Hepatitis C Infected Organ Transplant Offers Hope

Of the nearly 100,000 people waiting for a kidney transplant in the U.S., many will never get one. Meanwhile, hundreds of Hepatitis C infected organs are discarded because of the infection.

The doctors at University of Pennsylvania connected these events and led a study that successfully showed that it is possible to transplant Hepatitis C infected kidneys into a patient and treat the disease in the recipient thereby saving his life. This revolutionary treatment is good news for those in need of a transplant; particularly patients who are facing long wait times, often 7 to 10 years and spending much of their daily lives on dialysis. We are talking to Dr. David Goldberg and Dr. Peter Reese from the University of Pennsylvania, who led the study, about their journey and how they are expanding this treatment process to transplant hearts and other organs.

Full Transcript:

Priya Menon: Good afternoon and welcome to Cure Talks. I am Priya Menon, your host and today we are discussing a very unique research that shows that transplanting Hepatitis C infected organs and then treating the condition in the recipient is possible, thereby saving lives, and we welcome the doctor who made this possible as a featured expert today Dr Peter Reese, transplant nephrologist and epidemiologist at the Hospital of the University of Pennsylvania and Dr David Goldberg, assistant professor of Medicine and Epidemiology at Penn and Medical Director for Living Donor Liver Transplantation at the Hospital of the University of Pennsylvania. Welcome to Cure Talks, doctors. The patient advocate on our panel today is Connie Welch, Connie advocates for Hepatitis C and liver disease. She's a certified life coach, writer and speaker and founder of life beyond Hepatitis C.com. We also have with us Kiran Shelat, who was part of the study that we'll be discussing in the hour and Kiran will be sharing his experience with us. Welcome to Cure Talks, Connie and Kiran. We will be addressing questions from the audience towards the end of the discussion so you can send in your questions to priya@trialx.com. All those of you listening to us on CureTalks pages, you can post your questions in the comments sections and we will take them up as time permits. So to start the discussion now, Dr Reese and Dr Goldberg, thank you once again for being here with us. I'm kind of very excited because we're talking about something very novel here and we are talking about deliberately infecting people with a virus and then treating them to save their lives. So my question to both of you first is why would anyone agree to infect themselves with a virus? Dr Reese, we will start with you and Dr Goldberg you can jump on with your comments.

Dr Peter Reese: I think that the short answer is that patients who need a transplant, are in a tough situation

much of the time. For kidney transplant, they're often enduring chronic dialysis, which Mr Shelat can tell us more about. Sometimes for patients who are in need of a heart or a lung or liver transplant they can be very sick spending most of their time in the hospital. And so because there's such a shortage of organs, we've been thinking more and more about, what are the organs that we can use that weren't used in the past. So a patient might accept an organ with a viral infection. Basically an imperfect organ might not be your first choice organ, but a very good organ nonetheless in order to get out of a tough spot that they're in. What happened with this study is that Dr Goldberg and I took a look at new therapies for Hepatitis C and recognized that the risks of Hepatitis C had become manageable and that we ought to use these organs that had hepatitis C in them.

Dr David Goldberg: And I think just to add on here, anytime someone is accepting an organ for transplant, there's always risks of known infections, but also unknown infections and all of the patients were presented with the data that although Hepatitis C treatment in the exact setting that we were doing haven't really been studied, that the new therapies had been studied for many years and with cure rates of 98% or higher, many of these patients were willing to take that risk rather than door years and years of dialysis, which is assuming that you'll even make it to transplant because we talk about the average waiting time being five to seven years, but based on certain criteria, older age, diabetes, half the people may not even survive to get a kidney transplant. So I think faced with those odds, it was something that many people were willing to take.

Priya: That's interesting, we can also hear from Kiran. Kiran, you're here and you've gone through this. So, what were your thoughts going forward for this study?

Kiran Shelat: Sure. First of all, thank you for giving me this opportunity. I'm really glad to be here discussing this. And I completely 100% agree with both the doctors, they kind of describe me perfectly. So, early 2016 around that time I was in advanced kidney disease called Stage 4 of ESRD and I was in a pretty bad shape. So just to summarize it and I was on a 10 hour per night to peritonial dialysis and I was already on the list for little over a year and PPD that I was doing nightly had caused some complication, and in that particular week I was actually scheduled to go for hernia surgery. So, in short, I was in a pretty bad state of health and everything that the doctor described physically as well as part of the mental, it does affect you mentally, socially as well. So, I was suffering and it looked like I was staring at the very dark long tunnel. And that is when this opportunity came in the form of a wonderful call from Dr Goldberg. So, 2016 was a life changer year for me and I was suffering from kidney disease for a long time, probably 25 years prior to receiving the kidney, although the symptoms were not present back then, they were coming back with a vengeance in 2014, 15, 16. And my GFR was getting lower by the minute. So, it was definitely a game changer when Dr Goldberg first called me and explained me about the THINKER study.

Priya: So, of course this was a difficult decision to make, but a game changer of course. What was your family's response towards this, were they supportive for this?

Kiran Shelat: Yeah. So just to start, how the conversation with Dr Goldberg started, he explained to me about the THINKER study in general. The phone came when I was at work and completely unexpectedly. And he told me about this study and how it works and he said when kidney is received from a Hepatitis C positive donor, you're sure to catch the infection, the virus through the donor and at that time I really didn't know much about the Hepatitis C at all. I mean, I knew it was a serious disease, but to those concerns or quickly faded away when Dr explained more about the new Merck medication that they will be administering as soon as the virus was detected. So the conversation went on, I was really thrilled about the prospects of getting a kidney here within several months rather than waiting several years. And as Dr had said, to be that sick and to still wait for four long years, you never know. Patients may not even make it to the surgery, be healthy enough to receive a kidney. So yeah, when this first came about, I shared the news with my family, my daughter who is a nurse, she came along with us to couple of meetings that we had with both doctors, Dr Reese and Dr Goldberg and the doctors during our meetings, explained very thoroughly and in a very transparent manner as to how the study would proceed. And it looks to me like they have thought of every single possibilities and as to what will the patient need right after the surgery, the medication and how they will monitor it. And the fact that they will be treating with the Hepatitis C medication called Zepatier

immediately after detecting the virus was comforting to me because they were planning on going aggressive in terms of treating the disease.

So my family, when I shared the news, several of them are doctors and some of them were concerned because of the newness of the procedure. But a couple of them were very excited. They say, rather you should try this. This is definitely exciting and we have definitely thought about this thing and when I signed my consent, I was completely relaxed in my own mind, with a lot of faith that things are going to be working out just fine. I was just telling, being a research engineer at one point in my career I knew that when somebody comes up with a trial procedure, definitely a lot of planning, lots of intelligent thinking goes into coming up with a plan as large and as novel as this one. So definitely I was comforted by knowing the details of the plan and my wife and my daughter and my extended family as well as all the friends, coworkers, they were all very, very supportive. It was like a rock solid.

Priya: Awesome to know Kiran. Thank you so much for sharing that. Dr Goldberg, as Kiran was saying that he received a call from your office. So did you and Dr Reese actually call up every patient you enrolled for the study?

Dr David Goldberg: Yes. So when we initially designed the trial, we had a lot of internal discussions about how to do this to educate the patients properly. We decided that we would first call them to give them a brief introduction then have them come in separately for an educational session and then if they were interested to consent. Then after we called a couple people here, Dr Reese and I said we will call a few people and then we would see if the research coordinator would then be able to help. It became clear to us right away that it needed to be one of us because patients had a lot of questions both in terms of the study but also their own health and about the infection. So we would literally just split up the list and if it was a given day that Dr Reese had more time, he would make the calls. If it was me, I would make the calls and we would cold call these people. And like I say, it was probably more awkward than a blind date call because we were calling these people saying, we're from the Penn transplant team. We're calling to talk to you about a study where you could get transplanted faster but get a kidney from a donor with Hepatitis C. I think over time we became more comfortable with the conversation, but it was something that took some work that we did have an IRB approved script to ensure that we were giving people the information in the same manner.

Priya: And so Dr Goldberg what was the criteria that was followed to make the selection of people who were approached?

Dr David Goldberg: So the way we thought about this, and obviously this is with a lot of inputs from Dr Reese and the other nephrology colleagues, was we wanted to identify people who seemed to have the most to gain because there were potential risks. So there had to be benefit. So we looked at people that didn't have much time on the waiting list and thus would be expected to wait the longest for kidney transplant. We also sought out people that didn't have any underlying liver disease and we did beyond just the routine blood tests that were done for all people on the kidney transplant waiting list. We did extra testing and a special ultrasound to make sure that they had what we call "a normal liver" to really maximize safety for the patients. And then there were a few other exclusions and I think the other big one is that when we spoke to people, we had to make sure that they didn't have a potential living kidney donor because we would tell them that ultimately that would be their best option. And those are sort of the main criteria that we looked at.

Priya: Interesting. And so, Dr Reese, this one question that has come up from the audience as well, and I guess this something that even I was a bit curious about. In the US apparently the average waiting time for kidney transplantation is more than five years, and for especially the patients with type A, B and O blood group. And I understand from the study protocol that was online that patients with AB blood group were excluded from the study. So does blood group or type matter for kidney transplantation in general?

Dr Peter Reese: Yeah, it matters a lot. And basically I think that it becomes difficult to really give a clean answer to the question of how long will it take for you to get a kidney transplant unless you know the

patient's blood type. So just to reinforce what Dr Goldberg was saying, we really tried to choose patients who were not likely to get a transplant without Hepatitis C anytime, certain patients who were in the toughest spot that they had to wait a long time. And I just wanted to say that, and of course, the implication here is that patients with AB blood group are a little bit more likely to get a transplant sooner because they're compatible with more donors than people with living donors. And I just wanted to comment also that listening to Mr Shelat, was it, this was great because he provided such an excellent example of, he was a very educated person, understood technical information, brought family members at a thought about it a lot. And we worked very hard on the informed consent process. And I think we should all be so lucky to have, well educated patients like him. I think one other, struggle that we've faced and that was important to have the IRBs then put on was just to try to make the materials as straightforward as possible. And I think whenever you're dealing with some complex consent procedures like we faced here, we learned very quickly together that when people brought in their friends and family, that was a very good sign because I think when people undergo research like this with so many complexities, the more kind of support they have behind them, the better off they are because there's just a lot of information to take in. And that was definitely true with Mr Shelat having a daughter who was a nurse for instance, made us feel much more confident that they'd really had a chance to understand what was being said and make the right decision for them.

Priya: Thank you Dr Reese for that input. So actually I'm trying here to walk through the entire process of having to approach people and get them to consent for the study, do the preliminary test, make sure that the recipient is ready, make sure that the kidney is available. So I know Dr Goldberg, you did touch a little bit about how the kidneys are one of the exclusion criteria and what are some of the inclusion criteria that you use for selecting the patients and the organ that we're going to be transplanting. So, how do you select these for transplant? I know you did mention, do you do any tissue mapping or any of the procedures performed and how are they just matched with the rest, just a quick comment in layman terms so that most of the people listening can understand how this actually happens?

Dr David Goldberg: So there are several things that go into compatibility of the donor and the recipient and it's more than just a blood type, but there is tissue typing that goes along at the time the kidney is offered. And that involves both what's entered into the electronic donor matching system, but also blood samples are sent from a donor blood to the recipient hospital for matching. That is done in any kidney transplant. Now, the one unique part of our study is that the drug that we're using, that was donated from Merck – Zepatier only works against type one and type for Hepatitis C. So as a result, we had an institute with immense help from our molecular pathology lab, a system where at the same time, tests are being run to make sure the donor and the recipient are compatible were to check the phenotype or the Hepatitis C subtype of the donor's blood to make sure it was a Type 1 or Type 4 donor. Because we only use donors that those two types, because Zepatier works best against them, is only FDA approved for those two groups of patients. Now we were looking, we had a fairly broad criteria for kidney donors. They had to be younger donors, the kidney quality score had to be below a certain value, but there was a lot of discretion ultimately to the kidney transplant surgeon on call, because ultimately they were the ones that would be implanting the kidney and doing the procedure and we want to make sure that they still retain their ability to make the decision about whether a kidney was usable or not.

Priya: Okay, are there any special precautions that are needed to be taken for transplanting an infected organ?

Dr David Goldberg: No, because this is, it's just, we always talk about, we call universal precautions, but the same thing that can be done for a recipient's Hepatitis C or one without was done here. There was obviously extra checks, to make sure that this is a patient that had consented for one of these kidneys, but nothing else was done especially at the time of the operation.

Priya: So when was the antiviral drug Zepatier started after the transplant?

Dr David Goldberg: So we started it. We tested people's blood on day three and if it was positive, it almost always the result came back that day we started the therapy that day, the world, a couple of instances just

due to timing that was tested on day two or day four, but we wanted to test early on and to get people started at the time or prior to discharge. But again, that was something that we sort of discussed as a group and we decided just for practical purposes to do.

Priya: Dr Reese, what do you like to comment on, what the indications are to start off the drug and how long does a patient have to take this?

Dr Peter Reese: So basically our view was that we would treat any patient who had detectable Hepatitis C in their blood. One of the things that we weren't 100% sure about was that all the patients would become infected with Hepatitis C. But we were able to detect Hepatitis C in the blood of all the recipients and as soon as we could detect it, we started to treat. What we learned from this, which really nobody knew is that in the early days after you get infected with Hepatitis C through transplantation, the viral load levels can be very diverse, some very high, some very low, but we treated right away on day three. And then we would continue the treatment usually for 12 weeks. There were a few cases where we had to extend it to 16 weeks just to follow recommendations from the Food and Drug Administration if there was what's called the resistance phenotype. But for most patients have one pill a day for 12 weeks. And, what we found is that by measuring the virus in the blood, time after time and study visits that, the viral loads almost invariably went down very fast and were often undetectable even after a month. That I think that was great news to be able to deliver to the patients. I remember many of these phone calls and they would feel really good knowing that they were responding quickly to the treatment and after a short period you couldn't even detect the virus in their blood. Dr Goldberg being the real expert in hepatology and Hepatitis C could comment on whether or not he saw the same thing for a patient who's had the infection longer, but I think what we've learned in the transplant setting is that when you know the day of the infection and you treat right away, the virus responds very quickly and become eradicated pretty fast.

Priya: Dr Goldberg, would you want to comment on that further?

Dr David Goldberg: Yeah. So I think the success and the cure rates that we're seeing match that in people with chronic Hepatitis C. The one thing that's different is that we noted that many of our patients, because we were testing and treating them three days after infection, the viral levels that they started were much lower than someone normally. So if I see someone in my clinic who has Hepatitis C for years, usually they have a viral load, one, two, three, 4 million. But most of our people, not all of them, but most of the patients when we started their drug, they had levels of 3000, 10,000, so orders of magnitude lower. So they were becoming, getting to a level of zero much faster and we still continued the treatment for the recommended duration just to make sure that we optimise their chances of cure. But we did notice that they went to zero much faster than we normally see.

Priya: That's interesting Dr Goldberg, was there anybody who did not get the infection at all in the trial?

Dr David Goldberg: No. There were a couple of people whose levels were zero on day three. And then when we checked it a couple of days later they were positive. But every transplant we did the recipient developed Hepatitis C.

Priya: And can you talk a little bit as to whether this new drug that is Zepatier, has any side effects that the patient should be aware of?

Dr David Goldberg: No, so all of the Hepatitis C medications that have come out over the last several years have really minimal to no side effects. And if you look at trials when they compared it to a placebo, to a sugar pill, the side effects are very rare. People can have nausea, headache, fatigue. We didn't note any side effects above what we expected, the medications that a patient takes after transplant to prevent rejection, were much more likely to cause any side effects than the Hepatitis C medication.

Priya: I'd like to hear from Kiran now. Can you talk a little bit about the treatment phase and when you started taking the new drug and if you're back to normal life now?

Kiran Shelat: Sure. Yeah. So, just to confirm what Dr Goldberg just mentioned about side effects. I had absolutely no side effects at all, zero. We were totally surprised because in the previous treatments with high doses of Prednisone and some other medication, I was definitely being bombarded with lots of side effects. But during this treatment with, I was on dozens of various medications. Plus, Zepatier, but fortunately there was no side effects at all. Absolutely none whatsoever to the extent that I didn't even have any surgical pain per se, I didn't even take a over the counter Tylenol for any kind of pain. So I really was very lucky and especially Zepatier did not offer any side effects and I was feeling really well within a first just few days. Even while I was in the hospital, I started walking around and feeling better and I'm just too excited to, get out of the hospital and return to the normal life. And I started feeling better every day after the surgery and if I have to talk about today, I'm feeling 100% back to where I was maybe 10, 15 years ago. So in terms of side effects, there were none whatsoever. And during the recovery time, there was some issue regarding blood pressure, but that was corrected after few adjustments were made. And I had some potassium level problems, which I still do to a certain extent. So I'm not completely out of the woods in terms of potassium, but that is a separate issue. But other than that in terms of any side effects due to medications, right after surgery and up until this point is basically none. I'm dealing with potassium, I'm on some medication for that, but watching the diet and exercise and rest of the good stuff is keeping everything in a pretty good balance.

Dr David Goldberg: So just want to bring up one point because I know we've used the term, I mean I've talked and Kiran and Peter, we mentioned the drug Zepatier, sort of the trade name and the reason why we had done that. So one of the things that was sort of important to get this study off the ground was we both ethically in our own internal safety board said that we could only do the study if we could guarantee that we can treat the patients Hepatitis C, after transplant. And because insurance is not 100% guarantee. We had to go to pharmaceutical companies applying for grants to help cover the infrastructure cost. But also to ask for donated drug. Merck was one of the companies that we went to, that had agreed to sponsor it. Neither myself or Dr Reese were paid by Merck, but they were willing to help you know, cost to the university for infrastructure but also to donate the drug. So it's not like this is the only drug that can be used in this setting, but that's why for the audience, why we're using that drug's name is that that's what we use because that's who we partnered with and who donated the drug for all of the patients.

Priya: Yeah. Thank you for that information. When Kiran said that you're back to normal life and I'm so, so very happy for you. This is like a great thing. I can totally understand what you went through and how you're feeling now. So Dr Goldberg, how much do we know the effect of training activity, both transplantation and effect on graft survival and what does the data say for now?

Dr David Goldberg: So I think there's a lot we know, but there's still a lot we don't know. Before this study, we knew that Hepatitis C can be treated before transplant or after transplant with the same cure rates and that's though in the setting of people having been chronic hepatitis C based on what we've seen so far and other published studies or things that are presented in meetings, It seems that even in the setting of acute Hepatitis C, when you're acutely infecting people the cure rates are no different. I think the jury is still out on how does this affect graft function. Historical data and Dr Reese can speak better to this, has suggested that kidneys from donors with Hepatitis C weren't "as good" as from those for people without hepatitis C. However, those organs were largely used in people who already had Hepatitis C and liver disease. So it was very difficult to parse out do the organs not do as well because there was something with the organs or did the organs not do as well in terms of who they were used in. The data that we published, they came out officially, in September in the Annals of Internal Medicine though showed that at least at a year in this subset of our patients who had reached a year, their graft function sort of how well their kidneys were functioning was better than we would have expected based on their kidney quality score. But I think though that's only a year and I do think this is why this is still an evolving field and one that is still, I would argue still sort of has a lot of unanswered questions and is still in the realm of experimental because we can't tell patients at this point, five years down the road, we seem to your kidneys going to work just as well as just the donor was Hepatitis C negative. We're very hopeful and the early signals that that will be the case, but it's far too early to be able to conclusively say that.

Priya: So I have just one more question before I bring Connie on, I know she has a quite a few questions for both of you. So, I believe that this treatment has been tried out for other organs as well and there's a trial for heart transplant also going on. And can you talk a little bit about that?

Dr Peter Reese: The question is what's the experience been with heart transplantation? Well, I think the results of the THINKER trial and the experiences of the patients encouraged us to try out a similar model in heart transplantation and so far the results for were pretty gratifying. So we have conducted and continue to conduct a trial in heart transplant where we take Hepatitis C infected hearts and put them into uninfected recipients. I can say qualitatively, our experiences in talking to patients have been really different because many of the heart transplant patients are just, even across the room, much sicker than the kidney transplant candidates were. Many times they're continuously receiving drips of fluids to try to give their hearts a little bit of an extra push. They're often, very fatigued and shorter breath walking across the room. Some of them we've talked to while they were in the hospital because that's where they were spending most of their time. So I feel the informed consent process was sometimes, even more intense, but I think the need is every bit as great. And so we partnered with some great people in the division of cardiovascular surgery and cardiac medicine, including Micheal Acker (unclear 35:12) among others. And, they were great partners and all the patients who have been in that trial who were able to finish the treatment have also been cured. The other thing that's been very gratifying for us at Penn is that, many other centers have kind of asked us for our materials and ask how they could develop similar programs and so we now are aware every week of programs elsewhere who've taken up similar programs. For instance, at Vanderbilt, they've also done a trial where they transplanted nine patients where the donors also had Hepatitis C and the recipients didn't. So, I think slowly the story is starting to grow and it's happening in other places and heart transplants besides that.

Priya: Thank you, Dr. With that I would now hand over to Connie Welch. So Connie, please go ahead with your questions for the doctors.

Connie Welch: Okay. Well first, thank you so much for the opportunity to be here today. I appreciate that. My first question really is for Dr Goldberg in regard to liver transplant. Has this study ever been done transplanting a Hepatitis C infected liver to a patient who perhaps had cirrhosis and was in the later stages, but that the transplanted liver was as not as damaged? So there was a greater, outcome as far as when the patient could go ahead and start on the antiviral drugs.

Dr David Goldberg: Yes. So, this in transplantation, we routinely have used liver from donors infected with Hepatitis C, especially. Obviously those that are younger with less time with the infection whose livers were normal. Historically. These were though used in people with Hepatitis C. There was a recent study that was just published online from Stanford. They performed 10 liver transplants from donors, with Hepatitis C into recipient without Hepatitis C. The thing that's different in livers as opposed to other organs is because there's still many, many people on the waiting list who are infected with Hepatitis C. We as a transplant community use liver from donors this Hepatitis C as much as we do livers from donors without Hepatitis C, meaning that we're just as likely to transplant one of those because there are so many recipients. So using at least now liver, some donors with Hepatitis C into people without Hepatitis C allows us to transplant someone who's maybe a little more sick than the patient with Hepatitis C. But won't necessarily lead to a market increase in the number of transplants because these organs are used with such frequency.

Connie: That's good to know. That opens up a definitely a lot more organs with this. Wonderful. My next question would be, is there any information that would, or any evidence showing that there is any problems with anti-rejection drugs, along with taking the Hepatitis C into barrels?

Dr David Goldberg: Short answer is yes. So it depends though. So the main immunosuppression drug that we use in all transplant recipients is something called Tacrolimus or Prograf. There is, it varies by drug, but the interactions between the Hepatitis C drug and Tacrolimus is fairly minimal and very clinically manageable for people who might be intolerant or have an allergy or something to that they sometimes then we'll require a medication called CycloSporin. There are getting this, that is different than there are very important

interaction between Cyclosporine and, and the Hepatitis C medications that really affect the dosing. Now, almost always, you don't know if someone is going to be intolerant to Tacrolimus prior to transplant and require Cyclosporine for him. But on the odd chance that you have a patient who does that in our study, we would not have enrolled someone who we knew ahead of time, couldn't take Tacrolimus and would require to take Tacrolimus because that interaction is so profound.

Connie: Okay. That's good information. I appreciate you sharing that. Now one thing I'd like to recap a bit, you had mentioned earlier that you do not wait necessarily for the patients who get a significant viral load before you start treatment. Do you see this standard protocol to be used in the future?

Dr David Goldberg: So I think that is something that's been discussed a lot in the community, for us it was partially, and I had asked Mr Shelat this when we had all spoken at a meeting, what he would have said if I told him we have the medication, but we're making you wait six weeks. And he told me he wouldn't have been as enthusiastic. So we had the medication, so we felt that it was important to start it early. Now in the real world, outside of a trial, I don't foresee a way that you would be able to start treatment that early because unless the hospital were to purchase the medication up front, you would require sort of a clinical practice to have the patient get a viral level, apply to the insurance company, get approval and get the medication which would take several weeks. So what we do in our study may not be what would happen were this to become standard of care.

Connie: Right. I understand that. And, I appreciate that information because there is a lot of patients who have, maybe have to apply for the insurance company and maybe have to work through some paperwork and everything. So it's just good information. My next question would be, from my understanding, the United Network for organ sharing, based here in the US has had a policy guidelines that throughout the country, anywhere in the US, it's divided into 11 regions, which includes 58 territories known as the donation service areas. But up to this year, a general transplant policy states that each area has first vide organs collected from their area in which the sickest patients from that area are first in line, only when an organ isn't suitable for all patients in the area is it made available to patients within the region or nationwide? Do you see this policy change in any way with Hepatitis C infected organs becoming more widely available?

Dr Peter Reese: I think I'll take this one. I guess what I would say is that organ allocation is really changing quickly and it's changing a lot for different organs sometimes because there have been lawsuits, sort of, demanding changes in allocation and sometimes because the community has recognized that it could be done better. I think Dr Goldberg and my general view is that Hepatitis C infected organs really should follow the same allocation process that other organs do with the sole exception that I think it's fine that people have to opt in to get these offers. But do you know in general when we allocate organs, the allocation systems should balance what's fair with what's gonna get the most benefit for the patient population. And so in general there there's always gonna be trade offs here. On the one hand you want people who live in different geographic areas of the United States to have the same access to organs but it's a lot easier said than done to make that happen just because, as an example, if a heart becomes available in Seattle, the neediest person, the person who might have a really strong claim to it by living in Philadelphia, but if you fly that part all the way here might get damaged on the way. So I think, I think there are some tough compromises being made, but I think the simple statement that I try to sort of push towards people about Hepatitis C infected organs is that in the past they were treated as sort of higher risk and maybe just to be reserved for people who already had Hepatitis C and now I think what we're starting to show is that these are high quality organs, Hepatitis C can be cured. There's no real reason to sort of only give these to patients already with Hepatitis C and so I think in general, the allocation of these organs in the future, I hope will just follow in general the same process that all other organs do, whether or not they have this infection.

Connie: Okay. That's very good. Thank you for that information. Dr Goldberg in the case of liver transplant, is there any liver damage acceptable to be transplanted like in the case of fibrosis, is there any liver damage that's excluded, to be transplant eligible?

Dr David Goldberg: So you're saying from the donor's perspective? Yeah. So I think there there's some

variability amongst centers. Now some places will always biopsy the liver of a deceased donor was Hepatitis C before using it to make sure that there's not significant scar tissue. The challenge though becomes is how accurate is that going to be, especially if it's in the middle of the night in their remote hospital where there may not be a pathologist familiar with liver tissue to say how much scar tissue there is in the liver. So there are some places where they will only will, they will biopsy and they require minimal to no fibrosis. Some will say only stage zero, some stage one and some will go up to stage 2. Anecdotally some surgeons I've spoken to at our center and others really go by feel and appearance and if it doesn't appear abnormal or fibrotic or stiff in any way, they'll accept it, but it usually has to have know minimal scar tissue. They wouldn't take a liver with cirrhosis, but if there's a little bit of scar tissue, especially all of the things, if it's adult, a younger donor or things like that, they will use it. It does not have to be completely devoid of any scar tissue.

Connie: Okay. That's very good information as well. Thank you. My next question would be, what is the recovery time period that you saw in this study for the patients?

Dr Peter Reese: For kidney transplant patients the time course, I think for the THINKER trial really looked a lot like it did for patients without Hepatitis C. The way I kinda look at it is that, there was kind of like a storm around transplantation. The patient emotionally keyed up. They go through a surgery, they get a lot of fluids, afterwards there briefly and the ICU setting, the transition to the floor, they started, they came to the hospital on 10 medications. Suddenly we're giving them IVs and then they leave the hospital on 10 medications, most of which are different. And all these people are talking to them about, all the education and what life means now that you have a transplant inside you. And in many ways, I think the fact of getting Hepatitis C was unimportant but sort of medium sized part of a big event. And I think Mr. Shelat could probably tell a lot more about that, but usually these patients were in the hospital, you know, maybe three or four days. And then, for a period and even on the first day you got out of bed walking, maybe by the second day starting to eat fluids and starting to have some of the tubes removed and the dressings changed. And then, they would usually be discharged to home or to a local thing that we have called the transplant house. And then it's sort of a period of two weeks of getting back into a daily routine. We encourage them to walk. We encourage them to really spend a lot of time sending their medications. But often they can't drive for several weeks. And well I think they could usually do self care at home for that first two to three weeks. We really encourage them to have someone there just so that, if you have to take a nap or you have to be driven to the pharmacy to pick up some medicines or you just need a little time, need a little help with dressing changes. There's someone kind of there for you. So anyway, I think it's huge to me it's usually around when patients are about three to four weeks out that they start saying, wow, I really kind of getting my energy back and starting to feel like myself and feeling like I've kind of mastered this new set of things that are demanded from me in terms of keeping track of my medicines and everything else.

Connie: Very good information because, that is something I think patients have to consider, especially after being discharged from the hospital and kind of in terms of what they can expect for recovery as well. My next question would be, does this study include working with living donors who have Hepatitis C?

Dr David Goldberg: So it does not. I think in theory you would with the living donor, you're just, ultimately from a societal perspective, from a cost perspective, you would want to treat the donor first and then if everything's okay then do the transplant just because treating, doing the transplants and then infecting someone which does pose a risk to me, I think ethically wouldn't make sense when you could treat the donor and just delay the transplant by a few months and not put the recipient at risk.

Connie: I appreciate that as well. I didn't know like it's a requirement for a match for a kidney patient and if they're only relative that had a match for kidney, happened to have Hepatitis C. I didn't know if they would be considered even if they had not been treated yet with antibiotic drugs. So, that I would think that would be something they would have to take us with the doctors and insurance company and see what they could do to help resolve that.

Dr David Goldberg: Anecdotally, I do know of a few colleagues that told me that they had a somewhat

similar situation, but they opted to treat the donor first and then do the transplant. So they didn't increase any risk to the recipient.

Connie: Well that's very good because that very likely could come up and, have a plan in place. Well, my last question would be from my information, this was a pilot study and if that's correct, could you explain what the difference is between a pilot study and a clinical study?

Dr Peter Reese: Well, I think what's going on now just sort of a debate in the transplant community is whether or not you goes, these organs should really be transplanted under research protocols or whether or not sensors should kind of have the latitude to just accept the organs and do the transplants. And, then maybe report their outcomes later. But, our view is that it's still pretty early days using these organs and everyone from the patient to the transplant community at large will benefit more if, first of all, if there's research oversight and there's an institutional review board from the institution saying, we've approved your protocol. We're making sure that you follow your protocol, your informed consent is safe and thorough because, if someone does have a side effect or a bad outcome, I think it's important that everyone felt confident that the way this study was conducted with the best. And also that, if this study didn't go well, that people could step in and say, I'm sorry, you have to stop it. So, we consider this a pilot research study with oversight, there are other centers that are doing this just as part of routine clinical care, with less oversight. We're not exactly sure what kind of consent processes that are putting in place, and then publishing the results. So we think that we know the right way to do it or the safest way to do it, but there's definitely some debate and also some debate about when it would be okay for this to transition to standard of care. We don't think we're quite there yet, but we will get there soon.

Connie: That's wonderful. Well thank you both Dr and Dr Goldberg for your work, pioneering this new frontier and making more lifesaving organs available to patients. Thank you so much.

Priya: Thank you Connie. Really wonderful questions there. We have some questions from the audience, doctors. I see that we have kind of covered quite a few of what has been asked. Just we just quickly summarize it again for the people who have asked the question. So the question has come both to my email as well as there on the website, is that whether this transplant treatment is being done on other organs, and I believe we talked about heart transplant, and so maybe one of the doctors, Dr Reese or Dr Goldberg, can just reinstate that?

Dr David Goldberg: So this is being done in liver, lung, heart transplants. We at Penn, have our ongoing kidney transplant trial and are now launching our lung transplant trial. Other centers are doing this, some as normal trial, some as just single center sort of protocols or experiences. So it's variable how it's being done, but those, all four of the major organs are being used in some fashion.

Priya: Thank you. Dr Goldberg. The next question is again something that we have answered, but let's revisit it, it says, how long does the patient have to be on the Hep C meds after the transplant?

Dr David Goldberg: So for our study, we are following the FDA package labels. So for 95% of the patients, they get the 12 weeks of Zepatier. A small subset who have a specific variant of one of the types of Hepatitis C have required 16 weeks. We felt like because the medication was being donated by the company, cost was not an issue and sort of other than side effects, the main reason to give someone a shorter course of therapy was cost, but we felt like it was safest and sort of most ethical if we were going to be doing this to give patients the full course of therapy.

Priya: Thank you doctor. So, the thing is I'm just going to wrap up and that now. To the nearly 100,000 people waiting for a kidney transplant in the US many may never get one. Meanwhile hundreds of Hepatitis C infected organs are discarded because of infection. We've just heard Dr Reese and Dr Goldberg talk about how is just possible to transplant Hepatitis C infected kidney into a patient and treat the disease and

the recipient thereby saving his life. This revolutionary treatment is certainly good news and we look forward to more data from trials on this treatment as well as those using this to transplant other organs as well. Dr Reese and Dr Goldberg. Thank you for your time and for sharing all this information with us. Kiran Shelat thank you so much for participating and sharing so much and thank you Connie. Thanks a lot for bringing in the patient perspective to the discussion and we also thank University of Pennsylvania and the audience. The talk will be available on curetalks.com and CureTalks at Penn pages. Please visit our website for details on upcoming talks. Thank you everyone and have a great evening.