32 (56.25%)	0.001
Tocilizumab	0 (0%)	3/32 (9.37%)	0.54
Outcome			
Severe respiratory illness[a] (%)	0 (0%)	15/32 (46.9%)[b]	0.007
Acute renal failure (%)	1/16 (6.25%)	8/32 (25%)	0.23
Use of vasopressive drugs	0 (0%)	8/32 (25%)	0.04
Graft loss	0 (0%)	0 (0%)	0.99
Death	0 (0%)	3/32 (9.4%)	0.54

[a]Severe respiratory illness is defined by the need for high oxygen support, that is, high flow nasal oxygen, noninvasive ventilation, or mechanical ventilation.
[b]Fourteen of the 15 patients who developed severe respiratory distress were given dexamethasone.
mTOR, mammalian target of rapamycin.

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