

Monoclonal Antibody Therapy for SARS-CoV-2 Infection in Kidney Transplant Recipients: A Case Series From Belgium

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Kidney transplant recipients (KTRs) are particularly vulnerable to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and may remain at risk after complete vaccination because of poor response rate.^{1,2} Neutralizing monoclonal antibodies (Abs) have been shown to be safe and efficient in reducing viral load in immunocompetent outpatients with coronavirus disease 2019 (COVID-19).³ In immunocompromised patients, including solid organ transplant recipients, few reports have reported similar results.^{4,5}

In this article, we report the efficacy and safety of monoclonal Ab therapy (intravenous casirivimab 1200mg and imdevimab 1200mg, Regeneron Pharmaceuticals, Tarrytown, NY) in 12 KTRs infected by SARS-CoV-2 who

were treated in our center between June and September 2021. The study received institutional review board approval.

The mean age was 47 (range, 21–78) y and 6 patients (50%) were male (Table 1). The mean time from transplantation was 112 mo (range, 2–264). Eight patients (75%) were treated with an association of tacrolimus (Tac), mycophenolate (MPA), and steroids, and 4 patients (25%) were treated with dual therapy (Tac/MPA n=2; Tac/steroids n=1; Tac/azathioprine n=1). Ten patients had received 2 doses of the mRNA BNT162b2 (Pfizer-BioNTech), with a mean time of 111 (range, 39–200) d before SARS-CoV-2 infection. Two of the vaccinated patients had a prior history of COVID-19.

TABLE 1.

Characteristics of patients at SARS-CoV-2 infection

Patients	Age (y)	Gender Male/ Female	Delay from KT (mo)	IS at diagnosis	Prior vaccine (Y/N)	Last dose to infection delay (d)	Anti-RBD titer before diagnosis (BAU/mL)	Last titer to infection delay (d)	Symptoms	Viral load ($\times 10^6$ copies/mL)	Genotype
1	64	Male	264	Tac-MPA-St	Yes	57	0	13	F	10	Gamma
2	43	Female	60	Tac-MPA-St	Yes	85	10.6	49	C	28	Delta
3	52	Male	2	Tac-MPA-St	Yes	116	0	42	M	—	—
4	23	Male	55	Tac-MPA-St	Yes	99	257.22	45	C-R	36	Delta
5	31	Female	22	Tac-MPA-St	Yes	39	0	0	M	0.17	Delta
6	65	Female	133	Tac-MPA	No	—	—	0	F-H	6	Delta
7	43	Male	196	Tac-MPA-St	No	—	—	0	F-C	0.43	—
8	35	Female	190	Tac-AZA	Yes	200	257.22	75	F-C-H	—	—
9	78	Female	262	Tac-MPA	Yes	139	159.77	0	F-R	85	—
10	52	Female	69	Tac-St	Yes	119	5.35	0	F-C-H	9	—
11	21	Male	28	Tac-MPA-St	Yes	117	239.71	4	F	5.7	—
12	60	Male	61	Tac-MPA-St	Yes	139	1.31	34	F-C-D	18.8	—

AZA, azathioprine; BAU, binding antibody units; C, cough; D, diarrhea; F, fever; H, headache; IS, immunosuppressive drugs; KT, kidney transplantation; M, myalgia; MPA, mycophenolate; R, rhinorrhea; RBD, receptor-binding domain; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; St, steroids; Tac, tacrolimus.

Received 1 October 2021.

Accepted 4 October 2021.

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G.F., A.D., and N.K. participated in research idea, study design, and data analysis. G.F. participated in data acquisition. A.S. and B.K. performed analysis. A.S. performed statistical analysis. G.F., A.D., A.S., B.K., T.D., A.B., J.D.G., L.B., J.C.Y., E.G., and N.K. took care of the patients. All authors discussed and reviewed the article.

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ISSN: 0041-1337/20/00XXX-00

DOI: 10.1097/TP.0000000000003974

Out of the 7 patients who mounted a humoral response after vaccination, the mean anti-receptor-binding domain Ab titer (Elecsys anti-SARS-CoV-2, Roche Diagnostics GmbH, Mannheim, Germany; positive threshold ≥ 0.8 BAU/mL) was 133.03 (range, 1.31–257.22) BAU/mL, which was assessed a mean time of 22 (range, 0–75) d before infection.

Patients presented with mild symptoms (fever $n=8$; cough $n=6$; headache $n=3$; myalgia $n=3$; rhinorrhea $n=2$; diarrhea $n=1$) and tested positive for SARS-CoV-2 using polymerase chain reaction on nasopharyngeal swab. The mean time between the beginning of symptoms and diagnosis was 3.75 (range, 2–7) d. The mean viral load at diagnosis was 3.62×10^6 (range, 171×10^3 – 85×10^6) copies/mL. Viral genotyping (available for 5 patients) revealed the Delta variant ($n=4$) and the Gamma variant ($n=1$) according to World Health Organization nomenclature.

MPA was discontinued for 10 d in all patients. Nine patients were discharged the day of the diagnosis after receiving the Ab therapy. Three patients were hospitalized, and interestingly, the 2 unvaccinated KTRs required oxygen supplementation for 24 h. All were discharged the day after.

One patient experienced a mild allergic reaction during Ab infusion that required a brief interruption of the perfusion. No other side effect was reported.

The follow-up consisted of a repeated polymerase chain reaction on nasopharyngeal swab 7 d after treatment administration. The viral load was <1000 copies/mL in all patients. All KTRs reported a rapid resolution of symptoms and none necessitated a new hospitalization.

Our results show that monoclonal Ab therapy is safe and associated with favorable outcomes in SARS-CoV-2-infected KTRs. Additional studies are required to assess the efficacy of this treatment in larger cohorts and in more severe forms of COVID-19 infection.

REFERENCES

1. Caillard S, Thauinat O. COVID-19 vaccination in kidney transplant recipients. *Nat Rev Nephrol*. [Epub ahead of print. September 27, 2021]. doi:10.1038/s41581-021-00491-7
2. Georgery H, Devresse A, Yombi J-C, et al. Disappointing immunization rate after two doses of the BNT162b2 vaccine in a Belgian cohort of kidney transplant recipients. *Transplantation*. [Epub ahead of print. June 24, 2021]. doi:10.1097/TP.0000000000003861
3. Weinreich DM, Sivapalasingam S, Norton T, et al; Trial Investigators. REGN-COV2, a neutralizing antibody cocktail, in outpatients with Covid-19. *N Engl J Med*. 2021;384:238–251.
4. Catalano C, Servais S, Bonvoisin C, et al. Preemptive antibody therapy for vaccine breakthrough SARS-CoV-2 infection in immunocompromised patients. *Transplantation*. [Epub ahead of print. August 27, 2021]. doi:10.1097/TP.0000000000003942
5. Del Bello A, Marion O, Vellas C, et al. Anti-SARS-CoV-2 monoclonal antibodies in solid-organ transplant patients. *Transplantation*. 2021;105:e146–e147.