Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

SUPPLEMENTARY MATERIAL

Supplementary File (Word)

Table S1. Characteristics of the patients who underwent belatacept withdrawal.

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REGEN-Cov antibody combination to prevent COVID-19 infection in kidney transplant recipient without detectable antibody response to optimal vaccine scheme

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To the editor: Many kidney transplant recipients (KTRs) do not respond to an anti–severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine. Indeed, concordant data indicate that about 30% of KTRs do not develop antibodies after 3 doses of mRNA vaccines.[1,2] However, KTRs are at a high risk of severe forms of coronavirus disease 2019 (COVID-19) infection. Mortality rates are reported to reach 15% to 20%, and the need for hospitalization in an intensive unit care is even more likely.[3]

In this setting, consideration for an alternative prevention strategy of COVID-19 infection is particularly required. Recently, the REGEN-Cov antibody combination (casirivimab + imdevimab; Regeneron Pharmaceuticals) has been proven to be efficient to prevent infection in persons at risk for infection because of household exposure to a person with SARS-CoV-2 infection.[4]

Nevertheless, no data are available for preexposition prevention in patients at risk.

The French government recently authorized the use of REGEN-Cov to prevent COVID-19 infection in immunocompromised patients without any antibody response after 3 doses of anti–SARS-CoV-2 vaccine (https://www.has-sante.fr/jcms/p_3281999/fr/covid-19-autorisation-d-acces-precoce-accordee-a-un-traitement-prophylactique).

We report the use of REGEN-Cov in preexposition prevention in KTRs.

Among 402 KTRs having received 3 doses of vaccines and for whom serology was available, 119 (29.6%) had no antibody response (anti-S titer < 50 arbitrary units [AU]; SARS-CoV-2 immunoassay; Abbott; designed to detect IgG antibodies to the receptor-binding domain of the S1 subunit of the spike protein of SARS-CoV-2). Preexposition prevention was proposed to all of them.

During the study period, the delta variant accounted for >99% of COVID-19 cases. REGEN-Cov is effective against the delta variant.[5]

The first dose of REGEN-Cov (1200 mg) was administered i.v. The subsequent doses (600 mg) were administered s.c. every 4 weeks. Nasopharyngeal swabs were obtained for patients to test for SARS-CoV-2 by quantitative reverse transcription polymerase chain reaction before each administration of REGEN-Cov. Anti-S antibodies were also measured before each treatment.

Ninety-one patients (76%) accepted, whereas 28 refused. Among the 91 patients, only 88 received a first dose of

Table 1 | Characteristics of study patients

Characteristics	Participants (n = 88)	Nonparticipants (n = 31)	*P* value
Age, yr	62 [55–70]	61 [51–70]	0.973
Sex, % male	63	59	0.664
Transplant vintage, mo	29 [14–91]	158 [60–194]	0.145
eGFR, ml/min per 1.73 m^2	48 [30–68]	47 [31–79]	0.352
CNI use, %	81	74	0.629
MPA use, %	81	84	0.695
mTORi use, %	8	10	0.767
Belatacept use, %	10	10	0.928

CNI, cancineurin inhibitors; eGFR, estimated glomerular filtration rate; MPA, mycophenolic acid; mTORi, mammalian target of rapamycin.
Data are presented as median [interquartile range], 25th–75th interquartiles.

REGEN-Cov. One experienced COVID-19 infection 3 days before the scheduled perfusion of REGEN-Cov, and 2 declined treatment after initial acceptance.

Characteristics of the patients are depicted in Table 1.

All of the 88 patients received at least 2 maintenance injections after the initial perfusion. No patient reported having been in contact with a COVID-19–positive person. No adverse effect was observed in any patient. No acute rejection occurred during the study period. Immunosuppressive treatment was not modified.

During treatment, anti-S antibody titers were >40,000 AU in all patients.

During the observed period, no patient of the prophylaxis group developed COVID-19 infection. By contrast, in those without prevention, 5 (16%; $P < 0.001$) experienced COVID-19 infection, and 2 of them required hospitalization in intensive care unit. One died 3 weeks after admission.

REGEN-Cov is safe in preexposition prevention in KTRs without detectable vaccine response. High antibody titers are achieved in all patients. Preliminary data suggest efficient prevention of COVID-19 infection in this high-risk population.

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Daratumumab for multidrug-resistant phospholipase-A2 receptor–related membranous nephropathy

To the editor: At least 10% of patients with anti–phospholipase-A2 receptor antibody (aPLA2R)–associated membranous nephropathy do not attain immunologic remission with standard therapies. Anti–plasma cell therapy with bortezomib has been suggested.[1,2] We report the disease course in a patient treated with daratumumab, a human monoclonal anti-CD38 antibody approved for treatment of multiple myeloma and amyloid light-chain amyloidosis.

Our patient (a woman, aged 38 years) was diagnosed with membranous nephropathy in 2016. Subsequent treatment with mycophenolate mofetil/prednisolone and rituximab (cumulative dose, 4 g) did not induce immunologic or clinical remission. Cyclophosphamide and bortezomib/dexamethasone were largely ineffective because of drug intolerance. Although, after bortezomib, a rapid decline of aPLA2R was noticed, and severe adverse effects forced us to withdraw therapy (details in Supplementary Table S1).

Introduction of daratumumab (weekly doses of 16 mg/kg i.v.) resulted in a rapid decrease of aPLA2R, followed by clinical improvement. Extending the interval to 2 and 4 weeks (dose schedule used in hematological disease) resulted in a steady increase in aPLA2R (Figure 1). Immune cell phenotyping showed a marked increase in naive B cells and undetectable plasma cells (Supplementary Figure S1). These findings are possibly related to B-cell hyperreactivity, which is also seen in other autoimmune diseases,[3] and led us to withdraw daratumumab and reintroduce rituximab (2 g), resulting in a rapid and long-lasting reduction of aPLA2R. Seven months after rituximab, the patient is in partial clinical remission with stable kidney function.

In conclusion, anti–plasma cell therapy with daratumumab induced a rapid clinical and immunologic remission; however, the effect was short-lasting, likely related to the rapid proliferation of B cells. We cannot exclude that continued therapy with bortezomib would also have been effective (see Supplementary Discussion). Our data suggest that combination therapy (anti-plasma and anti–B cell) may be most effective. Prospective studies are needed to define the best type and/or combination of anti–plasma cell and anti–B cell therapy.

SUPPLEMENTARY MATERIAL

Supplementary File (Word)