



Early treatment with sotrovimab monoclonal antibody in kidney transplant recipients with Omicron infection

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In patients (57.8% men, median age 72 [56; 79] years), 15.6% had a history of immunosuppression (Supplementary Table S1). At 15 [14; 22] days after the fourth “booster” dose, antispikes Ab titer significantly increased from 923 [369; 2019] to 21,883 [10,234; 42,870] AU/ml (Figure 1; Supplementary Figure S3), which corresponds to a 19-fold increase (median) in antispikes Ab titer. Ab titer after the fourth dose was 3.4-fold higher (median) than the Ab peak reached after the third dose. Dose 4 appeared well-tolerated (Supplementary Figure S4), and no serious adverse event was observed. After the fourth dose, only 2 patients developed a breakthrough infection (vs. 7 cases of coronavirus disease 2019 after the third dose; Supplementary Table S2).

To conclude, our finding shows that a 3-dose regimen of an mRNA-based vaccine with a fourth booster dose appears to produce an important antibody response in dialysis patients, with a significant increase in antispikes Ab titer. Long-term follow-up studies are needed to assess if this vaccination strategy elicits a durable and robust protective immune response against SARS-CoV-2 in dialysis patients.

DATA STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

DISCLOSURE

All the authors declared no competing interests.

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AUTHOR CONTRIBUTIONS

PH and A-LF researched the idea, created the study design, acquired the data, and analyzed and interpreted the data. A-LF provided statistical analyses. SK performed the antispikes serology testing. Each author contributed important intellectual content during manuscript drafting or revision.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Supplementary questionnaire on vaccine reactions and global tolerance after the fourth vaccine dose.

Table S1. Characteristics of the study population.

Table S2. Characteristics of the patients with breakthrough coronavirus disease 2019 (COVID-19) after the third or the fourth vaccine dose during the fifth wave pandemic.

Figure S1. Vaccination strategy in dialysis patients.

Figure S2. Flowchart.

Figure S3. Kinetics of the antispikes antibodies.

Figure S4. Self-reported tolerance.

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Early treatment with sotrovimab monoclonal antibody in kidney transplant recipients with Omicron infection



To the editor: Early data about coronavirus disease 2019 (COVID-19) related to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron variant (B.1.1.529) suggest that it may be less severe than prior variants of concern in the general population.^{1–3} However, our preliminary data (NC, personal communication, January 28, 2022) about Omicron infection in kidney transplant recipients (KTRs) suggest that the disease is associated with severe forms in this vulnerable population with low postvaccinal immune responses.

Sotrovimab monoclonal antibody has been demonstrated to reduce disease progression in high-risk patients with mild-to-moderate COVID-19 before the Omicron era.⁴ Recent studies assessed that, in contrast with other monoclonal antibodies, it remained active against the Omicron spike.⁵

We aimed to compare the clinical outcomes of the first 25 KTRs treated with sotrovimab for mild-to-moderate Omicron COVID-19 with KTRs who did not receive sotrovimab.

Sotrovimab was available in our institution (Necker Hospital, Paris, France) from January 25, 2022. KTRs with a high risk for progression of COVID-19 (because of older age [≥ 55 years] or because they had at least 1 of the following risk factors: diabetes, obesity [body mass index >30 , estimated glomerular filtration rate <30 ml/min], coronary artery

Table 1 | Baseline and COVID-19 characteristics of KTRs infected with Omicron variant who received or not sotrovimab

Variables	Sotrovimab-treated KTRs (N = 25)	Nonsotrovimab-treated KTRs (N = 100)	P
Age, median (IQR)	54 (46–62)	53 (37.8–52)	0.599
Sex (males), n (%)	21 (84.0)	54 (54.0)	0.006
BMI, kg/m ² , median (IQR)	24 (22–25.6)	25.5 (22.6–30)	0.162
BMI >30 kg/m ² , n (%)	2 (8.0)	23 (24.5)	0.101
Hypertension, n (%)	20 (80.0)	81 (82.7)	0.773
Coronary artery disease, n (%)	6 (24.0)	13 (13.3)	0.217
Diabetes mellitus, n (%)	8 (32.0)	34 (34.7)	1.000
Chronic lung disease, n (%)	5 (20.0)	4 (4.1)	0.017
eGFR <30 ml/min per 1.73 m ² , ^a n (%)	8 (32.0)	7 (7.1)	0.003
KT >1, n (%)	5 (20.0)	21 (21)	1.000
Induction immunosuppressive therapy, n (%)			
Antithymocyte globulin	7 (31.8)	46 (46)	0.246
Basiliximab	14 (63.6)	44 (44)	0.105
Rituximab at induction	4 (16)	8 (8)	0.256
Maintenance immunosuppressive therapy			
Calcineurin inhibitors, n (%)	20 (80.0)	75 (75.0)	0.794
Azathioprine, n (%)	2 (8.0)	6 (6.0)	0.660
Mycophenolic acid, n (%)	18 (72.0)	84 (84.0)	0.246
Dose, mg/d, median (IQR)	1000 (1000–1500)	1000 (1000–1500)	0.407
mTOR-i (everolimus), n (%)	1 (4.0)	3 (3.0)	1.000
Steroids, n (%)	24 (96.0)	96 (96.0)	1.000
Dose, mg/d, median (IQR)	8 (6–10)	7.5 (5–10)	0.179
Belatacept, n (%)	3 (12.0)	21 (21.0)	0.402
Anti-SARS-2 mRNA vaccination (Pfizer–BioNTech), n (%)	23 (92.0)	88 (92.6)	1.000
1 injection	1 (4.0)	1 (1.1)	0.377
2 injections	1 (4.0)	5 (5.3)	1.000
3 injections	16 (64)	58 (61.1)	0.822
4 injections	3 (12.0)	24 (25.3)	0.188
Positive serology at Omicron infection, n (%)	7/23 (30.4)	21/45 (46.7)	0.298
Anti-S titer, BAU/ml	192 (30–744)	260 (60–1010)	0.349
Previous history of COVID-19, n (%)	2 (8.0)	13 (13)	0.734
Characteristics of Omicron infection			
Time between KT and Omicron infection, yr, median (IQR)	7 (5–14)	6 (2.8–11)	0.140
Clinical symptoms at presentation, n (%)	N = 23	N = 86	
Cough	16 (69.6)	46 (51.1)	0.236
Asthenia	10 (43.5)	45 (50.0)	0.489
Fever	14 (60.9)	37 (41.1)	0.160
Rhinitis	6 (26.1)	36 (40.0)	0.229
Myalgia	5 (21.7)	31 (34.4)	0.223
Sore throat	8 (34.8)	30 (33.3)	1.000
Diarrhea	5 (21.7)	23 (25.6)	0.791
Headache	9 (39.1)	22 (24.4)	0.206
Dyspnea	0 (0)	15 (16.7)	0.037
Asymptomatic	2 (8.7)	7 (7.8)	1.000
Time between symptom onset and sotrovimab injection, d, median (IQR)	5 (3–9)	–	–
Follow-up after infection, d, median (IQR)	30 (27–34)	20 (11–27)	0.011

BAU, binding antibody units; BMI, body mass index; COVID-19, coronavirus disease 2019; eGFR, estimated glomerular filtration rate; IQR, interquartile range; KT, kidney transplantation; KTRs, kidney transplant recipients; mTOR, mammalian target of rapamycin; S, spike.

^aDetermined with the Modification of Diet in Renal Disease equation.

Bold values of $P < 0.05$ were considered statistically significant.

disease, or chronic lung disease) who presented with mild-to-moderate Omicron COVID-19 after this date were treated with sotrovimab (a single 500-mg, 1-hour infusion). The control group consisted of the first 100 consecutive KTRs who experienced Omicron infection before January 25. We excluded patients who received pre-exposure prevention with tixagvimab/cilgavimab.

A total of 25 patients (21 men [84%], median age of 54 years, interquartile range: 46–62 years) who developed an Omicron infection between January 14 and February 13, 2022, received sotrovimab (Table 1). Sixteen of 23 (69.6%)

patients with available data had a COVID-19 serostatus predictive of a poor protection against Omicron (seronegative or weakly seropositive [<264 binding antibody units/ml] and/or treated with casirivimab/imdevimab). Antibody titers of seropositive patients are available in [Supplementary Table S1](#)). No infusion-related reaction was observed. Median time between symptom onset and sotrovimab infusion was 5 (interquartile range: 3–9) days. (Eight patients [32%] were treated after day 5 [up to day 13] of symptom onset.) Although sotrovimab-treated patients presented more risk factors associated with severe COVID-19 (significantly more

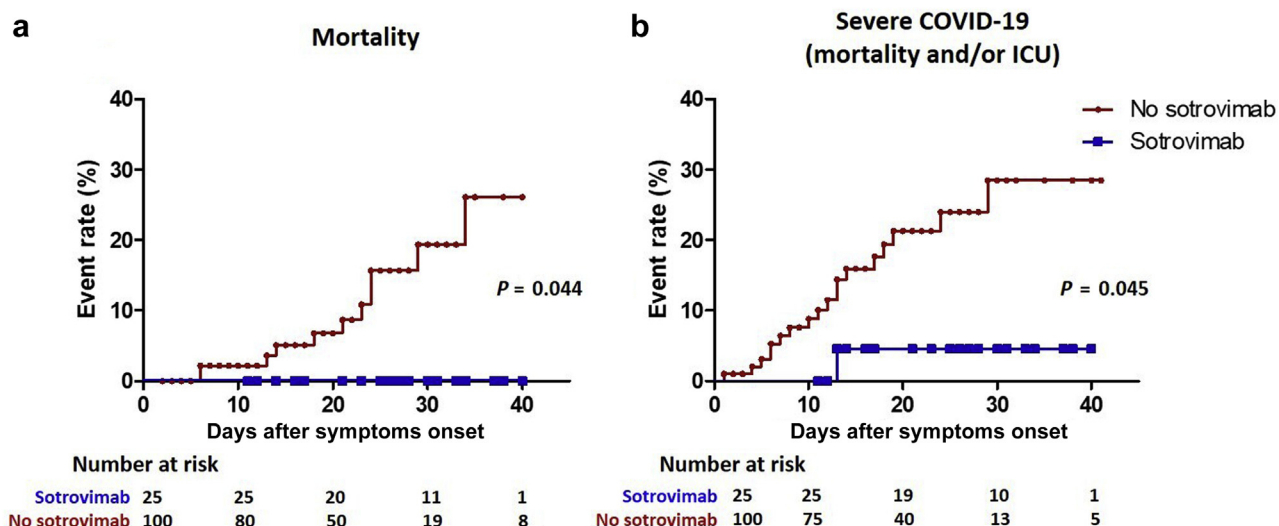


Figure 1 | Kaplan-Meier curves representing (a) mortality and (b) severe Omicron coronavirus disease 2019 (COVID-19) in kidney transplant recipients infected with Omicron variant and treated or not with sotrovimab.

men and more underlying comorbidities; Table 1), Omicron infection was less severe (less mortality and less severe disease [mortality and/or intensive care unit admission]) compared with controls (Figure 1). In the sotrovimab group, 4 (16.0%) patients were hospitalized, of whom, 1 patient required intensive care unit admission and no patients died. The patient admitted in intensive care unit received sotrovimab at day 11 after symptom onset. In contrast, 35 patients (35%) were hospitalized for Omicron disease in the control group. Among them, 17% required intensive care unit admission (9% needed mechanical ventilation) and 11% died.

Omicron infection appears to be severe in KTRs. Our study reports the first cohort of KTRs treated with sotrovimab for Omicron infection. Although these patients presented high risk for progression to severe disease, the severity of COVID-19 was lower than the historical control group, concordant with findings in the general population. Interestingly, the rate of patients with SARS-CoV-2-positive immune response was similar (and low) in both groups.

Despite its retrospective character and the relatively short follow-up, our findings show that the sotrovimab-neutralizing anti-SARS-CoV-2 antibody can prevent severe COVID-19 in KTRs infected with the Omicron variant and can be safely proposed in outpatient KTRs.

DATA STATEMENT

The data that support the findings of this study are available from the corresponding author at Nathalie.chavarot@aphp.fr.

DISCLOSURE

All the authors declared no competing interests.

SUPPLEMENTARY MATERIAL

[Supplementary File \(Word\)](#)

Table S1. Antispike titers in postvaccinal seropositive kidney transplant recipients treated or not with sotrovimab.

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Management of refractory lupus nephritis: rationale to consider tacrolimus



To the editor: We read with great interest the review article by Mejia-Vilet *et al.* about the management of lupus nephritis (LN).¹ The authors mentioned that few uncontrolled studies had evaluated tacrolimus in combination with mycophenolate mofetil for LN.¹ In a recent prospective observational study from our group, similar proportions of patients with refractory LN treated with tacrolimus ($n = 12$) or treatment-naïve LN treated with cyclophosphamide (Euro-Lupus Nephritis Trial protocol; $n = 16$) attained at least partial kidney response at 3 months of therapy (risk ratio for refractory vs. treatment-naïve LN, 1.07; 95% confidence interval, 0.61–1.85).² Moreover, tacrolimus significantly reduced P-glycoprotein expression and function on peripheral blood mononuclear cells in refractory LN 3 months after treatment.² A subset of T helper cell 17 (Th17) lymphocytes expressing both interleukin-17A and interferon- γ (Th17.1 lymphocytes) has been recently identified in LN and other immune-mediated inflammatory diseases.^{3,4} Th17.1 lymphocytes are refractory to corticosteroids due to P-glycoprotein expression. Tacrolimus might be useful in a subset of refractory LN by blocking P-glycoprotein on T lymphocytes, including possibly Th17.1 lymphocytes.² Therefore, we suggest the exploration of tacrolimus or other calcineurin inhibitors, such as voclosporin, in refractory LN. Future studies might also prospectively evaluate tacrolimus or voclosporin on Th17.1 lymphocyte frequency and P-glycoprotein expression in LN.

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Ecuzumab impairs killing of *Neisseria meningitidis* serogroup B in atypical hemolytic uremic syndrome patients vaccinated with MenB-4C



To the editor: Recent reports suggest that ecuzumab may not only compromise MenB-4C vaccination-induced serum killing of meningococci, but also opsonophagocytic killing.^{1,2} Using pre- and postvaccination serum from 5 patients with atypical hemolytic uremic syndrome (aHUS) on treatment with ecuzumab and 2 controls (Supplementary Table S1), we showed that vaccination increased MenB-specific IgG (Figure 1a) and complement C3 binding to the bacterial surface (Figure 1b), which confirmed an effective anti-MenB vaccine response.

A high level of C5b-9 formation as a measure of terminal complement pathway activation was observed using postvaccination serum from controls, whereas this was 10-fold lower using postvaccination serum from patients with aHUS (Figure 1c), which resulted in defective serum-mediated and whole blood-mediated killing in comparison with controls (Figure 1d and e). Vaccine-induced IgG-dependent serum-mediated and whole blood-mediated killing was restored to levels like controls when ecuzumab was discontinued (Figure 1f–h). Altogether, our results suggest that vaccination with MenB-4C does not increase opsonophagocytosis of MenB in serum from patients with aHUS at the time of ecuzumab usage.

The lack of whole blood-mediated killing of MenB suggests that patients with aHUS using ecuzumab remain vulnerable to meningococcal infection, but this might be reversed after ecuzumab withdrawal. Subtherapeutic C_{trough} levels could be beneficial when vaccine-induced antibodies increase complement activation during infection in patients with aHUS. Although various studies showed that it is safe and effective to temper or discontinue ecuzumab treatment in patients with aHUS, in-depth studies are needed to look at the effect of lowering C_{trough} levels to prevent severe infections, but still reducing the risk of aHUS relapse.^{3,4}

It remains important to state that concerning today's knowledge in the treatment of aHUS patients with ecuzumab and in the prevention of invasive meningococcal infections, the use of preventive antibiotics and/or immediate supply of antibiotics in case of signs of systemic infection is an urgent advice.