LETTERS TO THE EDITOR

Response to the KDOQI US Commentary on the 2018 KDIGO Hepatitis C Guideline

To the Editor:

In 2018, KDIGO issued a clinical practice guideline for the prevention, diagnosis, evaluation, and treatment of hepatitis C virus (HCV) infection in patients with chronic kidney disease.[1] Recently, KDOQI published a commentary on the KDIGO guideline in which members of the appointed group disagreed with Recommendation 4.2.2 to direct HCV nucleic acid test (NAT)-positive kidneys to HCV NAT-positive recipients.[2] They commented that recent studies demonstrated viral eradication with direct-acting antivirals (DAAs) in HCV NAT-negative patients who received HCV NAT-positive kidneys, thus providing evidence that such kidneys could be allocated to any recipients regardless of their HCV status.[2] This is an important issue that deserves clarification.

The 2018 KDIGO guideline did not recommend that HCV NAT-positive kidney allografts should be preferentially given to NAT-positive recipients over NAT-negative patients. Instead, we recommended that NAT-positive kidneys be allocated to NAT-positive recipients rather than be discarded. The discard rate of such kidneys in several countries, including the United States, has been high.[3] This recommendation was based on contemporaneous literature that reported excellent long-term patient and graft survival in HCV-positive recipients of HCV-positive kidneys.[4]

As acknowledged by the KDOQI work group, at the time of the KDIGO guideline there was evidence from only 20 NAT-negative patients who received NAT-positive kidney allografts. Nearly all articles reporting the use of NAT-positive kidneys in NAT-negative recipients appeared after publication of the 2018 KDIGO guideline. We have thus conducted a preliminary review of the recent evidence, identifying 7 relevant studies (with at least 10 patients each) that included a total of 240 NAT-negative patients who received NAT-positive kidneys. Sustained virologic response at 12 weeks and graft survival at 6 to 12 months were excellent (99% each), but no long-term graft survival and limited safety data are available. About one-quarter of patients had delayed graft function and 4% had acute rejection. The excellent short-term graft survival needs to be confirmed for longer periods.

As a global guideline, KDIGO aims to address transplant practice worldwide. Transplanting NAT-positive kidneys into NAT-negative recipients is not yet embraced in many countries. This strategy requires that DAAs are readily available and that patients undergo stringent NAT monitoring after transplantation. Furthermore, the timing for initiating DAAs and the treatment duration remain highly variable, as reported in the literature. Thus, what KDOQI recommends for transplantation of NAT-positive kidneys in the United States may not be appropriate globally.

Nevertheless, based on recent studies, we endorse the allocation of NAT-positive kidneys to HCV NAT-negative recipients provided that patients have access to DAA therapy and comprehensive HCV monitoring, national/local regulations permitting. There remains uncertainty of the long-term adverse effects of such practice (eg, fibrosing cholestatic hepatitis, DAA failure, and de novo glomerular disease) and as such, extended follow-up of patient and graft survival of these recipients is still warranted.

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In Reply to 'Response to the KDOQI US Commentary on the 2018 KDIGO Hepatitis C Guideline'

The authors of the 2018 KDIGO hepatitis C guideline[1] have provided a valuable service in clarifying their position on the allocation of HCV NAT-positive

kidneys. Their original guideline statement read: "We recommend that transplantation of kidneys from HCV NAT-positive donors be directed to recipients with positive NAT." As expressed in the KDOQI US commentary on this guideline,[2] our plain-language interpretation of this recommendation was that HCV NAT-positive donor organs should be preferentially directed to recipients with HCV viremia versus transplant candidates without HCV viremia. After reviewing recent publications,[3,4] the KDIGO authors now "endorse the allocation of NAT-positive kidneys to NAT-negative HCV recipients provided that patients have access to DAA therapy and comprehensive HCV monitoring, national/local regulations permitting."[5] We agree with this endorsement, which focuses on the autonomy of the kidney transplant recipient and the ability of the treating clinicians to provide timely HCV DAA treatment after transplantation. Otherwise, we point to the principles of utility and equity as the main concepts that should guide the allocation of deceased donor organs, including those from donors with HCV-NAT positivity.

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Favipiravir for COVID-19 in a Patient on Hemodialysis

To the Editor:

Favipiravir may be an effective option for treating infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of coronavirus disease 2019 (COVID-19), in maintenance dialysis.[1] There have been few reports of favipiravir administration in hemodialysis patients. We administered favipiravir to a hemodialysis patient with COVID-19 and found that blood concentrations of favipiravir were similar to those seen in patients not receiving dialysis.

A 72-year-old man presented with fever and cough at an outside hospital. After computed tomography of the chest showed left lower lobe consolidation, he was transferred to our hospital. Medical history included diabetes mellitus and kidney failure treated with hemodialysis since early 2016. A polymerase chain reaction test performed 1 week before hospitalization was negative but a test day 2 of hospitalization proved positive. Oxygenation worsened and he was intubated and ventilated. Favipiravir administration started on day 4. He continued receiving hemodialysis 2 or 3 days a week. Blood concentrations of favipiravir (determined as described in Item S1) are shown in Figure 1. On day 38, he experienced sudden clinical deterioration and died the next day.

The course of the decline in favipiravir blood concentrations that we observed was similar to that reported in patients not receiving hemodialysis.[2,3] This was unexpected because the molecular weight of favipiravir is 157 Da, 53% to 54% is protein bound, and the volume of distribution is ~20 L, suggesting that dialysis would eliminate favipiravir.

The half-maximal effective concentration of favipiravir against SARS-CoV-2 infection is 9.7 μg/mL, but blood concentrations after day 9 were all below this level.[4] Previous reports also indicated favipiravir that blood concentrations were lower than predicted and therapeutic drug monitoring may be necessary.[2]

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