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.

Efficacy of anti–SARS-CoV-2 monoclonal antibody prophylaxis and vaccination on the Omicron variant of COVID-19 in kidney transplant recipients

To the editor: Solid organ transplantation (SOT) recipients are at very high risk of developing severe coronavirus disease 2019 (COVID-19).[1] Despite the implementation of a third dose of mRNA vaccine, the efficacy of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination on humoral and cellular immunities is reduced in this population,[2] resulting in increased incidence of severe infection and mortality, including in fully vaccinated patients.[3] In this context, monoclonal antibodies (mAbs) providing passive immunization have been developed to enhance immunity against SARS-CoV-2 in immunocompromised patients.[4] The results of a very recently published randomized trial support the use of a single i.m. dose of Evusheld (tixagevimab/cilgavimab; AstraZeneca) for the prevention of symptomatic and severe COVID-19 (mainly the Alpha, Beta, and Delta strains of SARS-CoV-2), but a relatively small number of immune-suppressed patients and chronic kidney disease patients were included.[5] However, although clinical data remain very scarce, several *in vitro* studies have suggested that mAbs may have reduced efficacy against recent variants, especially Omicron[6]—the effect of casirivimab-imdevimab was likely to be lost, and that of tixagevimab/cilgavimab was reduced (to an uncertain degree), which led the US Food & Drug Administration to recommend use of a higher dose.

In France, prophylactic use of mAbs (Ronapreve [casirivimab-imdevimab], from September 12, 2021; Evusheld [tixagevimab/cilgavimab], from December 2021) is recommended in solid organ transplantation patients with a complete vaccine scheme and no or weak humoral response (<264 binding antibody units [BAU]/ml)[7] 1 month after the last injection. Here, we report the occurrence and severity of COVID-19 in 860 fully vaccinated kidney transplant recipients (KTRs) between December 23, 2021 and March 7, 2022, during the Omicron outbreak, from a single kidney transplantation center. During the study period, the BA1 variant was predominant, until February 14, 2022, and then BA2 became predominant.[8] Baseline characteristics of the

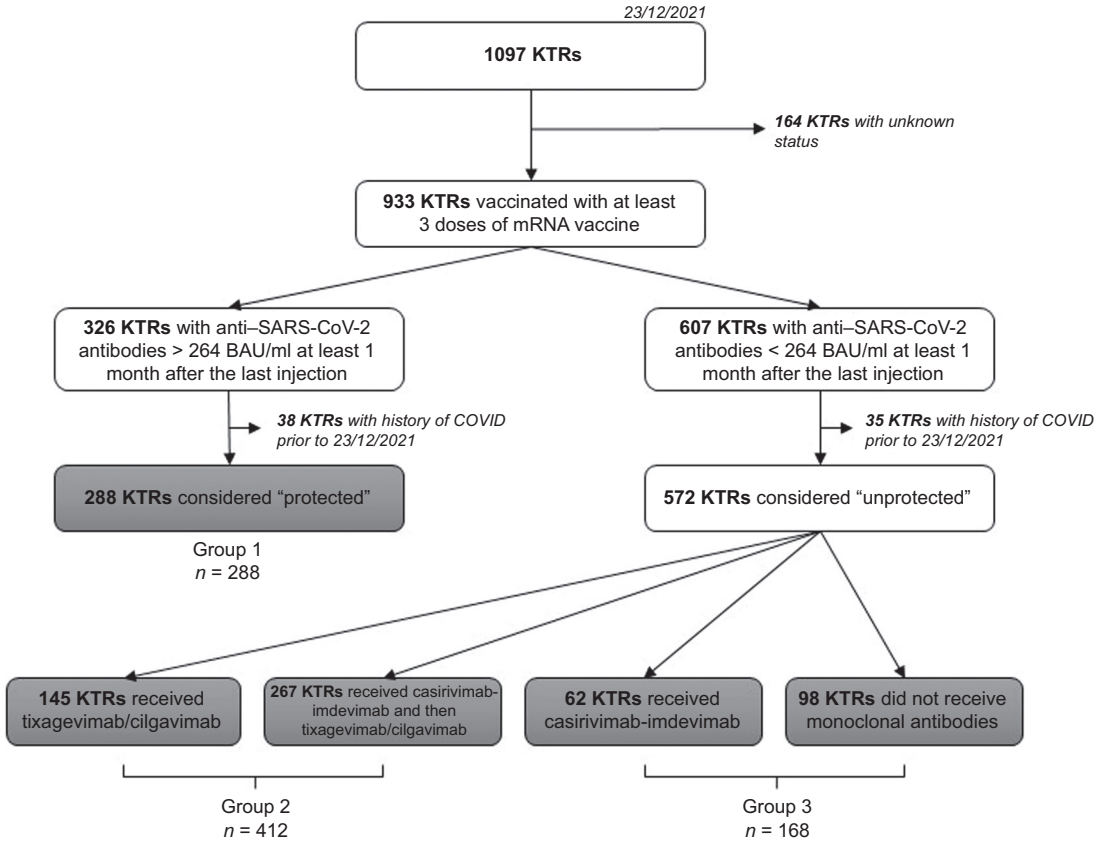

Figure 1 | Flowchart. BAU, binding antibody unit; COVID, coronavirus; KTRs, kidney transplant recipients. SARS-CoV-2, severe acute respiratory syndrome coronavirus-2.

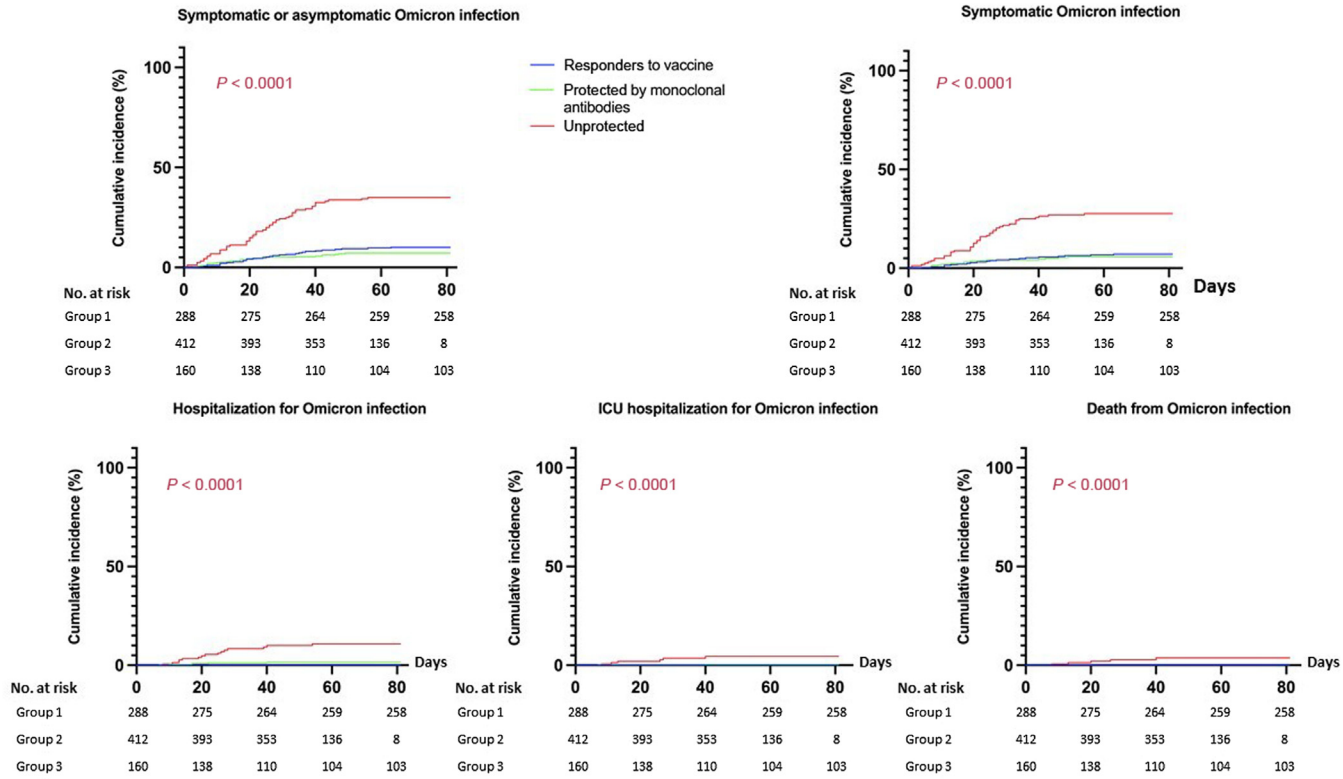

Figure 2 | Cumulative incidence of Omicron infection. Log rank test was used to compare the 3 groups, andresults were considered significant when $P < 0.05$. ICU, intensive-care unit.

study population are summarized in Supplementary Table S1. All patients were instructed to systematically report potential symptoms of COVID-19 and/or the positivity of a nasopharyngeal swab for SARS-CoV-2. Outcomes were studied according to immunization status, as described in Figure 1, as follows:

- group 1: vaccine-induced immunization, 288 patients;
- group 2: passive immunization with tixagevimab/cilgavimab, 412 patients. In this group, 267 KTRs received casirivimab-imdevimab as a first step of protection before receiving tixagevimab/cilgavimab. All KTRs of group 2 received 2 i.m. injections of 150 mg tixagevimab + 150 mg cilgavimab between December 23, 2021 and February 7, 2022; and
- group 3: insufficient immunization, 160 patients. In this group, 62 received casirivimab-imdevimab.

During follow-up, 113 patients (13.1%) presented an Omicron infection, of which 85 were symptomatic (from December 23, 2021 to February 14, 2022—103 cases of infection [91.2%]; from February 14, 2022 to March 7, 2022—10 cases of infection [8.8%]). Twenty-one patients required hospitalization, including 8 in the intensive care unit. Five patients died of COVID-19. The occurrence of infection, symptomatic infection, hospitalization, intensive care unit hospitalization, and COVID-19 death were significantly increased in patients in group 3 (Figure 2; Supplementary Table S1). Patients who received passive immunization with tixagevimab/cilgavimab had outcomes similar to those of patients with vaccine-induced immunization, but they had significantly fewer infections (both severe and nonsevere), compared to KTRs considered unprotected.

Despite its potential bias, per the retrospective design, to our knowledge, our study shows for the first time the potential clinical usefulness of mAbs against Omicron in KTRs with weak or no response to vaccine, as a prophylaxis strategy. These results challenge the reduced efficacy of mAbs that has been shown *in vitro*. No serious adverse event was reported in our cohort who received tixagevimab/cilgavimab. Multicentric prospective or retrospective studies are needed to confirm these encouraging results for the protection of immunosuppressed patients against COVID-19.

DISCLOSURE

All the authors declared no competing interests.

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AUTHOR CONTRIBUTIONS

DB designed the study. DG and DB wrote the paper. All authors provided feedback and critical review.

SUPPLEMENTARY MATERIAL

Supplementary File (PowerPoint)

Table S1. Baseline characteristics of the patients and occurrence of Omicron infection in the 3 groups. The χ^2 test (nominal variables) and the *t* test (continuous variables) were used to compare the 3 groups; results were considered significant when $P < 0.05$. *P: comparison between groups 1 and 2. **P: comparison between groups 2 and 3. ***P: comparison between groups 1 and 3. AZA, azathioprine; eGFR, estimated glomerular filtration rate, estimated by Modification of Diet in Renal Disease (MDRD) formula; F, female; ICU, intensive care unit; M, male; MMF, mycophenolate mofetil.

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Pre-exposure prophylaxis with 300 mg Evusheld elicits limited neutralizing activity against the Omicron variant

To the editor: Immunocompromised patients show an impaired vaccine-induced immune response, resulting in an increased risk of severe coronavirus disease 2019 (COVID-19).[1] In an effort to address this issue, health authorities in the US and various European countries have subsequently authorized the use of anti–severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) monoclonal antibodies for pre-exposure prophylaxis. Although the combination of casirivimab–imdevimab (Ronapreve, Roche Regeneron) has been shown to confer satisfactory protection against the Delta variant, it has limited neutralizing activity against Omicron.[2] In March 2022, the combination of cilgavimab–tixagevimab (Evusheld, AstraZeneca) was approved in the UK for protecting transplant recipients with poor response to vaccination against the Omicron variant.[3] In France also, Evusheld was granted approval as of December, 2021. Although the Phase III Double-blind, Placebo-controlled Study of AZD7442 for Pre-exposure Prophylaxis of COVID-19 in Adult (PROVENT) study showed good efficacy for 300 mg Evusheld in the context of Delta-variant circulation, the question of whether this dosage is sufficient to prevent Omicron infection remains unanswered. Previous data indicated that the serum-neutralizing capacity against SARS-CoV-2 is positively associated with protection against severe forms of COVID-19.[4] Here, we analyzed the neutralizing capacity of Evusheld against Omicron in a cohort of kidney transplant recipients who received the drug for pre-exposure prophylaxis.

Both anti–receptor binding domain (RBD) IgG titers and neutralizing antibody titers against the Omicron BA.1 variant were measured in serum samples collected from 63 adult kidney transplant recipients who received gluteal i.m. prophylactic injections of Evusheld (150 mg tixagevimab and 150 mg cilgavimab) in the Lyon and Strasbourg University Hospitals. Recipients with a history of COVID-19 or positive anti-nucleocapsid IgG were excluded. Patients who received prophylactic Ronapreve (600 mg casirivimab and 600 mg imdevimab, $n = 39$) and those who were infected with SARS-CoV-2 during the fifth wave of the pandemic ($n = 14$) were used as the negative and positive control groups, respectively. The study protocol was approved by the local ethics committees (identifier: DC-2013–1990 and DC-2021-4460), and written informed consent was obtained from all participants.

After a median interval from injection of 29 days (interquartile range: 29–33 days), patients who received Evusheld had a low level of neutralizing activity (Figure 1a), and only 9.5% of them (6 of 63) were able to neutralize the Omicron variant, compared with 71% of patients (10 of 14) who were infected with SARS-CoV-2, and 2.6% (1 of 39) of those who received Ronapreve. Interestingly, convalescent patients displayed higher levels of neutralizing antibodies than those who received Evusheld (median: 2.3 log IC50, interquartile range: 1.5−2.7 vs. 0.00 log IC50, interquartile range: 0−0.05; $P < 0.001$). Although anti-RBD IgG titers were generally low after Evusheld injection (median: 2583 binding antibody units (BAU)/ml, interquartile range: 1906−3611 BAU/ml), a high interindividual variability was observed (range: 262−7032 BAU/ml; Figure 1b). This variability was explained largely by the patients' body mass index, which showed an inverse