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MEETING TRANSCRIPT

Externally–Led Patient–Focused Drug Development Meeting on Kidney Xenotransplantation

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POINT OF CONTACT

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00:02:54

Heather Murphy, MA

Excuse me, everyone we're going to get started shortly.

All right. Good morning, everyone. I'm Heather Murphy, a medical project director at the National Kidney Foundation and the lead facilitator of this meeting. Thank you all for coming this morning, whether you're joining us here in person or attending virtually online welcome to this meeting, the externally led, patient-focused Drug Development meeting on Kidney Xenotransplantation. We are looking forward to a great discussion today, and I would like to introduce the chief executive officer of the NKF. Kevin Longino, who would like to provide some welcoming remarks.

00:08:10

Kevin Longino, CEO [National Kidney Foundation]

Thank you, Heather. Thank you. Thank you. Thank you. Welcome welcome to this fantastic day. We're all excited to be here. I hope you are. I know the NKF Staff is. I know the sponsors are. I know the administration is. So thank you. I can't stress enough the importance of having patients at the at the beginning, at the end, throughout the process for any new technology and any development. And I'm grateful for the FDA. Hearing that and wanting to be a part of that as well.

You know, I am going to go on a limb a little bit and say that the current transplant system that we have is not patient-centric. What we have in the transplant community is a lot of skillful brilliant, committed, hardworking, dedicated people, trying to save lives. But what we have is a system that is full of processes, regulations, metrics, incentives, and disincentives and barriers that don't necessarily align with what patients need in Xeno. Among the many things we're trying to do at NKF to really change that model.

Xeno is a great opportunity for us to really put patients back in the center and move us to a definitive, shared, decision-making model. And this today is the beginning of that.
So, to the patients that are here virtually or here in the room. I really ask you to step into this.

And I know you want to, but really step into this event and ask questions and say what you need to say really, probe on what we're going to be talking about. Think about not only the best case scenario, but think about the worst case scenario and how that needs to inform policy. How that needs to inform how we move forward in this. This is such an exciting opportunity. But the patients that are here on the phone, myself included. I had a kidney transplant 19 years ago. I feel a burden of that. And I think the patients here need to recognize that we represent the 14 people that died on the wait list yesterday and the day before that, and the day before that the 20 people that were told yesterday that they were on the late. The wait list is too long, and they're too sick to stay on the list, and they've been taken off. and the 800,000 people that are living with Stage 5 kidney failure right now. and all the future patients. So we represent them, and we have the honor and the privilege and the burden to represent all those people and their families today. So, I really hope you lean into this and really take advantage, and to the folks that are that are here listing and want to be a part of that. I hope you recognize that we, as patients, are carrying that burden. And to the FDA. I just wanna thank you for your commitment to listen to patients and put patients at the beginning and the center of this. And I just want to thank you in advance for taking all of this input and integrating into your policy and your thoughts, your thinking. So thank you.

00:11:19

Heather Murphy, MA

Okay, thank you, Kevin. Hello, everyone. And again, welcome to the externally led patient focused Drug Development meeting, or EL-PFDD, meeting on Kidney Xenotransplantation. This is the National Kidney Foundation's seventh EL-PFDD Meeting, and we are proud to host this meeting.

As of this morning, about 90 people registered for the in-person meeting, and over 260 people registered, virtually including patients, care partners, FDA staff representatives from Xenotransplant companies, and other stakeholders from over 40 States, and also internationally from India, Taiwan, England, Philippines, and France.

The purpose of this meeting is to explore the patient perspective of kidney xenotransplantation. Kidney xenotransplantation is an experimental procedure involving the transplantation into a human of a of a pig kidney that's been genetically modified to reduce the chances of rejection.

You will hear this said many times today. But we want to emphasize now that kidney xenotransplantation is an experimental procedure. It is not, FDA approved, and, as you will hear, has not yet been tested in patients. Because this is still an experimental phase of development. There is a degree of uncertainty about many aspects of this procedure. Today we are asking you to look into the future and tell us how you might think how you would make decisions about whether or not you would enter a clinical trial or accept a Xeno kidney as a patient advocacy organization. The National Kidney Foundation is holding this meeting to gather patient input to support the FDA's regulatory responsibilities in this area as well as to help guide those research centers and companies developing these experimental organs.

If developers and regulators don't know what is important to patients. They can't guide the development of a modality or design clinical trials that will matter to the patients during today's meeting. We encourage you to tell the FDA and researchers what is important to you regarding the benefits the risks you might accept as well as the risks you might not accept with kidney, Xenotransplantation. They want to hear your input, because they know that you are the experts in living with kidney disease.

We want to hear from patients and care partners, regardless of your age, or how severe your symptoms are, or what stage your disease is in. In fact, the more voices we hear each of you speaking to your own experiences and perspectives, the better understanding we will have as research advances. Your feedback today can actually help influence the development of kidney, xenotransplantation. Please don't be shy and make your voice heard.

If you are a patient or care partner, both here in the room and online, please contribute to this discussion you will be given instructions on how to do this later. Beyond our patients and care partners attending today. We have several other stakeholders in the room to hear here to listen and learn: a warm thank you to the FDA for the opportunity to host this meeting, and for all of you who are joining today's meeting.

Welcome also to the researchers, clinicians, and developers who are attending. In particular. We would like to thank our sponsors for your financial support for this meeting. They are eGenesis, Makana Therapeutics, and United Therapeutics.

If you are listening online, the meeting agenda and instructions for how to participate are located on our meeting webpage to get to this web page, go to www.kidney.org/el-pfdd-xeno you will receive more information about this later, and we will also provide a link in the Webinar chat now.

Just one last word: in each of the National Kidney Foundation's 6 previous EL-PFDD Meetings there is 1 point that has consistently stood out: Patients, care partners, and families are looking for hope. Hope for better lives, and better treatments that will relieve the tremendous burdens they face from their diseases. So, we hope that today's meeting will give you a sense of hope that groups who are who are responsible for developing and evaluating experimental modalities for kidney transplantation are listening and working through advancing this new area of xenotransplantation in a way that will be meaningful to you.

So, let's get started. I'm happy to introduce our first speaker, Dr. Patricia Beaston, who is a clinical reviewer in the center for Biologics, Evaluation, and Research for the FDA. Dr. Beaston is vested in the area of Kidney Xenotransplantation approaches. She presented at the FDA's cellular tissue and Gene therapies Advisory Committee meeting in June of 2022 on the current regulatory expectations for Xenotransplantation products. She has also addressed academic and industry groups who are working to bring transplantation of Xeno organs and cells to the clinic. So, Dr. Beaston will talk about why today's EL-PFDD Meeting is important to the FDA. Thank you.

00:17:14

Dr. Patricia Beaston, MD, PhD [US Food and Drug Administration]

Thank you for that kind introduction. I'm Patricia Beaston. I'm an endocrinologist, and have been at the FDA for 23 years serving as a member of teams of clinicians and scientists that are responsible for providing scientific advice to developers of new products and performing regulatory review of applications for human studies and marketing applications for a range of drugs and devices and biologics.

For the past few years I have worked in the center of biologics, evaluation and research, where I participate in the review of organs sourced from pigs that are being developed to address the shortage of available human organ donations needed to meet a growing demand.

I have represented the FDA at meetings discussing the potential of xenotransplantation and consideration for product developments. This includes the use of pig techniques for human transplantation.

You may wonder why an endocrinologist is part of this team. Well, the kidney and eyelets are, namely, the biggest considerations for an endocrine product that we could source from the pig and it is my responsibility to make sure that when we talk to developers that we understand the potential benefits and mitigations that may be needed to address any kinds of physiological differences between humans and pigs.

Over the years I have participated in meetings in which patients were invited to speak during public comment, sessions, or a patient representative has been a member of the panel.

In addition, I have had the honor of volunteering at Walter Reed, National Military Medical center and Provin care. Hearing from patients their families and caregivers at meetings or in clinic helps provide perspective on their experience and goals.

FDA protects and promotes public health by evaluating the safety, effectiveness, and quality of new products. But we do not develop medical products or conduct clinical trials. It is, however, FDA's responsibility to ensure that the benefits of a product outweigh its risks. While FDA plays a critical role in medical product development. We are just one part of the process.

PFDD meetings give FDA and other key stakeholders, including medical product developers, health care providers and Federal partners an important opportunity here, directly from patients, their families, caregivers, and patient advocates.

The currently available treatments for end-stage kidney disease are dialysis and transplantation. Much is known about the science and medical management of end stage kidney disease, the limitations of these treatments, and the shortage of donor kidneys.

However, there is so much that we do not know about your everyday experience. The impact of the disease has on your life, and your experiences with the currently available treatments are how your end-stage kidney disease affects you and your family and caregivers.

While the criteria for organ selection and procedure for transplantation, immunosuppression and post-transplant management are well defined for traditional human-to-human kidney transplantation, this is not so for the transplantation of a pig kidney to a human recipient.

Therefore, this PFDD is somewhat unique in that the members of the review team have worked with the organizers of this meeting to develop discussion topics specific to xenotransplantation, so that we can hear about your experiences with end-stage kidney disease. How you think about the possibilities of xenotransplantation, and how you weigh the potential benefits and unknown risks of xenotransplantation compared to currently available treatments.

We look forward to incorporating what we learn today into the agency's thinking and understanding of how patients view potential benefits and risks of Xeno kidney transplantation for ESKD.

Thank you for inviting me to participate in your meeting today. I would also like to thank the National Kidney Foundation, all the staff that were involved in planning this meeting and my colleagues at the FDA. Who provided input into the discussion topics.

Once again, we are all here to hear the voice of the patient. So, thank you for your participation. We are grateful to each of you for being here to share your personal stories, experiences, and perspectives.

00:22:08

Heather Murphy, MA [National Kidney Foundation]

Thank you, Dr Beaston, for the important context for today's meeting. Now, I would like to introduce the speaker for the first clinical overview. Dr. Vineeta Kumar who will provide an overview of kidney xenotransplantation. And let us know what the current state of research of these experimental products are. This will set the foundation for many parts of our discussion today.

Dr. Vineeta Kumar is a transplant nephrologist and director of the High Risk Transplant program and is involved in the Xenotransplantation efforts at the University of Alabama in Birmingham. Dr. Kumar will provide an overview of Xenotransplantation. Welcome, Dr. Kumar.

00:23:03

Dr. Vineeta Kumar, MD

Thank you. Heather. Good morning. Everybody. Can everybody. Hear me. Okay.
great, thank you. So in the next 10 min we'll do a tour to force review of all the advancements and Xeno transplantation. So without further ado. Some disclosures. And what I'd like you to focus on this disclosure slide is the word investigational. Heather's already used that word, and that's something that needs to be front and center. As we talk about both the kidneys and the immunosuppression, both the modified kidneys and the investigational immunosuppression could go hand in hand as we move this forward.

The other things that we need to focus on as a group are the knowledge that we have gained both from the animal and the brain-dead decedent model and the risks we've understood, the benefits we've understood, the unknowns that are still out there, you as a group take into consideration, what next?

This is the overview that we're going to explore today. And without further ado, let's talk about the need. Why do we even have to talk about Xeno transplantation? Most of you are aware of a slide like this that shows the mismatch between the people waiting for a organ transplant versus the number that actually gets a transplant, and that bar in the bottom. The bars in the bottom represent the flatness of that bar versus the curve that represents the people waiting, and they just represent a fraction of the people who have kidney failure, one in 7 actually make it to the waiting list.

But the saddest thing is this fact down here that Mr. Longino already referred to, where this is an underestimate 25 patients per day are either removed from the wait list or they die, and that adds up to about 9,000 patients a year that never make it to transplantation. And that's where we need a solution. Play on words at the impossible. Or I am possible solution of xenotransplantation.

And why, then, are we thinking about pigs as a potential source non-human primates were potentially something that could be used. Early data suggested. Perhaps they could have had more success. But where are we going to find enough of them, and they also harbor deadly viruses. Which is why the use of that was banned in the late nineties and pigs were preferred, and I won't enumerate each of those reasons, but they're there for your review. But more importantly, pick sources are already news for some of these things like heart valves, cornea skin. We are using pig sources at the present time. In medicine.

So, with that background, if we what was one of the first progress that was made in Xeno transplantation. We needed a model. We needed to study this. We needed to figure out how we could use a pig into clinical into the modern medicine, but not do it in humans. So, we had this model of trying it into a baboon which was a surrogate for a recipient.

So today, if we took a non-modified donor pig and put it into a baboon, that kidney from the pig into the baboon immediately would look really pretty, and then within minutes would turn black. This is what we refer to as hyper acute rejection, and what we learned was that baboons. By the same token, humans have naturally occurring antibodies that would then attack anything from the pig. So, the pig organs and immediately destroy it. And the way. The solution to overcome that in the beginning was, let's just treat the baboons with immunosuppression.

Let's give them immunosuppression and more immunosuppression. We discovered other things that got in the way. If we treated this first antibody, there was some other antibody and some other antibody, and soon it was just way too much around the same time we were learning something called genome attempting where scientists could fundamentally change DNA of organisms. And that led to this Eureka idea is hey? Instead of doing too much for the recipients? Why don't we change the donor?

Why don't we make the donor look more human-like so that we don't have to do so much immunosuppression for the recipient. Here is a example of how that was done. Remove genes that could potentially be looked at as foreign, so that's called knockout, and introduce genes into the pig that could then make that organ come with its own immune system, sort of protect its own self sort of the knockout
model, and there could be one gene knockout, 3G. Knock out 10 gene knockout but the question that we need to ask ourselves is, can there be too many edits? What are the long

term effects of these gene edits? And that's an unknown. That's something we'll have to content with as we move forward now, as we figured out these gene knockout pigs.

How did they work? Right? The non modified pig we know but now, with the modified edited pig into the baboon, what were some of the lessons learned?

This is where we found out that physiologically it worked similar to human kidneys. But there were some important differences, and these are differences that could then extend into when we do in human clinical trials. If we do? In human clinical trials. And what were these differences? Doctor Beaston has already referred to the very important differences between pig and human hormones.

So, for instance, the pig kidney will make a hormone called EPO. Human kidney makes a hormone called EPO, that works on the human bone marrow, and prevents us from. Get anemic dialysis. Patients take erythropoietin. The pig EPO will is not, doesn't seem to work on baboon bone marrows. So, the baboons need erythropoietin supplementation. So the mitigation strategy, the strategy to overcome this is then to give people lifelong for our in human trials. If it comes to that, there are other things.

There's other hormones that are made either by the pig kidney that have to work on humans or other hormones made by humans that have to work on the pick kidney vice versa, and if that so the translation of that could be, you could end up making so much urine output. It could affect your blood pressure. So we'd have to have mitigation strategies. We have to drink a lot of water. We may have to add additional medication. We may have to leave the native kidneys in for the recipients. These are some considerations increase in size of the kidney from a few centimeters to much more and if that happens, the placement of the kidneys sort of the usual placement it may have to be in the abdominal cavity where there's space for patients or pulses to kidney diseases. Those kidneys get up to 30Â cm of normal kidneys at 12Â cm. So, there's way you have. We'll have to think around those things transmitter rejections. these modifications, short-term rejections, hyperacute rejections, acute rejections we could do away with but long-term rejection still persisted that required that the baboons were continued to be treated with more immunosuppression.

Now - we were trying to create these, to reduce immunosuppression, to allow for us to use conventional immunosuppression. But here, even with the modified pigs we were using more immunosuppression. And so the contention became. Look, we were making these modified pig kidneys to look more human like. But we were studying them in baboons. And so that's why we were using more immunosuppression. Maybe we won't need as much immunosuppression in humans. But how are we to know that one way to consider doing that was to think about the human, decedent model. the human, decedent model? Was the brain dead? A human where you could put these modified kidneys test them under usual standard immunosuppression, or even experimental immunosuppression, and see if they would work. But it would only still give us short term data a week, 10 days, 30 days but it was something worth looking at just to sort of test out our hypotheses and what we have found from the decedent studies both done at our center at UAB and at NYU The 3 days, with standard immunosuppression at our center. And now it's 7 days. We just published that. That there's no

early hyper acute redaction. Though recently there was the NYU media release. We're waiting for the actual peer-reviewed publication of that. But at one month, supposedly, there was no rejection. We do know the xeno heart recipient ultimately had rejection of the heart. And this is something Dr. Reese is going to touch on more in the 3-day experiment with our first deceit, and one there was no poor scene. Virus transmission. We shop, but that's a short time we do know. In that heart, xenotransplant. There was the poor scene we presence detected in the heart, recipient. Not necessarily disease. And this is something, again that Dr. Reese is going to touch upon more recently, as far as function, we were able to show function. That's up to 7 days, these kidneys function. Normally, we were able to maintain blood pressure electrolytes with what we would be able to do a with usual fluid intake and medications that we could give with the standard of care therapy.
and that's the two-min thing that I was mentioning to you with and by you, so to wrap it up. What are the implications for first inhuman trials. First, again, a reminder that this is still an investigational therapy.

2. The first concern. But the first thing to address is safety is taking care of our patients, any potential risk? That we know of, and the unknowns that we can take care and rescue patients from, and that will require intensive monitoring both inpatient and outpatient.
It will. The question then becomes, will the pig kidney work? And the answer question. The subsequent question also is compared to what committed to human native kidneys, or living donor transplant kidneys, or the good deceased donor or marginal disease donor, or, you know, we know they're deceased donor kidneys that don't work. They end up in primary non function. We remove them or dialysis. I can purely speculate and say that at the present time that probably hopefully will be there. But do I know that? No, that's my wish list. And hopefully that line will move up further? And you know as we move to first in human trials, we'll still need to figure out the optimal immunosuppression and the question about viruses, future transplant rejection. And as we've talked about in those scientific circles is, it's probably not going to be the first inhuman trial. It's probably going to take multiple trials learning from each one to apply to the next one to get where we need to.

So, with that, thank you for your attention. There are too many people to think, but this is the work of on the shoulder of giants that have worked in this field for over 100 years, and the work has really accelerated over a period of time. And I'm really grateful that we're all here in this room, willing to work together to inch this needle forward. So, thank you for your time and attention.

00:35:34
Heather Murphy, MA:
Thank you, Dr. Kumar, for that wonderful overview. Later we will have another clinical presentation that will focus more on the known and unknown risks for that future discussion.

So now we get to the core of today's meeting, which is to hear from you people living with kidney conditions and their care partners and family members to lead us. It is my pleasure to introduce our meeting Moderator James Valentine, who has been working with us over the past several months as he's helped us plan this meeting.

James has worked the last 15 years as a champion for the patient voice. James previously worked at the FDA, where he was a patient liaison helping to incorporate the patient voice into medical product review.

There he helped to develop and launch the patient-focused Drug Development initiative. In private practice James has worked with many patient organizations to ensure their community's voices were heard by decision makers relevant to today's meeting. James has been involved in helping plan and moderate 60 of the 80 externally led, patient-focused Drug Development meetings, including having moderated all 6 of NKF's previous EL-PFDD Meetings. So, we are in good hands with James. Take it away, James.

00:37:06

James Valentine, JD, MHS [Meeting Moderator]

Thank you so much, Heather. And it's so wonderful to be here with this community today to explore this really important topic of patient's experiences that inform their preferences around the possibility of investigational kidney Xeno transplant.

So now that we've heard an overview of kidney Xenotransplantation from a transplant expert. We are turning to the core of today's meeting, which is to hear from you people living with kidney disease and their parents, spouses and other direct care partners.

Patient-focused drug development is a systematic way of gathering patients, perspectives on their condition and on available treatments. As you heard from FDA's Dr. Beaston, your input can help inform the agency's understanding of kidney disease specifically today to inform the development and potential review of kidney Xenotransplantation while FDA has held many of its own meetings today actually marks the 80Â s externally led, patient-focused drug development meeting. So, this is truly a unique opportunity for this community, especially knowing that there are tens of thousands of known conditions that FDA could and industry could be spending their time with today.

So, today's meeting is interactive. So let me tell you a bit of what we'll be asking of you and how today's meeting will be organized.

First, we're going to have 3 different discussion sessions. Our first session, which will occur this morning, will be exploring the patient and care partner experience of living with kidney disease and how those experiences inform. Why, you may consider kidney xenotransplantation after lunch in the afternoon. We're going to have 2 discussions. Our second session of the day will bring everyone back together to explore your considerations of risks and other downsides of kidney, Xenotransplantation. Some are that are known, but many that are unknown prior to first in human clinical trials and then we will end with our third discussion of the day, where we will explore considerations for participating in those first and human clinical trials. So, what will those 3 different discussions look like? Well, you'll be seeing a combination of some different methods that will be bringing your voices into the discussion to kick us off for the day. We'll be hearing from a panel of patients and care partners of individuals that are living with kidney disease that's intended to help set a good foundation for our discussion. Those individuals reflect a range of different experiences with different kidney diseases at different stages in their journey, and will give us a sense of what the community may be thinking. But we know that a single panel can't reflect the full range of different perspectives, which is why, following the panel, will be launching into these different audience discussions.

These discussions will be open to all of our patients and care partners that are in the audience, both here in person as well as on the web. The ideas to build on the input that we'll have heard from the panel, and I'll be asking discussion questions and inviting you to state your name and provide a comment to help answer those.

This can be done in one of 2 ways for those of you in the room. You'll just raise your hand, and I'll call on you, and we'll actually bring a mic to you to have you share your thoughts.

For those of you who are on the web. We have a web form for you to submit written comments, and I'll go over how to join that a little later, and we'll be reviewing those comments and reading them out during the program today as well. So, your voices can be heard.

The final way. We'll be bringing all of our patients and care partners into the discussion is through the use of polling questions. So we ask that our patients and care partners only use their phone or for those who are following along on the web. Today, you can actually do this in a web browser. And I'm going to ask that we actually go ahead and get you into the system now. So again, for our patients and our care partners for those in the room, you can flip your agenda over, and you'll see that there's a QR. Code for slide. Oh, and if you use that with your phone's camera, it'll actually take you what right to the web page, or if you're following along and wanna on the web or here in the room. You can also type in that URL directly. It's just www.slido.com and you'll be asked to enter a code, and that code is 7004787. Again, you can go there now www.slido.com and enter code 7004787 and we'll be getting to some polling questions very soon. We'll be using these polling questions to help get broad in the discussion to everyone and get a sense of the range of experiences and perspectives in the audience.

I also want to mention that following today's meeting, we'll have the opportunity for you all to provide written comments for 30 additional days after the meeting. So, whether you just walk out of the meeting, and something pops into mine. You wish you had, you know, had thought of earlier to share, or for those of you who may be watching the recording of today's meeting within the next, you know, 30 days from the live meeting day, you can submit your written comments as well.

All of today's input. And all of the written additional written input we receive will be summarized in what's called a voice of the patient report which will be provided to the FDA and made available for researchers and product developers.

So, I have a few ground rules I want to cover before we get into asking you all to participate.

So first, we encourage people living with kidney disease as well as again, their parents, spouses, and other care partners to contribute to the dialogue. And again, you can do that through polling by raising your hand here in the room, or for those on the web submitting written comments. The discussion today is limited to our patients and care partners.

Also, I want to mention that today, we want to explore the direct potential benefits and potential risks of kidney Xenotransplantation to patients directly. So, we will not be focusing on issues of animal ethics or other ethical considerations. I also want to mention that our colleagues from the FDA drug developers and clinicians are here to listen.

And finally, views expressed today are inherently personal, and the discussion may get emotional at times, so respect for one another is paramount, and to that end I do ask that you try to be focused and concise in comments, so that way we can hear as many voices as possible.

So, without further ado, let's get into our first set of questions to get a sense of who we have in our live audience here in the room today, or as well as on the web again for those of you in the room. You can go to that QR code on the back of your agenda right now, or you can type in www.slido.com and enter in code 7004787.

Once you get into the system, you'll be able to keep this up throughout the day, and you'll be able to make your selections. Every time we go to a new question it will automatically appear there and then we'll be able to actually see the results here, live in the room.

So, if we can go to our first polling question and we'll give everyone a few moments to get into the system here, so we can make sure to capture your responses throughout the day. So here, we want to know, are you currently, or in the past, an individual who has experienced kidney disease, the care partner of someone who has experienced kidney disease, or both, both a patient and a care partner.

So, give everyone a few moments here to make sure you're in the system. If you're having any issues getting into the system, you can just give a little wave of a hand, and we'll send someone over to help you. We have one person right here, Heather.

These first questions will be more straightforward. As the day goes on, they will become more complex and require a little bit of thinking. But we do want to give everyone just a few moments here to get into the system. So, we make sure you're in throughout the course of today's meeting

Alright. So, as it stands, it looks like of our individuals represented today, we have about a little under 2. 3 of our audience are individuals who have experienced kidney disease, a little under a third of our audience are those care our care partners. And then just under 10% of our audience today represents a person living with kidney disease who is also a care partner of a loved one with kidney disease if we can go to our second polling question.

So here we want to understand where our audience lives. And so we would like to ask you, where, where do you or your loved one live? The options are A, the Us. East coast or Eastern time zone, B, the Us. Midwest or Central time zone C. The Us. West or mountain time zone, d. The Us. West Coast, which includes the Pacific, Alaskan and Hawaii, time zones E. Canada. Mexico, or the Caribbean Islands, or G outside of North America, such as Europe or South America.

Again. Give everyone a few moments here to get. Make sure you're in the system, and can answer these questions ot surprising, for in person meetings on the east coast that we have a little higher representation there, but I do am pleased to see that we do have representation across all of the US Time zones or in regions.

If we go to our next polling question. So here we want to know what is you or your loved one's age. So, this is the person living with kidney disease, and if you are both a patient and a care partner, please answer on behalf of yourself.

And so we'd like to know, are you? Is the person living with kidney disease, a. From birth to age, one B. Age 2 to 12 years, C. Age 13 to 17 years, d. 18 to 29 years E. 30 to 39 years, F. 40 to 49 g. 50 to 59, age 60 to 69, i. 70 to 79, or JJ. 80 years of age or older.

I see a few responses are still trickling in we do have good representation across most of the age ranges. We see that the greatest represented today are the 40 to 49, and 60 to 69, although probably just right there. Pretty in that. The same mix is 50 to 59.

So, we're seeing that kind of total in totality, age 40 to age 69, heavily represented. We have a good representation from the 18 to 29, age, range and representation across all range age ranges besides birth to age one and 13 to age 17.

We go to our next polling question. So here we'd just like to know? If or ask you to describe you or your loved ones. Race or ethnicity. The options are a American, Indian or Alaskan, native B, Asian, American, C. Black or African, American, d. Hispanic or Latino. E. Native, Hawaiian, or other Pacific Islander, F. White or Caucasian G other or H. If you prefer not to answer. We'll give just a few more moments. Make sure everyone has a chance to get their response into the system here. It looks like the majority of our participants today are representing. Represented are white or Caucasian.

We do have about over 15% represented a black or African American, 5% Asian, American as well as representation from those who are Hispanic or Latino, as well as other recent ethnicities that weren't listed here one last polling question here just again to get a sense of who's in our audience? Both in the room and virtually so. Here we want to know the person living with kidney disease. What is your or your loved ones? Gender a female B male C. Nonbinary, or D, if you prefer not to answer.

We'll, give everyone a few more moments here, we're seeing some flip flopping, if whether it's male or female here in the room and on the web.

But we're seeing a good equal balance close to equal balance between male and female. No one is reporting that they are non binary, or that they prefer not to answer

Well, thank you all for being willing to participate in those first polling questions again. You can keep this up. We're going to be going to polling throughout the session today to get your help, get your input, and help launch into some of our discussions.

Oh, sorry about that. We missed that but one last one, which is an important one. Apologies for that. So please pull your phone right back out here. We do want to know is what is the cause of your kidney condition.

And so the options here are A. acute kidney injury, B. aHUS, C. alport, syndrome, D. C3G. Or MPGN, E. Diabetic and or hypertensive kidney disease. F. Fabry, G. FSGS, H. IGA nephropathy, i. Lupus nephritis, J. Membranous nephropathy, K. Polycystic kidney disease, or L. If you have some other form of kidney disease, or if you're unsure or it's unknown to you.

we'll give everyone just another moment. Here we're seeing a lot of it is impossible to list all of the different types of forms of kiddie disease in a single question.

So, we are seeing about a quarter of our audience saying others, or unknown. About 20% representing FSGA, another 20%, almost with Ig nephropathy, nephropathy, just over 15 with PKD. and then representation across a number of others. And a number of others that aren't included here today.

So now, thank you so much for answering those polling questions. It is good to get a sense of who we have in our audience as we explore a number of the different topics throughout today. But at this time I'd like to invite our panel to the stage. As I mentioned, we have a number of your peers. Come on up. Don't be shy.

Who are going to be sharing some of their experiences and expectations both on around. You know, the possibility for themselves or their loved ones. You know, of undergoing a kidney Xenotransplantation as well as some of their thoughts and perspectives on risk and their tolerance for risk around kidneys. Xenotransplantation.

So today our panel is made up of Brie, Sandy, Ed, Katherine, Wendy, Maria and Victoria and I'm going to go ahead and ask Brie to kick us off and take it away. Thank you so much, Brie.

00:53:36

Brie [Testimony Panelist #1]
Can you all hear me? Is that good?

Hi! I'm Brie, from Birmingham, Alabama. I'm a wife and a mother to 3 young children, 2 daughters and a son. I'm also the marketing director of an Alabama-based pharmacy.

In May of 2019 I was diagnosed with atypical. I'm sorry I'm atypical hemolytic uremic syndrome or AHUS. A very rare genetic disease that causes blood clots to form in your blood vessels blocking blood flow to your kidneys. I received a kidney transplant in August of 2021. I prayed for many years to be a mother. However, during my 2 and a half years on dialysis I felt less than a mother.

2 and a half years is a long time to miss out on life's emotions, especially with young children. When I was diagnosed and immediately placed on dialysis. I had a 6-month-old, a 3 year old and a 5 year old. 2 years later, when I received my transplant, My kids were then 3, 5, and 7. Those were 2 crucial years, and during that time I sat in the background missing out on all the mesand castles were creating, such as building sand castles at the beach, and simple neighborhood walks.

During those 2 years I was forced to wait on an aloe transplant due to Covid as well as finding a matching donor. If Xenotransplantation had been available, I most likely wouldn't have spent that time waiting on the list. I could have rejoined my life as a mother much quicker. I would have volunteered to be in the first Xeno clinical trials. My quality of life had diminished to that point other than losing my life. No risk was too great.

No matter how they spin it. Dialysis is not a pleasant option. the years spent only being able to consume 32 ounces of liquid a day, the struggle over which shoes to wear, because I wasn't sure how badly. My feet were going to swell at the end of the day, the random throwing up spells, and so on. All of that could have been reduced had Xenotransplantation been an option. everything mentioned and living that life would have greatly influenced me to volunteer for a xenotransplanted kidney.

I would have seen it as a life raft in the tumultuous sea I was living in.

Xenotransplantation could cut down on the months or years. Patients are waiting on dialysis while the clock ticks by on a kidney hopefully to come. You can't live a normal life on dialysis, you can with a transplant and a Xenotransplant kidney could fill that need

I have experienced an allotransplant. I'm very well aware of the surgery itself. The post-transplant medication regimen, the follow-up appointments, the physical pain and anxiety that comes with receiving a human kidney transplant. I would happily go through all of that again if it meant I didn't have to suffer on dialysis. and I could get back to living a normal life.

I know a human kidney transplant last, on average, 12 years. I sit here today at 40, so most likely I will need another transplant or 2. I would whole heartedly volunteer for a Xeno kidney if it meant my time on dialysis would be cut down. I assume there would be many more follow-up visits, the possibility of added post-transplant medication, more blood work, and even daily monitoring for some time. But I would gladly accept that if it meant I would be able to return to my life as a wife, mother, and friend.

Of course there's going to be risks with Xenotransplantation. I knew them going into my own human transplant, but as a mother I would risk everything for the chance to actually be there for my children.

Honestly, I would only 47% of those on dialysis are still alive 5 years out, if I knew my time on dialysis was running out, and Xeno was an option. I would seize it. The way I see it. My only other option would be death. In the year since my transplant I've taken advantage of my second chance. I'm the room mom at my kids classes.

I've blown my work goals out of the water. My husband has his wife back. My parents have their daughter back. and I actually love. I relish in the mundane. I mean, I really like packing my kids lunches every day. We have sleepovers in the den. I love taking them on long walks and just being an active part of their everyday lives.

This this type of bonding with my kids is what xenotransplant could provide if I need another transplant. The heartbreak I felt while waiting on dialysis for a transplant was almost unbearable. 2 and a half years. That was 2 Christmases I missed out on playing Santa because my cord wouldn't reach far enough into the den. 2 easters. I couldn't play the bunny. not to mention I couldn't be the one to collect the lost teeth nor could I be the one to run to my children as they cried from their bed as a mother that goes against your natural instincts. For those reasons I would accept the risks of failure, the risks of pain of sickness, and whatever else Xenotransplants could throw at me.

I am a mother that is my God-given blessing, and I wouldn't let anything stand in the way of that. Thank you.

01:00:23

Sandi [Testimony Panelist #2]

Okay. Good morning. My name is Sandy. I live in the nation's capital, the District of Columbia and I'm a native Washingtonian. I retired from the Federal Government in 1996 after 30 years of service. I suffered from kidney disease for many years before being diagnosed with end stage kidney disease and 2019. I had been a hemodialysis patient on Monday, Wednesday, and Friday at 3 and a half hours for 4 years

I was told by 3 different hospitals that I was not an viable candidate for the kidney transplant donor list. For several reasons: My age. my ethnicity, my blood type. O positive, And my health challenges, such as diabetes and high blood pressure. Since I'm not a viable candidate for the kidney transplant donor list. I must depend on a living donor.

I don't have one as yet. so I am open to other options. Xenotransplantation is not something I have heard of until now. If the procedure is approved and is successful, it could save the lives of many people who would otherwise receive a kidney transplant like me.

My major concern at this time would be the rejection of the foreign object by my body. I need to know the percentage rate for rejection before agreeing to participate. If the rejection percentage is too high. I don't think I will be willing to take that chance, especially at my age. If I am told that XY and Z would be done to decrease rejection. and if it lowered the percentage rate, then I would reconsider.

If the rejection rate is minimal. I need specific information on the meaning of minimal. If studies are done that prove the rejection rate is the same as human kidney transplant, then I would definitely participate in the program. You may ask what percentage rate is acceptable for me. To be honest, I don't know what this time I would need to compare the substance and rejection percentage statistics before making a decision.

I am looking at things from a different perspective. I am 78 years old because of my age. I don't know how much time I have left. I want to live a full, productive, and useful life with the time I have left. I won't go out willy-nilly to accept something with the high failure rate just cause. I am also concerned about the time it will take for the necessary studies to be completed before the first xenotransplantation would even begin.

At my age I am unsure if this would even be an option for me. However, I would accept an approved kidney xenotransplantation if I needed another kidney to live because there was no other alternative and was assured that it would effectively replace my kidney function.

Another major concern regards the infection risks: specifically zoonosis for the patient and for those around them. Xenotransplantation would not be an option for me if nothing was done about this problem. However, I understand that peaks can be screened and quarantined, which dismisses the infection risk to nearly 0%.

If this proves to be true, then I would accept xenotransplantation with 0 infection risk. Since I have end stage renal disease. I don't know how long dialysis will work for me. I do know that dialysis is what is keeping me alive. At my age my chances of receiving a kidney donation of any kind are so. I would consider it if dialysis was no longer working for me, and I had absolutely no other options. Medication is another concern.

Are the medications the same as those for a human kidney transplant? I've been told there are many. I've also been told that the medications are harsh. What does Harsh mean? I will need to make a comparison of the medications to determine whether this would be an option for me. Thank you for your time and interest.

01:06:39

Ed [Testimony Panelist #3]:
Good morning, everyone. My name is Ed.

1986. While stationed at Howard Air Force Base in Panama, I was diagnosed with IgA Nephropathy. I was told that I would need dialysis and eventually need a kidney transplant.

I was medically retired, and months later started hemodialysis. At that time, I was 23 years old, married, and had 2 small children.

After nearly 6 years of serving my country, my lifelong dream of having a career in the Air Force was over, and the courses of my life, and the lives of my wife and children were dramatically changed.

Today, at 60 years old I am married and have 5 adult children, 4 grandchildren, and 2 Yorkie pups that keep my life full. I've had a full and blessed life, and I want more. After one year on hemodialysis, I received a kidney transplant which lasted 34 years. When it failed. I went on peritoneal dialysis. Nearly 3 years later. I had my second transplant in May of this year.

I am doing well now and remain grateful for another chance at embracing life. Dialysis saved my life. It also negatively impacted the quality of my life. I felt a sense of hopelessness and doom. I was surviving on dialysis, not thriving.
I longed for the freedom from dialysis and to spend quality time with family and friends, go to work, or go to school or travel the world.

Waiting for my kidney transplants was terrible. The uncertainty of not knowing when I would get a kidney, or even if I could survive the years. Long wait was extremely taxing on the body, mind, and spirit. My marriages suffered, I was divorced twice, my careers were derailed, and my family's dreams were crushed.

I mention all of this because reducing or eliminating the weight for a human kidney with all the associated trauma of that weight would have driven me to strongly consider entering a trial for kidney xenotransplantation.

Nevertheless, I have fears about xenotransplantation. They are based not on not fully understanding the evidence that it will be safe and effective for humans. Some of these risks are acceptable to me.

Animal-to-human transplantation, unknowns, including infections or potential diseases or unanticipated viruses that could emerge in the future. This is the biggest fear I have about xenotransplantation but it will not determine acute or chronic rejection possibilities similar to human kidney transplants. I know these risks exist. Infections that directly impact only me direct, different or new immunosuppressant medications and potential negative side effects. Mental health impacts like depression and anxiety, post transplantation.

and some risks that are unacceptable: threat of porcine or other infections to my loved ones. I'm around family members with immunocompromised health, and I would not want to jeopardize their health. If xenotransplantation required extensive long term monitoring that would prohibit me living a full quality. Life, it would be a deal breaker for me.

Knowing there are many unknowns to consider when my life is literally on the line. I also worry that I would be more willing to take risks in order to sustain my life without fully thinking, through the long-term implications of Xenotransplantation. Yet these fears seem almost irrelevant when given the chance to avoid or minimize dialysis treatments and the harsh life I described previously reflecting back on my dialysis experiences. If the opportunity was available. Back then to be part of Xenotransplantation trials. I most certainly would have moved beyond the fears with medical guidance and had the transplant in the hopes of getting my life back.

Finally, as a Latino, it would be important to know that my race and ethnicity was included in preparation for xenotransplantation.

Thank you for your time and for hearing my story.

01:11:20

Katherine [Testimony Panelist #4]:
Okay. Good morning. Good afternoon. Only the Creator knows when my life will end, and in the past I took life for granted. However, when I was diagnosed with end stage renal disease. I began to cherish each day. I am graced with.

My name is Katherine. I live in Jacksonville, Florida, with my husband, and I have grandchildren living in Atlanta and Cleveland, Ohio. In 2021 I was diagnosed with end stage renal disease and put on the transplant wait list. That same year

I spend 3 and a half hours on hemodialysis. On Tuesday, Thursday, and Saturday. I was on peritoneal dialysis for 6 months but after an additional 3 surgeries. I had to stop because my body rejected the catheters.

The time spent on hemodialysis is difficult, mentally, physically, and it is time consuming being on. The waitlist is another burden because I am on the inactive transplant. Wait list until I can transition over to the active list, and I fear that I may not live long enough to see my grandchildren grow up as the youngest is now 4 months old.

Side effects of medications. I take my dialysis treatments and the emotional effects of my kidney disease are depleting and compromise my quality of life while the transplant list fills me with hope. Having the option of a human or xenotransplant is even better. Any new treatment or medication has risks and side effects. but when I think of the alternative without treatments. I would rather take the risk.

The shortage of kidneys for transplant time on the wait list time on dialysis, and hope to extend my life. To be with my family are the reasons why I have no fear of xenotransplantation.

When I consider the risks of xenotransplantation. I think of the potential benefits, such as such as an increased freedom in my life, less pain and less of the numerous medications I take when I think of it this way. I am willing to endure Xeno kidney that will last for even a few years to allow me the time off dialysis. However, some of the risks I would be more concerned about. or if the kidney fails or needs additional surgery to remove it. life-threatening infections, extreme pain, and if it was, and if I was worse off than if I did not endure a Xeno transplant.
I believe we need to define what a successful Xenotransplant is and that definition needs to involve the patients. What defines the successful Xenotransplant?

I think the definition should include answers to questions like: How long will the pig kidney last? Will there be side effects and or increase immunosuppressive medications? Will these side effects be more tolerable than the effects of kid of kidney disease and dialysis.

In my view, at least one year free from dialysis, minimal pain and sickness would be a successful definition and beneficial results for a xenotransplant. My hope for a xenotransplant is stronger than my fear of the risks.

My future is unknown. Will I receive a human kidney? Will I be on dialysis for the rest of my life will treatment like xenotransplantation become available or if I will live long enough and stay healthy enough. I don't know. I'm living on borrowed time.

However. Well. Whatever time I have left, I want to spend it with my spouse, grandchildren, and rebuild relationships with my daughter and sister is, you know transportation is that opportunity I do not want to fear. I do not want fear to stand in my way.

I understand and accept. No one is promised tomorrow but when you have a condition where the only option for staying alive are dialysis or transplant. I want the transplant. whether it be human or pig. Science and medication keep me alive physically but my strong faith in God and His accepting grace and mercy keep me hopeful to be able to leave a legacy for my grandchildren to remember that I did not give up. and I was willing to take one of the biggest risks of my life when I think about it from a grandmother's perspective, I would join the first clinical trial to help advance science for future generations.

When I think of my grandchildren if they are ever confronted with kidney failure, I want them to know that their grandmother offered her life to improve the number of treatment options, to extend their lives with xenotransplantation. Thank you for your time and a chance to express my opinions.

01:17:50
Wendy [Testimony Panelist #5]
Hello! My name is Wendy. I am 50 years old, and I live with my husband and our 23-year-old daughter in Hemingway, South Carolina. I am the caregiver to my daughter in 2012, at age 12 she was diagnosed with SLE Lupus nephritis, who class III which has progressed and is now class IV. The highest class is Class 6.

Last year she went into renal failure and began dialysis. While on dialysis she endured multiple procedures for access that kept clotting and ended with a failed graph and fistula. It was found her lupus was the cause of the failed dialysis access point and was only able to receive her treatments through a temporary tunnel catheter which led to 2 bacterial infections and sepsis. A few months ago her kidneys began functioning around 30%. She is now off dialysis and the transplant list.
Samantha's health journey has been traumatic for her to experience and as her mother has been excruciating the watch. Her nephrologist expects her kidney function to decline again and plans to place her back on the transplant list once her renal function falls to 20% to avoid going back on dialysis.

I think Xenotransplantation would be a good match for my daughter. and I would encourage her to enter a clinical trial, because I've seen the effects dialysis has had on her quality of life.

She doesn't want to live the rest of her life on dialysis or waiting for an allotransplant which may never happen.

My daughter and I fully understand there are risks with any transplant such as organ rejection or side effects from immunosuppressants. We're as prepared as we can be to deal with organ rejection. As for side effects, I have talked with the allotransplant team about the medications used. Post transplant. There are medications she's already taken previously to treat her lupus. So, I'm already familiar with most potential side effects.

What worries me is the unknown risks of xenotransplantation. Throughout my daughter's life, I have researched everything I could about her disease so that I could better understand each phase of treatment she has undergone, and the risks involved with Xeno transplantation. There isn't much public information available for me to research with due diligence.

However, my daughter has a lifelong condition, and our future is full of unknowns
Without Xenotransplant, I don't know if my daughter will have a future that allows her the freedom of living that most of us take for granted.

If xenotransplantation achieves FDA approval. I believe it will make these dreams a reality for my daughter, because she will have an option to receive a functioning kidney without prolonged wait times or chronic dialysis. Even the possibility she may be monitored several hours daily is not a deal breaker. as she's already been hooked to a machine for several hours during both chemo and dialysis.

I would like to share with you a conversation I had with Samantha recently. After explaining Xenotransplantation and its known risks. I asked if she'd be willing to enter phase one trial if she were selected as a candidate. Her response was. *"I'm not going to lie. I'm nervous about zoonotic infection because I could make others sick if I get it. But if they have safety precautions and I'm able to enjoy living life again, it's worth it, and I would be willing to participate in a phase one trial. Being hooked up to a machine, multiple times per week for hours, with no end in sight isn't living. And I want to live."*

In conclusion, I can tell you, as a mother and a caregiver. although she is not currently on dialysis or the transplant list. I would support and encourage Samantha to be one of the first trial participants. If she's an appropriate candidate. As you just heard, she agrees. I do not want to watch her deteriorate on a machine again. I am certain she would be closely monitored and receive the best of care while undergoing clinical trials for us, the benefits and the hope of living a full life once more outweigh the risks and the dread of watching Samantha live hooked up to a machine and simply existing. Thank you.

01:23:45

Maria [Testimony Panelist #6]
Hi, I'm Maria. I live in Midlothian, Illinois, which is a suburb of Chicago

in 2019 I sought care after a year of suffering, with swollen feet and blaming menopause a primary care. Doctor noticed several irregularities in my lab work. But it wasn't until 18 months later that I was finally referred to a nephrologist biopsy and diagnosed with IgA Nephropathy or IgAN, a rare kidney disease that has irreversibly damaged the filtering function of my kidneys. I undertook a grueling regimen of high dose prednisone in 2021, but have not been able to rise above Stage 4 with my kidneys functioning at less than 30%.

I have not done dialysis yet. but the need could arise at any time any infection I contract could kick off an autoimmune response that could damage my kidneys further and push me into end stage renal failure where the only options available today remain dialysis or transplant. Talking to you today about Xeno kidney transplantation is important to me because with my condition, even after receiving a living donor kidney. The hygienic property would still exist within me, and could damage that kidney as well. I don't have firsthand experience with either of the treatment options, and I hope to put those decisions off for a long time.

But neither of those options would end my battle with IgA Nephropathy. The 2 available options come with their own sets of issues, concerns, and conveniences that may keep me alive, but perhaps not really living.

There are numerous risks associated with xenotransplantation, known and unknown. And if you asked me today to participate in the first human clinical, clinical trials, I would simply say, No. I am sick, and my blood carries 70% more toxicity than most people. I am sluggish and foggy much of the time but participating in the first human clinical trial, would come with way too many risks for someone who has not yet reached that decision, making point the risk of a serious poor sign, disease being contracted by me or passed on to anyone close to me is simply not something my family or or I would take on today. Today, even in my diminished health, my husband and I enjoy family dinners, game nights, and other get-togethers with our adult children.

We both come from sizeable Greek and Irish families that we entertain a lot each year my siblings and our families spend vacation time with my aging parents. We also have a very large array of friends. My 5 best girlfriends have been by my side for 45 years. We have shared everything together.

These are the things I live for, and that I love doing, and being among the first to undertake a Xeno kidney transplant would most likely render that life extinct. even if death or disease were not risks. The close monitoring, severe medication, loss of privacy and other demands of being first would take away too much of the life I am still able to enjoy with my loved ones today.

If you asked me again in a few years, and my health had declined to the point where I was eligible, and seeking a living donor transplant. and the Xeno trials had entered later phases. The answer could be, maybe I would want to know if any IgA Nephropathy patients had participated in the earlier phases of the trials.

I would want to know more about their particular experiences and any other patients with a rare kidney disease. Similar understanding, the unique data points collected but I think I would be most interested in knowing if the disease had resurfaced in the Xeno kidneys or not.

If there was evidence that a Xeno kidney transplant did not pose a significantly higher risk of death, infection or rejection than an allotransplant, and could provide a kidney that would not be damaged by IgA Nephropathy I could definitely see us saying, Yes.

However, if there were no IgAN, or similar rare kidney disease patients being assessed in the early trial phases. I'm not sure what we would say to participating in even in a later trial.

I would probably have a lot of questions and expect the doctors to provide data from the trials that was critiqued against my specific condition. It would then depend on my personal situation, meaning, if I did or didn't have a match for an Allotransplant, and how much of my busy and full life was already fading away with age and disease.

The truth is, when I need to make the choice, I will always choose transplant over dialysis period. If I had no living donor match, and the waiting was requiring me to do dialysis, my life would probably no longer feel like my own. I would feel like a burden to my husband, my aging parents, my adult children and my friends, and I believe we would all say yes for joining a clinical trial for a xenotransplant.

That being said, I would want my participation to specifically collect data points that could be used to help. IgA Nephropathy and similar rare kidney disease research move forward in any way possible. Thank you.

01:29:26

Victoria [Testimony Panelist #7]

Friday, April 5th, 2019, the day my son and our family's lives changed forever.

Hello! My name is Victoria. I live in Howard County, Maryland. Prior to that dreadful day. My 12-year-old was the epitome of health: a travel soccer, baseball player, avid mountain biker, skier, and a great student.

I couldn't have imagined flu-like symptoms leading to debilitating dizziness. Sending us to the ER was life-threatening low hemoglobin. the cause: acute renal failure on that April day in our local ER we learned he had less than 10% kidney function due to the complexity of his case. We were transferred to Hopkins where he endured a series of invasive tests and procedures. This visit, the first of many, ended 37 days later when we were told he would never regain kidney function and would need a transplant.

The next 13 months were an emotional and tumultuous time for my son and our family. We were so thankful he was alive, but the dialysis he had to endure was short of torture: 9 to 10 hours per night, his tiny body filled with 1,500 CC's of fluid. That's 50 ounces filling, dwelling, draining up to 6 times in the night while he slept.

In the morning the last cycle left 1,300 c seats of fluid in his body to collect toxins until evening. when he would endure the cycles all over again. He'd often say he felt like a human water balloon. This the primary reason that prevented him from enjoying sixth grade with his peers. Our family was and is traumatized by the journey Z. Has endured

As a mother and primary caregiver. I felt helpless. I couldn't fix this for him. He lost a vital part of his childhood to his kidney failure, but thankfully, after 13 months he received a deceased donor kidney being so young, who knows how long his current kidney will last? If it fails? I hope he gets priority on the living organ donor list from my non directed kidney donation and our National Kidney registry voucher.

But what if that second kidney fails soon after I worry 1, 2, or even 3 transplants later. Will he be out of options if faced with the threat of dialysis while waiting for another kidney.

We would have to consider the alternatives. In this case we would consult the Xeno Research and our transplant team, including Xenotransplant surgeons, my son and our family experienced lasting trauma from his kidney failure, and he suffered multiple complications from dialysis. But if a human kidney is not available for a future transplant, we will have to choose between dialysis or experimental procedures like xenotransplantation. We would want to know if a xenotransplant would be a more stable solution and present less complications over dialysis.

I don't want to see my son suffer on dialysis or have to endure complications like high blood pressure, seizures, and constant fear of infection. As a mother I want my son to live a long and healthy life, so in the early trials I would hesitate to sign him up as one of the first patients.

We cannot know if Xenotransplant will lead to a better quality of life until we learn more about it. With Xenotransplant, what scares me most is the possibility of his other organs failing, leading to death.

Another worry is after Xenotransplant. He would be in much worse physical state and be subject to more intensive daily testing and lastly, if he received a Xenotransplant and it failed, would his body reject a human kidney if one became available as things stand now, if these proved true, I think you know transplantation would have to be a last option.

However, if we were faced with needing a kidney while my son Z. Is still under 18, and none was available. I would strongly consider alternatives like xenotransplantation. A Xeno kidney would offer a timely solution to years on dialysis, allow him to be free of fear of complications and restrictions, and he could get on living his life.

If Xenotransplantation becomes more predictable and successful in human trials, it seems very much a good alternative for him for these reasons. My son was blessed to receive a 19-year-old deceased kidney, but someone had to die for him to receive it. That comes with conflicting feelings of gratitude and guilt.

Xenotransplantation would help ensure my son would have a transplant when he is in need. That alone seems a good reason to try. Xenotransplantation makes tremendous sense, filling the gap between the number of deceased and living donors. I never want my son to be one of those waiting and dying on the transplant list. I hope the first trials begin and are successful, so he and all those in need can get a kidney when deemed necessary. I just don't think I am ready now to enter my son. In one of those early trials.

I look forward to a world where my son has a future that doesn't include the impending threat of kidney failure to hold him back. Thank you for your time and consideration.

01:36:20 | AUDIENCE POLLING

Discussion A: Patient Experiences with Kidney Disease

Why patients may consider Kidney Xenotransplantation (Expectations & Outcomes)

James Valentine, JD, MHS [Meeting Moderator]

Wow! Truly truly incredible testimonies, and thank you all for being so brave to share first and be the first to add to this discussion, and if everyone could just join me in thanking our panel one more time.

So now we get to our first opportunity today to broaden the discussion here. Everyone's good to go. Broaden our discussion to all of you and our audience, our patients and our care partners.

Both here in the room as well as virtually online and to as we go into our first discussion, we'll be focusing really on your experiences living with kidney disease, and how those experiences inform how you may consider a kidneys, you know, transplantation, either now or in the future.

So, if we could pull up our first set of discussion questions.

Here, as we start to get into these discussions, I want you to think as you're answering these questions a little bit about your condition and your treatment experience, as we heard from Dr. Beaston in her remarks this morning. It's so important to understand your lived context as you help us answer and provide your preferences around Xeno kidney transplantation.

So, as you do, I want you to think about you know your kidney disease, how it's progressed over time. And your experiences with some of the treatments for end stage renal disease, whether that's, you know, being on the transplant waiting list, dialysis or Allokidney transplant.

Well, we'll get to the discussion questions in just a moment. In this first session. What we really want you to do is think about what would motivate you about your Xeno kidney or about your experience that would again inform your interest in a Xeno kidney transplant.

So, for those of you who are on the web, if you want to contribute at any point during this first discussion, or really throughout the day, we're going to drop a link into the comments in Zoom now. Th, that will bring you to the EL-PFDD Website, and you'll see if you scroll down under the join Webinar button. There's a comment form, and we invite you to submit your comments throughout the discussion, and we'll be reading those out live here today. So that way you can have a voice in this.

But now I would like to take us to our set of polling questions. That will help us understand a little bit about your medical history. Some of those things, again, that we want to understand how that might inform your preferences about whether or not you might be interested in a kidney xenotransplantation.

So again, you can go pull your phones out. Go to www.slido.com. Type in the code 7004787. If you were not a part of the earlier polling. You can go ahead and join. Now, this is for our patients and our care partners.

So here we just want to understand what is your you or your loved ones? Current level of kidney function, also known, or alternatively stage of disease. The options are A and EGFR of 90, or above or stage, one B. eGFR. Of 60 to 89, or stage 2 C. eGFR. Of 30 to 59, or stage 3 D. eGFR. Of 15 to 29, or stage 4, eGFR Of less than 15 or stage 5 F. If you don't know, or G. If you're a care partner and your loved one is currently or is deceased.

So as it stands, we have a good representation across the various stages of chronic kidney disease and the Associated eGFRs. It looks like we have about a quarter of the audience that are representing Stage 5 with eGFRs of less than 15, but we do have representation in each of the other stages, as well as amongst some that are unsure of their or their loved ones. Current stage of kidney disease. Nobody represented in the audience today of a patient who is deceased. We go to our next question.

So, here again, exploring a little bit of your medical history that might inform how you would think about a potential kidneys. You know, transplantation. We want to know what best describes you or your loved one's experiences with different treatment approaches, or where you're at in your journey.

So here we want to know, are you or your loved one? Have a functioning native kidney. So you're not currently on dialysis or transplant wait list are you: B end stage disease with your native kidney? So you're on dialysis and or the transplant wait list. Do you: C. have a functioning transplant. So you have a transplant, but are not currently on dialysis or the transplant wait, list or D, do you have end stage disease with a transplanted kidney? So are on dialysis and or the transplant waitlist.

We see so far with the results still trickling in that the majority of our audience are those with a functioning transplant. And so, even though you're not yet in end stage disease. We do want you to reflect on how your experience with transplant on some of the risks associated inherently with an allotransplant might inform your thoughts around a potential. Xeno, transplantation. we do see. We have representation. Both represented representatives of those with functioning native kidneys and stage disease with native kidney as well as individuals who have end stage disease with a transplant kidney. We do want to hear from all of these groups throughout our desk discussion today. Not just those that are currently an end stage disease, but your thoughts for those who currently have functioning kidneys your thoughts about the potential for a Xeno transplantation in the future.

We go to our third polling question here.

We'd like to know if you've ever been on, or are currently on dialysis. And if you are, how long? And if you were, how long were you on it? So the options here are a less than 6 months B. 7 to 11 months. C. One to 5 years, d. 6 to 10 years, E. 11 to 15 years F 16 to 20 years, or G greater than 20 years. Either on dialysis in the past, or currently. you have just a few more moments for everyone to get the response in here. See? Responses still trickling in.

It looks like just under half of our audience have. Their experience with dialysis has been between one and 5 years. After that we see about 20 that had dialysis between 7 and 11 years. 15% between 6 and 10 years. Just over under fif under 15 at less than 6 months. and we do have some individuals who experience dialysis, for between 11 and 15 years

We go to our next question. It's very similar. But here we want to instead, ask if you've ever been on the transplant waiting list, either currently or in the past. How long have you been on it, or were you on it?

And so the options here are the the same less than 6 months between 7 and 11 months. between one and 5 year, or between one and 5 years. between 6 and 10 years. between 11 and 15 years between 16 and 20 years and were greater than 20 years.

Yeah, everyone. A few more moments here. Let us know if they have ever been on the transplant letting list how long either they were on it in the past or currently.

So, as it stands, we're seeing a little bit of a difference from the responses we saw to the last question, where I'm seeing a slightly larger representation for those who are on the waiting list for less than 6 months when they were on it.

But we're seeing that one to 5 year range. Still as the top response and then the the ranges that follow are fairly close to what we saw, although we're seeing a slightly higher percentage in that or actually, we're seeing for the first time a percentage of people who were on the waitlist for 16 to 20 years.

One last question. And this is shifting gears a little bit from your past experiences.
And here we want you to think a little bit now, for the first time, about your considerations for a Xeno kidney transplant, either now or in the future.

And as you think of these things, we want you to select the top 3. So the options are in terms of motivations. Would it be A. avoiding or shortening time on dialysis? B. Avoiding or shorting time on the transplant wait list. C. Being ineligible for allotransplant or waitlist. d. Having no matched living donor, and having a concern with Matching on the waitlist E. A concern that you may lose eligibility for any transplant in the future. For example, from declining health. F. Your age, including the number of future transplants you may need. G. Improving quality of life. H. An interest in helping advance science and future treatments. I. some other motivation that isn't listed here on the slide or J. non-applicable, because you're not interested in a Xeno kidney transplant now or in the future.

And again, we're asking everyone to select their top. 3 we know many of these things may be important motivators that would in inform whether or not you're interested in Xeno kidney transplant. As you make your selections, I want you to think about what again, about your history of living with kidney disease and other treatments is informing your selections here. Because shortly we'll be asking you to share some of that thinking with us.

So, it looks like avoiding and shortening time on. Dialysis is rising to the top as the one of the top. Consider, top 3 considerations for why, you might consider a Xeno kidney transplant followed by that improving quality, but of life as well as the fact. You know your age, or the number of future transplants you may need.

After that we're seeing considerations related to helping advance the science and treatments, avoiding time and avoiding or shortening time on the transplant wait list or concerns about not having donors. But I think as we're seeing we're there's each of these things are in some people's top. 3.

And I should note that we do have some individuals who are denoting that they're not interested in Xeno kidney transplant now or in the future, and we want to hear from those folks as well. You know. What about your experience? You know, and your thoughts from around the possibilities of this are informing you're not being interested now or in the future in this type of treatment approach.

So, with that. Now we're going to broaden our discussion and ask for you to tell us a little bit about what you're what you were thinking there, as you weighed in on those questions.

So again, if for those of you who are on the web, we encourage you to submit written comments, and we'll be sharing those throughout. But now I'd like to welcome our all of you that are here in person. And have been participating in these questions, you know again bait. And you're seeing our some of our discussion questions posted here, based on your kidney disease to date, and some of those treatments, some that we just explored in this polling questions.

You know how, you know, could you describe your interest in Xeno kidney transplant? And if you do have an interest. What factors would be important to you in deciding whether to pursue a Xeno kidney transplant and if you just raise your hand we'll bring a mic to you, so you can help us understand some of your thoughts and perspectives.

01:48:22 | AUDIENCE DISCUSSION

Topic A: Patient Experiences with CKD & Considerations for Xeno (Expectations & Outcomes)

James Valentine, JD, MHS

Who wants to get us started here? Oh, yes.

Discussion A | Patient Participant #1
So I was diagnosed with polycystic kidney disease when I was 21 right out of college. I'm now 57. I had a first transplant, unrelated living donor transplant from a remarkable, amazing woman, my best friend from college. who had never told me she was saving her kidney for 20 years until I needed it. That transplant is now failing.

I had it for 12 years. I'm now on peritoneal dialysis, and this is something I don't hear people talk about a lot. But A. It's really hard to get a living. Donor. B, when you get a living donor you worry about. I worry about them all the time, in part because she had some trouble. It ruined a friendship of 20 years. It was very unusual, I know, but so now I'm in this position of. Do I get another living donor or not? And that is much more complicated for me this time around. Now that I've seen what could happen. So the for me. The idea of xenotransplantation removes a lot of that. I like pigs, but I'm not as worried about them as I am about Brenda, so that would make a huge difference to me. I'm still young enough that if I do get a transplant now, I might still need a third one. that makes a difference. And the last thing I'll say is people I'm really blessed. I'm very lucky with a good support system, and people jumped to try to donate the first time.
Not so much the second. And I I'm a therapist, and I make all kinds of thoughts about what that's about, Covid. We're all 12 years older, you know. There's a lot of factors. but I don't think that's the only thing. I think people don't understand that you need more than one, and it's hard to ask a second. It's hard to ask, and it's hard to ask a second time.

James Valentine, JD, MHS
Sure. Well, if you don't mind me following up on a couple of things you said just to understand. I mean, when you talk about, you know weighing for yourself. You know you think about, asking a living donor to donate a kidney that you're concerned about them, and that there are, you've experienced it, Practical consequences of that. Can you just speak? Is that specifically about their health? Is that about something else? Can you maybe just describe that a little for us?

Patient Participant #1 | Discussion A: Patient Experiences with Kidney Disease
Great question. Thank you. Yeah, absolutely. The primary thing is their health. Yeah. She had some health complications. Or can you function is at about 50%. Now, post donation, which yeah, thank you, for whoever made a noise is lower than was expected.

She got understandably terrified. looked to me to support her, because I'm the only person she knows who has a kidney disease, and I was sick as a dog recovering from a transplant. So health is the number one worry. the number 2 worry that I don't hear people talk about. And I think we need to talk about it. Her care from my transplant center was nonexistent. When she was done she was done. And that is a huge deal. I mean, we are back friends now. After 12 years. And that is the one thing she would change. You've gotta do after care for donors. She was on her own, and she was scared, and there was a lot of No, no, we did everything right. And you're fine from a very, very good transplant center, right? So health. And then. just yeah. The impact on their lives that people go into this and every living donor says, I wish I could do it again. It was fabulous, and I think for a lot of people it is. But it's not that way for everybody.

James Valentine, JD, MHS

The other thing that you mentioned was, you know, because of this experience that you've had wanting options besides living donors. How do you think about? You know some of the other transplant options that are available. And how does that factor into your interest that you just described related to a Xeno kidney?

Patient Participant #1 | Discussion A: Patient Experiences with Kidney Disease

I've now been on dialysis for a year and pretty sick for about 3 years. I went into this one saying, I would only accept a cadaver kidney because I just wasn't going to do that again after a while. Sick. That changed and after seeing the statistics. potential differences between living donors and deceased donors. So I think if I had the option of a Xenotransplant, and we were at a place where we knew it was safe enough, I would go for that before a living donor, maybe before deceased donor, but for sure, before a living donor.

James Valentine, JD, MHS

Sure. Well, thank you so much for sharing your thoughts. There we have a hand here in the middle of the room. We got mic coming right behind you.

01:54:00 | Topic A Audience Discussion [Continued]

Patient Participant #2 | Discussion A: Patient Experiences with Kidney Disease

Yes, Hi! My name is Gary, and I'm here. I donated a kidney to my son about almost 2 years ago, and this was a pair type thing. 6 people were involved 3 donors and 3 recipients. And I, personally had no problem. A post off. I was back to work in 3 weeks and I'm fine.

My son's fine, and we thank God for that. I'm also a physician and it's I know about medical research and trials, and it's time that we start with a a phase, one trial we have to do this because it takes a long, long time to see the results of this.

So I'm all for investigating Xenotransplantation. I'm also, I will make a comment, each transplant center has their own criteria for donors! I, personally was turned down at 2 transplant centers before getting another opinion, and I was taken immediately.

So there III think that has to be looked into. Because in my own case. For about 5 or 6 months. II sort of just said, well, I can't be a living donor. My son's going to have to be on the go for deceased kidney, and I have my bags packed to help him when, if that time comes. So I think you know, if you have chronic kidney disease you cannot give up. Yeah, you cannot give up. You have to ask for a second opinion. Yeah, please keep in a third and a fourth, and keep going, and I'm just so happy to be here. Thank you.

James Valentine, JD, MHS

Very, very happy to hear that you are doing well, and your son's currently doing well.
You mentioned that, you're hopeful that you know Xeno kidney can make it into, you know, start clinical trials that it'd be important, you know. Can you share, you know, any reflections that you have? You know, thinking about your son? You know where that might fit in for him,

and why? That, you know, and some point in the future. You know, given what you've described it that you think kidney would be valuable.

Patient Participant #2 | Discussion A: Patient Experiences with Kidney Disease

Yes, I just think there has to be more options again. I try my best to encourage, live, live kidney donation. But there's not enough kidneys, and we have to start a clinical trial and answer all the questions you know. How safe is it? Is it? What's the risks? And so forth. going forward. We don't know what will happen 10 years from now, 20 years from now. We, have to advance science. All this. We didn't have kidney transplants years and years ago. I mean, just think of what if someone didn't investigate this years ago, we wouldn't even be where we are now. So, we have to continue to advance with everyone's concern. We have people that are researchers, and they're so intelligent for science to see what molecular genetics can be adjusted to go forward. So, I think it's yeah. I'm all for xenotransplantation to again to start. We have to start. You have to start, and I would encourage the FDA to please consider it. That's all I have. Thank you.

James Valentine, JD, MHS

Yeah, well, I really appreciate you sharing. And thank you very much. Have a hand right here, and then we'll tell me. See you right after.

01:58:00 | Audience Discussion [Continued]

Patient Participant #3 | Discussion A: Patient Experiences with Kidney Disease

So, I think both of those stories resonate with me. So, I was 21 when I went on dialysis and undiagnosed kidney disease. I was on dialysis for 9 years. Part of the reason I was on for that period of time was, I was also diagnosed with cancer in between that so luckily with thyroid cancer, which is a very curable cancer. But it took me off the transplant list for 3 years, and I had to jump through many, many hurdles. To prove to the transplant team that I was cancer free at that point, and that giving me a transplant and putting me on immunosuppressants was not going to be a major factor in me, you know, losing my transplant later on. So, you know. between having cancer, you know dialysis for 9 years in your twenties, which was not fun, how. I went through both Peritoneal and hemodialysis probably had one, you know some of the most complications of any person you can think of, of, both of those. But I'm also a researcher I happen to research in in the transplant field, and, like, you know, the gentleman before me said, I understand the complications we have. And ultimately we get to a point where we can only do so many studies. We can only put this into animals for so many times we have to get these into humans to see what's going to happen.

And you know, in terms of where I'm at right now, I've had a transplant for almost 20 years, and so I'm very stable. But I also look ahead of going. I'm not 20 years old anymore. And there's a big difference between being a 20-year-old, with their life ahead of them versus being, you know, coming into my fifties and sixties where I'm being towards the, you know, at the end of my life. But you know, getting towards the best years of my life right? And I kind of look at it in 2 ways. I also had a deceased donor, and part of the reason I had a deceased donor was there were no live donors for me. There were not. Now, you know, granted this was back in the nineties as well, and things were a lot different, but I also had a lot of apprehension, and I still do about if I had a relative that could donate to me, I do not want that person to have to go through any of the stuff that I went through of dealing with even chronic kidney disease. And so for me the only options are: It's a deceased donor, or it's a Xenotransplant. And so, I think xenotransplant for me at this point. If I were to in the next 10 years or so need to have another transplant. I would probably look upon it on myself. Going. I'm old, you know. I'm older at this point, and for me it's a way of giving back. It's a way of *let's see what happens* if it prolongs my life if it makes it so, I'm not on dialysis, if it makes it because of whatever reason, I'm not eligible for another one. I'll go for it because we need the information. We need the data.

So hopefully. You know, the first couple of people who go through these transplants, you know, will be brave enough and understand that it. It's one. It's hopefully, because it'll make their lives better. But 2, it's also contributing to science. It's contributing to the legacy of transplant, and that hopefully later on, some kid in their twenties doesn't have to sit on dialysis for 10 years waiting for a transplant, right? Someone like your son would not have to wait on dialysis waiting for a transplant.

James Valentine, JD, MHS

So, and is that something for you as well, you know, just thinking about? Where you might be at that moment in the future, where you might need a new transplant. Would you have a concern for yourself about another long, prolonged period of time on dialysis? And can you speak to that a little bit?

Continued Patient Participant #3 | Discussion A: *Patient Experiences with Kidney Disease*

Yeah. So definitely, you know it, it's and I was having conversation with someone earlier.

There's a big difference between being on dialysis in your twenties. You know you're you're likely here to survive on dialysis is much longer. By the time you hit 30 or 40, you know, those odds starts coming down pretty quickly. Right thing like you know, even in my stage of life right now I had a heart attack when I was 42 in part because of the new suppressants that I'm on. And so, being on. Dialysis at my age is a huge risk compared to when I was 20. And so that that is, you know, something in the back of my mind of II may not actually survive that long and dialysis if I had another transplant.

James Valentine, JD, MHS

Thank you so much for sharing that I think we have a comment right here.

02:02:00 | Audience Discussion [Continued]

Patient Participant #4 | Discussion A: Patient Experiences with Kidney Disease

Thank you. I realize we're ready for lunch, so I'll be quick. 18 with FSGS 10 years post-transplant. and I was thinking 10 years ago, I was told “You know, when you get a kidney. You name your kidney”, and I love France, and I love to travel which I'll talk about in a minute. But A teacher came the day of my surgery, and she said, Melanie, I found a name for your kidney and a Cersei. Cersei is a French word that means a small gift.

It means I'm thinking of you, and it can also mean I love you. But my favorite meaning is something that I thought you needed that you would never ask for. I would never have thought that I would be asking for a 0 kidney. That is definitely a different Cersei that I know I'll need

I think about my donor who is now living. Who told me 10 years prior to me, needing it, that she would give it to me. Her mother in law now is on dialysis.

I haven't been able to call her since I found out cause there's a guilt that she gave [her kidney] to me. And now her mother-in-law is in need. I think about her children. My God, children, what if they need something in the future, and having this option will just save so many lives. Personally, I think about my cousin, who is 4 miles down the street from me Who does not have the same options that I have.

I get to travel, and I spent 2 weeks in Greece and Italy, and she's at home and not even active on Facebook anymore. And I know she's terribly sick. And so I am also one of those who are waiting on a phase one trial. Not just for me, but for all the people who I love and care for and who are in need, who are on that list.

And I think, 9. What did I write down? 14 dying every day? Yeah, it's time to move forward.

James Valentine, JD, MHS
Yeah. Well, thank you so much for sharing. We have a comment right here, and then we'll break for lunch.

02:04:00 | Audience Discussion Continued [Topic A]

Patient Participant #5 | Discussion A: Patient Experiences with Kidney Disease
My son, is 16. I can’t do this without crying. He had a kidney transplant when he was 2. It was a congenital problem.

He's had a wonderful life. He's you would never know he was had a transplant. It's been fantastic, just, you know, medicine 2 times a day. He's like totally normal, but his kidney is failing. He's had it for 12 years. I have to talk to this man, we, my husband and I have been rejected for donating so we're now in the process of like sort of just a huge amount of work.

However, I will say that I would not, of course, not put him in a clinical trial, for you know, xenotransplantation. I you know the more kidneys into the system the better. I will say it's a little vaguely distasteful to me.

I would worry about medicines. I already am worried about the medicines he takes. I'm also worried about kind of taking the taking our foot off the gas on other options, man-made organs, improving medicines for donated kidneys.

That is really where I'm like hoping science takes us. But I do. You know, again more kidneys into the system. If it were Dylan's last option. I would take it so I'm in favor of the research. I just hope we continue and surpass this phase and get something better.

James Valentine, JD, MHS

Absolutely. Thank you so much for sharing that I think we'll take this comment here. And then we will need to break for lunch. But we'll have a lot more opportunity to continue the discussion after.

02:06:00 | Topic A: Audience Discussion [continued]

Patient Participant #6 | Discussion A: Patient Experiences with Kidney Disease

I'll try to keep this real brief. But I was, I guess, 56 when I was when I found out I had glomerular nephritis and I did get on the transplant list and my transplant worked very, very well. I'm 68 now, and so all I was really trying to get at is when I was offered the opportunity to go on a transplant list. They asked me if I had a donor, or would I rely on a cadaveric kidney and at that stage of my life. All the people that I could think of that might be donors had what was referred to as cruddy kidneys because of their age, and that was the only reason. So I held out for a cadaveric and maybe it was so successful because she was an 8-year-old girl which the donor was which has its own issues attached. Right now, I'm 68.

I think I would take a Xenotransplant just because I am either at an age where I wouldn't be put on a transplant list, or I'm soon approaching that age, and I certainly would take a pig kidney. There would really be no question about that for me. The last thing I'll say, and what does bother me a little bit when I watched those or I also participated in those online pre-meetings. Yeah. And one of the physicians was talking about the possibility of not only yourself getting a virus, but the people in your own home getting it and being quarantined.

And you know that is something that I think about. And from a practical standpoint, typically the caregiver lives in the house. Well, if she or he is being quarantined: how does she or he continue to be a caregiver? That was it.

James Valentine, JD, MHS

Well, I really appreciate your comments and your thoughts, as you about it at your age. The possibility of whether you would even be able to be eligible on the wait list, and what that would look like. And I appreciate your comments about risk as well. Because actually, as we come back from our lunch break, we will be getting a clinical overview talk for those of you that weren't able to join the pre meeting webinar discussing and sharing with you all some of those known and unknown risks. And we really want to dive into that with you and explore your thoughts and preferences around some of those different specific areas of risk.

But this has been a great start to our discussion. We heard a range of different degrees of interest and degrees of interest today versus in the future from so many of you in about a potential kidneys, you know, transplantation. And so I think we want to kind of dig deeper into to that interest, and see what your thoughts are, and different tolerance for risks that you might have as we build on this in our next discussion. So I want to thank everybody for their participation this this thus far, we're going to take a lunch break until one Pm. Eastern for those of you that are here in the room. Lunch is just a couple of doors down

Heather, any other announcements before we break for lunch? Alright, thank you so much. We'll see you at 1:00pm.

LUNCH BREAK

02:12:00 | Topic B: Introduction

Patient Considerations of Risk & Other Downsides of Kidney Xenotransplantation

James Valentine, JD, MHS

Welcome back, everybody. I'm James Valentine, your meeting moderator, and it's my pleasure to have you all rejoin our externally led patient focused Drug Development meeting on Kidney Xenotransplantation. We had a wonderful morning discussion where we began to explore some of your considerations about you know the potential for kidney Xenotransplantation, and you and your loved ones lives.

And now we want to expand that and dig a little deeper as we explore some of the known and unknown risks that relate to this product class, and so to help us get an understanding and a lay of the land about these potential and risks of Xeno kidney. It's my pleasure to introduce Dr. Peter Reese.

Dr. Peter Reese is a transplant nephrologist and ethicist at the University of Pennsylvania in Philadelphia. And he's Going to provide that overview of benefits and risks of xeno-Kidney transplantation which was going to help set the stage for the discussion that we're going to have right after that. So, Dr. Reese.

02:13:00 | Expert Presentation

The Known and Unknown Risks of Kidney Xenotransplantation

Peter Reese, MD

Great, what a pleasure to be here! It's a big honor. It's amazing to follow the talks from the patients. Incredible perspective we can't hear enough. And people really made their views known so eloquently. It was great.

So, I just want you to look my disclosures for a moment. I do have a project ongoing with eGenesis, a grant to my institution.

So, here's what I'm going to talk about. I'm going to talk about longstanding ethical problems. One of the things that's really interesting about Xenotransplant is that these ethical problems have been with us for 40 or 50 years.

I'm going to talk about known and unknown risks. And I'm going to talk about how I would counsel patients about xenotransplant what I think they would need to know, and I'm going to emphasize kidney transplant the most. But I think these problems are pretty generalizable to say heart.
So, we think about the longstanding ethical problems. I think the biggest one is this fear? What if we put a kidney into someone and it doesn't work well.

What if they reject it? Or it minimally functions? Or they become dependent on complicated medications? How are they going to feel? How are we going to feel?
I'll talk about, you know, rejection. But in addition, the other sorts of bodily functions that could go off bleeding, blood clotting. I'm going to talk about infections in the way I think about that problem. I'm going to mention death and something that you know hasn't come up as much here which is loss of privacy for the patient and for the close contacts. We live in a world where information spreads really fast, people have very different senses of how important maintaining their privacy is.

So, what did we learn about rejection risk? We've been lucky, in a sense, that some scientific groups have done some fold work.

And a few lessons have come out of it. So, I think we, as Vineeta mentioned, we learned that immediate rejection has been avoided, and that is progress. It's a big step. But it does seem that if we take together all of what's known, what's been in peer reviewed publications that rejection is still a big issue. We're not quite sure how to treat it. For those of you who like pictures. You can see here that this was the first Maryland heart transplant, and that's healthy heart tissue on one side, and some pretty, unhealthy, swollen heart tissue on the other side. Maybe that was rejection.

If we look at the published studies from NYU. you know there was a lot of excitement at first no hyper acute rejection, but then some very careful scientists, chiefly from the Paris transplant group.

They worked with Bob Montgomery. They got the tissue. They did some special standings and some deep work, and the immune-phenotyping and other sorts of molecular investigations suggested. Well, there probably was emerging rejection there.

So, I think we have to assume that rejection is going to be a difficult problem. Probably.

So, I see a rapid learning curve ahead. A patient involved in one of these trials might not necessarily feel like they're dealing with a team that knows exactly what to do. They might be dealing with a team that is doing their best to figure it out as the as the days pass and we do have a lot of therapeutics to treat rejection. That's the good news. The toolkit is bigger than it ever was. But the side effects of that toolkit are the same ones that we've always dealt with before.

So, if you use strong rejection medications, you might expose the patient to infection. You may not have heard of CMV. Before you came into this room, but those of us who have dealt with CMV. Know that that's a really difficult infection to deal with, and then there are more common infections that can come in a very severe form, and an immunosuppress person you or I might get, and a urinary tract infection. Take some antibiotics and forget about it. But I admit a lot of my patients to the hospital with a urinary tract infection, sometimes to the Icu.

So, the good news is that we can treat rejection. But the bad news is that treating rejection can lead to other problems. Lymphomas are another one.

So, what did we learn about infection risk from the recent Xenotransplants? So, this pig CMV, a virus that usually just causes trouble in pigs was transmitted to the first Maryland Heart recipient. It's unclear. If this was a virus that was active, I'm not using the word infection. But the virus was transmitted, and I think that we probably do have tools to really limit this. My sense is with better screening, with redundant screening with careful quarantine of the pig herd these different sorts of testing, maybe biopsies. We can probably really limit the risk of transmission infection. There's also this concern about retroviruses that can potentially be knocked out of the pig with genetic engineering. So, my sense is that this risk can be mitigated. But we're never going to be 100. Sure, we're never going to be able to say to the patients, I'm sure there's no, you know, there's no chance of infection transmission. I think that they're just going to have to accept. That's part of the risk.

And then there's this privacy issue. So, I've had the privilege of talking to some of the surgeons who were working that day at the University of Maryland, and what I'm going to say is, I have in my mind an institution that wanted to do the right thing. Very professional thought about it. A lot had a plan in that context. The name of the patient was out there I don't know. things were coming out in the Washington Post really fast. And why could that be? It could be because there are dozens of people involved in one of these transplants. There's someone sweeping the floor. There's someone doing patient transport. There's a team of pathologists, nurse respiratory therapists. Everybody. It's hard to keep a secret these days.

The other really weird thing that happened was that the Washington Post decided that they were going to start doing research into this person's personal life and found out about a crime that he'd committed like more than 10 years earlier, was that relevant to the story at all.

Not at all. Was it a headline in the Washington Post? It was. Did they ever apologize for the spend? They didn't. So, you know my take is that part of what patients and their families need to think about is that they could be in the spotlight. It may be really hard to prevent that, even in the best circumstances it might not. But it might.

So, what does this mean for families in close contacts? I think that I know the FDA has dealt with other things like live viruses, where the implications for the family and close contacts were front and center. But it is different than the average drug or device. There's some needs, and there's some interest from caregivers that have to be taken into account. Now, any of us who've worked with transplant knows that there's never one patient going for a transplant. The family goes for the transplant, basically. But in this case it's a little different than most transplants, and that the family is being brought into, brought under the umbrella a little bit of risk

risk to privacy, risk to infection. So, I think there is some work that is being done, and probably needs to be done to a more intense degree about the needs of the caregivers, how to educate them, how to talk to them, because they're going to be in there, too.

And I'll leave it out of this talk. But that's sort of true for hospital staff, too. Most people who went to the hospital didn't necessarily, when they went to say nursing school think to themselves, Wow, I'm going to potentially one day and be exposed to a pig virus. That wasn't probably quite what they were thinking about.

But so, what should the patient understand? So, I think it should be a pretty intense education and informed consent process. We've done some of this stuff a little bit, say, with hepatitis C transplant, but this will probably take it to a slightly different level. So, I would need the patient to say to me, I know this is an experiment. I know I'm involved in an experiment. I would want to make sure that they weren't harboring a secret hope that they were going to do this, because if it didn't work out, they'd get a great human transplant. No one has made that promise, I think, would be a hard promise to keep, and I think, most importantly, I'd want the patient to say, look.

I know that you can't tell me how big these risks are. They might be small; they might be medium sized. There might be complications. You don't know, you can't know. I don't think anyone in this room could know, so I think that they would embrace that kind of uncertainty would be necessary.

So, I'm going to talk now about the potentially catastrophic complications. I don't expect to see these, but if I heard that they happen I wouldn't be surprised, either. so, the pig kidney might function poorly. Maybe the person winds up back on dialysis. the immune system and the bleeding and blood clotting system are really closely intertwined. Could there be uncontrolled bleeding or blood clotting? Could the patient have a stroke or become disabled. they could. I don't expect this, but I think it's something that I would want to talk about.

It's possible that the person could wind up with quality of life was worse than what they expected on dialysis, either because of medicines, they had to take fluids, they had to take in dependence on complicated treatments, rejection, treating rejection that could have complications, infection, cancer, pain, side effects, and the person could die, and they could die at an unpredictable moment. So again, these are the potential catastrophic outcomes. I think part of my mission here is to lay out the worst case scenario. It's not what I expect, but I think it's all there. and I think we should think about quarantine hum. Unless you've worked with a disease like tuberculosis, you probably rarely had to deal with the operations of quarantine with patients or people that you know. But if the patient seems like he or she is infected. and the specter is raised, that this could be an infection that came from the pig person might have to quarantine, and that could be very awkward. It could be kind of a public health consideration. It might be hard to enforce. I don't know if you've noticed, but in the

United States people are really into their rights, and really not into what the Government can tell us to do.

But this, this is something that they would need to think about, and maybe and I know one of the patients brought this up. Maybe not just them, but also their family members in quarantine. For how long I'm not quite sure. Again. I don't think this could happen. This will happen, but it could.

So, all of these things are necessary to think about. I think the patients really have to look in the mirror and think to themselves. Well, if this doesn't go well, the good news is they could take the pig kidney atomy. But the bad news is, I don't think anyone can say with confidence that they might get a human transplant later. They might be too sick, too frail, too sensitized.

And I think that as others like Dr. Kumar have brought up. I said a lot of scary things. but we will always have to sort of have our benchmark about what else is scary, and a life on dialysis, you know, that can be scary. There is a known high death rate. There is a reduced quality of life.

Complications are common. Fistula's clot. People are in the hospital a lot. Human kidney transplant. That's a complicated life for some, too. A lot of people die waiting. Rejection. That's a word that you all know a lot about infections after transplant are also common. The difference, basically, is that when I counsel someone about human transplant, I can say, well, here's my, here's my reasonably accurate prediction of how susceptible you will be to that. In this case I can't really say what the rates will be. I don't think anyone can really say what the rates of rejection are likely to be after xenotransplant. So just a big question, mark there.

So, what are we here to figure out?

I think these questions have come up. How do we choose the right patients? I have my own opinions. I've written about them. I'm happy to talk to you about them. I think we probably have some pretty clear and strict inclusion and exclusion criteria for the first trials. I don't think it's for everybody. I think when I listen to the people at the table, this is not for everybody. This is, maybe for people with a generous spirit who are up for something with a lot of uncertainties, and are looking to give back for the person who's thinking this could be better than what I'm doing. I don't want you to have that thought. This could be worse than what you're doing.

I think the question about what kind of multi-step education and consent process will be enough is a big question. It's not going to be a one session. It's going to be a multi-session. It's going to be a lot of discussions might involve some testing. To make sure that we know what people think.

How much risk will patients be willing to set? My sense is, it depends a lot. I think people are really different. I don't think there's an average patient on dialysis. I think some people can't stand it. They don't want to do it another day. I think others are like, you know what? I don't like it, but I've adapted pretty well. I'll keep going with this. So we kind of probably have to find the patients for whom more dialysis is basically intolerable.

Caregivers need a lot of support. We got to work with that we need to work with them.

And we need to kind of think about, how do we frame the risk of xenotransplant? We can name them, but we don't know the likelihood that they're going to appear versus the large risks and dialysis that are known.

So, thank you very much. Privilege to be invited.

02:27:00 | Topic B: Live Polling & Audience Discussion Introduction

Patient Considerations of Risk & Other Downsides of Kidney Xenotransplantation

James Valentine, JD, MHS

Thank you, Dr. Reese, for walking us through that. You know, we've been alluding from the beginning of the meeting today that there's a lot of uncertainty that's associated with this experimental product type. And so hopefully, this gives you a little bit better of a sense of just how much uncertainty that there is with these different risks. And now we'd like to, you know, start to expand, and have you all help share with us your thoughts about you know, how those risks would factor into your own thinking for yourself or your loved ones.

For those of you who are following along on online. I would like to remind you that if you would like to submit written comments, we will be sharing those throughout the afternoon, and we will make sure to put the link again for this afternoon into chat. So that way you can find that comment box which is under the join the webinar button on that web page.

this in this discussion around risks we have some questions that we want you to contemplate and consider. So, we want you to think about a number of those different risks. That that Dr. Reese just kind of walked us through, and we want, you know, you know, we know that you might not be able to definitively always tell us for sure whether or not that risk would be a deal breaker, in fact, we heard from some of you this morning about how you need information and so, we'd like to explore what information would you need to know? And then how likely would you know? You know that information help impact your decision to undergo a Xenokidney transplant in a situation where you would be considering one. We heard a lot from you all this morning about how you know some of you and your loved ones might be, con, you know, more likely to consider in the short term versus at some point in the future.

If we also want to explore a little bit about you know the different, you know, beyond just the direct risk. But the fact that there would be some intensive medical treatment and monitoring required. And how would that impact your decision?

And finally, you know, if, having a Xeno kidney transplant, you know, caused issues. I would make it so you would be ineligible to receive another kidney, you know, Xeno or human in the future. How would that impact your decision. So, we're going to ask you to reflect on some of these questions. But to get us started, I kind of want to take it off, you know, bite size here. Bite by bite. So, we're going to kick it off our discussion here with a polling question.

So, if we can go to our first afternoon polling question for the all of our patients and care partners. If you were already logged in this morning. That's great. You can go right to that webpage. If not, you can go to www.slido.com, and you'll be asked to. In our code. That code is 7004787. You can keep this web page up throughout the remainder of the afternoon, and we'll be coming back and asking you different polling questions.

So here we want to know: How likely would you be to undergo a Xenotransplant if there was a risk of a catastrophic event? And this could be things like Dr. Reese just spoke about severe organ damage, a life-threatening event, some kind of other severe worsening of you or your loved ones. Health. The options here are: A: not at all. B, somewhat likely. C: Moderately likely. D, very likely E unsure or F. Not applicable because you're you are not interested in a Xeno-kidney transplant.

It's totally okay to select unsure, regardless of whether you picked that or picked one of the other options. What's most important is to understand your thinking about this topic, and I'm going to ask you to in just a moment share kind of what you selected and why

I know these are difficult. These are going to be tricky questions to answer. It's what's more important than the numbers we see on the screen is to get you all thinking about these topics. And again, to have you explain to us your thinking about these risks. So, it looks like the highest response here is unsure with about over just over 40% of our participants reporting that they're unsure if they would undergo a Xenotransplant. Given a risk of a catastrophic event.

However, we also do see that there's kind of a fairly equal spread across willingness from some that are about 15% that would not at all be willing to undergo a xenotransplantation. Given this type of risk all the way through around 10%, that would be very likely.

So, no matter where you fall in that spectrum, we want to hear from you. And again, have you explained to us why, given your personal situation, and where you would foresee a kidney Xeno transplant fitting into your own health journey with kidney disease. Why, you made that selection. So, at this point, let's like to hear from our audience, again, what did you pick in that question? Why.

02:32:00 | Topic B: Audience Discussion

Patient Participant #1 | Discussion B: Risks and Downsides of Xenotransplantation

Okay, I'm Silke. I've been a transplant patient since 1988. I've had kidney disease since 1986, at a time when transplantation was not yet an established treatment, and the drugs we had were really pretty terrible at 1 point in time, after my first transplant, the surgeon said, 50 50 this last year.

We've come a long, long ways since then, and you know, if we hadn't taken that risk, I probably would be dead by now, because dialyzing a 10, 11, 12-year-old. Undersized child is an extremely difficult endeavor.

And I think we've a little bit lost focus in the transplant world in terms of our outcomes. So right now, transplant programs get shut down. If they're one year patient survival isn't greater than 95-90%. Their graft survival isn't greater than 95%. I dare say most of us patients in the room would be happy to accept the chance of an organ transplant with an 80% 1-year survival rate for the patient, not the graft.

Right? I accepted a 50-50 failure rate at age 11 or 12 and that was totally fine, so I think, in terms of considerations of risk. You need to know your other options. You need to know where you are in life at a certain point in time. Right now, I'm a mom, right? I have responsibilities that are other. My risk tolerance, at the moment, is a little lower. I have a perfectly functioning kidney, right? Number 2,

5 years ago, when I was on the wait list, and after 5 years of waiting not a single organ offer had come along. I couldn't work. I was working one day a week, sleeping 14 hours a day. Right? That's the effects of kidney failure, not even on dialysis yet, right that people neglect to talk about. And it's ignored. Kidney disease is not curable. Cancer is, in many circumstances kidney disease is there for a lifetime, and we need to do better. Right? So, I picked moderately but it's because the question wasn't worded perfectly, right. If you told me the risk is 1%. My answer will be different. If you tell me the risk is 10%, my answer will be different. If you tell me the risk is 50, my answer will be different. So, I think there's a lot of different answers I could have given to that question if it had been asked in a slightly different way. But I think one thing that we could do immediately to change availability of organs is to just get rid of all these gradings and outcomes that we have for transplant programs that say, if you have such poor outcomes, you get shut down, you lose insurance coverage, right? And we're throwing a lot of organs in a bucket, and I'm a transplant surgeon with my other hat. I did that as a result of being a patient for so long. I wanted to learn everything there is to know about it.

And I think we're wasting a lot and a lot of opportunity of life for a lot of people, just because monitoring has become too tight. And I think if we embark on Xeno transplantation, which I think we should, we need to approach this with a mind of where were we 50 years ago? Where were we 100 years ago?

And what expectations that people have? If this helps in the beginning, 20 more people. I'm okay with that. That's a risk, I think, is fine.

But we need to consent the patience to that right. I think a lot of us have the expectation. This is the panacea that'll solve all of our problems. I don't think in the beginning it can be, and without studying it we won't get to that point either. So, I think we've been held up far too long. I was hoping that by the time I'm 30 we'd have xenos available, or bioartificial organs available. But I think we've lost control of autonomy for patients.

5 years ago, I would have said yes to this right, but I wasn't given the opportunity. And so the field has become extremely paternalistic from an IRB and regulatory standpoint. And I think that's wrong.

James Valentine, JD, MHS
Well, I'd love to follow up with you a little bit here, if you don't mind. Now, I first want to fully acknowledge that these are intentionally imperfect polling questions, because we don't have.

We don't. Wanna. We did not. As the organizers wanna make up a a particular percentage. But I actually love what you said in terms of you know, had it been a 2% risk versus a 10% risk that that would factor in differently. And I think you have an incredible perspective of someone who faced a very se significant benefit risk decision at such a young age. That that informs where you're coming from.

But if you were to reflect back to that situation you were in like 5 years ago, and thinking about a 2% risk of a catastrophic event as we were talking about versus a 10%, is there a percent? Is it 50-50 like you know what you were in some ways faced with as a child., since you spoke in terms of percentages, you know. Is there somewhere in your own mind? 5 years ago, when if Xeno kidney had been available, you would have said, This is my threshold.

Patient Participant #1 [Continued]| Discussion B: *Risks and Downsides of Xenotransplantation*
Sure, I mean for organ failure rate, I would have accepted 100% at 3 months. Okay, because I don't think that the first few will be super successful. But if we don't study it in humans, we will not figure out what's different between humans and primates and the immune systems between those differ. Having done research with that right?

I think, in terms of catastrophic events. When I go under general anesthesia I have a less than 1% threshold right for heart attack, strokes, pulmonary embolisms, and death. It's never 0, even for the best option available. Right? I'm a healthy, patient, right? I know my own mortality on dialysis at age 40. If I go on with IgA nephropathy no diabetes right? That's not a super high mortality.

So, I'd have a higher standard on that than, for example, if I was 60 and had diabetes, and my mortality was a lot less. And so, I think you have to really take that into account. Right? I'm not sensitized. I can easily get another transplant. I know all these details about my own healthcare, and I think the decision has to be informed by what's the risk of waiting? What's your estimated waiting time? What's the estimated risk, you know? If you have an allotransplant? Are you even a candidate for an allotransplant. Are your vessels healthy enough? Is your heart healthy enough? Right? So, there's a lot of individualized decisions that go into these kinds of things, and then the willingness to risk take right? I mean, if I look around the room, some of us would be willing to jump out of an airplane for fun and would think that'd be the best day of our life, right. Others would not want to get on an airplane to visit their dearest loved one across the country, because that's just too terrifying, right? And so, I think there needs to be some allowance for differences in people's risk taking and willingness.

James Valentine, JD, MHS
Beautiful kind of ending comment there. Because I think that's exactly what we are hoping to bring out today is what is that range of risk, tolerance, and willingness? Yes, right.

02:39:00 | Topic B: Audience Discussion

Patient Participant #2 | Discussion B: Risks and Downsides of Xenotransplantation
Hi, I'm Hayley. I'm approaching my 15-year anniversary of a deceased donor kidney transplant, which I received as a teenager after acute renal failure with the cause was never found.

And I've been in incredibly fortunate that my graft has functioned really? Well, I've been able to have 2 kids. Pursue a wonderful career in the space. Ultimately, and I just II had to jump in after what he said about this should be up to individual patients based on their individual situation. And I think that there needs to be the freedom to make that decision. So, I need for me right now 2 young kids.

I'm not going to take a Xeno transplant, even if I if I didn't fail you tomorrow, I would say No, but II that that that will change over the course of my life. I anticipate needing more kidneys at some point or one hopefully, right? As few as possible. But it's just been extraordinary to hear the number of people in this room who are at completely different places for that. And what I would just, I think, in terms of these risks, and knowing them or not knowing them, the more that we put that I don't want to say, put that on patient, but allow patients to hear those things and make those decisions rather than saying, You know I, your physician, I the FDA. I *whomever* am going to try to make that decision for you makes it really difficult to kind of control all of these things that we can't control and predict the things we can't predict, like I and I respect completely those challenges as someone who's trying to care for another human being and wanting to protect them and give them the best possible outcome. But the reality is that's not up to you like that's up to me. And then I can choose to take those risks or not. So again, you know, for me today it's a no, but that I suspect that won't be the case forever. And so, I just am really appreciative of the fact that the these risks are unknown. Now we never will know them if we don't try, and that there are people willing to take those risks, and we need to give them the chance to do that if that's what they want. Yeah.

James Valentine, JD, MHS
Well, just to follow up, I think one of the things that helps us advance development is exactly knowing who is willing to tolerate what risks, at what points. And so, just as we're trying to collect many of those data points today, I'm going to put a question back to you, you know.

On the topic of these really catastrophic risks, we leave you off worse than where you started, or you know the possibility of death, you know is that a risk you said at some point, you know, might be a transplant might be something. Where does the catastrophic risk consideration fit into that? Clearly not today, is that you know I mean understandably, as you, you described your mother, you have responsibilities beyond yourself. Can you kind of share? You know what? What would be that? How would you factor those catastrophic risks in at that point in the future where you would start to consider Xeno?

[Continued] Patient Participant #2 | Discussion B: Risks and Downsides of Xenotransplantation

I think for me, the balances against sort of like my other options, right? Like, what's my risk of death on dialysis is obviously a part of that. But the quality of life on dialysis is also so bad. I mean, II was what 1415 when I started dialysis. I lost 30 pounds that I had no business losing. I was. I was in a really, in bad shape and getting worse quickly. And I would weigh that, too, right is, is like, what is the life that I have? If I just stay the course? And would I rather take a chance? And I know that there will be a point at which I am willing to take that chance, even if the risk is greater than like a human transplant. Because it's no life. For after a certain point it's really no life on your own dialysis.

Patient Participant #3 | Online Comment

So, this is coming in from Gigi, who is a caregiver and will be her son's kidney donor. And she is saying she and her son would be willing to consider Xeno transplantation as it stands today. If all other options were unavailable, even she would assume that a catastrophic outcome could be possible. They would be willing to do it if their other options were worse.

James Valentine, JD, MHS

Well, thank you for those of you who are writing in, and as we get on different topics, we'll make sure to bring those into the discussion. I think I saw another hand that wanted you wanted to speak to this topic.

02:44:00 | Topic B: Audience Discussion

Patient Participant #4 | Discussion B: Risks and Downsides of Xenotransplantation

Hello, everyone! My name is Stacy War. I'm 33 years old, and I spoke to several people about this. But one of my concerns about the Xenotransplantation is: what about women who were to receive this transplant, and they decide to have children? How would that affect them? And also, the medications? I was diagnosed with chronic kidney disease about 4 years ago, at the age of 29.

I've been struggling with high blood pressure since I was in college, and as a college student I did not take that seriously. I didn't know much about high blood pressure or chronic kidney disease, or anything of that nature. So, when I was diagnosed, it was a complete shock to me. my nephrologist. I don't have any children as of now, but my nephrologist recommended that I wait until I receive a transplant to have a child. And I'm a bit concerned about that, because I don't know how long I'm going to be on the transplant list. I've been on it under a year now, and I was just thinking about how if I if we did have that option right now to have this, you know transportation, and I want to have a baby and start a family. How would that transplant affect me? The medications! How would that affect the baby? And how would it affect me carrying a child. So, I just wanted to. I'm not sure if that risk was even considered. But I just wanted to put that in everyone's mind, especially some of the physics. Well, doctors that are here, and medical professionals that are here. Have you all just thought about women who want to have children after they receive this transplant. And what would that look like?

James Valentine, JD, MHS
Yeah. And I don't know that we have the answer for that for you today. But I guess you know. You know, as we're trying to understand what risks are. Ones that that are of concern and might impact decision making. It sounds like this is one that's top of mind, for you know, is this I guess. Could you talk about is essentially, a kidney xenotransplantation were to you know, kind of be contraindicated to, then go on to, you know, child bear have children, you know, is that you know a risk you would not be willing to take on. Can you just kind of speak to what your thoughts are. Since you, you brought it up, and I think it's really great to hear it.

Patient Participant #5 | Discussion B: Risks and Downsides of Xenotransplantation
I would consider only if there were minimal to no complications to the baby. I know now, with the human transplant that it's already a high-risk pregnancy. So, I'm also probably expecting that that would probably be a high-risk pregnancy. But I would be more concerned. What are the complications, and

How would that affect the baby like what I have a very small baby. Would I miscarry? What kind of medications would I take or not take? And how would those medications affect the birth defect of the child.

So that's just some of the thoughts that I have. I know that I'm speaking too far in the future. But maybe that's something that some of the doctors here can start to think about raising it.

James Valentine, JD, MHS
It wasn't on our list, but I think, very valuable to hear about. And I definitely, you know, I think perfectly fits in that ballpark of catastrophic events. So, I do want to bring up our next polling question just to keep us thinking about some of these other risks. So again, you can go to your pull out your phone, go to Slido, com

02:48:00 | Topic B Polling Question
Here we want to know: How likely would you be to undergo a Xenotransplant if there was a risk you would not be eligible for the Allotransplant waitlist in the future?
And the same response options, you'll see here on some of these different questions, you know, could be not at all somewhat likely moderately likely very unlikely, unsure, or not applicable cause. You're not interested in Xenokidney transplant. As we heard a little bit already. Some of the reasons that may become ineligible for future allo transplant waitlist eligibility would be if you're less left worse off healthwise from some complications.

Perhaps there might be damage to tissue or surrounded physiology needed to have another transplant or your immune system is sensitized. So, if for one more, or maybe a different reason. you would become ineligible. How would that that risk of potentially becoming ineligible fit into your thinking?

We'll give you just another moment here to get in your response. It looks like we're again seeing a wide range of different tolerance for the potential to not be eligible for allotransplant waitlist in the future. We're seeing the top response about just under a third of our audience would not at all be likely to undergo a xenotransplant if this was a risk to them. We're seeing about a fifth of the audience say that they'd be somewhat likely, or maybe even moderately likely, to undergo a xenotransplant and about 10% saying they'd still be very likely to undergo a Xenotransplant, about 15% saying unsure, and nobody reporting that they're not interested. So, not applicable.

So again, here, as we consider, you know, this this kind of multi-faceted risk. There might be different things that lead to this result, but that there could be some risk that that you know, by undergoing a Kidney Xenotransplant. You're, you know. You would make yourself ineligible for the allotransplant waitlist in the future. How important is that to you individually?
In other words, what did you pick? And why? Yes.

02:51:00 | Patient Participant #6 | Discussion B: Risks and Downsides of Xenotransplantation
Just a quick observation that I was very fast on the "no way" for me. That was the deal breaker. Right, please don't fix me and break me, and then not be able to fix me. I know absolutely that some people are going to have to go through that because we don't know what happens. I didn't hear an option that would have made a difference for me, which is, if I wasn't able to do a human transplant. But I was able to do another pig transplant that would change my risk benefit. A lot. Sure the question would be, can I get another transplant that would work?

James Valentine, JD, MHS
Yeah, I think maybe just to address that for a moment. Perhaps the bar to being on the transplant list is a little higher, but there still could be risk to no transplant whatsoever. So, I think that some of the things I listed could relate to either of those risks. But, understand that that's a kind of a deal breaker out of the gate, for you have a comment right here.

Just one moment. We'll get a mic to you. Sorry, those of everyone on the web and in the far corners of the room can hear you.

02:52:00 | Patient Participant #7 | Discussion B: Risks and Downsides of Xenotransplantation
Yeah, I think. Similarly, you know for me, I answered pretty quickly, and said that I would in that case not enroll in a trial for Xenotransplantation if I knew that it was going to prevent me from getting an allotransplant in the future. I guess part of my thought process was really almost reversing. It is, you know, perhaps something to consider meaning. There's quite a bit of discussion that's been ongoing about How do we incentivize patients to look at a living donor transplant? and part of that has been to say, Well, if you donate, say, through the National Kidney Registry, you're going to be at the top of the list in the future. If you need a kidney one way to incentivize. And maybe this is not appealing, but it may work, incentivize people to enroll in a phase 1 trial with a lot of risk around, transplantation would be to say that you're going to go to the top of the list if this kidney fails. So, that was my thought.

James Valentine, JD, MHS
So just to follow up a little bit, even if in that hypothetical where that kind of promise could be made, you know what you were saying is for you. And you're thinking, you know, if there were

medical reasons why that wouldn't be possible, a risk of a complication that would make another transplant.

Kind of not either physically possible or be a risk to the patient. You know that would be the type of risk that would, you know, be a deal breaker for you. And is that I mean, obviously, we're not putting percentages on anything. But you would weight that very highly?

Patient Participant #7 | Discussion B: Risks and Downsides of Xenotransplantation
I would. I would weight it very highly. And it probably goes, you know, to broader topics as well as where would the trial be done? Would there be consistency?

Across those different trial sites? I said there would, from doing device studies and pharmaceutical studies. But at the same time. Right now. The reason I mentioned that right is that there's huge variability between all the different transplant centers in the United States. So, I understand they would likely have one similar identical protocol, I should say, at the different trial sites.

But then, if you were in a sense out of that trial, and then facing many different Id is about whether or not you could get on the waiting list or jump to the top of the list. and that was different, depending on where you were. That just adds more variability, confusion, and concern. Sure, at least for me.

James Valentine, JD, MHS
Yes, well, thank you very much other thoughts and perspectives on. You know how you think about this risk of, you know, potentially being, you know, ineligible for the wait list or another transplant. Let's go here, and then we'll come to the back.

02:55:00
Patient Participant #7 | Discussion B: Risks and Downsides of Xenotransplantation
I mentioned earlier that I'm 60 years old, yeah, and spent 4 years on dialysis one year, when I was much earlier, and then 3 years on peritoneal. And for me, it's you know, I think, about the difference for me would be, how long have I been on dialysis, and how old am I? Because taking these risks would likely save my life at the same time, the longer I'm on dialysis, the sicker I'm going to get. I mean, I lost my spleen. I have arthritis. I have a bunch of other stuff going on.

And so, these risks. If it's going to save my life as opposed to living the poor quality life that many of us live on dialysis, I'm more apt to say, let me take these risks and see if this is going to save my life in some kind of way, increase the quality of my life, as opposed to saying, "Let me just stay on dialysis for another 5 years", or whatever it is, and take a risk that I'm going to get sicker and be completely ineligible for any kind of transplant. I see.

James Valentine, JD, MHS
I understand what you're saying about length of time on dialysis, worrying that you would get sicker and become ineligible. Can you maybe just explain? So, we understand where age fits

into that, and how your risk tolerance might change, as you know, from where you are now versus in the future. Much, much younger. Back when I was 23 years old.

Patient Participant #7 | Discussion B: Risks and Downsides of Xenotransplantation
I'm like, Hey, man, I have my whole life in front of me. Now that I'm 60, I'm thinking, do you have a little bit of life left in me?
And so, it makes a big difference for me to say, well, you know how much of a risk am I willing to take to stay on dialysis, as opposed to say, let me increase the quality of my life through a xenotransplant. and do what I said earlier, spend quality time with my family, with my friends, travel the world go to school. Those kinds of things are important to me. But staying on dialysis, you don't have those options very much. Most of you know, talking to several of the transplant recipients here. It's the same thing. We want a quality of life. We want a good quality of life, just like anybody else.

But the older I get. and the zipper I get the more apt I am to willing. Take take the risks necessary to stay in my life, and that's it's a bit of a concern that, as I mentioned earlier, too, because, you know I don't.
I'm not a big risk taker. but when my life is on the line you think differently, you think you know I'd be more willing to take risks, and that's a concern for me. Am I willing to take too much risk? But when your life's on the line, I mean, you know...

James Valentine, JD, MHS
absolutely well, thank you so much. I think we had a comment in the back.

02:58:00
Patient Participant #8 | Discussion B: Risks and Downsides of Xenotransplantation
I mean again, I think it's not just age, right? So, I picked again, moderately likely, because it'll depend on my time in place right if I'm still raising a small child. Well, no, I'm less risk tolerant once I hit 65, and I know my waiting time will be 10 years, and I know my survival at age 65, on dialysis is 5 50, at 5 years or less.

Well, at that point in time, while I'm 65, and acceptably healthy, I might say. Well, alright, the kid's happy. The kid's married. The Kid can take care of himself. I don't need to be there right if I die at 70. I have by far already today outlive my life expectancy at age 11, right? So any day to me is an added Bonus, and in the end, if I go. But I help hundreds of thousands of other people, and I die a few days sooner to me. That's a life worth lived. And that may be a little fatalistic. But I also grew up in Europe. Where? How long you live is not the end? All be all right. But how well you live, and what you did with the time you had matters just as much.

And so, I mean, I don't. You know, I don't know if at age 70 I'll even be a candidate for a third or fourth human kidney transplant, right? And the risks of that are not low either. Right? All these, even these catastrophic risks, are things I discuss with every patient that I take for a transplant right, and depending on their comorbidities. Those are not 0 risks.

And they do happen right. And so I think we can't aim for 0 risk with a Xenotransplant, and still have a reasonable risk with an hallow transplant. I think that's unreasonable. And so, I think, depending on your time and life and stage in life, and what all the circumstances are. You have to approach this on a very individual scale.

James Valentine, JD, MHS
Yeah, I really appreciate that. And you helping put kind of your thinking of what age and stage, both in terms of what's going on in your life, but also how that corresponds to health outcomes not only with the disease. But you know the current treatment approaches so yes, we have.

03:00:00
Patient Participant #9 | Discussion B: Risks and Downsides of Xenotransplantation
So, I guess I have a question for everybody, too, because it sounds like the age, the weight, the quality of life. You're going to end up with only people who are very sick or very old to be in these trials. How are you going to entice younger, healthier people to? You know? II mean, there's so many other complications when you're old and already so sick from dialysis, or whatever like. How do you? I don't know. Incentivize like the healthier, younger, more. Whatever

James Valentine, JD, MHS
the risk of asking questions is the questions come right back at you. So. The question here is so you know, in in considering risks, you know, is are there? You know certain information that you would need to know?
I mean, I kind of want to, take off the plate for incentives that we couldn't guarantee like, Dr. Reese said. You know we could Say that Maybe you would get kind of some kind of priority for allotransplant, but that could never be guaranteed or promised. But are there things that you think of that would be an incentive for you all?

Patient Participant #9 | Discussion B: Risks and Downsides of Xenotransplantation
I don't know I can't. I have a hard time thinking that far ahead, but I do think that it is. You know those are the things that you know need to be addressed is, how
how do you entice people to do that? You have to have something, you know. I mean everybody, I understand, wanting to push science forward. But you also. You're not going to get maybe the highest quality.

James Valentine, JD, MHS
Yes, we'll take one quick comment here, and then we'll go to our next polling question.

03:02:00
Patient Participant #10 | Discussion B: Risks and Downsides of Xenotransplantation
I'm actually not sure if incentivizing is a good idea at all. To take a completely different view. Because I think if we incentivize, then people will feel pressured into it. And I think that poses a lot of ethical issues of, you know, if there hadn't been an incentive, would you have still done it? I do think, however, that there are plenty of young people that are not transplantable currently, for whom Xenotransplant could work beautifully. There are young people who are relatively healthy, who have chronic low blood pressure in whom doing a human kidney

transplant would likely fail, and has failed in my experience many times right now, if you take a small pig kidney whose normal blood pressure, by the way, is lower, right? And you put it into a person like that, they might actually have a better outcome with that than with current options for our transplant or not even being able to be listed right.

Same with patients who suffer from diabetes, who are not candidates for a kidney and a pancreas transplant their waiting time on dialysis often makes it such that they die and they die waiting because diabetes plus renal failure, even at a young age is a very, very morbid disease that kills.

And so those patients don't currently stand a chance on barring them having a living donor or being able to get a pancreas with their kidney and thus shortening their wait time, have no chance to get transplanted in a timely frame, and so I don't think there's any need to incentivize in the current system.

James Valentine, JD, MHS

Thank you for that additional perspective. We will now go to our next polling question again. We're having great discussions about each of these different topics. We've heard this risk come up a few times and people's remarks. So we'd like to now explore this with you.

03:04:00

Topic B Polling Question

How likely would you be to undergo a Xenotransplant if there was a risk of a zoonotic infection that could, as we've talked about, could be transmitted to friends or family?

You know, I think we've heard in our clinical presentations that there are some opportunities to mitigate this risk, but it would never be a nonzero risk. So, the options are the same as we've been seeing A, not at all. B, somewhat likely. C, moderately likely. D, very likely E unsure or F. Not applicable because you're not interested in a Xeno kidney transplant.

We'll give you a few moments here to answer this question. It looks like close to 50% rate. This is something that they would not at all be interested in a Xenotransplant. If this was a risk followed by a pretty even then spread amongst those who are very likely unsure, and somewhat likely some reporting moderately, and again, no one's saying that they are not interested.

So, I know this has been top of mind for some of our audience members who spoke on the panel earlier shared some thoughts on this who would like to share their thinking. I we see, I think, a little bit higher, of a rate of not at all here, compared to some of the other risks we were asking about, so would be interested to hear what you selected and why?

03:06:00

Patient Participant #11 | Discussion B: Risks and Downsides of Xenotransplantation

Well, I selected. Somewhat likely because one is, and maybe it's my ignorance of how bad zoonotic infection is, and how long it lasts, and how long is actually isolation, or but aren't we? And haven't we been dealing with this recently in the last few years? I don't wanna say the C Word, but I know we all know what we're talking about here. And aren't we doing that already? I mean, we, you know, I see I wear a mask quite often today. Ironically, I didn't. But I think that there has to be again a percentage of how long does that last? What are we talking about? Is there going to be eventually vaccines that could possibly be developed to overcome that just like we did in a very short amount of time for the last, you know, in 2019, when they ramped up all this research that maybe it was possible to actually create a virus a vaccine in a shorter amount of time. But maybe there's so much funding that they didn't do it quick enough, they were just not doing it. And that's just another thing.

James Valentine, JD, MHS
The idea here is we want to hear as many different perspectives of people who, and sharing their thinking of how they would Consider this risk. So, for you. It's what I'm hearing. I'm hearing you right is, you know, somewhat likely, because there's maybe mitigating, you know, factors, maybe beyond what we talked about like vaccines. But if there were mitig ways to mitigate the risk that helps kind of increase the interest that you have but also that this is even if complex in terms of managing it and needing to quarantine. It's something that can. You know there's there's some approaches to managing It is that my hearing you that those are the things that led you to say somewhat.

Patient Participant #11 | Discussion B: Risks and Downsides of Xenotransplantation
Yes.

James Valentine, JD, MHS
Well, thank you very much for adding that. We have a hand in the corner there and then we'll come right over

03:08:00
Patient Participant #12 | Discussion B: Risks and Downsides of Xenotransplantation
Kind of piggybacking off of what you said previously. The pandemic was very serious, and people had to quarantine, but it also that quarantine made. You see that your family was suffering, and if there's a possibility that my family can, you know, be infected with zoonotic disease or infection after I've contracted it, and I can pass that on just from dealing with Covid. I contracted Covid from my wife, who contracted it from work, and my daughter ended up contracted that now she has, you know, asthma. So now she has a long-term ramifications from something that we tried to prevent, but couldn't prevent, and that is something that you want to try to prevent, but can't prevent. And what could be the long-term ramifications from that that could be passed on to the members of our family.

James Valentine, JD, MHS
Right? Yeah. So, the concern for you. It sounds is at least you didn't speak as much of your the concern to you yourself in terms of the health risk of the infection, but it's really the fact that you may convey it to friends and family that that would make you.

you know, kind of give a lot of weight to this particular risk, right?

Patient Participant #12 | Discussion B: Risks and Downsides of Xenotransplantation
Because then they'll possibly be in the same situation as me, needing a transplant because of organ failure due to a disease that could have been prevented if I didn't bring this to them.

James Valentine, JD, MHS
Sure. Well, thank you very much for adding that to the conversation.

03:09:00
Patient Participant #13 | Discussion B: Risks and Downsides of Xenotransplantation
so I was in the completely opposite group, right where I was actually more likely to accept this risk. And part of my answer is that I actually think while it's a risk, I think this is a remote risk. Right? When I think about the things that we don't talk about. And this just literally came to mind sitting here is one the patient at highest risk from these infections, is the recipient of the organ, because they'll be immunocompromised right? Once your immune system is weak, that infection will harm you and hurt you more than anyone who has a normal, healthy, immune system. I'm sure all of you have at some point had family that went to the Zoo went to a farm, went to petting Zoo and played with the animals, and nobody got sick. The normal, healthy people are unlikely to get super sick from it. Right number 2 is, I have friends whose cats are getting immunosuppression and chemotherapy, and nobody's talking about the risk of transmission from immunosuppressing these animals to now having viruses and other diseases replicate in immunocompromised animals that spread to their human owners. And that's even true for immunocompromised people who have pets right. So, I think we do a lot of this already, unknowingly, without thinking about in our society. But I do recognize that, you know viral replication is higher and immunocompromised. People in mutations are more frequent in your compromise. People that is very well proven and true. And could something crazy happen? Yes, but I think the chance of that happening is much, much lower than any of the other risks we've previously discussed.

James Valentine, JD, MHS
Sure, in a very helpful context. any other comments on this point. Yes, let's go here.

03:11:00
Patient Participant #14 | Discussion B: Risks and Downsides of Xenotransplantation
Good afternoon. I indicated that I was not interested at all. As I had said during my testimony. It concerns. First of all, because of my age. there's a lot of things going on and bringing something like zoonosis into the picture would not be good for me first of all because of my age, and then, secondly, because I would put it out there for my family. and I don't think that's even though it's my life, I don't think that is fair for them. I also indicated, they said, that there was a way that they could quarantine the pigs and do something different for them to lower the risk of zoonosis. Yes, and if that was the case, that would be different for me.

Depending upon what the percentage was, I would consider it, but only if the risk could be lowered, so that it would not affect me or my family and friends and my support team.

James Valentine, JD, MHS

Sure, thank you so much - seeing no other hands on this, let's go to our next polling question. I know we're covering a lot of territory here. But again, I think it helps to try to take these one at a time. So, this. This has come up a little bit in discussion.

03:13:00

Topic B Polling Question

Here we want to know. How likely would you be to undergo a Xeno transplant if there was an increased risk of a failure or rejection of the kidney and perhaps somewhat differently from Allotransplant where kidney could remain intact, that some of the reasons for failure or rejection of a Xeno kidney may increase the chances that it needs to be removed at the time of failure of course, also and rejection. So, the options are similar here. A. Not at all. B, somewhat likely. C, moderately likely. D, very likely E unsure or F not applicable because you're not interested in a Xeno kidney transplant.

Alright, we'll give you a few more moments to answer here. It looks like a little over. A third of our audience would be very likely to undergo a xenotransplant in light of a risk of increased failure or rejection of the kidney that would require surgery to remove it. We see a little over 25% saying moderately likely. And then we're seeing around 10% for each of the others, saying, I'm sure not at all, or only somewhat likely.

So, we're kind of here seeing a a greater tolerance overall with our audience. For this potential risk, but would like to explore how people are are thinking about this possibility of an increased risk of failure or rejection. And your likelihood to undergo a Xeno kidney transplant in light of that. Who wants to share what they? What they picked off of this poll, and a little bit of why. yes.

3:14:00

Patient Participant #15 | Discussion B: Risks and Downsides of Xenotransplantation

I'll just say, and I'm curious if others are thinking the same thing, I'm thinking or not. But to me this feels like kind of normal risk. This feels really similar to the risk that I took on when I got a kidney transplant, is, it could fail and honestly like, if you need a surgery to take out dials like a like I had. Pd. I may have needed a surgery to get a catheter out. I may have needed a surgery for another 1 million other reasons. If I was still on dialysis. So, this one kind of just feels like it comes with the territory for me, sure.

James Valentine, JD, MHS

And yeah, so certainly, you know. risk of rejection, risk of failure. You know, obviously, that exists for allotransplant, risk of surgery exists, for, as you mentioned dialysis.

How would you, think about and consider this risk relative to that did it, would it? If there was a much greater risk relative to allo I think we heard, to date. We only know that there's, data out to one month, showing, yeah, and not even a patient. Yet you know that the kidney can stay intact and function, you know, is that. you know, kind of where does that degree of uncertainty fit into your thinking?

Patient Participant #15 | Discussion B: Risks and Downsides of Xenotransplantation
Yeah, I mean, I think for me, this one actually feels still feels like the more manageable risk, because to me, if this was the worst-case scenario. This is like a risk I'm willing to take to not be on dialysis, sure, for sure, relative to, you know, dying or giving my family, a disease or something like that. Sure.
Even if it is a higher risk than a human transplant.

James Valentine, JD, MHS
And very interesting to hear, kind of relative to some of the other things that we've just talked about. Where that fits in. There were a lot of heads nodding. But you know, we wanna hear as many individual perspectives as possible.

Anyone else want to speak to their risk tolerance here? It may end up in me asking you questions. But yes, of course.

3:17:00
Patient Participant #16 | Discussion B: Risks and Downsides of Xenotransplantation
This this kind of relates to an earlier question. So, when you talk about rejection, and in the earlier question it was, you may not be eligible for human kidney after you do the Xeno transplant. My question is, isn't that knowable?

We can't. We know that I had so like not whether I know each kidney sensitizes you more and more. But can't we know that like if you get a pig kidney. Now you're going to be wiped out from human. Kenny's count.

James Valentine, JD, MHS
So not necessarily. So, you know. I think we heard that, you know there's certain risks that again we don't know how likely they are, but you know that there could be some damage, you know, to you, you know in internally that would make it impossible to do another kidney transplant, and that might not be knowable. What the what the OP. You know. Chance of that happening is we also for this particular question, don't know.

You know, in patients you know how long a kidney will either function or you know, be able to, you know, withstand possibility of rejection and you know we'll only have trends of that over time. But certainly at this stage. We don't know

what the likelihood of that is. So again, just to try to get different perspectives on this. How you know, kind of knowing that that there is some unknowability. You know. How does that factor into your thinking about these risks?

Patient Participant #16 | Discussion B: Risks and Downsides of Xenotransplantation

I'm sorry I don't offer a different perspective. I'm with her, I think that you know that is something in the transplant world you are aware of.

James Valentine, JD, MHS
It doesn't, and certainly does. We like hearing similar perspectives, too. That's actually helpful to know. So, thank you.

03:19:00
Patient Participant #17 | Discussion B: Risks and Downsides of Xenotransplantation
so it's even a crapshoot for allo transplants. Right, I mean, who gets sensitized, and by what and when is something that none of us even understand? For Allo transplants you can have one transplant and next have a Pra of 99% and be almost impossible to match, or you can still be close to 0. So if we don't predict it or know it for what we do. Currently, I think we are just in the same place. Yeah.

3:20:00
Patient Participant #18 | Discussion B: Risks and Downsides of Xenotransplantation
Hi, my name is Larry. I'm 60 years old. This is some good lawyering questions, because it sounds like you're asking the same question differently to see if you get a different answer. But I think one thing that is consistent is that it depends on what stage or age you're at. So I answer this question somewhat likely. because, statistically speaking. you know, I'm in the fourth quarter of my life and this surgery is, it's so traumatic. I wouldn't want to do it again and again. But if I were 40 or 30, yeah, I might be willing to take that risk, like, if this doesn't work, let's try something else. But at this point in my life. and so like. Here's my one shot.

James Valentine, JD, MHS
And what about being, as you put it in? You know, kind of this point, this place in your life makes it so. You're you'd be less likely to want to have to undergo, potentially repeat, surgeries, procedures. Can you kind of help me understand that?

Patient Participant #18 | Discussion B: Risks and Downsides of Xenotransplantation
But sort of like you know, I feel like maybe you get one bite at the apple, you know. I mean, you've kind of lived 60 years. And like, I'm saying, statistically speaking.
you know you may. You know your estimated life might be 80 years. So it's like, Okay.
I've had my chance. I don't want to put myself or my loved ones through this kind of trauma again if it does not work. And so that's that would go into my thinking, like, okay. It's not completely, not at all. But it's somewhat likely that I would just say, Okay.

James Valentine, JD, MHS
and I didn't work, and I think part of what I also heard you say was, you know, that it might be harder to. you know, if you had to at this stage undergo multiple procedures. Surgeries at this stage versus earlier. Is that also factor into, to your thinking on this?

Patient Participant #18 | Discussion B: Risks and Downsides of Xenotransplantation
Oh, absolutely as many of the other folks have said.

you know you're not as strong as you were. If I were 20, I would, you know. have a greater expectation of rebounding, but as you get older you have other elements, and you know no surgeries are guaranteed. So it's like, I don't want the the cure to be worse than the disease, you know, so to speak. So

James Valentine, JD, MHS
I see. Yeah, yeah, no, thank you very much. Did. Oh, we have a hand?

3:22:00 | Patient Participant #19 | Discussion B: Risks and Downsides of Xenotransplantation
Hello again. Everyone. I'm on. I'm unsure if this is related, but I read an article. I believe it's from University of Maryland, where a patient received a pig's heart. I know that's completely different from a a pig's kidney, but the patient only survived about 2 months and I believe one of the reasons that that patient passed away was because of underlying like infections within the pig's heart.

So, I also voted, as the gentleman is somewhat likely, because I would hate to finally get a transplant right. And then. 2 months later, or one month later, it. you know. it's rejected, or I get an infection, or I pass away. I think that's one of my concerns is how healthy is that pigs kidney, and wouldn't work for me, so I don't. I don't know if I should compare the 2. But when I did read that article I was a little concerned about, how would that work with the pig's kidney?

James Valentine, JD, MHS
Sure. No, and it's, I think, valuable to have you reflect on that. I guess I do. Wanna follow up if you don't mind me asking. You kind of talked about, for only a couple of months. That amount of time is something that you would really want to avoid right getting finally getting a kidney, turn around one to 2 months later. Have it fail or get rejected? You know, do you have, And it's okay. If you haven't any thoughts about, you know... Is there any minimum amount of time that you think you would want to see, you know, at the kidney function or not be rejected if there was this risk? Obviously not. It's not one or 2 months. But you know, do you have any thoughts? You know around, you know, if you read an article that said it was a year, you know, and that's just totally hypothetical throwing it out there. How would you react to that article versus this one that said it was one to 2 months later?

Patient Participant #19 | Discussion B: Risks and Downsides of Xenotransplantation
I will still feel the same way, because getting a kidney, you know, to me is improving my quality of life, and to live as long as possible, so I would still be a little nervous.

On how you know if the kidney, the pig's kidney, would fail or my body rejects it. In in 2 months, or even a year, I would be really sad in in, in hurt by that.

James Valentine, JD, MHS
Sure. Thank you. Yes, we'll take these as our last 2 comments on this topic. So, we'll start here.

3:25:00
Patient Participant #20 | Discussion B: Risks and Downsides of Xenotransplantation

So, I think it's an interesting question. I in my mind when you were just talking. I think your comments very valid, are we talking right now about a trial situation, or are we talking about an approved therapy? Right? And if you're talking about. Xeno is an approved therapy. I agree with you. We need to have better outcomes than that. If you're talking in a trial situation, and I'm a patient enrolling in a trial. I'm honestly fine. If the kidney works for a month, I'm honestly fine, if it never works at all, because we won't move the science forward. If we don't take that risk upfront. Should we approve it as a therapy for everyone or as a standard of care, until it's really good, absolutely not but I think we need to separate that as a talk. And then the other thing is , you know, even with allo transplants. Right? We know there's a 2 to 3% primary nonfunction risk. 2 out of 100 kidneys don't work that we put in currently.

So, I don't think that, you know, we need to have superiority. We need to have something somewhere close in my mind if that gets to 5% of them don't work. But you have the next kidney available the next month. Potentially. Okay, with that failure rate. Right? But again, very situational. Sure. Thank you.

James Valentine, JD, MHS
Well, we'll come here.

3:26:00
Patient Participant #20 | Discussion B: Risks and Downsides of Xenotransplantation
My concern is similar to the concern that I addressed at the last question. My age I'm 78 years old. As Larry said, you know he's 60. He doesn't know what else, how much more is left for him. Of course, at 78 I definitely feel the same way, because and also I was not allowed to be on the kidney transplant list. So, if I have this surgery and it doesn't work what's left for me.

I mean I can't. I'm not on the list where I get another xenotransplantation that that that bothers me. I don't know what I would do.

James Valentine, JD, MHS
No, absolutely. Thank you very much.

3:27:00
Patient Participant #21 | Discussion B: Risks and Downsides of Xenotransplantation
Mine is just a statement that I think this just comes to mind, and I'm sorry, a little off topic, but maybe not. But my idea, when I'm thinking about all of this. And after my son got sick, and I do a lot of research, and looking down the road at what's possible, because I know he may have another, you know he'll need more kidneys. So, my question is, you know, I read also about, you know, people getting pregnant and picking the color of their kids, eyes and genome editing that is happening within vitro and the in vivo and animals. Perhaps, can't we? At some point. And maybe this is down the road, too, can't we? We breed chickens for eggs? We breed, you know, animals for meat we could potentially. Couldn't we start with reading animals and pigs? Obviously, in this case, to be genetically modified? I know they take 4 or 5 out and put 4 or 5 in. But can't we do this from birth? Is this happening when they're older? And they've already developed these diseases within themselves?

James Valentine, JD, MHS
Yeah, again, I don't know that II think what is well, just to come back cause you ask a question. You get you get a question back. It's the tradeoff here. So, I don't think we can answer like that scientific question today. But you know what you know you had in mind when you were saying that certain thing risks that you hoped could be better mitigated. You know what was in your mind when you were saying that?

Patient Participant #21 | Discussion B: Risks and Downsides of Xenotransplantation
In regards to this? I said, somewhat likely because and again I'm answering. I started answering for myself because I donated kidney. Should I need a kidney? Someday? I can't answer. I mean, I can't answer with my son in mind, but it would be different. We had this discussion. Our children are young, and when I started positioning the answers according to what I would do, my answers changed. Because, again, I might need a kidney something, and I the fact that I gave one. I don't know that I gave him. I gave a kidney, so, my son, for to help people, and to get a voucher for my son, which I know he'll eventually need right. But again, will it fail soon, whatever. But in my case, if I need a kidney. I don't know if I'll go to the top of the list. I think that you get one shot, and I want to give it to my kid. I would. But that changed the way. I answered the question. Because if I am, I'm 54 now. You know. I want to live a long and healthy life. I love to do all everything. Yeah, we all want to do travel, live, enjoy our family

So, my answers. I'm now answering from that perspective. And I hope that doesn't skew any results. It's not scientific polling. It's to help get the discussion going.

James Valentine, JD, MHS
Yeah. So. I think we've had a really good discussion here about a number of the risks, and even though we tackle a lot of them one off time here and again a lot of the comments many of you shared earlier reflected on a lot of these as well. I do want to shift gears to kind of our third discussion topic of the day, which, to a comment that was just made. You know, we weren't being specific up until this point about whether we were talking about a Xeno kidney that's approved versus a Xeno kidney for a clinical trial. And then, in part that was purposeful because we wanted to hear. You know about how people think about benefits, and bris in a general sense, cause in some ways that helps us

Think about who might actually be interested, or the right candidates for a first in human study versus who would need in for more information and need to wait until there was a potentially approved product or a product that maybe at least had more clinical evidence behind it. And I that diversity has come out a lot but in this session we do wanna kind of focus in on that first in human clinical trial, and I'd like to invite our panel here to the stage. Who will be helping us think through? Some of these questions.

So, Carrie and Gregory? So, as they're coming up to the stage. I want to frame this.

3:32:00
Intro to Discussion C: Considerations for Participating in Xeno Clinical Trials

So here we want to talk a little bit about this phase, one study, and there's not a phase, one study that's currently designed. So this is, you know us somewhat, you know, taking a guess just to again, put out a hypothetical to have people react and respond to and I think, for many of you who, living with a chronic disease, are aware of different clinical trials and trial designs, and I think we should erase a lot of that, because this isn't going to look like a maybe typical clinical trial where we're recruiting cohorts of people, even small coats of cohorts of people all at once. This is going to probably going to look like one patient getting a. kidney xenotransplantation at a time spaced apart from one another, so patient one's level of information that they have could be very different from even patient. 2 or patient 3. Who knows what that duration apart would be. 6 months something. But it's not like everybody coming in at once, and we're collecting all that information in parallel.

I think we've talked a lot about the uncertainties around benefit and how long kidneys will function or not be rejected. We talked about how to date. We only have, you know, some data that goes kind of 3 days. 7 days won't 30 days so we don't really know a lot yet about whether.

There's a lot of uncertainty about the benefit of these products. We've talked a lot about risks, the unknown risks, and some that could be pretty severe. That kind of degree of uncertainties also the greatest, if we're thinking about a phase 1 study, and I think that, and probably makes sense to a lot of you, because we've been talking about how, as we, you know, go into a first in-human study. If we go into first clinical trials you know we have. We don't have that experience yet to see how many of these different risks will pan out to what degree, in terms of how likely, to what degree, in terms of severity.

Some things that we haven't maybe talked about as much: monitoring. We should expect that there's going to be greater monitoring required than after an allotransplant.

Again, thinking through this. Imagine that you need to stay in the hospital 24, 7, monitoring for, you know, a month long, you know, a real instead of maybe a week after an outlet transplant, much longer here. And then, once you're released from that inpatient experience, Imagine that you might need daily monitoring for at least another month and maybe even longer, depending on how things are going in terms of what monitoring needs to continue so significant, monitoring in terms of other aspects of what might need to go, and we don't know how again, how rejection will work. So, there might be a need for not just the same immunosuppression regimen as we use for Allo. We might need to add other immunosuppression that adds additional side effects additional issues on quality of life.

And then there might be some things that are lifelong, you know, in terms of these medications or other supplementation even increased fluid intake might be lifelong. So I think probably you know, we I have even heard it from some comments that, participating in a phase. One study is not for everyone. In fact, it's probably not for most people.

But we do want to try to make some progress towards kind of thinking through who would be the right kind of candidates for that. And by doing that we want to hear from you individually again, thinking about yourself now, your loved ones. Now, thinking about your past experiences, living with kidney disease, thinking about where you might be in the future. Each of you has a perspective to share that can help us kind of collectively think through this.

So, let's maybe try to take on the monitoring piece first. I think that's one concrete place.

3:36:00

Discussion C: POLLING QUESTION

We can start. So, if we can go to our first polling question. Again, we don't have a very specific thing to respond to. But what is the greatest level of monitoring that you'd be willing to accept. and for an extended period of time, so think at a minimum one, maybe 2 months of this most intensive monitoring.

And we'd like for you to think about. Would you be willing to be in a trial if it involved inpatient or other? 24/7 monitoring for that long of a period of time? The next option would be daily monitoring a few hours a day. Of course this would have to follow some amount of inpatient, but for that more extended period of time. Would you be willing to undergo daily monitoring? C would be just. You know you would only accept weekly monitoring, D would be something less frequent, or E not applicable because you're not interested in enrolling: You never foresee a situation where, past, present, or future, you would be willing to enroll in a phase one clinical trial for some other reason.

Alright! We'll give everyone a few more moments here. It looks like we're seeing the inpatient as well as the weekly monitoring being kind of the top 2 greatest levels of monitoring you'd be willing to accept for an extended period of time.

We see about a quarter of the audience saying that for an extended period of time they would actually be willing to accept daily monitoring less than 10%, saying only if it was something less frequent and 3% of people saying not applicable because they're not interested in this type of trial, so I'd like to welcome our 2 panelists here. We've agreed to kind of kick us off on some of these discussion topics. So, as you were thinking about this and thinking about what monitoring might look like over time, can you describe kind of your thoughts and preferences. And, Carey, maybe you can get us started.

3:38:00

Discussion C Panelist: Carey | Considerations for Participating in Xeno Clinical Trials

Can you guys hear me? Okay, yes, great. So, I think the automatic thought that comes into my mind is, I want to be number 3. Please don't make me number 4. However, under the right circumstances, I would happily be number one, because we have to find out about this. So the idea of inpatient monitoring for a month makes me throw up right in my mouth. I've been in-patient quite a bit. It's not fun. But I would do it for the research. I would do it under the right circumstances. Right now. I'm fairly healthy, so I wouldn't go do that today. But under the right circumstances I absolutely wouldn't put up with pretty much any of that, not only to help me, but to help move this forward.

James Valentine, JD, MHS

And I guess, as you think about being inpatient, for some extended amount of time is that in general, if you had otherwise made the decision that kidney was now the right thing for you other risks kind of balancing benefits here, you're saying at least a month? Would you even think of being willing to stay if you needed to beyond a month Inpatient?

Discussion C Panelist: Carey | Considerations for Participating in Xeno Clinical Trials

I think. Then we get into burden benefit questions. If it's going to give me 5 years of healthy life, sure, I'll stay as almost as long as you need me. If it's short term, and I'm ending up spending 2 months in the hospital. And then I have a year. Harder answer.

James Valentine, JD, MHS

in some ways, you know, you're what you're saying is the more information you know about how much it would benefit you the longer you'd be willing to stay. But in a phase, one study where we would know the least amount of what would be willing. This might be harder for you to agree through. Okay. Gregory?

3:40:00

Discussion C Panelist: Gregory | Considerations for Participating in Xeno Clinical Trials

I think somewhat similar I'd be, if I enrolled, which would be still a large “if” for me depends on, I think, as we've discussed where you are in your life span and how you're doing health wise, and what do you think your other comparative options are of other types of transplants, etc.? Then I would be willing to stay in for a month. that it probably be the Max, and then I'd be glad to do daily home monitoring the other part that colors my answer for me a little bit is that I've participated in observational studies and also some clinical trials in the past and depending on the funding. And it seems like also the thought process to the investigators. Some of them can be pretty low- burden, and you know very, if you would, thoughtful. where you may, for example, be able to take an Uber or a lift from home. So, transportation is no longer an issue, and you have meal tickets for you while you're there. During the day, and just many other small things that make it a much less effort. Type of engagement.

James Valentine, JD, MHS

Sure. And when you say you know a month that would be, you know it for inpatient. Can you just speak to a little of why, that's in your mind. Kind of the cut off what? What makes one month okay, beyond that, it's too much of a burden?

Discussion C Panelist: Gregory | Considerations for Participating in Xeno Clinical Trials

Probably experience. yeah, I guess thinking about that. So, I'm a physician. And maybe we're some of the worst patients, I've been told. but as part of that, I guess, having dealt with short-term and some long-term patience.

You know, after a month it just feels like you become most to me a fixture in the hospital. You're like the person there who seems like they're never going to go home. And again. I actually was very, very fortunate, and got a living donor match in May of this year, so I still remember staying in the hospital, and there's no question, you know. I couldn't get any sleep, you know. Everyday somebody was coming in at 2 o'clock in the morning to take my blood pressure. The vampire would wake me up at 3 in the morning, while I was still half asleep, just taking my blood and not try to go back to sleep. Then you've got, of course, all these tubes and things coming out of you. So, I had to sleep on my back, which is not normal. the food was hospital food. So, if you kind of go down the line, it's like, Wow, this is not the club med for sure.

James Valentine, JD, MHS
Thank you. Audience members, I want to bring you into this discussion. How did you think about the question of monitoring? Yes. right here

3:44:00
Audience Participant #1 | Discussion C: Considerations for Participating in Xeno Clinical Trials
So, I kind of have that that same opinion. And unfortunately, I was one of those that was in and out of hospital a lot. And my biggest problem is less about if I'm feeling well, I drive the nurses crazy. Because I don't want to be there anymore. I'm up walking around my room. I can get up walking around, so it's much less about how much time I'm in there. If I'm not feeling well, if I'm kind of stuck in the room a month. That wouldn't be a problem. But if I'm you know the kidneys working, hey? Everything's great. And then, even after my transplant. I was stuck in the hospital for 10 days, and I drove everybody insane. And so I think it has more to do with as we've been talking about, for it's really a a continuum right of are, are they keeping you in the hospital for observation? And for, you know, for data points as opposed to. Yeah, you're healthy enough to leave versus. We're still concerned. You're correct and still high. You know your blood pressure still uncontrolled. We still have these other issues. So I think there's it's, you know. I kinda as you mentioned before, which is, what's the protocol for? Is there a specific cut off, or milestone that you have to reach, to be able to get out the hospital, and I think if I knew what those clearly were, I would have a much more likely chance to say. Sure, I can stay in for daily monitoring for a month if it's not a problem. But if I reach these goals. Let me out

James Valentine, JD, MHS
Is there, for you. A minimum, or I guess a maximum rather amount of time that you know. Say they regard there is no protocol based off of how you're doing. We need to observe you, because you know the unknowns that that we might not be able to see you know. So, there could be that you're feeling good, but they still want to observe. So, Imagine you're consenting to participate in a trial. Is there a maximum amount of time? You would that that you'd be willing to agree to?

Audience Participant #1 | Discussion C: Considerations for Participating in Xeno Clinical Trials
Yeah, that's a tough question. I think it's still right along that month. I think one month is when you start to get mentally, it starts to affect you more than anything, because then you're you know, and then that also brings in questions in terms of is the mental health issue that I'm now having, because I'm bored because I'm starting to get antsy. I'm getting depressed and getting this is this now affecting the overall output, you know, and outcomes that you're looking at.

Because those two factor in, you know quite readily, especially if you're on a lot of those drugs. The prednisone, any transplant patient here knows they make you crazy. So, on top of everything else. I think those are what we discussed before, which is very clearly defined protocols. Even if there is an unknown. We still have to have a way of. I think, in some way giving hope to a patient that you know you can get out of the hospital at some point.

James Valentine, JD, MHS

Yeah, that's really helpful.

3:46:00

Audience Participant #2 | Discussion C: Considerations for Participating in Xeno Clinical Trials

So I can't stand hospitals and I really thought highly of my sales skills when I tried to convince the transplant that I could leave after the second day, and they wouldn't allow me. We had my yoga clothes. I was going like I was out. So I went with the daily monitoring, even if it was for hours one, just because of my mental health being in the hospital. But also, I know hospitals can be very germy, and so I think not only of myself in the hospital for that amount of time, but then family coming to visit me, especially having small kids

showing up there. I mean, what if they were to contract something that they got because they came to see me in the hospital. Sure. Yeah, no very helpful. Thank you for adding that. Yes.

and then start in the back and then work our way back towards the front.

3:47:00

Audience Participant #3 | Discussion C: Considerations for Participating in Xeno Clinical Trials

I think it depends on the hospital setting. I mean, you know, if I'm lying in bed and deteriorating, and you lose a lot of strength by just lying around that would be disincentive. I put that, I mean, I'm cool with daily intensive monitoring. I'm imagining, like a sec. You bed like an ICU I'm imagining being excavated right but hourly. Vitals hourly this hourly that please automate it all right. They're very nice technologies to keep track of my heartbeat.

Don't need someone to come stick me right. I can walk around with an a line, for example. Put a peloton there, give me good TV streaming services. Give me a yoga mat and something to do, and I'll be happy as a clam to be observed for 3 months, right? But if I need to be lying in bed and be treated like, you know. I can't walk. I can't get out of my room because of infection concerns. I have no place to move, and I'm stuck lying in bed. That's not going to go so hot. Not on steroids. oh, and vital sign frequencies, you know, like you can check the numbers, but don't send people in at night like there needs to be those limits on the door. Yes.

3:48:00

Audience Participant #4 | Discussion C: Considerations for Participating in Xeno Clinical Trials

I chose weekly. Being in a hospital when I was first diagnosed I was in hospital for 2 weeks, and for those 2 weeks I lied in bed and I couldn't do anything, and it was very miserable for me. I'm a person who loves the sun. I have to go outside. I have to go outside and get some fresh air. I think I would consider daily. Only if there was a way to go outside. Get some fresh air, or, you know, like some others said, do maybe like exercises, have some entertainment, better food? but if not, if we're going to be just in bed and being treated.

I don't think I will be able to survive just staying in the hospital bed for a month, or even longer than that. It was a very, you know miserable, tough time to just lay there all day every day with no good TV.

James Valentine, JD, MHS
You also mentioned you said weekly monitoring. Talk a little bit about the difference in your mind between needing, maybe to spend a few hours a day being monitored daily versus the weekly. And why, that is was something that you said you wouldn't be interested in.

Audience Participant #4 | Discussion C: Considerations for Participating in Xeno Clinical Trials
So when you said weekly what my mind is, I come in for like a day for a few hours every week. I think that's something that I could do and commit to for a long period of time. I wouldn't mind doing that like if we had the trial for about 3 months, 6 months, coming in once a week for a couple of hours to be monitored. Easy, peasy. I can do that. But every day for 3, 6 months, just land in bed. I don't think I can

James Valentine, JD, MHS
Well thank you so much for adding that hope. We have 2 comments here, so let's go here first, then we'll come to the web comments.

3:50:00
Audience Participant #4 | Discussion C: Considerations for Participating in Xeno Clinical Trials
Thank you. II haven't heard this said yet, but I think if you have a job or a career to which you are really devoted. you know, I think it would be hard to do some of this monitoring. So you know I chose. You know. What was it? Less or well, more than a something left? Yeah, I chose that just because again, if you're invested in a career, you may not be able to do it to do both.

James Valentine, JD, MHS
And we'll give the final word on this topic to our some of our web commenters.

3:51:00
Online Comments | Discussion C: Considerations for Participating in Xeno Clinical Trials
So we're getting a lot of comments that are about the same of what's coming in through the room. Teresa was saying that she feels like with. She's a transplant recipient with today's technology. As long as your labs are good and you can be monitored at home daily better than you can in the hospital.

3:52:00
TOPIC C POLLING QUESTION
Speaker: Alright. So, let's try. Yeah. We spent a good amount of time there talking about monitoring. If we can go to our next polling question. Here, again, we're talking about a phase, one clinical trial. highest degree of uncertainty about how well the product the Xeno

kidney will function, not be rejected all of the risk that we've talked about also. Now, this context of the additional burden and regimen associated with that, you know. But if you were, considering you think you would at some point, past, present or future. Consider yourself a candidate for phase, one clinical trial given everything we've talked about. I'd like to know what of these factors would most likely influence your decision to participate in that trial. And so, it's totally okay. If you don't think phase, one trials would be a fit for you again, past, present, or future. that's the final option here which is not applicable. But we'd like to, for those of you who, could proceed that potential possibility like you, to rate the options of a: the urgency or immediacy of the need that you would have for a transplant. B: the increased medication and immunosuppression compared to allotransplant, C: the inability to withdraw from the study due to the need for follow up d, the unknown duration of trans. The transplant lifespan; e: the unknown or and potential risk which we've discussed quite a bit so far today F: Your and your doctor's general understanding around xenotransplantation or G: some other factor that we haven't listed. That is one that you would view as being most likely to influence your decision to participate. And then, again, you can select H. If not applicable, because you don't foresee phase one phase, one clinical trial. Being relevant to you, which is again totally. We've heard many people state that sentiment today so no worries, if you that is your selection. So again, you can select all that apply to you as the ones that you would view as the most likely factors to influence your decision to participate in a phase 1 trial.

We'll give you a few more moments to make any selections. It looks like most of you have answered. So, it looks like the thing that has risen to the top is the urgency and immediacy of the need for a transplant and I think that this even may vary. You know, in terms of what each of you are individually thinking of. You know. What is that contextual situation that would lead to you seeking, you know, something that's so experimental. So, we want to definitely hear about that from you and discussion. After that we see a bit of a drop off. We see kind of a cluster of the increased medications and immunosuppression being a a factor that's likely to influence your decision the unknown duration of the transplant lifespan and unknown and potential risk

After that we do see a number of people selecting general understanding about xenotransplant, the inability to withdraw, and some others. I definitely want to hear about what those are as being top factors for you. And then we do see a number of people selecting not applicable.

So, I'd like to come to our panel, and maybe I'll pick on Gregory first this time, you know, kind of thinking about these factors, these different considerations. You know what kind of one or 2 rows to the top in your mind.

3:56:00

Discussion C Panelist: Gregory | Considerations for Participating in Xeno Clinical Trials

I think the unknown duration of the transplant lifespan would be number one or 2 for me. and then the other would be the urgency or immediacy of the need for the transplant. to give it a little context. I think for me. I'm driven quite a bit by the appeal of quality of life as opposed to just strictly the quantity of life. So though I put the duration fairly high. That's because I would not necessarily want to go through the same process over again. If they said, this is going to last, maybe a year, or the best estimate was, and that have to be back through the whole mill again if you would. And again, just to give it context. I suppose nobody enjoys going through the transplant process. But I found it. you know, very, very challenging. I was just surprised at how. for better term, I guess inefficient. It was yeah. And so I. And then also, you know the people you sort of have to drag along with you. Going through that process. I had relatives who were kind of throwing their hands up in there saying, You know I can't go through this anymore. You know they're not returning my phone calls. I can't seem to get in. They're just qualifying me over XYZ. So I think between myself, my friends, relatives, all those sorts of things. I would take that all into account. Yeah.

James Valentine, JD, MHS
So really, w what we're talking earlier about in terms of...In some ways it's a risk as well as you know, an unknown duration itself is a risk, because there's a need then to have a surgery to potentially to remove it. And then, being kind of put back in the cycle of, you know, another meeting, another transplant. You want to avoid that right?

Discussion C Panelist: Gregory | Considerations for Participating in Xeno Clinical Trials
And then, I suppose, just maybe it's obvious. But yeah, I'm assuming that the for better term the ride would be bumpy after the transplant. And so I'm anticipating a lot of side effects from the medications and those sorts of things. So again comes back to quality of life. yeah. And I think that's the other reason.

James Valentine, JD, MHS
And then, on the other one that you said was in your top 2, which is the emergency or immediacy of a need can describe, like in what situation you might consider a kidney xenotransplantation. What? What is that? What need would you need to have to consider potential phase one trial participation? Or, if not that, just a Xeno kidney? More generally.

Discussion C Panelist: Gregory | Considerations for Participating in Xeno Clinical Trials
Yeah, I think, in terms of attracting me to enrolling in that related to the urgency, it would be knowing that I still could qualify, at least theoretically for a allo transplant, either a living donor preferably, or else the deceased donor. If I knew going in that, I couldn't. I think really the biggest driver for me personally would be to say, rather than just. in a sense. dying for no good reason. I could help to advance it, but it would be going in with a knowledge or expectation, I guess, is a better phrase that this is going to be a really terrible pool board quality of life, and I'm just going to put up with it for X amount of time. And I'll almost look forward to dying in, you know. moving on to something a little bit more pleasant. Yeah.

James Valentine, JD, MHS
and I you know you. You said it in a very cheerful way. But it's a very serious thing that you're saying and you know so just again to probe a little bit deeper here, you know the way that you framed it was, you know, essentially your interest in, you know, kidneys and transplantation is as really a last resort. You know. And so when you know, how would you articulate when you.

you know, would be at that point like, how would you describe your health, your treatment options? You know. When would it start popping up. Oh, I should consider this, you know. Possible clinical trial, or you know. You know, product?

Discussion C Panelist: Gregory | Considerations for Participating in Xeno Clinical Trials
Yeah, I'm I'll try to answer it, and if I don't know for me, I right, we're all comparing, I think, different options. So for me, given that point in time and so on. Fairly recently I put it at. I would put xenotransplant right now probably tied with probably dialysis, and for me and I guess I should start. It would be a living donor because they do last longer. You're on less immunosuppression so little lower of a chance that you're going to need to go through the process again. And deceased kidney donor, for instance, other degradations. You're not going to have it lasting as long, etc. And then, when it got down to dialysis. In part, because I've again treated patients in acute kidney failure and had put them on dialysis and etc. And I've seen that I'm also a researcher. So I know how bad the stats are as you get older for morbidity. Mortality. I had decided there's no way I was going to go on dialysis. I had pretty much chosen. I was going to go to hospice in, just, you know, short amount of time on EGFR was pretty low, and everything you could crash any day. so it would only be really, if somebody had said we would like you to do the Xenotransplant trial. It won't prevent you from getting another transplant, and I saw it at least personally, even if the investigators didn't put it this way, that it's really a bridging strategy. and it would be painful in a sense, and difficult, but at least be generating some data, and I'd be bridging myself to hopefully. Then getting an allo transplant again, preferably living donor. Right? Does that help answer?

James Valentine, JD, MHS
It helps a lot. One kind of clarification, though, is, you did kind of mention the possibility that other transplants weren't an option. So, your only option is dialysis. So, in that case, if I'm understanding you correctly, that you know, and most likely mean that it's not, in that case a bridge, because transplant is off the table. Is that also a situation? You view Xeno kidney, as if dialysis becomes your only option. Would you be then more open to the risk that you know it would make you further ineligible for Allokidney transplant some of those risks that could lead to that?

Discussion C: Gregory | Considerations for Participating in Xeno Clinical Trials
I think yes, that if my only option was dialysis, that I probably would do it, as I mentioned earlier, and I realize, you know there's some pros and cons. But I feel that many clinical trials have incentives for patients. For very similar reasons. I've done a fair amount of cancer research, for example, and there's no question. You know, cancer patients enroll with the idea of. Well, if I don't try this new drug, there's almost no question. My 5-year survival is known as X right? And so I'm going to enroll in it and then there's other incentives. I would argue for it. I suppose. in a sense. To a related aspect of why, I would see this as a bridge. I was quite surprised at how slow and long, very slow the process was. So if I thought that this would buy me more time. I would do it for that. So unless they had said, No, you totally will not qualify for kidney. If it was just this time factor going on. Let's say I don't understand why it's taking so long. But okay, let me buy some more time if I can

James Valentine, JD, MHS

Thank you so much for letting me probe and understand that a little better, Carrie. Same thing as you kind of consider. You know the range of different factors, you know, some relating to what we've already talked about as well as others, what it's kind of top of mind as as those kind of most things that are most likely to influence your decision.

4:04:00

Discussion C Panelist: Carey | Considerations for Participating in Xeno Clinical Trials

So I selected with the 83 that urgency and immediate immediacy of need would make probably the most difference. Okay, Gregory covered a lot of things that came through my mind.

I'm presuming I'm patient one right? If I don't have another option. Why would I not do something that could help other people, and further it along, if it's my only option?

The thing that is a big consideration for me is quality of life, and how long it takes to recover. I was better at 3 Years post-transplant than I was at one year. Post transplant at 6 months post-transplant. I went in pretty healthy, so I should say that oh, no, great. So to risk potentially all of that being worse or very little time. I'm not sure I would take that sacrifice.

This may sound crazy, but it's very similar to what you said. If you accidentally kill me with the research. Okay, if you make me suffer for 3 months, and then I die at some point, and I know I couldn't know that. So, I guess for me again. It goes back to that number one. How urgent is it? Yeah.

James Valentine, JD, MHS

So, the way you've described it was, you had no other options. What does that mean to you?

Discussion C Panelist: Carey | Considerations for Participating in Xeno Clinical Trials

I think for me it would mean that I couldn't get a living donor transplant, that I couldn't get a disease transplant, and that dialysis was miserable right now on Pd, it's not. I'm not a fan. but it's not miserable. Okay, so if I were in a situation where Pd. Still worked, and I could have a quality of life. I wouldn't go in. But if I was really sick already, which can very much be the case. Umhm, then, yeah, I would. I'm pretty risk tolerant. So I would definitely go in.

James Valentine, JD, MHS

No, that's very helpful. So again, would like to now broaden and include our audience here on thinking through these different factors, it can be whether it's the same factor understanding your personal. Take on that, or maybe something we haven't heard about yet. Oh, yes, let's see what the web comments have to say on this topic.

4:07:00

Online Comments | Discussion C: Considerations for Participating in Xeno Clinical Trials

So, Andre, who's a transplant recipient? Says Similar to what Carrie was just saying. It might be a minority opinion, but as a scientist I would appreciate being a member of a clinical trial for the aspect of extending the science and my own comfort benefit is secondary and then

Linda, who's a transplant recipient, said, yes, she'd be willing to listen to the options about Xeno. Of course she'd be scared about the possible outcomes. I she was fortunate, didn't have to be on Pd. As long as many others, but as the process can wear you down, loss of energy, loss of dreams, difficulty, traveling, etc.

James Valentine, JD, MHS
Thank you. To those of you who have been writing in, and you've had comments that came in on some of the other topics that we haven't had a chance to read out, know that we have all of your comments, and will be including them in the voice of the patient report.

So, our audience here in the room. You've been so thoughtful and sharing all day long. I know we're getting towards the end of a very long program of me asking a lot of you. But I think this is a important topic, because I we heard from so many of you that we need to get to that first, you know. Clinical trial. We want to see the science advance and so we want to think about, you know, who might be the right population that would raise their hand to be in a clinical trial. Phase 1 clinical trial specifically like we've talked about. And so again, each of your individual perspectives, even if that's not you or it's not you today, I think, help kind of help us build that understanding.

So, any thoughts or perspectives on this. What factors would be important thinking about very specifically a phase, one clinical trial setting? Yes.

4:09:00
Audience Participant #5 | Discussion C: Considerations for Participating in Xeno Clinical Trials
I mean, I think one is not a guarantee, because you can't guarantee anything in life, but at least an assurance from authorities that there is an option for another transplant as a rescue therapy right? And you know, I mean, we have this currently right for people who are living kidney donors, that because they've donated they get extra points as they will on the waiting list. I think if you're willing to take a risk to further the science, maybe there should be extra points given either within the national deceased donor allocation system. Possibly even within, you know, other systems that involve living donor kidneys that become available later.

Is there going to be a guarantee for any recipient who goes through a transplant or an experimental procedure that they're going to be a candidate for another transplant. No, right? There's always naturally going to be a risk that you know the health will deteriorate. You know. Cardiac health, vascular health, the place to implant the kidney might not be there in the future.

But I think that should be one consideration. I think the other thing, and I stepped out for a minute, so I don't know if this was brought up is the option to opt for a transplant nephrectomy at some point If things become too severe and then strong support from a palliative care team, so that there's appropriate goal setting with the patient and the family, and that that risk and balance in the long run at the end of a phase. One trial, you know, are in the place. Where do we decide to end this organ by taking it out? Versus? Do we keep it in and continue to have the patient forced to be taking immunosuppression. There should be some input from the patient. That is part of that at that time. Yeah.

James Valentine, JD, MHS

So if I can follow up with you on one thing that you said because it's a little different than what we we've maybe heard from others, which is you know, for many we're hearing that it's really, you know, if I have no other options, this is then become something I might consider, but you just mentioned that, and kind of it came up as you were talking about, you know, getting preference, or at least points, or what have you to? You know, if you're healthy enough and aren't otherwise contraindicated from getting additional transplants to have a priority for that? But that would also indicate that you know you might be willing to, raise your hand to be in a phase, one study before you get to that being your last option right? Because Allo might still be an option for you. If you're presuming that you can come out of the Xeno and have Allo as an option. So I guess what I'm saying is, wanna ask is, you know, in what for you kind of setting or stage would you'd be willing to raise your hand if, say, some kind of preference was for an Allo transplant was an option.

Audience Participant #5 | Discussion C: Considerations for Participating in Xeno Clinical Trials

Yeah, I mean, I think there's a variety of circumstances in that setting for me. So, for example, one is, you know, I'm waiting. I have kidney failure. I'm feeling not so great. I don't have any major obligations in life right to other people that are dear to me, and maybe at that point in time I am willing to undertake a trial and have a kidney for a month or 2 or 3 or 4 and if at that time it's working in, my life is reasonably okay. Being half home, half in the hospital. I'm cool with that.

On the other hand, yeah, I mean, I think there are people who are just natural risk takers. You see what I mean. And I mean, I'm not a skydiver. I'm not super interested in it. Personally, I'm not that level risk taker. You see what I mean. But you know not that level. But, on the other hand, I've participated in many trials, and frankly, they care. I've gotten within a research trial has always been more detail oriented, more thorough, and almost more caring than outside of a trial.

So, I have great faith in our in our current system that it would make that work. But I think there are some circumstances where you know. For example, if I struggle with my dialysis access if fist chill after Fischel on graft after graph lots and say, I'm now on Pd. And nothing's working, and there's the option to do a phase 1 trial, and I could do some good, you know, and my iliacs are free of disease. But that's not a place where normal people put in access. Well, why not give this a try? Right?

And you know, I think the other important part to this is, I think if we're only looking at people who are not candidates for Allotransplants to participate in Xeno trials. We're going to have different outcomes because those people are not candidates for allotransplants for a reason. And then you're going to try to have similar outcomes among sick or patients. And that's not going to lead to a fair comparison. So, I think the trials should be open to a broad population of different backgrounds and in different disease states, and in different states of health and with the proper consent, and you know, respecting patient autonomy and understanding of where they are in life, they should have the ability to participate, even if another transplant down the road may be possibility for that. Sure. Thank you so much.

James Valentine, JD, MHS
Yes, right here.

4:15:00
Audience Participant #6 | Discussion C: Considerations for Participating in Xeno Clinical Trials
So, I think the one thing I haven't heard too much of, and I think Gregory kind of touched on this, which is in terms of the clinical trial. You know. We assume hopefully, that there's nothing that's going to go wrong. Note that there may be some pain, management, and other stuff.

But I think the other thing that may need to be addressed is the end of life care at what point do we have a patient where they're like done? II can't no more no how do the protocols? How do clinicians' kind of come to the conclusion that okay, you know, we're going to take everything off. We're going to boot pain management. It's going to be just basically hospice at this point. And that has to be the patient's choice right? That has to be a conversation between patients. The doctors. and I think that's something that should be a conversation even prior to going into any of these clinical trials which I know in clinical trials, in in a lot of these discussions. There are things of you know. At what point? You know. Are we going to end the trial? And what point. Is it too far to push? But I think you know that that's something that even in in our field of transplantation dialysis that we don't discuss a lot of which is, there is always another option besides dialysis and transplant, and that is.

you know, just end of life care, and that's and that's perfectly fine for a lot of people who they've lived their life. They're done with it. And they just don't want to have to deal with this anymore. And I think if a patient, as you said, if you're the first patient in, that reassurance that you're not going to let me suffer is, I think very important, especially for those of us who've been through the ringer already with dialysis transplants and everything else. Sure, really appreciate. Yeah.

James Valentine, JD, MHS
saying that I saw lots of nods around, as you were saying. any other thoughts on important factors, that for you and you would consider Yes, Gregory.

4:16:00
Gregory | Discussion C: Considerations for Participating in Xeno Clinical Trials
so this is really just, perhaps reinforcing the the point that I think I heard about a preference to move to the top of the list for transplant. It's something II mentioned earlier, just to expand on a little bit. If you are familiar, many of you probably are. Hope with the National Kidney Registry right? They give you a voucher, and that's part of their program. Is that then you go to the top of their list, so it doesn't guarantee that you are going to get a transplant, but

they're giving you preference just in my situation, to clarify a little bit, too. If this were a bridging strategy for me, and someone said, You're going to go to the top.

I had had a number of donors come forward, and I was surprised that they were declined by some of the transplant centers. So, there was that variability going on. Then they'd go to another transplant center, have to be worked up again. Meanwhile the clock is ticking, and I'm getting worse and worse and worse and yet. And then they're getting approved at other transplant centers, which is great. But it's basically chewing up the time. So it wasn't that I wasn't transplantable for a living or from a deceased kidney. It's just the time was ticking away. Right?

James Valentine, JD, MHS
I think we've heard that experience of people's donors that you ultimately were successful. Finding that they weren't at multiple centers, right?

Gregory | Discussion C: Considerations for Participating in Xeno Clinical Trials
Which itself, you know, leads to a different topic. But yeah, you know, I'm surprised we don't have a national standard when I found that out.
Yeah, right? Yes. So any final thoughts on factors that would be important to you. Yes. I'll put 1Â s. We'll get you a mic.

4:18:00
Audience Participant #7 | Discussion C: Considerations for Participating in Xeno Clinical Trials
I'm sorry, and bear with me. Have a lot of thought swirling. I think originally, I answered, that if there were no other options. but also really not interested in being phase one. but going back to if there are no other options, and looking at what that patient might look like. I kinda wanna put some color to that. I am single. No children, my Nico family pretty much is my mom and myself. And let's just say my mom's deceased. And it's just me. Then, definitely, I would make that decision to be a part of a phase, one clinical trial. And much like all of you said, you know a bridge, or possibly this idea that you know I would be eligible for something else later. But as you all were talking, I really thought about at 33, I had to make some really hard decisions. Getting a will, paying prepaying for my burial. So all those things are already taken care of and well thought out about what happens to me later.

And you know again, looking at who that patient might be for phase one individuals who are interested in being a part of medical research, as I said earlier, so that others don't have to walk down on that same road and street. If you know, I had to kind of decide of like my later thoughts. And a lot of I'm sorry I want to go back a little bit.

To a question I didn’t make comment on about the monitoring piece the 30 day. I think all these questions is, Larry said earlier are related, so I would do like a monthly thing because I don't have any of those external pieces. And again back to clinical research. So they're just like thought swirling in my hand. I hope I didn't scare you there, but when Greg said, You know, Hospice, I'm like there's nothing wrong with that and you know it. and it's not discussed. It's like these are your options. You get a transplant or you go on dialysis. I'm very unique in the fact that I never went on dialysis. And to be very honest with you, I don't wanna ever have to go on dialysis.

James Valentine, JD, MHS
Well, I really want to thank everybody so much and thank you to our 2 panelists for being willing to get us started in this discussion. Okay, but I really just want to thank everyone for all of the input, today. we are at the point in today's program where we need to start wrapping up, but it has been an incredible day. We asked a lot of you to not only reflect on your own experiences, which were very personal and you know, but and very important for us to understand, so we could appreciate what you then shared. As we ask for you to consider a lot of really hypothetical kind of kind of situations.

But I think we needed to have this discussion and conversation so we could. You know, understand how you know all of you living with kidney disease or care partners of those living with kidney disease at all different stages. You know of your disease and of treatment to know how you think about these things. And I think you know, we heard a wide range of different perspectives. But that's what we wanted to hear. We needed to know. You know how you thought about it, and maybe in some ways, not the answer of what you selected on the polling question. But all the context that you shared around what kind of led you to make that choice was the more important thing for all of us to hear, you know, because it's not black and white, and these things do all relate to each other. So

I just wanted to thank you as the meeting moderator today, for so all of you being willing to be so open and share your personal experiences and go on this thought journey with me as your meeting moderator. So just from the bottom of my heart, thank you all for being so willing to do that. So, at this stage, we're going to shift to a meeting summary. It's an impossible task to truly summarize everything that was discussed today but we have the perfect guy to do it. We have David Feldman, who's the senior medical project director at NKF.

He has decades of experience in the kidney space doing research, working in industry at Nkf, he's helped organize all of the different patient-focused drug development meetings that have been held today, and he was integral to the planning of today's meeting. So, David, I'd like to welcome you up to offer some summary comments.

4:24:00

David Feldman, PhD (National Kidney Foundation)
Well, thank you, James. and thank you for your as usual. excellent job at leading this meeting. and I would like to give the audience the opportunity. But thank you.

So good afternoon, everyone. This really has been a wonderful meeting. I was thinking a few minutes ago that since 10'clock this morning we've really come a long way toward understanding how the transplant community, or at least this small segment of the community, thinks about xenotransplantation.

So, we asked you to do something today that was quite difficult to look into the future and to try to visualize decisions you might make about xenotransplantation for kidneys. Even while this modality is still being developed. and you did it really well. And so now I'm going to try to summarize what we heard today, and I'm not going to be able to cover all of the fantastic insights that we heard today. So please don't feel left out.

If I don't mention something that you said during the meeting, and of course I'm talking to the online community as well. So, we started the day with Dr. Patricia Beaston from the FDA. And Dr. Beeson told us about the importance of El Pfd. Meetings to the Agency's regulatory responsibilities in particular, with respect to kidney xenotransplantation.

We also heard 2 excellent expert presentations from doctors. Vanita Kumar and Peter Reese on what Xeno transplantation is and possible benefits and risks associated with this modality.

And we started the patient input part of this meeting with 7 insightful and very moving testimonies from a panel of patients and care partners with diverse experiences in kidney transplantation. And I want to spend some time on this portion of the meeting.

So first let me talk about the common experiences that shape the panelists thinking about kidney xenotransplantation. Victoria, Brie, Ed, and Katherine spoke of the trauma and the harshness of dialysis, and how that would affect their possible future decisions regarding xenotransplantation.

All the panelists who have waited for a kidney transplant talked about the high level of the stress associated with waiting for a human kidney and their desire not to go through this again.

And these 2 types of experiences combine to a third factor that colored the panelists thinking about Xenon transplantation, and that is improving, or at least avoiding a reduction in quality of life and a final common theme involved family, and especially children and grandchildren, and spending time with them and watching them grow so all these, these were common factors that influenced the panel's thinking about decisions on Xenotransplantation in the future.

Then there were concerns. Our panel spoke about their concerns regarding the risks of xenotransplantation, and how these concerns factored into their thinking about this modality.

And so I'll just list 8 of these concerns. The possibility of multiple organ failure leading to Death. Rejection of the Kidney and additional surgery to remove it. A zoonotic Infection. Side Effects of Immunosuppressive Therapies. How long a pig kidney would actually last recurrence of the original kidney disease in the transplanted kidney being subject to more intensive testing and other demands of being first in an early clinical trial. and of course, the unknown and unidentified risks of Xenotransplantation

so related to these concerns that I just mentioned. Some panelists gave us insights into their thinking about a decision to enter a first inhuman clinical trial or accepting a Xeno kidney. If the modality is approved for some panelists, the urgency of their clinical situation seemed to determine their openness to Xenotransplant, and we heard a lot about that. Just in the last few minutes this was expressed, I thought quite well by Maria. who has not undergone dialysis or a kidney transplant, and Maria said that she would not enroll today in a clinical trial, because it would take away too much of the life that I am enjoying with my loved ones.

But she said in a few years, if her health had declined, and there was no match for an allo transplant, and if waiting for a human kidney necessitated dialysis, and if my life would no longer would no longer feel like it was my own.

she would likely join a clinical trial. So, there was, and a lot of people expressed this kind of gradient of thinking, not today, maybe tomorrow.

In a similar vein, Victoria said that she would hesitate to enroll her son in a first inhuman trial now. but if the need for a new kidney arose, she would strongly consider Xenotransplantation. and some panelists express less ambivalence toward Xenotransplantation, for Brie and Ed and Catherine and Wendy and her daughter.

Their perspectives reflected the likelihood of a clear, choice dialysis or a long wait for a human kidney versus a kidney xenotransplant and faced with these scenarios in general, they would have chosen the Xenotransplant and somewhat different sort of refreshing view from what was expressed by Sandy, who has undergone dialysis, and she said she would pursue a very detailed understanding, including statistics and definitions of the risks of Xenotransplantation before entering a trial. and finally the panelists spoke about their potential.

What they thought were the potential benefits of Xenotransplantation, and the most common of these were avoiding dialysis and associated complications and problems and avoiding emotional trauma of the long waits for kidney transplant.

And even just a few years of extended life without dialysis, was thought to be a benefit to some of the panelists. so we thank the Panelists for their diverse and very important insights, and for setting the stage for the rest of the meeting which was devoted to hearing from all of you here in the in the room and online.

and largely your perspectives echoed what we heard from the panelists, and I'm going to briefly cover some of the important points that emerge from the audience discussion.

So, regarding why patients may consider transplant xenotransplantation. Many people are in strong favor of a phase, one trial, because. you know, the difficulties of and complications surrounding getting a donation, a kidney donation apart from just the weight. So we heard about when all possible living donors were too old, you know, that would be among among friends. We heard about a ruined friendship with a donor which xenotransplant would have prevented. Obviously, this difficulty in asking for in getting a second transplant donor. and we heard about concerns about you know the donor themselves worrying about the donors. Pre health! Health pre transplant and the burden of a people were were hesitant to put a burden on a relative as a donor. And so all of these things were factors that factored into deciding on Xenotransplant.

So that was discussion. A discussion. The second discussion, B was about known and unknown, known and unknown risks prior to first, in human clinical trials and so 42% of patients were unsure of whether they'd be interested in entering a trial if there was a risk of catastrophic event.

Haley said that basically individual decisions would be determined by changing individual situations and risk tolerance. And you have to balance the options of, you know other other options, for you know, kidney therapy.

There were one person asked about or raised a kind of concern about pregnancy during in the post transplant setting so these were reasons, you know for how people are thinking about the risk of a catastrophic event.

And then there was the question about likelihood to take a a transplant, a Xeno transplant, and if there was a risk for not being eligible for a Allo wait list. and the reasoning here from many participants was that age, current circumstances, quality of life, length on dialysis, whether or not you have young or adult children, all these things would factor into the decision making for you know accepting xenotransplant, and of course, the risk tolerance, one person said, Don't break me and not be able to fix me with an allo transplant.

So, another question was, how likely would you be to accept xenotransplant if zoonotic infection and transmission to the family was a risk 45% of people said not at all. Some people were talking about vaccines or other mitigating activities that might be available and these people there were. So, these people said that they would be somewhat too very interested in Xenotransplant if those, if there were mitigating factors.

And one person felt that, you know normal, healthy people are not dying of zoonotic infections. Very frequently. then, there was a likelihood to undergo xenotransplantation.

If there was a increased risk of breath, rejection and the rationals here were, well, it feels like there's this was felt like to be a similar risk. As for an allo transplant, so this is not anything new that that people have been encountering.

and of course age has a factor in it. Older the older you are, the that the individual is, would not want to do this surgery again. So if the graph fails, so sort of like 1 one bite of the apple, I think, was the phrase. and then we're talking about entering clinical trials. What's the greatest level of monitoring you would accept for an extended period of time.

One month seemed to be the maximum, and there were several factors that were discussed here, depending on where you are in your life and your options for transplantation, the logistics of the of the of the trial and the monitoring, like, you know, meal tickets and transportation. These would motivate more monitoring. More than one month was said to, you know you become a fixture in the hospital, and that's not very attractive.

And are you healthy enough to leave the hospital compared to is the team just collecting data. And somebody wanted to know, you know. wanted to know if that's going to be the case infections from a hospital setting being stuck in a bed compared to being move, being able to move around. These are all things that people were talking about home monitoring was also raised, and of course, if you have a job you don't want to be sitting around the hospital.
So for a phase, one trial, what would likely to influence your decision? To enroll the urgency was the predominant factor here. The urgency of need of, you know, further treatment quality of life, eligibility of for an allotransplant that would also factor in.

You know, eligibility after the trial. Greg said. If dialysis was his only option he would enroll in a trial if he thought he'd be able to buy more time. And Kerry said, if no other option, why not help science and then someone raised the topic of a rescue. Therapy. Should be, you know, if a rescue therapy was available that would factor into her decision and the option for a transplant and nephrectomy to remove the xenotransplant if necessary, and then followed by strong supportive care.

So that's, the summary that I could put together. Again. I want to thank everybody and congratulate you for all the comments that you made, and especially the panel, the testimony panel very brave and moving comments. And now I'm going to turn it back over to heather for her closing remarks.

04:38:54

Heather Murphy, MD [Meeting Facilitator]

Okay, so while thank you, David, for that thoughtful summary. And wow! This has been an incredible day, and has helped us all. Better understand your perspectives of kidney xenotransplantation as people living with kidney diseases and direct care partners.

First, to the patients who delivered testimonies today. Thank you.
Thank you for your dedication and hard work to develop your talks. It has been an absolute honor to work with each and every one of you, and you have taught us an enormous amount about your experiences and your thinking on xenotransplantation.

Next, thank you to the discussion panelists for the important insights that you contributed to today's discussions. Now, thank you to our expert presenters, Dr. Vineeta Kumar and Dr. Peter Reese. who set the stage for our discussions today with their informative and thought-provoking presentations.

I would also like to thank the FDA Staff, who tuned in today. We especially appreciate Dr. Patricia Beaston for her remarks, and Karen Jackler, Ethan Gabor, and Lena Murza for their support. During the many, many months of planning this meeting.

A special thanks to James Valentine and his team at Hyman, Phelps and McNamara for your support in planning and of course, moderating today's meeting. and then a big thanks to the

NKF. Staff who have given countless hours to the planning of today's meeting, especially David Feldman, who provided consistent support through the many months of planning the meeting, and has led all 6 of our previous EL-PFDD Meetings.

We are also greatly appreciative of our NKF Divisional chapters for their support with recruitment and raising awareness of this meeting.

And again, thank you to our financial sponsors for your support: eGenesis, Makana Therapeutics and United Therapeutics.

So finally, a huge, huge thanks goes to you. Each of you living with a kidney disease and direct care partners. Thank you for your for honesty sharing your lived experiences with kidney disease, and how that informs your views on Kidney Xenotransplantation.

The meeting could not have been as impactful or as enlightening without each and every one of you. I do have a few final remarks before we adjourn this meeting.

The comment box on the meeting website will be open until December 10th. So please continue to share your perspectives on the questions that we discussed today.

The discussions from the meeting and those additional comments will be analyzed and compiled into an executive summary, called a voice of the patient report. The report will be made public and will be shared directly with the FDA and Xenotransplant companies.

The recording of today's program will be available on the meeting website shortly as quickly as we can. And then today's meeting will have a lasting impact on the future of kidney xenotransplantation, research and development. So once again to all of our participants, both online and in this room. Thank you for making your voices heard today.