Expanding access: First clinical trial transplants hepatitis C-infected kidneys at Penn Medicine

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Patients who need a kidney transplant may have new hope, through an innovative Penn Medicine clinical trial using kidneys from deceased donors who had the Hepatitis C virus (HCV). The first study participant received a kidney transplant in July 2016, and after being treated with a full regimen of Zepatier - a recently-approved oral medication prescribed to eradicate HCV - her doctors announced today that there is no evidence of the virus in her blood. Irma Hendricks of East Stroudsburg, PA, faced upwards of five years on the transplant waiting list with dialysis three days a week for many hours, before enrolling and receiving a kidney transplant as part of this trial. The research team says if the new approach works, for patients who do not have HCV, there is the potential to provide a chance at a lifesaving kidney transplant for hundreds more patients each year.

The clinical trial, known as THINKER, led by David S. Goldberg, MD, MSCE, and Peter Reese, MD, MSCE, both assistant professors of Medicine and Epidemiology at Penn, aims to determine the safety and efficacy of transplanting kidneys from Hepatitis C-positive donors into patients currently on the kidney transplant waitlist who do not have the Hepatitis C virus.

"There are more than 99,000 Americans are awaiting a kidney transplant," said Reese, who is also an assistant professor of Medical Ethics and Health Policy at Penn and chair of the Ethics Committee for

the United Network of Organ Sharing (UNOS). "Yet despite very long waiting times for transplant, hundreds of otherwise good kidneys from deceased donors infected with Hepatitis C are discarded each year. If we can demonstrate that it's possible to eradicate HCV from patients who contract the virus from a transplant, this approach could open up access to an entirely new pool of donor organs that are currently being discarded. Ultimately, our hope is that this trial will show that it is possible, and will then afford far more patients who are on the waiting list an opportunity to receive a lifesaving transplant much sooner."

Reese and Goldberg estimate that if this experimental course of transplantation and treatment proves effective in the long term, at least 500 more kidneys could become available for transplantation each year. Currently, individuals who have Hepatitis C are only eligible to donate organs to recipients who also have the virus. But in most cases, these HCV-infected organs would be discarded, and never used for transplantation.

The study is enrolling patients between 40 and 65 years of age, with a blood type A, B, or O, with varying ethnicities and socioeconomic statuses, who do not have Hepatitis C and are receiving chronic dialysis, a treatment that often causes severe fatigue and medical complications and can require a tremendous time investment. Typically, patients must undergo dialysis to filter their blood often three or more times a week, for upwards of three hours each session. Though many patients who receive kidney transplants are able to obtain a donor organ from a relative or matching unrelated donors, thousands have no such option and can wait years for a kidney to become available from a suitable, deceased donor. After a rigorous informed consent process, participants in the new Penn study are enrolled and eligible to receive kidneys from donors with Hepatitis C.

In this study, only donated kidneys that are infected with a certain strain

of HCV are used. There are six genotypes of HCV that have been identified, but patients will only receive HCV genotype 1-infected kidneys, since the viral treatment used in this study has a 95 percent success rate in eradicating this type of HCV in the general population. Additional steps are taken to ensure that the kidneys study participants receive are high quality, with the best possible chance of successful transplant.

"While these kidney quality criteria may be more selective than our usual approach to choosing organs, we are aiming to evaluate safety and efficacy in only the most viable organs in this initial pilot phase of the clinical trial," said Goldberg, who is also the medical director for Living Donor Liver Transplantation at Penn. "We realized that the amazing transformation of treatment options for Hepatitis C should also transform how we think about organs with Hepatitis C. At this very early point in the study, we are pleased with how our first patients have responded to transplantation and antiviral treatment."

Researchers intend to transplant and treat 10 patients in this pilot study. Patients who receive an HCV-infected kidney, who are then treated with an extended regimen of Zepatier, can be classified as HCV-free or "cured" if they have undetectable levels of the virus three months after completion of the oral medication. One risk of participating in this clinical trial, which is discussed during the informed consent process, is that patients who receive the HCV-positive kidney may become infected with the Hepatitis C, and may never be cleared of the virus despite the mediation regimen.

There are an estimated 3.9 million Americans living with the Hepatitis C virus, a contagious viral disease that causes inflammation of the liver and can range in severity from mild illness lasting a few weeks to a lifelong disease leading to weakened liver function or liver failure. HCV often goes unnoticed as many of those infected don't show symptoms until

significant liver damage is detected. Those with ongoing HCV can develop cirrhosis - scarring of the liver - leading to complications such as bleeding, yellowing of the skin or eyes, fluid buildup, infections and even liver cancer. New treatments for Hepatitis C approved over the past several years have high cure rates and much better side effect profiles than historical treatment options.

Provided by Perelman School of Medicine at the University of Pennsylvania