Bebtelovimab for Treatment of COVID-19 in Ambulatory Solid Organ Transplant Recipients

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Solid organ transplant recipients (SOTR) are at a higher risk of morbidity and mortality from COVID-19.[1] COVID-19 therapeutics have been used in ambulatory SOTR in an effort to avoid hospitalization and other morbidity.[2,3] However, because of the rapidly evolving distribution of SARS-CoV-2 variants throughout the course of the COVID-19 pandemic, many previously effective treatment options, including some monoclonal antibodies (mAbs), can no longer be used.[4] Bebtelovimab is a recombinant neutralizing IgG1λ mAb that targets the S-protein of SARS-CoV-2. In February 2022, based on the results from the BLAZE-4 study and data from in vitro neutralization assays, bebtelovimab received emergency use authorization by the Food and Drug Administration for the treatment of mild-to-moderate COVID-19. Unlike other mAbs that have been used for SARS-CoV-2 infection, bebtelovimab has been shown to retain activity against Omicron subvariants, including BA.1.1, BA.2, and BA.4/5.[5] However, it is considered only as alternative therapy by the National Institutes of Health COVID-19 Guidelines.[6]

In this Institutional Review Board-approved retrospective study, we identified 25 SOTR who were treated with bebtelovimab between February 11, 2022, and April 25, 2022, in the outpatient setting after testing positive for SARS-CoV-2. During the specified time period, SARS-CoV-2 infections were predominantly caused by either the Omicron BA.1 or BA.2 subvariant. The choice of treatment (bebtelovimab versus oral antiviral therapy versus symptom management) was at the discretion of the treating provider and dependent on time from symptom onset, drug availability, and relative contraindications due to patient considerations such as drug–drug interactions or renal insufficiency. Baseline characteristics are presented in Table 1. Of the 25 patients, 19 (76%) had completed their primary COVID-19 vaccination series. All 25 patients who received bebtelovimab met emergency use authorization

TABLE 1.

Baseline characteristics and 30-d outcomes for the full cohort (N = 25)

	Bebtelovimab (N = 25)
Age at time of COVID-19 symptom onset, y	52 (44–67)
Male sex	15 (60)
Organ transplant	
Kidney	15 (60)
Liver	5 (20)
Heart	3 (12)
Lung	0 (0)
Kidney/pancreas	2 (8)
BMI, kg/m^2	25.8 (22.5–29.4)
History of previous COVID-19 infection	1 (4)
Time from transplant to COVID-19 symptom onset, y	3.7 (1.5–9.3)
COVID-19 symptom severity[a]	
Asymptomatic	0 (0)
Mild	24 (96)
Moderate	1 (4)
Vaccinated[b]	19 (76)
Immunosuppressive agents administered within 6 mo before COVID-19 symptom onset	
Lymphocyte-depleting agent	2 (8)
High dose steroids[c]	2 (8)
Rituximab	0 (0)
Bortezomib	0 (0)
Maintenance immunosuppressive agents before COVID-19 symptom onset	
Tacrolimus, ng/mL	6 (5–7.5)
Everolimus, ng/mL	–
MMF equivalents, mg/d	1000 (1000–1500)
Azathioprine, mg/d	–
Prednisone, mg/d	5 (2.5–5)
Belatacept-containing regimen	0 (0)
Time from symptom onset to COVID-19 treatment, d	3 (2–4)
Outcomes at 30 d after treatment	
Time from symptom onset to any hospitalization, d	12 (11–13)
Hospital admission for any reason	2 (8)
Hospital admission due to COVID-19 disease progression	1 (4)
Acute kidney injury[d]	1 (4)
Allograft rejection	0 (0)
Mortality	0 (0)

Continuous variables reported as median (IQR), categorical variables reported as n (%).
[a]COVID-19 symptom severity defined by the National Institutes of Health.
[b]Received at least 3 doses of mRNA vaccine or 1 dose of adenoviral vector vaccine as per the Centers for Disease Control and Prevention.
[c]Defined as at least 1 mg/kg prednisone equivalents (associated with treatment of allograft rejection).
[d]Acute kidney injury defined according to the Acute Kidney Injury Network classification.
BMI, body mass index; IQR, interquartile range; MMF, mycophenolate mofetil.

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criteria at the time of treatment and had at least 30 d of follow-up. Patients received bebtelovimab at an average of 3 d from symptom onset (interquartile range, 2–4). Within 30 d of treatment, only one patient who received bebtelovimab was admitted due to COVID-19 progression. This was a kidney/pancreas transplant recipient who was admitted 4 d after receipt of bebtelovimab for a submassive pulmonary embolism that was thought to have been provoked in the setting of COVID-19. The patient was additionally treated with remdesivir and dexamethasone for risk of worsening oxygen requirements. Of note, this patient had been recently treated for acute cellular rejection with antithymocyte globulin 39 d before COVID-19 diagnosis. One other patient who was treated with bebtelovimab was hospitalized for obstructive uropathy and acute kidney injury with electrolyte derangements, though the patient never reported any upper or lower respiratory tract symptoms. No patients experienced acute allograft rejection or death during the 30-d follow-up period.

Bebtelovimab, which maintains activity against Omicron subvariants, represents a potentially safe and efficacious treatment option for SOTRs with mild-to-moderate COVID-19. Because of the retrospective, nonrandomized nature of this study and the absence of a comparator group, additional reports characterizing outcomes of ambulatory SOTR (that include lung transplant recipients) treated with bebtelovimab will help further clarify its place in therapy.

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