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SARS-CoV-2 Neutralizing Monoclonal Antibodies for the Treatment of COVID-19 in Kidney Transplant Recipients

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Key Points

- Early outpatient severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mAb treatment of coronavirus disease 2019 (COVID-19) in kidney transplant recipients was safe and well tolerated.
- COVID-19–related hospitalizations were fewer in the mAb group despite having greater risk factors for disease progression.
- Angiotensin-converting enzyme 2 receptor blocking activity of anti–SARS-CoV-2 IgG acquired from natural immunity was weak on initial and follow-up serology testing.

Abstract

Background Morbidity and mortality associated with coronavirus disease 2019 (COVID-19) infection in kidney transplant recipients are high and early outpatient interventions to prevent progression to severe disease are needed. SARS-CoV-2 neutralizing mAbs, including bamlanivimab and casirivimab-imdevimab, received emergency use authorization in the United States in November 2020 for treatment of mild to moderate COVID-19 disease.

Methods We performed a retrospective analysis of 27 kidney transplant recipients diagnosed with COVID-19 between July 2020 and February 2021 who were treated with bamlanivimab or casirivimab-imdevimab and immunosuppression reduction. We additionally identified 13 kidney transplant recipients with COVID-19 who had mild to moderate disease at presentation, who did not receive mAbs, and had SARS-CoV-2 serology testing available.

Results There were no deaths or graft failures in either group. Both infusions were well tolerated. Four of the 27 patients treated with mAbs required hospitalization due to COVID-19. Four of 13 patients who did not receive mAbs required hospitalization due to COVID-19. Patients who received mAbs demonstrated measurable anti–SARS-CoV-2 IgG with angiotensin-converting enzyme 2 (ACE2) receptor blocking activity at the highest level detectable at 90 days postinfusion, whereas ACE2 blocking activity acquired from natural immunity in the mAb-untreated group was weak.

Conclusions Bamlanivimab and casirivimab-imdevimab combined with immunosuppression reduction were well tolerated and associated with favorable clinical outcomes in kidney transplant recipients diagnosed with mild to moderate COVID-19.

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Introduction

Advances in supportive care and the identification of effective therapeutics have contributed to improved outcomes in patients hospitalized with coronavirus disease 2019 (COVID-19) (1,2). However, kidney transplant recipients remain at higher risk for COVID-19–associated complications and mortality (3,4). Compared with matched nontransplant patients, kidney transplant recipients experience a doubling of risk of COVID-19–related death after adjusting for age, body

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mass index, and other major comorbidities (5). Therefore, the identification of early interventions that can halt the progression from mild or moderate to severe COVID-19 is especially important in this vulnerable population.

Although there are several inpatient therapies, such as remdesivir, dexamethasone, tocilizumab, and baricitinib, that are available to treat patients with COVID-19 that require hospitalization, there are few outpatient therapeutic options for early intervention that could prevent the progression to severe disease. Like most transplant centers, we modify immunosuppression in kidney transplant recipients with COVID-19 (6). Our practice has been to reduce immunosuppression, usually by holding the antimetabolite immediately upon COVID-19 diagnosis (7). Since December 2020, we treated eligible kidney transplant recipients positive for COVID-19 with bamlanivimab. The increasing prevalence of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant CAL.20C in our region later prompted a change in our mAb treatment regimen from bamlanivimab to casirivimab-imdevimab in February 2021 (8).

Bamlanivimab is an mAb that binds with high affinity to the receptor-binding domain (RBD) of the SARS-CoV-2 spike protein on the viral surface. Casirivimab-imdevimab is a cocktail containing noncompeting, neutralizing human IgG1 antibodies that can bind simultaneously to different, nonoverlapping epitopes of the spike protein. Both drugs prevent virus entry into host cells by blocking the binding of the spike protein to the cell surface angiotensin-converting enzyme 2 (ACE2) receptor (9). On November 9, 2020, bamlanivimab received emergency use authorization (EUA) from the US Food and Drug Administration (FDA) for treatment of mild to moderate COVID-19 in outpatients at high risk of progressing to severe disease within 10 days of symptom onset (10). Casirivimab-imdevimab subsequently received EUA from the FDA later on November 21, 2020 (11). The European Medicine Agency's Committee for Medicinal Products for Human Use granted conditions of use for casirivimab-imdevimab and bamlanivimab on February 26 and March 5, 2021, respectively (12,13).

Here, we report our experience with bamlanivimab and casirivimab-imdevimab infusions combined with immunosuppression reduction for the treatment of COVID-19 in kidney transplant recipients.

Materials and Methods

We performed a retrospective analysis of kidney transplant recipients who were diagnosed with COVID-19 between July 2020 and February 2021. Demographic and clinical data were abstracted by review of electronic health records.

Patients

We abstracted data on kidney transplant recipients with COVID-19 who received treatment with either bamlanivimab or casirivimab-imdevimab under EUA. For comparison, data were also abstracted from kidney transplant recipients with mild to moderate COVID-19 at presentation who did not receive mAb treatment and had SARS-CoV-2 serology testing available. All patients had a functioning kidney transplant. Those who were on an antimetabolite (mycophenolate mofetil/mycophenolate sodium/azathioprine) were instructed to hold it at the time of COVID-19 diagnosis. Patients were eligible to receive either bamlanivimab (before February 10, 2021) or casirivimab-imdevimab (after February 10, 2021) if they met the FDA's EUA criteria (14), as outlined in Supplemental Table 1.

Diagnostic Testing

SARS-CoV-2 RT-PCR testing was performed on nasopharyngeal swab samples (Stanford Clinic Virology Laboratory) (15). IgM and IgG antibodies to the SARS-CoV-2 spike RBD were measured by ELISA. In patients with positive anti–SARS-CoV-2 IgG, the ability of the anti–SARS-CoV-2 IgG to block the binding of the SARS-CoV-2 RBD to the cell surface ACE2 receptor was assessed using an RBD-ACE2 competition ELISA developed by the Stanford Department of Pathology (16). This assay was developed as a functional assay to assess the quality, rather than the quantity, of antibodies against SARS-CoV-2. It has been compared with both the anti-RBD IgG assays and pseudovirus neutralization assays, and a strong correlation among them have been shown. The RBD-ACE2 competition assay is reported as a percentage of the SARS-CoV-2 RBD to ACE2 receptor blocking activity, where 0%–10% indicates the presence of little to no antibody blocking activity (comparable with a sample from an individual who has never been exposed to SARS-CoV-2), and 90%–100% indicates a high level of blocking activity.

Administration

Bamlanivimab and casirivimab-imdevimab were administered as a single outpatient intravenous infusion of 700 and 2400 mg, respectively, in 200–270 ml normal saline over 60 minutes with a 0.2–0.22 μm in-line polyethersulfone filter. All patients were monitored during infusion and for 1 hour after the infusion.

Statistical Analysis

Data are shown as numbers (percentages) for categoric variables and as medians (interquartile ranges [IQR]) for continuous variables.

This study was approved by the Stanford University Institutional Review Board (protocol number 59887, consent waiver). The clinical and research activities being reported are consistent with the Principles of the Declaration of Istanbul as outlined in the Declaration of Istanbul on Organ Trafficking and Transplant Tourism.

Results

Between July 2020 and February 2021, 27 patients met the EUA criteria (Supplemental Table 1) and received either bamlanivimab or casirivimab-imdevimab between December 2020 and February 2021. Thirteen patients who did not receive neutralizing antibody but had serologic data available were selected as the comparison group. Of these, seven patients met EUA criteria but did not receive either bamlanivimab or casirivimab-imdevimab due to their unavailability, five patients did not meet EUA criteria (had

Table 1. Patient demographic and clinical characteristics

Patient	Age (to Nearest Decade)	Lymphocyte-Depleting Therapy	Body Mass Index, kg/m^2	Sex	Diabetes Mellitus	Number of Other High-Risk Factors[a]	Maintenance Immunosuppression	Mycophenolate Mofetil Held, days	Symptom Onset to Diagnosis, days	Cycle Threshold of SARS-CoV-2 RT-PCR[b]	Symptom Onset to Infusion, days	Hospitalized	mAb	<1 Year Transplant
mAb (*N*=27)														
1	40	ATG	35.4	M	N	1	MMF/Tac	8	0	—	3	N	Bam	Y
2	30	ATG	41.3	F	N	1	MMF/Tac/Pred	20	0	—	8	N	Bam	N
3	50	ATG	32.0	F	Y	2	MMF/Tac/Pred	9	2	38.0	9	N	Bam	N
4	40	ATG	27.3	M	Y	1	MMF/Tac	25	(−2)	30.4	6	Y	Bam	Y
5	70	ATG	26.7	F	Y	2	MMF/Tac/Pred	13	1	—	5	N	Bam	Y
6	40	ATG/OBZ	28.5	M	N	0	MMF/Tac/Pred	16	(−1)	—	5	N	Bam	N
7	50	ATG/RTX	29.2	F	Y	1	MMF/Tac/Pred	16	7	—	9	N	Bam	Y
8	50	ATG	21.7	M	N	0	MMF/Tac/Pred	13	(−2)	—	1	N	Bam	N
9	30	ATG	30.4	M	N	0	MMF/Tac/Pred	13	2	—	5	N	Bam	N
10	80	ATG	25.8	M	N	1	Belatacept/Pred[c]	—	2	—	10	Y	Bam	N
11	60	ATG	23.5	F	N	0	MMF/Tac/Pred	17	0	—	3	N	Bam	N
12	70	ATG	19.4	F	N	1	MMF/Tac	13	2	17.3	8	N	Bam	N
13	40	ATG/RTX	35.1	F	N	0	Tac/Pred	—	2	—	4	N	Bam	N
14	60	ATG	30.0	M	N	0	MMF/Tac/Pred	14	1	15.7	3	N	Bam	N
15	30	ATG/RTX	39.7	F	N	1	MMF/Tac/Pred	17	3	—	5	N	Bam	N
16	40	—	23.2	M	Y	1	MMF/Tac	18	7	—	9	N	Bam	N
17	50	ATG	30.5	M	Y	1	MMF/Tac/Pred	9	2	15.6	2	N	Bam	N
18	30	ATG	22.1	M	N	0	MMF/Tac/Pred	13	0	—	3	N	Bam	N
19	70	ATG	33.3	F	N	1	Tac/Pred	—	1	—	7	N	Bam	N
20	70	—	26.0	M	N	1	MMF/Tac/Pred	8	1	—	8	N	Bam	N
21	60	ATG	28.1	M	N	0	MMF/Tac	13	3	—	6	N	CASIM	N
22	50	ATG	21.1	F	N	0	MMF/Tac/Pred	12	(−1)	—	4	N	CASIM	Y
23	30	ATG	26.0	M	N	0	MMF/Tac/Pred	20	0	—	1	N	CASIM	Y
24	60	ATG	23.5	M	Y	1	MMF/Tac/Pred	10	1	—	4	N	CASIM	Y
25[d]	30	ATG	22.5	F	N	0	MMF/Tac	11	6	—	10	N	CASIM	N
26	60	ATG	25.2	F	N	0	MMF/Tac/Pred	12	5	—	7	Y	CASIM	Y
27[d]	50	ATG/RTX	21.6	M	Y	1	MMF/Tac/Pred	16	8	—	10	Y	CASIM	N
No mAb (*N*=13)														
1	60	ATG	25.8	F	Y	1	MMF/Tac/Pred	48	14	—	—	Y	—	N
2	30	ATG/RTX	26.7	F	N	0	MMF/Tac/Pred	14	5	26.6	—	N	—	N
3	60	ATG	31.7	M	Y	1	MMF/Tac	16	4	16.5	—	Y	—	N
4	20	ATG/RTX	30.2	F	N	0	Tac	—	6	—	—	N	—	N
5	20	ATG/ALZ	20.2	F	N	0	MMF/Tac/Pred	14	0	28.4	—	N	—	Y
6	50	ATG	29.7	F	N	0	MMF/Tac/Pred	23	4	—	—	N	—	N
7	30	ATG/RTX	24.8	M	N	0	MMF/Tac/Pred	14	1	22.9	—	N	—	N
8	50	ATG	26.4	M	N	0	MMF/Tac	14	14	—	—	N	—	N

Table 1. (Continued)

Patient	Age (to Nearest Decade)	Lymphocyte-Depleting Therapy	Body Mass Index, kg/m^2	Sex	Diabetes Mellitus	Number of Other High-Risk Factors[a]	Maintenance Immunosuppression	Mycophenolate Mofetil Held, days	Symptom Onset to Diagnosis, days	Cycle Threshold of SARS-CoV-2 RT-PCR[b]	Symptom Onset to Infusion, days	Hospitalized	mAb	<1 Year Transplant
9	50	ATG	33.3	M	N	0	MMF/Tac/Pred	17	3	23.3	—	Y	—	N
10	50	ATG	35.1	F	N	1	MMF/Tac	11	3	—	—	Y	—	N
11	40	ATG	34.0	F	N	0	AZA/Tac/Pred	7	11	—	—	N	—	N
12	60	ATG	29.2	F	N	0	MMF/Tac	—	2	—	—	N	—	N
13	30	ATG/RTX	25.5	F	N	0	MMF/Tac/Pred	7	10	—	—	N	—	N

MMF, mycophenolate mofetil; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; ATG, antithymocyte Ig; M, male; N, no; Tac, tacrolimus; —, no data available/applicable; Bam, bamlanivimab; Y, yes; F, female; Pred; prednisone; OBZ, obinutuxumab (anti-CD20); RTX, rituximab (anti-CD20); CASIM, casirivimab-imdevimab; ALZ, alemtuzumab (anti-CD52); AZA, azathioprine.

[a]In addition to immunocompromised state, including BMI ≥35 kg/m^2, diabetes mellitus, age ≥65 years, and/or chronic respiratory disease.

[b]Data not available for all patients due to testing done at outside facilities.

[c]Delayed.

[d]Received full vaccination series before positive diagnosis.

Table 2. Summary of patient characteristics

Characteristics	mAb (N=27)[a]	No mAb (N=13)
Age, yr, median (IQR)	52 (37–61)	44 (32–54)
Female, *n* (%)	12 (44)	9 (69)
BMI, kg/m^2, median (IQR)	26.7 (23.2–30.5)	29.2 (25.7–32.5)
Diabetes, *n* (%)	8 (30)	2 (15)
Race, *n* (%)		
White (Non-Hispanic)	7 (26)	2 (15)
Hispanic	9 (33)	10 (77)
Black	1 (4)	0
Asian or Pacific Islander	10 (37)	1 (8)
Within 1-yr transplant, *n* (%)	8 (30)	1 (8)
Time from transplant, mo, median (IQR)	22 (8–68)	49 (26–63)
Number of additional high-risk factors, *n* (%)[b]		
0	11 (41)	10 (77)
1	14 (52)	3 (23)
≥2	2 (7)	0
Lymphocyte-depleting therapy, *n* (%)	25 (93)	13 (100)
ATG/anti-CD52	0	1 (8)
ATG/anti-CD52 within 1 yr	0	1 (8)
Anti-CD20	5 (19)	4 (31)
Anti-CD20 within 1 yr	1 (4)	0
Maintenance immunosuppression, *n* (%)		
MMF/Tac/Pred	18 (67)	7 (54)
MMF/Tac	6 (22)	4 (31)
Other	3 (11)	2 (15)
Duration of MMF/MPA/AZA held, d, median (IQR)	13 (11–17)	14 (8–17)
Symptoms, *n* (%)		
Fever	12 (44)	6 (46)
Cough	17 (63)	7 (54)
Muscle pain	12 (44)	5 (39)
Headache	11 (41)	2 (15)
Fatigue	7 (26)	6 (46)
Gastrointestinal	11 (41)	5 (39)
Shortness of breath	4 (15)	3 (23)
Loss of sense of taste/smell	2 (7)	3 (23)
Other (poor appetite, congestion, chest pressure, chills)	9 (33)	6 (46)
Symptom onset to diagnosis, d, median (IQR)	2 (1–3)	5 (3–11)
Symptom onset to initial serology, d, median (IQR)	5 (3–8)	18 (13–29)
Diagnosis to initial serology, d, median (IQR)	3 (2–6)	13 (9–19)
Ct values, median (IQR)[c]	17.3 (15.7–34.2)	23.3 (19.7–27.5)
AKI, *n* (%)	7 (26)	4 (31)
Symptom onset to infusion, d, median (IQR)	5 (3–8)	—

Categoric variables are presented as numbers (percentages). Continuous variables as medians (interquartile ranges). IQR, interquartile range; BMI, body mass index; ATG, antithymocyte Ig; anti-CD52, alemtuzumab; anti-CD20, obinutuxumab, rituximab; MMF, mycophenolate mofetil; tac, tacrolimus; pred, prednisone; MPA, mycophenolic acid; AZA, azathioprine; Ct, cycle threshold of SARS-CoV-2 RT-PCR tests; —, no data available/applicable.

[a]Bamlanivimab or casirivimab-imdevimab.

[b]Body mass index ≥35 kg/m^2, diabetes mellitus, age ≥65 years, and/or chronic respiratory disease.

[c]N=5 for each group.

symptoms present for >10 days), and one patient declined bamlanivimab treatment despite meeting EUA eligibility.

Demographic and clinical characteristics of both groups are shown in Table 1 and Table 2. Those in the mAb group had a shorter median time from transplant to SARS-CoV-2 infection, with a numerically higher number of risk factors for progression to severe COVID-19 as defined by the EUA. The median (IQR) time from COVID-19 symptom onset to positive diagnosis was two (1–3) days for the mAb group, with four patients developing symptoms after a positive SARS-CoV-2 RT-PCR test (Table 1). Mycophenolate mofetil/mycophenolate sodium/azathioprine was held for a similar duration of time between the two groups. The median (IQR) time from COVID-19 symptom onset to mAb treatment was five (3–8) days.

There were no deaths or graft failures in either group. After receiving bamlanivimab, one patient complained of transient and self-limiting chest tightness and another of headache; both resolved within 24 hours after the infusion. None of the seven patients who received casirivimab-

Table 3. AKI in mAb and no-mAb group

Characteristics	mAb (N=27)[a]	No mAb (N=13)
AKI, *n*	7	4
Baseline creatinine, mean±SD	1.4±0.4[b]	1.0±0.2
Creatinine at time of COVID-19 infection, mean±SD	1.5±0.5[b]	1.3±0.3[c]
Creatinine >2 weeks after COVID-19 infection, mean±SD	1.3±0.3[d]	1.0±0.2

Categoric variables are presented as numbers. Continuous variables as mean±SD. COVID-19, coronavirus disease 2019.
[a]Bamlanivimab or casirivimab-imdevimab.
[b]N=26.
[c]N=10.
[d]N=25.

imdevimab developed reactions. Four patients who received mAbs were subsequently hospitalized (two after receiving bamlanivimab and two after receiving casirivimab-imdevimab). Two were hospitalized with COVID-19 pneumonia later on the same day that they received their mAb treatment. One did not require intensive care and recovered to discharge after 3 days. The other patient did require monitoring in intensive care while on high-flow oxygen therapy but recovered to discharge on room air after 6 days. The third patient was admitted to hospital 3 days after bamlanivimab infusion with a foot cellulitis that was deemed unrelated to COVID-19. The fourth patient was admitted to hospital the day after receiving casirivimab-imdevimab with volume depletion and AKI in the setting of nausea, vomiting, and diarrhea. Four patients in the comparison group were hospitalized due to COVID-19. One was hospitalized for severe diarrhea and AKI. Three patients were admitted for acute hypoxic respiratory failure due to COVID-19 pneumonia about 1 week after symptom onset, with two out of the three patients requiring intensive care. Seven patients in the mAb group and four patients in the comparison group had AKI, which was defined as an elevation in serum creatinine either 1.5 times baseline or 0.3 mg/dl above baseline (17). AKI episodes were considered prerenal in the setting of COVID-19 gastrointestinal upset, occasionally exacerbated by supratherapeutic tacrolimus levels, in the majority of patients. Serum creatinine returned to baseline in all patients. There were no biopsy sample–proven rejections in either of the two groups. The trends in creatinine for all patients in both groups are illustrated in Table 3.

Initial and follow-up anti–SARS-CoV-2 IgM and IgG details are shown in Table 4 and Figure 1. In the mAb group, all but one patient with available pretreatment serology testing were anti–SARS-CoV-2 IgG seronegative (23 of 24 patients). Three patients did not have a pretreatment "baseline" anti–SARS-CoV-2 serology because blood work was inadvertently drawn immediately after infusion. Twenty-three patients had post-mAb serologies available, and all were anti–SARS-CoV-2 IgG seropositive with strong ACE2 receptor blocking activity. Seventeen of the 23 patients remained anti–SARS-CoV-2 IgM seronegative. Two of the 23 patients had further serologic testing up to 83 and 95 days post-treatment, which showed persistence of anti–SARS-CoV-2 IgG with strong ACE2 receptor blocking activity (Figure 1 and Table 4). In the comparison group, six of the 13 patients were seropositive for both IgM and IgG on initial testing, at a median (IQR) of 14 (11–19) days after diagnosis. One of the 13 patients was seropositive for IgG only on initial testing at 115 days after diagnosis. Five of the six patients who were seronegative on initial testing seroconverted on later testing at a median (IQR) of 40 (22–94) days after diagnosis. At both initial and follow-up testing, ACE2-blocking anti–SARS-CoV-2 IgG activity was weak in most patients who were not treated with mAbs.

Discussion

In this series, we found that bamlanivimab or casirivimab-imdevimab combined with immunosuppression reduction for outpatient treatment of mild to moderate COVID-19 in kidney transplant recipients was safe and associated with good outcomes. Only four of the 27 patients treated with mAbs required hospitalization for COVID-19. One of the 27 patients treated with mAbs required intensive care, whereas two of the 13 patients in the comparison group required intensive care. Hospitalization for COVID-19 complications was more frequent in the comparison group, despite fewer risk factors for disease progression than those treated with mAbs. The infusions of bamlanivimab and casirivimab-imdevimab were well tolerated. Only two of the 27 patients developed mild and self-limiting reactions postinfusion.

In the three clinical trials that have published findings on the use of SARS-CoV-2 neutralizing mAbs (bamlanivimab, casirivimab-imdevimab, and bamlanivimab-etesevimab) for outpatient treatment of mild to moderate COVID-19, solid-organ transplant recipients were excluded from the study cohort (18–20). Serologic testing after administration of SARS-CoV-2 neutralizing mAbs has also not been reported previously. Our findings are consistent with another US transplant centers' reported experience of using bamlanivimab and casirivimab-imdevimab in a small number of solid-organ transplant recipients positive for COVID-19, where none of the recipients required hospitalization for disease progression (21,22). Furthermore, the availability at our center of a functional assay to evaluate the ACE2 receptor blocking activity of anti–SARS-CoV-2 IgG allowed comparison of passive immunity with bamlanivimab and casirivimab-imdevimab versus natural immunity, and its evolution over time. High ACE2 receptor blocking activity of anti–SARS-CoV-2 IgG is suggestive of greater viral inhibition and immunologic protection. All

Table 4. Evolution of anti–SARS-CoV-2 IgM and IgG over time

Patient	Symptoms Onset to Initial Serology, days	Diagnosis to Initial Serology, days	Initial SARS-CoV-2 IgM	Initial SARS-CoV-2 IgG	Angiotensin-Converting Enzyme 2 Blocking Activity, %	Next SARS-CoV-2 IgM	Next SARS-CoV-2 IgG	Angiotensin-Converting Enzyme 2 Blocking Activity, %	Time Between Serologies, days	Last SARS-CoV-2 IgM	Last SARS-CoV-2 IgG	Angiotensin-Converting Enzyme 2 Blocking Activity, %	Time from Initial Serology, days
mAb (*N*=27)[a]													
1	3	3	Neg	Neg		—	—		—				
2	8	8	Neg	Neg		Neg	Pos	90–100	95				
3	9	7	Pos	Pos	90–100	Pos	Pos	90–100	7	Pos	Pos	90–100	75
4	6	8	Neg	Neg		Pos	Pos	90–100	5	Pos	Pos	90–100	21
5	5	4	Neg	Neg		Neg	Pos	90–100	10	Neg	Pos	90–100	59
6	5	6	Neg	Neg		Pos	Pos	90–100	11	Pos	Pos	90–100	58
7	9	2	Neg	Neg		Neg	Pos	90–100	15	Neg	Pos	80–90	41
8	1	3	Neg	Neg		Neg	Pos	90–100	9				
9	5	3	Neg	Neg		Neg	Pos	90–100	5				
10	10	8	Neg	Neg		Neg	Pos	90–100	9	Neg	Pos	90–100	32
11	3	3	Neg	Neg		—	—		—				
12	8	6	Neg	Neg		Neg	Pos	90–100	3	Neg	Pos	90–100	83
13	—	—	—	—		Neg	Pos	90–100	—				
14	3	2	Neg	Neg		Neg	Pos	90–100	7	Neg	Pos	90–100	29
15	5	2	Neg	Neg		Pos	Pos	90–100	9				
16	9	2	Neg	Neg		Neg	Pos	90–100	12				
17	—	—	—	—		Neg	Pos	90–100	—				
18	2	0	Neg	Neg		Neg	Pos	80–90	43				
19	3	3	Neg	Neg		—	—		—				
20	8	7	Neg	Neg		—	—		—				
21	6	3	Neg	Neg		Neg	Pos	90–100	4				
22	—	—	—	—		Neg	Pos	90–100	—				
23	0	0	Neg	Neg		Neg	Pos	90–100	15	Neg	Pos	90–100	25
24	4	3	Neg	Neg		Pos	Pos	90–100	7				
25	7	1	Neg	Neg		Neg	Pos	90–100	7				
26	4	(−1)	Neg	Neg		Pos	Pos	90–100	6				
27	10	2	Neg	Neg		Neg	Pos	90–100	3	Neg	Pos	90–100	11
No mAb (*N*=13)													
1	15	1	Neg	Neg		Neg	Pos	10–20	55				
2	16	11	Pos	Pos	20–30								
3	19	15	Pos	Pos	10–20	Pos	Pos	10–20	8	Pos	Pos	10–20	15
4	35	29	Pos	Pos	10–20								
5	7	7	Neg	Neg		Pos	Pos	10–20	12				
6	13	9	Neg	Neg		Pos	Pos	<10	14				
7	14	13	Neg	Neg		Pos	Neg		68				

Table 4. (Continued)

Patient	Symptoms Onset to Initial Serology, days	Diagnosis to Initial Serology, days	Initial SARS-CoV-2 IgM	Initial SARS-CoV-2 IgG	Angiotensin-Converting Enzyme 2 Blocking Activity, %	Next SARS-CoV-2 IgM	Next SARS-CoV-2 IgG	Angiotensin-Converting Enzyme 2 Blocking Activity, %	Time Between Serologies, days	Last SARS-CoV-2 IgM	Last SARS-CoV-2 IgG	Angiotensin-Converting Enzyme 2 Blocking Activity, %	Time from Initial Serology, days
8	27	13	Pos	Pos	90–100								
9	12	9	Pos	Pos	60–70								
10	5	2	Neg	Neg		Neg	Pos	10–20	130				
11	25	14	Pos	Pos	40–50								
12	117	115	Neg	Pos	40–50								
13	68	58	Neg	Neg									

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; neg, negative; —, no data available; pos, positive.
[a]Bamlanivimab or casirivimab-imdevimab.

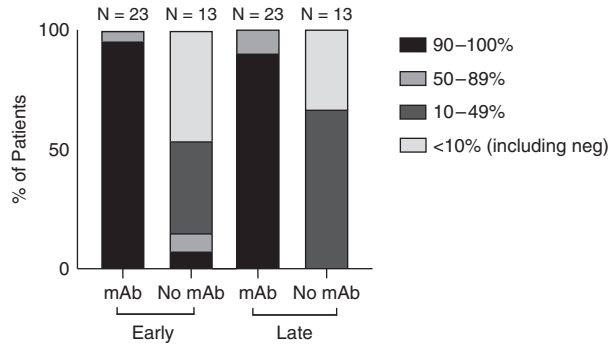

Figure 1. | High and sustained anti-SARS-CoV-2 IgG ACE2 blocking activity on early and late serologic testing in patients treated with mAb compared to non-mAb treated patients. ACE2, angiotensin-converting enzyme 2; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

patients who received either bamlanivimab or casirivimab-imdevimab with available postinfusion testing had measurable anti–SARS-CoV-2 IgG at the highest level of ACE2 receptor blocking activity detectable (90%–100%). In contrast, only one patient in the comparison group developed a similar level of ACE2 receptor blocking activity from natural immunity. Ten of the 13 patients in the comparison group eventually developed anti–SARS-CoV-2 IgG. Only four of these patients did not have detectable anti–SARS-CoV-2 IgM, and one of the four did not have detectable anti–SARS-CoV-2 IgM and IgG at day 58 postdiagnosis. This rate of seroconversion is consistent with reported findings of 51%–67% anti–SARS-CoV-2 IgG seropositivity in kidney transplant recipients with confirmed positive SARS-CoV-2 RT-PCR (23,24). Only one patient in the mAb group was seropositive for anti–SARS-CoV-2 IgM and IgG at first testing, compared with six of 13 patients in the non-mAb group. This may have been due to an earlier time of testing from symptom onset (median of 5 versus 18 days) in the mAb-treated versus nontreated groups. However, only five of 22 patients who received mAbs on subsequent testing had detectable anti–SARS-CoV-2 IgM antibodies. One possible explanation is that the early administration of either bamlanivimab or casirivimab-imdevimab impaired the host immune response by either reducing SARS-CoV-2 viral load or by directly inhibiting the virus-host immune interaction, resulting in a lower seroconversion rate. A better understanding of the durability and decay of bamlanivimab and casirivimab-imdevimab may be important when considering timing of subsequent vaccination against COVID-19.

The demonstration of a high ACE2 receptor blocking activity against SARS-CoV-2 achieved with bamlanivimab and casirivimab-imdevimab in our patient cohort additionally raises the possibility of using neutralizing antibodies for immunoprophylaxis in the peritransplant period, particularly in the context of emerging knowledge of the poor response to SARS-CoV-2 vaccination in the transplant patient population (21,25–28). In transplant patients with negative SARS-CoV-2 antibody titer after two doses of mRNA vaccine, humoral response to a third vaccine dose remained disappointing (29). Beginning June 30, 2021, the FDA has now expanded authorization for casirivimab-imdevimab to be given as postexposure prophylaxis for patients who are at high risk for progression to severe disease and either (*1*) not fully vaccinated, or (*2*) immunocompromised patients who are not expected to mount adequate immune response to complete SARS-CoV-2 vaccination and who have exposure to individuals who tested positive for COVID-19.

Our study has several strengths, including a sizable number of transplant recipients treated with bamlanivimab and casirivimab-imdevimab under the EUA, pre- and post-infusion serologic monitoring, availability of a functional quantitative antibody assay, and an untreated group in whom COVID-19 serologic testing was available for comparison. However, our study has several limitations. It is a nonrandomized, noncontrolled, observational, single-center study. The comparison group is not matched, which limits generalization. Specifically, some patients in the comparison group did not come to our attention until later in their illness and did not receive mAb treatment because they were outside of the 10-day symptom onset window for administration of the mAb. There was a greater number of Hispanic/Latino patients in the comparison group (75%) than the mAb group (33%), and Hispanic/Latino patients have been reported to have greater odds of COVID-19–related hospitalization and death, even after adjusting for socioeconomic differences (30). Another limitation is that we were unable to further trend the ACE2 receptor blocking activity levels because our patients started getting vaccinated against SARS-CoV-2 in March 2021. Comparing passive immunity to the intensity of adaptive immunity is limited, because other aspects of the immune response were not evaluated. Despite these limitations, comparison between the two groups could remain valuable because the patients without neutralizing antibody intervention may illustrate the natural evolution of the disease in this patient population.

In this review of our experience, we found the use of bamlanivimab and casirivimab-imdevimab under the EUA criteria to be safe and associated with favorable outcomes for the treatment of mild to moderate COVID-19 after kidney transplantation.

Disclosures

A.X. Wang reports receiving research funding from CareDx. S. Busque reports receiving honoraria from Genentech; having consultancy agreements with, and serving as a scientific advisor for, or member of, Genentech and Gigagen; and having ownership interest in Gigagen. G.M. Chertow reports having consultancy agreements with Akebia, Amgen, Ardelyx, AstraZeneca, Baxter, Cricket, DiaMedica, Gilead, Miromatrix, Reata, Sanifit, Unicycive, and Vertex; serving on data safety monitoring boards for Angion, Bayer, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), and ReCor; having ownership interest in Ardelyx, CloudCath, Durect, DxNow, Eliaz Therapeutics, Outset, Physiowave, and PuraCath; serving as coeditor of *Brenner & Rector's The Kidney* (Elsevier) and on the board of directors for Satellite Healthcare; and receiving research funding from the NIDDK and National Institute of Allergy and Infectious Diseases (NIAID). C.R. Lenihan reports receiving research funding from Astellas and CareDx, and honoraria from Veloxis. J.D. Scandling reports serving as a scientific advisor for, or member of, AlloVir; receiving

research funding and honoraria from CareDx; and having consultancy agreements with Horizon Pharma. U. Singh reports serving as a scientific advisor for, or member of, Gilead; and receiving honoraria from Gilead and Regeneron. All remaining authors have nothing to disclose.

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Authors Contributions

S. Busque, G.M. Chertow, J. Kuo, C.R. Lenihan, K. Röeltgen, J.D. Scandling, and A.X. Wang reviewed and edited the manuscript; S. Busque and C.R. Lenihan provided supervision; S. Busque, C.R. Lenihan, and A.X. Wang were responsible for formal analysis; S. Busque and A.X. Wang conceptualized the study; G.M. Chertow and U. Singh were responsible for funding acquisition; J. Kuo was responsible for resources; J. Kuo, C.R. Lenihan, and A.X. Wang were responsible for project administration; C.R. Lenihan and A.X. Wang were responsible for investigation and validation; B.A. Pinsky, K. Röeltgen, and A.X. Wang were responsible for methodology; and A.X. Wang wrote the original draft, and was responsible for data curation, software, and visualization.

Supplemental Material

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Supplemental Table 1. Bamlanivimab and casirivimab-imdevimab emergency use authorization.

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