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SPECIAL REPORT

Issues regarding COVID-19 in kidney transplantation in the era of the Omicron variant: a commentary by the ERA Descartes Working Group

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ABSTRACT

The Omicron variant, which has become the dominant strain of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) worldwide, brings new challenges to preventing and controlling the infection. Moreover, the widespread implementation of vaccination policies before and after transplantation, and the development of new prophylactic and treatment strategies for coronavirus disease 2019 (COVID-19) over the past 12–18 months, has raised several new issues concerning kidney transplant recipients. In this special report, the ERA DESCARTES (Developing Education Science and Care for Renal Transplantation in European States) Working Group addresses several questions related to everyday clinical practice concerning kidney transplant recipients and to the assessment of deceased and live kidney donors: what is the current risk of severe disease and of breakthrough infection, the optimal management of immunosuppression in kidney transplant recipients with COVID-19, the role of passive immunization and the efficacy of antiviral drugs in ambulatory patients, the management of drug-to-drug interactions, safety criteria for the use of SARS-CoV-2-positive donors, issues related to the use of T cell depleting agents as induction treatment, and current recommendations for shielding practices.

Keywords: antiviral agents, COVID-19, kidney donation, kidney transplantation, SARS-CoV-2

INTRODUCTION

Since the identification of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) at the beginning of 2020, the world has seen a rapid and wavelike spread of the virus. The currently dominant Omicron variant (B.1.1.529) spreads very fast but appears to cause less severe disease than previous variants. Consequently, the number of kidney transplant recipients (KTR) admitted because of coronavirus disease 2019 (COVID-19) is lower than before and attention is shifting to management of ambulatory patients, preparation for transplantation and planning of surgery. Herein we address

several questions that are related to these issues and rank high on the agenda in everyday clinical practice.

DO KTR STILL HAVE AN INCREASED RISK FOR A SEVERE COURSE OF THE DISEASE?

During the first wave, findings from the ERACODA database showed a 28-day COVID-19-related mortality of 21.3% in KTR and 25.0% in dialysis patients [1]. In European patients, mortality was 28% higher in KTR when compared with matched dialysis patients [2]. Goffin *et al.* reported that after adjustment for comorbidities and other confounders, KTR had twice the mortality of hemodialysis patients [3]. According to a recent meta-analysis, transplant patients with COVID-19 had a higher risk (+57%) of intensive care unit admission than non-transplant patients [4].

When compared with patients with COVID-19 in the first half of 2020, solid organ transplant recipients who were affected by the disease in the second half of that year had a lower mortality risk [5]. In a Spanish registry study, the case-fatality rate was overall lower in the second than in the first period (15.1% versus 27.4%), but similar in critically ill patients (66.7% versus 58.1%) [6]. A population-based cohort study showed that even after one or two vaccinations, COVID-19-related mortality was 8.1 fold higher in KTR as compared with the general population [7]. Recent US data showed a reduction in the rates of hospitalization (26% versus 60%) and mortality (2% versus 10%) in 347 infected solid organ transplant recipients during the Omicron surge, when compared with the first and second wave of the pandemic [8]. Finally, in a French cohort, the mortality in KTR infected with the Omicron variant was 4% [9]. Thus, the overall picture is that the COVID-19-related mortality in KTR is markedly lower in the Omicron era, but remains higher than in the general population.

WHAT IS THE RISK OF BREAKTHROUGH INFECTION WITH CURRENT VARIANTS IN VACCINATED KTR?

In the general population, the protection against infection and severe disease after two vaccinations is considerably less for the Omicron as compared with the Delta variant [10]. KTR have a lower antibody response after vaccination [11], and a higher risk of severe breakthrough infection [12–14]. Consequently, it can be expected that the risk of breakthrough infection with the Omicron variant is even further increased in this population.

The concentration of neutralizing antibody titers and the protection against infection with the Omicron variant can be increased by administering booster vaccinations [15]. However, 4 weeks after administering a third dose of an mRNA vaccine to 51 KTR, only 12% had neutralizing responses to the Omicron variant, compared with 61% and 59% to the wild-type and Delta variants, respectively [16]. Similar data were found in a cohort of 60 solid organ transplant recipients, with 18% of the patients having detectable neutralizing antibody responses to Omicron 1 month after completion of three doses of mRNA-1273 [17]. These data indicate that there will remain a relatively high risk of breakthrough infections with the Omicron variant, even after booster vaccinations. Nevertheless, a certain degree of protection against severe disease might still exist because of vaccine-induced cellular immunity, and non-neutralizing antibodies, supporting the policy of repeated booster vaccinations [18].

In brief, the risk of breakthrough infection with current variants is still high in vaccinated KTR. This emphasizes the need for additional protective measures including further vaccine doses (repeated boosters) and antiviral drugs.

SHOULD THE IMMUNOSUPPRESSIVE REGIMEN BE TEMPORARILY ADJUSTED WHEN A KTR HAS COVID-19?

In an earlier expert opinion paper by the DESCARTES Working Group, we provided recommendations on the management of immunosuppression in KTR who are beyond 3–6 months after transplantation [19]. We believe that in the current era with milder consequences of COVID-19 it is in general not necessary to change the immunosuppressive therapy in ambulatory patients who are asymptomatic or have mild disease without signs of COVID-19 pneumonia. However, when there are risk factors for progression to severe disease such as previous treatment with lymphocyte-depleting agents, we recommend temporarily reducing the intensity of immunosuppressive treatment. In more severe cases, we refer to the recommendations given in the previous paper [19].

WHAT ARE THE OPTIONS FOR PASSIVE IMMUNIZATION IN AMBULATORY KTR?

Monoclonal antibodies (mAb) directed against SARS-CoV-2 S-protein have been developed in record time, to provide immediate protection against developing disease. Almost all mAb are human IgG1 directed against the receptor binding domain or adjacent regions. In the general population, treatment with mAb has been demonstrated to be safe, and to significantly reduce hospitalizations or deaths in non-immunized high-risk individuals with early mild-to-moderate COVID-19, with a relative risk reduction of up to 85% [20–22]. In the most recently published study (TACKLE), progression to severe COVID-19 or death occurred in 4% of ambulatory patients treated with the combination of tixagevimab and cilgavimab versus 9% of placebo-treated patients ($P < .01$) [23]. Based on these results, treatment with mAb has replaced the use of convalescent plasma, for which a clear beneficial effect has not been demonstrated [24]. Unfortunately, KTR have been excluded from the main randomized control trials with mAb and data are therefore derived from case series and small retrospective studies [25–29]. mAb seem to be safe in KTR, but no conclusive data are available so far on the efficacy of mAb in the transplant population. In a retrospective study on 95 KTR (of whom 20 received mAb) a significant decrease was observed in hospitalizations or emergency room visits (15% versus 76%, $P < .001$) [28]. A smaller effect of mAb was reported in a single center retrospective study on 165 SOTs

where the 30-day hospitalization rate was 8.7% in the mAb treated group and 15.3% in the comparator group (NS) [25].

mAb have also been proposed in the setting of pre-exposure prophylaxis. In an ongoing trial, non-vaccinated adults with an increased risk of an inadequate response to vaccination and/or an increased risk of exposure to SARS-CoV-2 received a single intramuscular administration of the combination of tixagevimab and cilgavimab (AZD7442) or placebo. Symptomatic COVID-19 within 6 months after administration occurred in 8 of 3441 participants (0.2%) in the AZD7442 group and in 17 of 1731 participants (1.0%) in the placebo group ($P < .001$) [30]. In 88 KTR who were non-responders to full-course vaccination, no patient treated prophylactically with the combination of casirivimab and imdevimab developed COVID-19 infection, while 5 of 31 (16%) of KTR without prophylaxis experienced COVID- 19 infection, 2 required ICU admission and 1 died [31].

Importantly, the data described above were obtained in non-vaccinated patients and before the emergence of the Omicron variant in December 2021. Since the risk of hospital admission and death is lower with the Omicron variant [8, 32], the absolute risk reduction obtained with these drugs may be smaller, which will increase the number needed to treat (NNT) to prevent one hospitalization or death. Furthermore, the effectiveness of mAb is different for the various virus variants and breakthrough Omicron COVID-19 infections have been reported in patients receiving a combination of mAb [33]. *In vitro* platforms are used for constant testing of the neutralizing activity of mAb against new variants of concern, suggesting which mAb to be used in the clinical setting [34]. Data on neutralizing susceptibility to mAb of the various virus variants are updated on a website from Stanford University registries [35]. Sotrovimab was shown to have a beneficial effect in a retrospective study on KTR infected with the Omicron variant circulating in January of 2022 [36], but it is probably ineffective for the current BA.2 subvariant. Likewise, the neutralizing efficacy of most mAb is considerably lower for the newest BA.4 and BA.5 subvariants.

From the currently available mAb, only cilgavimab and bebtelovimab appear to have reasonable neutralizing activity against the Omicron/BA.2 variant and have been authorized for pre-exposure prophylaxis in non-effectively immunized KTRs in European countries. Finally, the emergence of resistant variants among immunocompromised individuals treated with mAb has recently been reported [37].

Taken together, the use of mAb for treatment of early infection or as pre-exposure prophylaxis is a rational and safe approach. Based on the available data, treatment with mAb, either in case of early infection or as pre-exposure prophylaxis, can be considered in immunosuppressed patients who are unvaccinated or have an insufficient or waned immune response to vaccination, especially in the presence of additional risk factors for a severe disease course, such as comorbidity. The NNT for the prevention of one hospitalization or death is probably smaller for treatment of early infection as compared with pre-exposure prophylaxis. Notably, with each new virus variant the susceptibility for the currently available mAb appears to decrease, which limits the applicability and cost-effectiveness.

WHAT IS THE EFFICACY OF ANTIVIRAL DRUGS IN AMBULATORY KTR?

Currently, three antiviral drugs have been demonstrated to be effective in the treatment of ambulatory patients with COVID-19. Randomized placebo-controlled trials were performed in unvaccinated adults with at least one risk factor for progression to severe COVID-19 disease and included (COVID-19 related) hospitalization or death within 4 weeks after start of treatment as endpoint. Molnupiravir, a nucleoside analog started within 5 days after the onset of mild-to-moderate disease, reduced the percentage of participants who were hospitalized or died from 9.7% (placebo group) to 6.8% (molnupiravir 800 mg b.i.d. for 5 days), corresponding to a NNT to prevent one hospitalization or death of 34 [38]. Nirmatrelvir is a protease inhibitor that is used in combination with ritonavir to inhibit the CYP3A-mediated metabolism of nirmatrelvir. Nirmatrelvir/ritonavir 300/100 mg b.i.d. for 5 days, commenced within 5 days after the onset of disease reduced the percentage of patients who were hospitalized or died by day 28 from 6.3% (placebo group) to 0.8% (NNT 18) [39]. In patients treated with the nucleoside analog remdesivir, started within 7 days of symptom onset, hospitalization or death within 28 days occurred in 0.7% of the patients as compared with 5.3% in the placebo group (NNT 22) [40]. Of note, patients infected with the Omicron variant were not included in the trials summarized above. Moreover, the proportion of immunocompromised patients included in these trials was less than 5%, precluding any conclusion on the efficacy in these patients.

Like for mAb, we think that treatment with antiviral drugs (within the investigated time interval after disease onset) is a valid option in immunosuppressed patients who are unvaccinated or not protected by vaccination, especially when the risk for a severe disease course is increased. Remdesivir and nirmatrelvir/ritonavir appear to be most effective, but a major disadvantage of remdesivir is the need for i.v. administration. The use of nirmatrelvir/ritonavir is challenging because of severe drug–drug interactions due to the CYP3A inhibition by ritonavir, which can strongly increase the blood concentrations of calcineurin inhibitors (tacrolimus even more than cyclosporine) and mTOR inhibitors. A useful source for information on these interactions is the Liverpool COVID-19 Drug Interactions website [41]. A recommendation for how to manage these interactions has been published [42]. In patients who are at relatively low risk of acute rejection, a pragmatic solution could be to discontinue calcineurin inhibitors or mTOR inhibitors during the 5-day course of nirmatrelvir/ritonavir and to resume the use of these drugs 2–3 days later. In addition, the use of remdesivir and nirmatrelvir/ritonavir are not recommended when estimated glomerular filtration rate is less than 30 mL/min/1.73 m^2.

In conclusion, there are effective antiviral agents available for the treatment of early COVID-19. However, the most

efficacious agents either require i.v. administration (remdesevir) or have strong pharmacokinetic interactions with a wide array of other drugs (nirmatrelvir/ritonavir).

WHAT ARE THE CONSEQUENCES OF COVID-19 OR A POSITIVE SARS-COV-2 TEST FOR DECEASED KIDNEY DONATION?

A major concern in transplantation of organs or tissues from donors with COVID-19 is the transmission of SARS-CoV-2 virus to the recipient [43]. SARS-CoV-2 PCR examination in nasopharyngeal, pharyngeal or bronchoalveolar lavage specimens, and thoracic computed tomography (CT) scan are the most reliable techniques to rule out COVID-19. However, if there is any suspicion of COVID-19 (e.g. unexplained fever, respiratory symptoms, ground-glass lung infiltrates on CT-scan examination) donation should be rejected [44]. The recommendations are less clear for donor candidates with resolved or non-active COVID-19. In potential donors with prior COVID-19, a 14-day symptom-free interval with a negative SARS-CoV-2 PCR has been suggested [44], but there are differences between various guidelines [45]. Importantly, the transmission of SARS-CoV-2 through organs other than lungs has not been demonstrated, even when the donor had an active infection at the time of donation [43, 46]. This is particularly important, as we are now seeing an increased number of potential donors with positive SARS-CoV-2 tests who die due to other causes where there is uncertainty about the significance of the test. With the lack of demonstrated transmission of SARS-CoV-2 and other respiratory viruses through non-lung transplants [47], and the lower disease severity with the Omicron variant, the use of organs from asymptomatic SARS-CoV-2 PCR positive donors who died for other reasons could be considered in recipients who are effectively vaccinated and/or had a prior natural infection. Such a policy, with active follow-up of recipients, is supported by some national transplant organizations (e.g. from Spain and Italy), of course only after obtaining informed consent from the prospective recipient.

In summary, while active COVID-19 is an absolute contra-indication for organ donation, individuals with asymptomatic SARS-CoV-2 infection or resolving COVID-19 can serve as organ donors when certain conditions are met.

WHAT IS THE IMPACT OF COVID-19 ON DECEASED DONOR KIDNEY TRANSPLANTATION AND THE PLANNING OF LIVING DONOR KIDNEY TRANSPLANTATION?

KTR are faced with a higher risk of infectious complications due to immunosuppression. During the first wave, the mortality of COVID-19 appeared to be higher in KTR than in candidates for kidney transplantation [48, 49], supporting a delay of transplant activities. With less pathogenic variants, and the majority of patients being vaccinated, a delay of transplantation seems no longer warranted.

If a transplant candidate contracts COVID-19, transplantation is usually postponed, but the optimal duration of the delay remains unclear. A more than 3-fold increased mortality has been demonstrated in (unvaccinated) patients undergoing surgery during the first 6 weeks after COVID-19 [50]. Therefore, recently updated guidelines recommend (i) pre-operative COVID-19 vaccination with three doses should be applied, preferably the last dose at least 2 weeks before surgery, and (ii) elective surgery should not be performed within 7 weeks after a SARS-CoV-2 infection in unvaccinated patients, unless the benefits exceed the risk of waiting [51, 52]. There is not enough evidence to make recommendations for those who become infected after COVID-19 vaccination, and it is also unknown whether the data on an increased risk of mortality after surgery are similar for asymptomatic patients and those infected with the Omicron variant [52, 53].

Whether vaccination against COVID-19 should be mandatory for kidney transplantation candidates is an interesting question with several medical, ethical and legal aspects. For more extensive discussion of this topic we refer to some recent papers [54, 55].

Although kidney donors are healthy before donation, following surgical nephrectomy they will have reduced renal reserve, which may increase the risk of acute kidney injury in the context of severe COVID-19 infection [56]. Unless urgent indications exist, postponing living-donor transplantation could be considered during the highest waves of a pandemic until circumstances improve. This strategy may protect donors from extra risks and also increase their willingness to donate because some live donors may hesitate to donate their organs with the anxiety of contracting disease during evaluation or after donating. Especially when donors are vaccinated, a liberal approach is justified when the risk of acquiring infection is low and the prevailing virus variants cause less severe disease. The aforementioned recommendations on avoiding elective surgery within 7 weeks of SARS-CoV-2 infection apply for the unvaccinated donors as well.

HOW DO WE HANDLE THE USE OF T CELL DEPLETING AGENTS FOR INDUCTION THERAPY WHEN THE RISK OF EXPOSURE TO SARS-COV-2 IS HIGH?

When the COVID-19 pandemic started in 2020, most transplant centers were less likely to use T cell depleting agents, and more likely to use non-depleting agents [57]. The need for using T cell depleting agents was also reduced since high-risk transplants, such as recipients with donor-specific antibodies or ABO-incompatibility with the donor, were being deferred. There are few to no data available to support management decisions regarding induction therapy. The available data are weak at best [58]. Presently, the dominant virus variant is causing mild disease, few transplant patients are admitted for inpatient care and outcome has improved. Due to the lack of evidence, management decisions regarding induction therapy should be made on an individual basis by expert opinion. We should use available knowledge on risk factors for a severe course of COVID-19, including high age, obesity,

diabetes and cardiovascular disease. Accordingly, we suggest that induction therapy could as a main rule be carried out as before the pandemic in individuals at low risk for serious disease. However, in more frail individuals with many risk factors, transplant professionals should make individual assessments regarding the type of induction therapy, and consider using non-depleting or no induction therapy, if this is a possibility.

SHOULD KTR CONTINUE SHIELDING PRACTICES?

During the first waves of the pandemic and in the pre-vaccination era, many KTR have adopted shielding policies to avoid exposure to the SARS-CoV-2 virus. Currently, the large majority of KTR have received multiple vaccinations, experienced COVID-19 or both, with resulting development of at least some degree of protection against severe disease. With fewer pathogenic virus variants and a low risk of exposure in the community, we feel that very strict shielding policies are not warranted anymore and may even harm the patients due to unnecessary isolation from social intercourse. KTR with a low or absent antiviral immune response, may be reassured by the current availability in most countries of mAb and antiviral drugs that appear to be effective in early stages of COVID-19 [59].

CONCLUSION

The emergence of the Omicron variant of the SARS-CoV-2 virus and the widespread implementation of vaccination have dramatically changed the clinical appearance of COVID-19 in KTR. While the risk of getting infected is higher with the Omicron variant, current rates of hospitalization and mortality are the lowest since the start of the pandemic. In addition to active immunization by vaccination, passive immunization and treatment with antiviral drugs can further reduce the risk of a severe course of COVID-19, although the efficacy and cost-effectiveness of these agents in patients using immunosuppressive drugs is difficult to judge due to a lack of data. Ideally, prospective clinical trials should be performed especially in such high-risk patients.

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CONFLICT OF INTEREST STATEMENT

The results presented in this paper have not been published previously in whole or part.

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REFERENCES

1. Hilbrands LB, Duivenvoorden R, Vart P *et al.* COVID-19-related mortality in kidney transplant and dialysis patients: results of the ERACODA collaboration. *Nephrol Dial Transplant* 2020; **35**: 1973–83
2. Jager KJ, Kramer A, Chesnaye NC *et al.* Results from the ERA-EDTA Registry indicate a high mortality due to COVID-19 in dialysis patients and kidney transplant recipients across Europe. *Kidney Int* 2020; **98**: 1540–8
3. Goffin E, Candellier A, Vart P *et al.* COVID-19-related mortality in kidney transplant and haemodialysis patients: a comparative, prospective registry-based study. *Nephrol Dial Transplant* 2021; **36**: 2094–105
4. Ao G, Wang Y, Qi X *et al.* The association between severe or death COVID-19 and solid organ transplantation: a systematic review and meta-analysis. *Transplant Rev (Orlando)* 2021; **35**: 100628
5. Heldman MR, Kates OS, Safa K *et al.* Changing trends in mortality among solid organ transplant recipients hospitalized for COVID-19 during the course of the pandemic. *Am J Transplant* 2022; **22**: 279–88
6. Villanego F, Mazuecos A, Pérez-Flores IM *et al.* Predictors of severe COVID-19 in kidney transplant recipients in the different epidemic waves: analysis of the Spanish Registry. *Am J Transplant* 2021; **21**: 2573–82
7. Hippisley-Cox J, Coupland CA, Mehta N *et al.* Risk prediction of covid-19 related death and hospital admission in adults after covid-19 vaccination: national prospective cohort study. *BMJ* 2021; **374**: n2244
8. Cochran W, Shah P, Barker L *et al.* COVID-19 clinical outcomes in solid organ transplant recipients during the Omicron surge. *Transplantation* 2022; **106**: e346–7
9. Bertrand D, Laurent C, Lemée V *et al.* Efficacy of anti SARS-CoV-2 monoclonal antibodies prophylaxis and vaccination on Omicron COVID-19 in kidney transplant recipients. *Kidney Int* 2022; S0085-2538(22) 00382-9
10. Andrews N, Stowe J, Kirsebom F *et al.* Covid-19 vaccine effectiveness against the Omicron (B.1.1.529) variant. *N Engl J Med* 2022; **386**:1532–46
11. Sanders JF, Bemelman FJ, Messchendorp AL *et al.* The RECOVAC immune-response study: the immunogenicity, tolerability, and safety of COVID-19 vaccination in patients with chronic kidney disease, on dialysis, or living with a kidney transplant. *Transplantation* 2022; **106**: 821–34
12. Wright BJ, Tideman S, Diaz GA *et al.* Comparative vaccine effectiveness against severe COVID-19 over time in US hospital administrative data: a case-control study. *Lancet Respir Med* 2022; **10**: 557–65
13. Mazuecos A, Villanego F, Zarraga S *et al.* Breakthrough infections following mRNA SARS-CoV-2 vaccination in kidney transplant recipients. *Transplantation* 2022; **106**: 1430–9
14. Callaghan CJ, Mumford L, Curtis RMK *et al.* Real-world effectiveness of the Pfizer-Biontech BNT162b2 and Oxford-Astrazeneca ChAdOx1-S vaccines against SARS-CoV-2 in solid organ and islet transplant recipients. *Transplantation* 2022; **106**: 436–46
15. Garcia-Beltran WF, St Denis KJ, Hoelzemer A *et al.* mRNA-based COVID-19 vaccine boosters induce neutralizing immunity against SARS-CoV-2 Omicron variant. *Cell* 2022; **185**: 457–66.e454
16. Al Jurdi A, Gassen RB, Borges TJ *et al.* Suboptimal antibody response against SARS-CoV-2 Omicron variant after third dose of mRNA vaccine in kidney transplant recipients. *Kidney Int* 2022; **101**: 1282–6
17. Kumar D, Hu Q, Samson R *et al.* Neutralization against Omicron variant in transplant recipients after three doses of mRNA vaccine. *Am J Transplant* 2022; doi: 10.1111/ajt.17020
18. Tarke A, Coelho CH, Zhang Z *et al.* SARS-CoV-2 vaccination induces immunological T cell memory able to cross-recognize variants from Alpha TO Omicron. *Cell* 2022; **185**: 847–59.e811
19. Maggiore U, Abramowicz D, Crespo M *et al.* How should I manage immunosuppression in a kidney transplant patient with COVID-19? An ERA-EDTA DESCARTES expert opinion. *Nephrol Dial Transplant* 2020; **35**: 899–904
20. O'Brien MP, Forleo-Neto E, Musser BJ *et al.* Subcutaneous REGEN-COV antibody combination to prevent Covid-19. *N Engl J Med* 2021; **385**: 1184–95
21. Dougan M, Nirula A, Azizad M *et al.* Bamlanivimab plus etesevimab in mild or moderate Covid-19. *N Engl J Med* 2021; **385**: 1382–92

22. Gupta A, Gonzalez-Rojas Y, Juarez E *et al.* Early treatment for covid-19 with SARS-CoV-2 neutralizing antibody sotrovimab. *N Engl J Med* 2021; **385**: 1941–50
23. Montgomery H, Hobbs FDR, Padilla F *et al.* Efficacy and safety of intramuscular administration of tixagevimab-cilgavimab for early outpatient treatment of COVID-19 (TACKLE): a phase 3, randomised, double-blind, placebo-controlled trial. *Lancet Respir Med* 2022; **7**:S2213–2600(22)00180-1
24. Piechotta V, Iannizzi C, Chai KL *et al.* Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a living systematic review. *Cochrane Database Syst Rev* 2021; **5**: Cd013600
25. Sarrell BA, Bloch K, El Chediak A *et al.* Monoclonal antibody treatment for COVID-19 in solid organ transplant recipients. *Transpl Infect Dis* 2022; **24**: e13759
26. Fernandes G, Devresse A, Scohy A *et al.* Monoclonal antibody therapy for SARS-CoV-2 infection in kidney transplant recipients: a case series from Belgium. *Transplantation* 2022; **106**: e107–8
27. Dhand A, Razonable RR. COVID-19 and solid organ transplantation: role of anti-SARS-cov-2 monoclonal antibodies. *Curr Transplant Rep* 2022; **9**: 26–34
28. Klein EJ, Hardesty A, Vieira K, Farmakiotis D. Use of anti-spike monoclonal antibodies in kidney transplant recipients with COVID-19: efficacy, ethnic and racial disparities. *Am J Transplant* 2022; **22**: 640–5
29. Pinchera B, Buonomo AR, Scotto R *et al.* Sotrovimab in solid organ transplant patients with early, mild/moderate SARS-CoV-2 infection: a single-center experience. *Transplantation* 2022; **106**: e343–5
30. Levin MJ, Ustianowski A, De Wit S *et al.* Intramuscular AZD7442 (tixagevimab–cilgavimab) for prevention of covid-19. *N Engl J Med* 2022; **386**: 2188–200
31. Ducloux D, Courivaud C. REGEN-Cov antibody combination to prevent COVID-19 infection in kidney transplant recipient without detectable antibody response to optimal vaccine scheme. *Kidney Int* 2022; **101**: 645–6
32. Villanego F, Vigara LA, Alonso M *et al.* Trends in COVID-19 outcomes in kidney transplant recipients during the period of Omicron variant predominance. *Transplantation* 2022; **106**: e304–5
33. Flahault A, Touchard J, Péré H *et al.* Breakthrough omicron COVID-19 infections in patients receiving the REGEN-Cov antibody combination. *Kidney Int* 2022; **101**: 824–5
34. Hu YF, Hu JC, Chu H *et al.* In-silico analysis of monoclonal antibodies against SARS-CoV-2 omicron. *Viruses* 2022; **14**: 390
35. Coronavirus Antiviral & Resistance Database. Susceptibility summaries. Stanford University. https://covdb.stanford.edu/page/susceptibility-data/ (23 April 2022, date last accessed).
36. Chavarot N, Melenotte C, Amrouche L *et al.* Early treatment with sotrovimab monoclonal antibody in kidney transplant recipients with Omicron infection. *Kidney Int* 2022; **101**: 1290–3
37. Rockett R, Basile K, Maddocks S *et al.* Resistance mutations in SARS-CoV-2 delta variant after sotrovimab use. *N Engl J Med* 2022; **386**: 1477–9
38. Jayk Bernal A, Gomes da Silva MM, Musungaie DB *et al.* Molnupiravir for oral treatment of covid-19 in nonhospitalized patients. *N Engl J Med* 2021; **386**: 509–20
39. Hammond J, Leister-Tebbe H, Gardner A *et al.* Oral nirmatrelvir for high-risk, nonhospitalized adults with covid-19. *N Engl J Med* 2022; **386**: 1397–408
40. Gottlieb RL, Vaca CE, Paredes R *et al.* Early remdesivir to prevent progression to severe covid-19 in outpatients. *N Engl J Med* 2021; **386**: 305–15
41. University of Liverpool. COVID-19 drug interactions. https://www.covid19-druginteractions.org/ (23 April 2022, date last accessed).
42. Lange NW, Salerno DM, Jennings DL *et al.* Nirmatrelvir/ritonavir use: managing clinically significant drug–drug interactions with transplant immunosuppressants. *Am J Transplant* 2022; **22**: 1925–6
43. Kute VB, Fleetwood VA, Meshram HS *et al.* Use of organs from SARS-CoV-2 infected donors: is it safe? A contemporary review. *Curr Transplant Rep* 2021; **8**: 281–92
44. Domínguez-Gil B, Fernández-Ruiz M, Hernández D *et al.* Organ donation and transplantation during the COVID-19 pandemic: a summary of the Spanish experience. *Transplantation* 2021; **105**: 29–36
45. Boan P, Marinelli T, Opdam H. Solid organ transplantation from donors with COVID-19 infection. *Transplantation* 2022; **106**: 693–5
46. Eichenberger EM, Kaul DR, Wolfe CR. The pandemic provides a pathway: what we know and what we need to know about using COVID positive donors. *Transpl Infect Dis* 2021; **23**: e13727
47. Kaul DR, Vece G, Blumberg E *et al.* Ten years of donor-derived disease: a report of the disease transmission advisory committee. *Am J Transplant* 2021; **21**: 689–702
48. Clarke C, Lucisano G, Prendecki M *et al.* Informing the risk of kidney transplantation versus remaining on the waitlist in the coronavirus disease 2019 era. *Kidney Int Rep* 2021; **6**: 46–55
49. Mohamed IH, Chowdary PB, Shetty S *et al.* Outcomes of renal transplant recipients with SARS-CoV-2 infection in the eye of the storm: a comparative study with waitlisted patients. *Transplantation* 2021; **105**: 115–20
50. COVIDSurg Collaborative; GlobalSurg Collaborative. Timing of surgery following SARS-CoV-2 infection: an international prospective cohort study. *Anaesthesia* 2021; **76**: 748–58
51. El-Boghdadly K, Cook TM, Goodacre T *et al.* Timing of elective surgery and risk assessment after SARS-CoV-2 infection: an update: a multidisciplinary consensus statement on behalf of the Association of Anaesthetists, Centre for Perioperative Care, Federation of Surgical Specialty Associations, Royal College of Anaesthetists, Royal College of Surgeons of England. *Anaesthesia* 2022; **77**: 580–7
52. American Society of Anesthesiologists. ASA and APSF joint statement on elective surgery/procedures and anesthesia for patients after COVID-19 infection. https://www.asahq.org/about-asa/newsroom/news-releases/2022/02/asa-and-apsf-joint-statement-on-elective-surgery-procedures-and-anesthesia-for-patients-after-covid-19-infection (23 April 2022 , date last accessed).
53. Glasbey JC, Dobbs TD, Abbott TEF. Can patients with asymptomatic SARS-CoV-2 infection safely undergo elective surgery? *Br J Anaesth* 2022; **128**: 909–11
54. Gökmen R, Cronin A, Brown W *et al.* Kidney transplantation and patients who decline SARS-CoV-2 vaccination: an ethical framework. *Transpl Int* 2021; **34**: 1770–5
55. Hippen BE. Mandating COVID-19 vaccination prior to kidney transplantation in the United States: no solutions, only decisions. *Am J Transplant* 2022; **22**: 381–5
56. Lentine KL, Mannon RB, Josephson MA. Practicing with uncertainty: kidney transplantation during the COVID-19 pandemic. *Am J Kidney Dis* 2021; **77**: 777–85
57. Bae S, McAdams-DeMarco MA, Massie AB *et al.* Early changes in kidney transplant immunosuppression regimens during the COVID-19 pandemic. *Transplantation* 2021; **105**: 170–6
58. Weiss MJ, Hornby L, Foroutan F *et al.* Clinical practice guideline for solid organ donation and transplantation during the COVID-19 pandemic. *Transplant Direct* 2021; **7**: e755
59. Radcliffe C, Palacios CF, Azar MM *et al.* Real-world experience with available, outpatient COVID-19 therapies in solid organ transplant recipients during the omicron surge. *Am J Transplant* 2022, preprint

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