Correspondence

Trial of Transplantation of HCV-Infected Kidneys into Uninfected Recipients

To the Editor: Waiting times for kidney transplants exceed 3 to 5 years in many parts of the United States. Yet more than 500 high-quality kidneys from deceased donors with hepatitis C virus (HCV) infection are discarded annually. Direct-acting antiviral agents, which are associated with high HCV cure rates and manageable side effects, have created the potential to substantially increase the number of kidney transplants by making HCV-infected kidneys available to HCV-negative candidates on the waiting list.

In this open-label, single-group, pilot trial at the University of Pennsylvania (Transplanting Hepatitis C Kidneys into Negative Kidney Recipients [THINKER]; ClinicalTrials.gov number, NCT02743897) we sought to determine the safety and efficacy of transplantation of kidneys from HCV genotype 1–viremic donors into HCV-negative patients, followed by elbasvir–grazoprevir (Zepatier) treatment. An external data and safety monitoring board reviewed all aspects of the trial. The authors vouch for the completeness and accuracy of the data and analysis and for the adherence of the trial to the protocol, available with the full text of this letter at NEJM.org.

Adults who were undergoing dialysis and who had long anticipated waiting times for a kidney transplant were eligible for inclusion in the trial, and patients with conditions that substantially elevate the risks of liver disease, allograft failure, or death were excluded. A physician-led, three-step, informed-consent process was implemented.

Deceased-donor criteria ensured selection of high-quality kidneys (see the Supplementary Appendix, available at NEJM.org). Since elbasvir–grazoprevir is not approved by the Food and Drug Administration (FDA) for patients with HCV genotypes 2 or 3, and a direct-acting antiviral agent for the treatment of patients with those genotypes who have renal failure has not been approved by the FDA, donors were limited to those who had positive qualitative HCV nucleic acid test results and HCV genotype 1. We developed a new protocol for donor genotyping concurrent with organ allocation (see the Supplementary Appendix).

Intravenous glucocorticoids and rabbit antithymocyte globulin were administered to all recipients, followed by oral tacrolimus, mycophenolate mofetil, and prednisone. The HCV viral load was measured in recipients on postoperative day 3; elbasvir–grazoprevir was initiated when the results became positive, and therapy was maintained for 12 weeks.

Among 38 patients who were potentially eligible to participate in the trial, 22 attended an educational presentation, and 14 provided written informed consent and had their waiting-list profile changed to indicate eligibility to receive an HCV-infected kidney. Per protocol, 10 patients received HCV-infected kidneys. The median age of the recipients was 59 years (interquartile range, 51 to 63); half the recipients were men and 2 were black. The median time from eligibility on the waiting list for hepatitis C–infected kidneys to transplantation was 58 days (interquartile range, 53 to 100). The median Kidney Donor Profile Index score (on a scale from 0 to 100%, with higher values indicating a greater risk of graft failure for an individual kidney) was 42% (interquartile range, 32 to 48) (see Table S4 in the Supplementary Appendix).

On day 3 after transplantation, all recipients had detectable HCV RNA; viral loads ranged from less than 15 IU per milliliter (detectable but unquantifiable) to 193,000 IU per milliliter (Fig. 1). Elbasvir–grazoprevir was initiated in all recipients. Nine recipients had HCV genotype 1a infection; none had identifiable NS5A resistance. All recipients were cured of HCV; a cure was defined as a sustained virologic response 12 weeks after the end of treatment.

The median 6-month serum creatinine level was 1.1 mg per deciliter (97 μmol per liter; interquartile range, 0.8 to 1.3 mg per deciliter (71 to
115 μmol per liter), and the estimated glomerular filtration rate was 62.8 ml per minute per 1.73 m² (interquartile range, 51.8 to 83.1). One recipient had delayed graft function, transiently elevated aminotransferase levels developed in two recipients, and a transient new class I donor-specific antibody level (1800 mean fluorescence intensity units) developed in one patient. Proteinuria (at an estimated level of 2 g per day of urinary protein excretion) developed in one patient who had IgA nephropathy before transplantation; in this patient, focal segmental glomerulosclerosis was detected on biopsy after a sustained virologic response was reached 12 weeks after the end of treatment (see Table S6 in the Supplementary Appendix).

This pilot trial showed that transplantation of HCV genotype 1–infected kidneys into HCV-negative recipients, followed by the use of direct-acting antiviral agents, can provide potentially excellent allograft function with a cure of HCV infection.

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