

Welcome to PKD Chronicles, navigating life with polycystic kidney disease.

A podcast by the PKD Foundation presented generously by Otsuka Pharmaceuticals.

This podcast is all about helping you live your best life with PKD. In each episode, we'll explore the stories, science, and support and resources for families impacted by PKD. And here's your host, Alyssa Ealy.

>> Hello and welcome. Today we're going to talk about one of the treatment options for individuals with ADPKD, a medication called Tolvaptan. We are joined today by Dr. Craig Gordon from Tufts Medical Center in Boston, Massachusetts, who's an expert in ADPKD and the use of Tolvaptan. Dr. Gordon, welcome.

>> Thank you so much for having me. Nice to be chatting with you, Alyssa.

>> Excellent. We're glad, definitely glad to have you here. Before we get started, do you want to introduce yourself to our listeners and share a bit more about how you got involved in this area of medicine?

>> Yeah, absolutely. So, as you mentioned, I'm a faculty at Tufts Medical Center and associate professor of medicine at Tufts and have had an interest in PKD really dating back to when I was a fellow 15 or so years ago and found it interesting you know scientifically, the service to the community, et cetera and so I returned to Tufts about six years ago now and have recently taken over as director of the Tufts PKD center of excellence. So I'm very fortunate to be there and to be doing that.

>> We are just delighted to have you here today. So excited to hear more from you about the use of Tolvaptan. So as we're getting started, could you tell us a little bit more about the medication Tolvaptan itself and what it is? It's not a new medication. It's been around for a couple of decades, but the use of tolvaptan for PKD is actually a pretty recent development. So I'd love to hear a little bit more about how it came to be a medication we use so frequently for those with PKD

now.

>> Yeah, so great question. So as you point out very importantly, this medication has been around for a while and was something that can be used for some other conditions that we tackle in nephrology completely related to PKD, but in 2018, after the publication of two really critically important clinical trials, the FDA approved this drug for the use of people with PKD, and it's really limited to those who are at risk of rapid progression, meaning relatively fast decline in kidney function, or those who have already experienced decline in kidney function. It works as blocking one of the hormonal mechanisms that's thought to be involved in cyst growth, something called vasopressin. So what tolvaptan does, it's a blockage of the vasopressin effect on the kidney. And this is thought to lead to reductions in the rate of the growth of cysts, and as a result downstream from that, a slowing of the rate of the decline in kidney function. So, it's a really exciting medication and I think around the country there's lots and lots of people prescribing and using this medication.

>> How would somebody know if they're at risk of rapid disease progression? Is that something that they're told or is that something that they would know themselves?

>> I think that's something they, there's a possibility they may know themselves based on family history. People's family histories do sometimes follow relatively close to their either parents or other individuals in the family.

That's not precise enough. So what we like to do is there's a number of different ways you can assess someone who is either at risk or having rapid progression.

So rapid progression, first of all, is declining kidney function or GFR without another explanation, and if it declines at a fast enough rate, and not at the point where someone's approaching kidney failure, but earlier in the course, that's someone who would qualify for tolvaptan. But importantly, we'd rather make the diagnosis early in the game than at that point, and so imaging studies are really important.

And this is more sophisticated imaging than the ultrasound that's often used to initially make the diagnosis. So this is usually via MRI or occasionally CAT scan.

And what's calculated is something called the total kidney volume, which is just a

measurement of the size of the kidney, actually both kidneys, and then compared to individuals of the same age with also with PKD. And then people are placed into what's called the Mayo Imaging Classification Categories. And if the kidneys are larger than the average PKD patient for a given age, this is considered Mayo Classes 1C, 1D, or 1E, someone is expected to be at risk of progression in loss of kidney function would be a candidate for tolvaptan. So it's really important for people to get this, what we call cross-sectional imaging with an MRI or cat scan to really figure this out.

>> And so for these Mayo classifications, you mentioned the classes 1C, 1D, 1E. So the higher the alphabetical letter, the bigger the kidneys.

>> That's right.

>> Excellent. And if patients have a decline in their GFR already, is there a certain cutoff that we look for or that you look for in your routine practice that would make someone more eligible than someone else?

>> Yeah, so we will start it at any GFR down to perhaps something in the order of 25 GFR. There is some evidence for starting and continuing tolvaptan, even at these levels. And we absolutely continue it, but we generally don't start it below a GFR of 25 because at that point the benefit is relatively less.

The earlier you start in the course of course if you make a difference in a slope change of kidney function you're going to have a greater benefit starting in a GFR of 100 then you would at 25. So if you if I meet a patient with a GFR of 17 let's say I think the side effect profile may outweigh the benefits of the drug and it's probably not really worth at that point you're gonna gain or maybe a few months benefit however if you start maybe with the GFR of 80 or 100 we might see five or seven or so years of delay in the timing when the person gets to kidney failure and thinking about kidney transplant and dialysis and that of course is a

very significant difference, right, in that person's quality of life. So we really like using it as early as possible when that opportunity presents. But we're not afraid to use it in people with a GFR of 30 or 27. And we definitely see some benefit in those people.

>> Yeah, absolutely. So I think one of the important things that we should make clear here, though, is that so it sounds like Tolvaptan doesn't actually stop the cyst growth, but rather just slows it down and prolongs that slope of decline.

>> Yeah, unfortunately, in nephrology, we have very few treatments that stop the disease course. And tolvaptan, unfortunately, is also in a medication that doesn't stop the disease course. But that slowing of the rate of decline can be substantial.

It's estimated to be about a difference of one in GFR, one ML per minute per year difference. If you compare someone who receives placebo versus tolvaptan in the studies, this is a rough estimate. But that estimate, if you extrapolate it over let's say 10 years, you're now looking at a 10-point difference in GFR, 10 years down the road. And that can be the difference between someone being evaluated for kidney transplant and being a few years away from being evaluated for kidney transplant. So it really is a, the number seems small but the difference out years into the future really makes a big difference.

>> Yeah and that's why starting it early is of the highest benefit. So catching it before it's at GFR less than 25 where they may only get a few months instead of a few years.

>> Absolutely and if I could say one message to the patient community and to the physicians out there is to really do this MRI to get a measurement of TKV and Mayo classification so we can figure out who's a potential candidate or not early in the game as much as possible.

>> Yeah, now for those patients who may have the ultrasound ordered originally by their primary care provider or by a different type of provider than a nephrologist. Is this something that they could ask their primary care to order while

they're waiting to see somebody for management of PKD?

>> Yeah, ideally when we're getting referrals at Tufts, we're hoping to already have the imaging on hand when we're seeing the patient and actually be like to look at it ourselves. So either a referring nephrologist who we're co-managing the patient ultimately with or primary care can absolutely order an MRI or CT often it needs contrast that CT so that is a potential issue with people with reduced GFR but the key is to have that imaging as soon as possible in the course and if we can have that at a time, that's great. Now, in some circumstances, there's, you know, you have to, I know our center, and I'm sure yours as well, Alyssa, have to go through a lot of prior authorizations and places that are center of sort of excellence, like have the staffing and the experience to know what to say and how to navigate that. So I'm fully recognize, you know, the primary care office 150 miles from Boston may not have the capabilities of doing this, but if they can, that's great. We really like to see it so we can make decisions ahead of time.

>> Absolutely, the more knowledge you have, the better the conversation can go 'cause you have more information. It's a good opportunity for patients to be engaged in their care as well.

- Absolutely.

- We've talked a lot about the GFR decline changing changing by starting tolvaptan. Is there any change in the cyst growth or is there any change any other benefit for a patient with ADPKD besides the decline in GFR being slowed down?

>> Yeah, extremely important question. We're very focused on GFR and patients as well, right? Because they've seen the experiences potentially a family who've progressed to need dialysis or transplant, and that's a really important outcome for them.

>> Yeah, it's also something we can see. You get the numbers; you see the trends.

>> Yeah, exactly. And so people are like, "Oh my God, why did my

GFR do this?" But I think there's a lot of other very important additional benefits which relate to, you know, for instance, if the kidney cysts are not growing, people may have less pain, and that's been studied and shown in a few different publications, so there might be an impact on reduction in the experiences of abdominal, back, flank pain, and other types of things like that. The mechanism of action where there's a lot of urine output, and sort of, I view it as sort of flushing the kidneys, seems to prevent the development of kidney stones, probably a relation of the urine output that we'll talk about later with the sort of side effects of Tolvaptan and the need to drink a lot of water, but this seems to prevent kidney stones as well as other kidney complications like bleeding, etc. So there's a lot of these symptomatic things that get better and I don't know how much you've seen this, but in our experience we've had a lot of people who are like, "Oh my god, I don't feel my kidneys the way I used to." And so that's another added benefit we propose to people when they're thinking about this decision. And we'll talk a little bit later about some of the side effects, which I think are sort of where that, you know, the other side of the double-edged sword comes.

>> Of course. And so there's definitely a lot of benefits to taking Tolvaptan.

In the past, we used to treat patients with ADPKD with water prescriptions.

So how does Tolvaptan compare to that? You mentioned compared to placebo, we see about a change of one milliliter per minute in the GFR decline. But how does it compare to that older mentality of using increased water to kind of mimic the same idea?

- Yeah, so the idea here is, if Tolvaptan is blocking the effects of vasopressin, this hormone on the kidney and the cyst growth, that one of the ways we can shut off vasopressin is to have very high-water intake and that affects basically the levels of this hormone. They've never been head-to-head comparisons of tolvaptan to water, although probably the people in the placebo arm of the two pivotal trials, tempo and reprise, probably were drinking a lot

of water. So one potential conclusion of the data from those trials is those people in the control arms were already drinking a lot of water. The one study that compared, or the one largest study that compared water sort of prescribed versus standard of care water is something called the prevent ADPKD study and this was a multinational study trying to see if we could push the water intake to achieve the same effects as Tolvaptan and basically, it's unfortunately a negative study so what they were doing was trying to control the water intake by people measuring how dilute their urine were and to see if they could push to higher levels of water intake, would you see the same benefits as Tolvaptan, as far as changes in total kidney volume or GFR?

And unfortunately, it was negative. They didn't see any difference at all. My interpretation personally is that probably the difficulty here was it wasn't really being compared to low water intake. It was comparing high to higher because of the pretty well-understood idea in the PKD community to drink a lot of water. So for my patients who don't qualify for Tolvaptan or don't want to take Tolvaptan or have a contraindication, those ones I tell to drink two to three liters a day of water to try to mimic these effects of Tolvaptan, But it's probably not as good as Tolvaptan, you know, so I the people I'm doing this for are really those who are unwilling for let's say work reasons, unable to, or just have a reason they're not, or they don't qualify for Tolvaptan we still think they benefit from water We just think if you can qualify and are willing to take Tolvaptan, it's better

>> So that

leads me to another question. So who would be those people who don't qualify or it may be contraindicated for?

>> Yeah, it's a relatively small list who it's really absolutely contraindicated One would be someone who can't sense thirst or gets easily dehydrated that person's not going to be Candidate for tolvaptan. We've had some patients who have lower urinary tract issues, where they have trouble holding their urine, and those people will run into all kinds of

difficulty with Tolvaptan. Pregnancy and breastfeeding are contraindications, so we will, for our young women who are considering pregnancy and nursing, we'll tell them we're gonna wait until your period of child-bearing age, you know, the period we are considering having kids is over and then we can talk about Tolvaptan. There are some medications that have a metabolic relationship with Tolvaptan, where the levels of either one or the other can end up out of control high. And there's a small list of medications where we just cannot do Tolvaptan and that medication. So that's something you'll want to review with your doctor. Outside of that, there's not a huge number of contraindications. What I've observed and I'm curious to hear what you've seen in your practice is there are certain professions that is just not going to work. And, you know, so there are, you know, you know an example we sometimes see is like an emergency room or ICU nurse who just is running around all day and has no time to stop to you know, go to the restroom or drink water, certain like you know teachers and young kids have some difficulty but we've had success with people who are in all kinds of professions who really would be surprised that they can do this and they're really able to tolerate it.

>> Yeah, I've definitely witnessed that as well. We do have some professions that really just struggle, but what we have found is that a lot of people can generally work around it. I have not had any emergency room nurses, but I have had surgical nurses, which is a similar thing. you're in an operating room for a long time. But we have had patients succeed. It took a while to get used to it. But once you kind of get used to the medication, people were able to stay on it.

Same thing, I see you have not but having been a nurse myself, I understand the challenges of needing to run to the bathroom and just not being able to for several hours. And we have even had people who spend a lot of time in the car like those who may drive trucks or those who just may have a job that changes locations frequently throughout the day they have been able to tolerate. They just become very familiar with every restroom along the highway that you know may be available to them. So it definitely takes a little practice, a little negotiation.

>> We've done some strange things like providing male patients with the medical urinals to bring with them in the truck and other sort of strange things. But you're right.

And the other point I think for people listening to this call is we've had success with workplaces making accommodations for people. So people who worked, let's say a few people who worked in sort of scientific or pharmacy situations where they had to be in a special suit and were expected to be in that suit for it stuck in a room for extended periods of time. Their workplaces have made changes to allow them to be more tolvaptan friendly for lack of a better way.

>> Yeah, sometimes it just takes a little bit increased knowledge on all parts.

>> Exactly.

>> Absolutely. So I think now this kind of brings us to a very important topic, which a lot of patients are highly interested in whenever starting a new medication. What are those side effects? So we are alluding to the fact that there is a lot of bathroom activity. So what are my patients starting medications see?

>> Yeah, maybe before I get to that, maybe I should talk briefly about the monitoring required because and then we could talk about this may be this other thing subsequently. So the F, there is a Small but not zero risk of liver toxicity with tolvaptan and that was seen in the early studies without careful monitoring and so the FDA has a program called REMS, R-E-M-S, that exists for various medications where there's a potential risk, where the REMS program for tolvaptan requires prescribing teams, doctors, nurses, physician's assistants, pharmacies that provide the medication and patients to sort of partner to monitor liver function tests. And the monitoring protocol is to be tested at baseline to make sure liver function is okay, to be tested two weeks after starting Tolvaptan, and then at the four-week mark and then monthly, so every single month for 18 months after starting. After one gets for the 18-month period, it's loosened a little bit because most of the liver issues were seen in that first year and a half of being treated with Tolvaptan, and afterwards you have to do sort

of every three month testing of liver function tests. It's important and this one comes up a lot that you don't have to travel to a center that prescribes it to get the liver test. You can get this liver test done at your lab that's right down the street or close to work or close to home. So we try to make it as convenient as possible. This program puts a lot of burden on the prescribing individuals and we have a whole protocol in place at our center where our nurse is calling the patient to remind the patient that they need labs. We won't refill until labs have appeared, those labs are sent to me in a spreadsheet, I review and approve the next refill of the medication and I think a lot of programs are doing something very similar. The thing here that's really has to be thought of is you is a patient who their local nephrologist doesn't have the structure to do this, might want to partner with one of the dozens, actually, of PKD centers around the country where there's a lot of experience and also this infrastructure to get through this program. And that partnership can be really like co-management of a patient where the doctor who's prescribing might be located in One of these big programs the monitoring and the labs are being drawn locally and the patient is being seen in many cases More often locally than at that center. So they don't they don't have to drive frequently. I will point out also that in the early days of the REMS a lot of physicians were requiring the patients to come Physically to the office to see them. We've realized this is not You know patient friendly at all, so we're monitoring people remotely, and even using telemedicine as a mechanism to see them. We like to see them at Tufts. We like to see the patient and see, including telemedicine every three months during the period of monthly monitoring, so during that first 18 months, and then we loosen when they're getting labs three months, we loosen them to every six months for the visits just to monitor these tests.

>> Yeah, we do something similar. We do a lot of early monitoring and then as they've been more stable, separate them out a little bit. We definitely use a lot of telehealth as well. And then we do also do the shared management where, you know, they may have a nephrologist who is either not a specialist in ADPKD or they don't have the infrastructure to prescribe or they've chosen not to prescribe. And they will send that patient to us, we'll do all the counseling, start them on the medication, and then we'll see them maybe every six months, but they'll see their general nephrologist in between. And then that person will do a lot of the other routine chronic kidney disease management and we'll just do the REMS monitoring and making sure that everything's going smoothly with that medication.

>> Yeah and I think if I'm a patient listening to this call the PKD Foundation has a really nice layout of all these centers of excellence around the country and I know there's a desire to expand those centers. So if you look at that website and look at the map, there's a pretty good chance there's a center within hopefully a few hours, maybe up to five or six hours in some cases of home.

But again, that one, that's not a small ask to travel three or four hours to see a center, but if it's very infrequent and it's for your health, that may be worth it, right? And I wouldn't be dissuaded if I was a patient by saying my local person is unwilling to prescribe this thing that I would benefit from. I would, you know, personally, if I was in that circumstance, would get in the car and drive a long distance. Many of our patients do. I'm sure in your center too.

People come from very far away just to get this treatment and it's worth it for them.

>> They do. Some come from several hours away.

>> Yeah.

>> And we even have some who cross state lines to come.

>> Yeah, we do as well. And one of the challenges is to really expand this care into all 50 states. And this is, I think, something we really have to achieve as a community in the near future.

>> And there are even, in addition to the Centers of excellence, there's even a lot of partner clinics that are popping up, and you know, a lot of those clinics will have the same services just maybe on a smaller scale. So there's opportunity for all patients to be prescribed this medication. There's a will, there's a way, I think.

>> Yeah, and I think also there's a real commitment by the PKD Foundation, the Centers of Excellence, and you and me on this call to spread the word to these local or regional doctors and nephrologists to have more people offering this as part of what they can do for patients. It's not rocket science, it just requires developing that infrastructure.

And so we do believe that a lot of people can do this on a small scale as well.

>> Absolutely. We do a lot of kind of coaching other centers and other practices on how to really get a program up and running so that more patients can be exposed.

And I'm sure you do too. I'm sure people ask you all the time what your approach is.

>> Yeah, absolutely. And we will show people literally are exact protocol and approach and say bring this with you to your state and and and help your patients in your region. So yes, absolutely and I think my guess is most centers around the country are very engaged in this and very willing to help others.

>> Yes all hands-on deck for sure. All right excellent. So I guess if we go back to, now that we've covered the monitoring, we can go back to the side effects. Like I said, we've definitely talked a lot about the fluid management that goes into taking tolvaptan and we've hinted that there's a lot of bathroom trips. So those are definitely going to be the biggest side effects due to the way we're inhibiting vasopressin. You will ultimately have to go the bathroom a lot, urinate a lot. And then as a result, you have to drink a lot of fluid to keep up with the resultant thirst. What other side effects do you counsel patients on as you're talking to them about Tolvaptan?

Yeah, so this urine output and thirst is the big one. The urine output is something that's really a 24 hour a day experience. Tolvaptan is dosed twice daily and the second dose, usually an afternoon dose, is a lower dose than the morning dose and that's done to sort of prevent extreme impact with going to the bathroom at night to urinate. But our patients, we do counsel them to expect that they will wake up at night at least one, two, and sometimes a few more times to urinate.

I know, Alyssa, you and I spoke about some tricks of the trade to try to minimize that. We'll provide that as well on this call. But yeah, as you mentioned earlier, people are going to the bathroom a lot. They're needing to drink water a lot. They come to the clinic with quite impressive water bottles they find somehow online to purchase, and as we said earlier, there is, you know, where every bathroom is on your way to work, you know, that you're going to have to take breaks to go to the bathroom, and that's part, that's the other side of, the negative side of the benefit of tolvaptan. We encourage our patients I think people are probably willing to tolerate more they're going to the bathroom all day work or otherwise but I feel the urination being woken up at night to urinate is the biggest problem. So one there's a few tricks people should be aware of the first is the earlier you take the first dose, the earlier you could take the second dose. They're supposed to be split eight hours apart. So we counsel people, you know, don't sleep until 9 a.m. and take the dose. Try to wake up as early as possible in the morning and this is a good drug for morning people to take that first dose at 6 a.m. So the second dose eight hours later is now 2 p.m. and not affecting you quite as severely at night. As I mentioned earlier, the second dose is lower by design than the first because of this. I know I'm curious to hear what you tell people from a dietary standpoint. We're advising people at dinner time to reduce to the greatest extent possible the intake of salt, sodium and protein, because those sort of push increases in urine output for sort of complicated physiological reasons. So we tell people really to try to avoid those as much as possible with their last meal of the day. But actually what do you tell your

patients, Alyssa?

>> We do exactly the same thing. So definitely the earlier you can take your doses the better. Even for those people who may not be morning people. I certainly am a morning person, so it's fine. But I know firsthand, my husband, if he had to wake up at 6am to take a medication, it would never happen. But even if you just set that alarm, you know, try and roll over and go back to bed, it'll still help. You'll have to get up and go to the bathroom pretty soon. But you can still kind of set those alarms and get going. And then, you know, the earlier in the afternoon, you take that second dose, the better. We also counsel a lot on reducing that protein and sodium intake at dinner. And so even just the size of the meal, I try and encourage people to switch that mentality of having your largest meal be the final meal of the day and try and make it more towards lunchtime so that you're still getting in that sustenance that you need, but without pushing those solutes of sodium and protein into your kidney so late in the day, and that definitely helps a lot. Also for the fluid intake, I think a lot of patients who struggle with going to the bathroom at night, they are trying, they get so in the habit of just drinking and drinking and drinking all day that even towards the end of the day, they're drinking the same volume. And as that second dose is wearing off, they may not need to drink as much. And so sometimes just reducing a glass or two of water before going to bed as long as you're getting in enough fluid throughout the rest of the day, it'll at least help you keep that extra trip to the bathroom down to a minimum overnight. And so that does help a lot of people with getting through the night without having to go to the bathroom, but without falling behind on fluid because they are getting it in throughout the day. And I find those are usually the most helpful. One thing I do always encourage everybody I'm starting on Tolvaptan is to try and just give it a couple weeks because I

think those first two to three weeks are the hardest. And then I'm sure everybody on this call will have heard that, you know, it takes 21 days to make a habit or whatever the number of days is. So eventually drinking all this water, going to the bathroom, it just becomes habitual. And it's just kind of part of the day. And I have some patients who have been on this medication since they were participants in the clinical trials over 10 years ago. And they kind of forget that they take it or that they go to the bathroom. It's just kind of, it's just there. They don't even recognize that it's something abnormal anymore, because it just is their normal. And so I try and say just give me a month and just see how you feel after the month and I tailor what I do is I tailor my education on managing the side effects depending on what the side effect is. So if there's someone who is getting dizzy or lightheaded after they take their medication, They're probably not drinking enough fluid and so it's very easy to just say okay Let's start there your blood pressure might be a little too low and let's see what's going on. And then if we counsel around whatever their main complaint is, but generally the advice is around the fluid management.

>> Exactly, and one of the things we're doing with our monthly monitoring during of liver function, we're also monitoring, and I think this is required as well by the FDA, it's not talked about as much, but to monitor sodium levels and if those are starting to rise that's usually indicative of not enough water to keep up so if we see that even slightly above normal we're counseling our patients okay I don't think you're keeping up with the water output in the urine.

>> Yeah do you ever counsel your patients on changes that they might see in their GFR when they start medication?

>> Yeah, actually, that's a super question. So we do. So most, or many of the medications we use in nephrology, including Tolvaptan, result in an

initial drop in kidney function. So the thought here is the changes in the kidney relating to being sort of having a lot of urine output and maybe being a little it always on the dehydrated side leads to what's called a hemodynamic drop in kidney function. So you see a slight drop, but then the slope subsequently is slower than the slope would be if the person was untreated or on a placebo in a trial.

If a person stops tolvaptan and there's usually a bump back. So it's not like it's a permanent damage. It's just sort of a state of being on Tolvaptan that goes away when you stop it. A lot of people ask, I'm sure you've seen this question as well, how do we know it's working? I tend to tell people is we unfortunately don't have access to the parallel universe of you not being on Tolvaptan.

So we have to take it on faith as we do a lot of things in medicine that we're gaining a benefit. So we don't have any way to prove what would have happened if you weren't on it. You can try to approximate that if you're able to get enough data over time. But this takes years to get this. But if you could see the decline in GFR was faster and then slows down with Tolvaptan, you can really make a decent argument for this. But that takes years on Tolvaptan before we could see that. But even if you're not seeing that and you can't prove that, I think it's really important to keep on faith that your course is better than it would have been off of Tolvaptan.

>> Yes, absolutely. Which is a lot to ask of a patient to say, just believe. But I think especially for those who have been on therapy for a really long time. I do have that conversation a lot that, you know, we don't actually know, but what we do have is that you're still doing great. And we should take this for what we have and consider it a blessing.

>> Yeah, a little occasionally questions about, okay, we should be re-image to see if the kidneys are not growing. But again, it's the same problem as you don't know what that imaging would have look like off of Tolvaptan. So it's really hard to make a compelling argument of this, but I think it's really important. And what I've seen is, yeah, people who take it on faith, then they start comparing themselves to others, let's

say in their family, who are not on Tolvaptan, and they're at an age, that that person was running into problems with kidney transplant, EVAL, and our patient is not the tolvaptan treated patient. So I think at that point it becomes more apparent, but the studies have definitely shown the benefit. There are studies that have been done to sort of extrapolate what would be expected long-term as far as outcomes and even some studies that have looked at long-term outcomes. And it clearly does seem beneficial both from the size and the cysts growth, but also the slower rate of decline in GFR.

>> Yes, absolutely. I think this is one of those medications that we talk about so much. There's just so much to be said about it. Do you have any additional tips or tricks that you recommend outside of diet or water management? Anything else that you talk to people about?

>> No, those are the major things. I think the other side of it, perhaps, is the prescriber side of it, which is dosing. I think the approach I've taken is to try to get the patient to a dose that they tolerate, that we get the urine dilute, but not to be fixated on getting to the maximum dose. In some people, we do that, and many people we do that even, but it's not required. If the patient, I'd rather see a patient on a moderate dose and taking tolvaptan than being pushed to a dose they can't tolerate stopping it. So we recognize this is a medication that has an impact on the lifestyle and the quality of life. You're trading these quality-of-life issues short-term for delaying kidney failure down the road. And I think it really requires a partnership between the people prescribing it and the patients to make sure we're sensitive and understanding of the impact on people's lives.

>> Yeah, absolutely. I think that's actually a great kind of closing thought is that, you know, it's a partnership between provider and patient and all the relationship building in the world will be very helpful in tolerating and managing this medication that can have significant impact on somebody, both highly beneficial, but also, you know, requires some life adjustments.

>> Yeah, it takes a village, right? I'm sure it's the same. We have physician's assistants who live and breathe PKD and Tolvaptan nurses who participate in this program. Pharmacists, like this is not a one-person job. The whole group has to work in a partnership with each of our patients. And one of the things I really honestly love about doing this is getting to know the patient is very unique when you're thinking about Tolvaptan.

You have to think into account their work, their travel, their vacations, their all these different things. So you're really engaged in their, you know, whether they're having kids, you know,

>> yeah,

>> Some people say I will even some of my male patients who have young babies, like this is not the medication to be on perhaps for them at that time. So, So you're really engaged in in their lives in a very meaningful way It's really gratifying honestly to do that.

>> Yeah, absolutely. I agree. I think you get to know people so well just by Taking that time to really investigate what their life situation is and what they can and what there can do throughout the day And you know, I think it also is another area that we counsel on a lot in my practice is just, you know, what's what's going on in your life? Oh, you're going on vacation to Florida? It's really hot in Florida.

You're going to be on a plane. It's okay to hold the dose for a few days. It's a I think that's something that is really nice because you just get to know what's going on. And then somebody comes back from Florida and you say, hey, how was Disney or wherever you went? And You just develop relationships that are so much deeper, I think, than the routine patient -provider relationship.

>> Yeah, I totally agree. And it's like, you know, people are thinking about business trips or they have a wedding to attend. And we have to advise them about what to do. So you're really engaged in these life experiences. And I think it's really important to work with people to make those experiences good. You don't want them spending the whole wedding, you know, rushing off to the bathroom because they could miss, especially for the wrong wedding, but also just to enjoy themselves. They can take a break from this for a day. So I think it's a marathon, not a sprint.

>> Exactly. And it's a really rewarding relationship, I think, on both fronts. So.

>> Absolutely.

>> Excellent. Well, thank you so much for being here today. It's been so lovely to chat with you and hear more about your experience with managing ADPKD using tolvaptan. It's definitely really great to get an expert opinion on this topic. We do really appreciate you taking the time to share all this knowledge and insight into how to take this medication. And really just very grateful you were able to help us out with this.

>> Well, thank you so much for the invitation. I really enjoyed speaking with you as well. And it's nice to hear where our two centers are practicing pretty much identically. So

>> Yeah, it's funny when you see things that align so well across centers.

>> Exactly. That's the goal.

>> Absolutely. Excellent. Well, thank you so much.

>> Thank you.

Thank you for listening to this episode of PKD Chronicles, Navigating Life with Polycystic Kidney Disease, a podcast by the PKD Foundation, generously presented by Otsuka Pharmaceuticals. The PKD Foundation is the only organization in the U.S. solely dedicated to finding treatments and a cure for polycystic kidney disease, PKD. The Foundation Fund's research, education, advocacy, support, and awareness on a national and local level and is the largest private funder of PKD research. For more information, resources, or to donate to the PKD Foundation, please visit pkdcure.org and connect with us on social media.