

Seizing Life, episode 56
Epilepsy Drug Development: How Patients Can Make An Impact
Guest: Dr. Darcy Krueger
(Transcript)

- Kelly Cervantes: [00:00](#) Hi, I'm Kelly Cervantes and this is Seizing Life, a bi-weekly podcast produced by CURE Epilepsy.
- Kelly Cervantes: [00:17](#) Today on Seizing Life, we continue our series detailing the drug development process by taking a deeper look into the human trial phase of the process. I'm happy to welcome Dr. Darcy Krueger to the podcast. Dr. Krueger is a pediatric neurologist, director of the tuberous sclerosis clinic, and associate professor of Clinical Pediatrics and Neurology at Cincinnati Children's Hospital Medical Center. He also serves on the TS Alliance Professional Advisory Board, and he's joining us today to discuss the importance of participating in clinical trials, and provide insight about what patients should expect from a trial, what might be expected of them, and what questions they should ask prior to participating in a trial.
- Kelly Cervantes: [00:58](#) Dr. Krueger, thank you so much for joining us today. I'm really excited about this topic. It's such a nice culmination of our last two topics to bring us to this part of patient participation in clinical studies, which I know is something that you are very passionate about. And I'm curious why you're so passionate about it, and why you are an advocate for trying to get epilepsy patients into trials.
- Dr. Darcy Krueger: [01:30](#) Yes, thanks for having me onto this presentation and platform, and it's excellent question. It comes from my desire to help patients, and we can do all the scientific investigation in the world about wonderful treatment possibilities, new mechanisms that might help treat epilepsy when previous strategies are falling short of our desire, and if we can't get through clinical trials, then we never get approvals, and so these medications never get into patient's hands. So that is probably my number one passion and driving force for supporting clinical trials. Even if the science is there, we need the medications to get to the patients, and this is an essential step.
- Kelly Cervantes: [02:14](#) Brilliant. And so we've, in previous episodes sort of learned about the different phases that the trials go through, but before you can even get into a phase one, two, three, four trial, you have to be accepted into the trial. So what does that process look like? How can people even find out where to find out what trials are occurring?
- Dr. Darcy Krueger: [02:39](#) There are probably a couple different pathways for people to find out about clinical trials that they're interested in

participating. The first is a clearing house that's maintained on the internet by the government. It's called clinicaltrials.gov, and this is a place where any federally funded research, and many industry clinical trials that are seeking to be approved by the FDA, are required to post basic information about their study. It will have the study name. It will have the medical conditions for which they are studying this treatment for. It will have information of if there's age restrictions or other medical requirements. They will often list several of the primary ones of this, and they list about what the treatment is that they're testing, and what they hope to measure with this treatment.

Dr. Darcy Krueger: [03:35](#) Another example, is it trying to just gather safety data? Or is it gathering whether the drug works in addition to additional safety data? All of this is on there. And then ultimately it has the information of about who's doing the trial, who's paying for the trial, and who you can contact, both email or phone number, in order to learn more about the study. That is probably the most authoritative and reliable place to go.

Dr. Darcy Krueger: [04:01](#) The second place is your medical providers that you trust. This might be your primary care provider. It may be one of the specialists that you travel to, to receive specialty care. Asking them if they're aware of any clinical trials or opportunities for studies to participate in. Sometimes those individuals will be up to date on what the newest trials are available for your diagnosis and particularly for epilepsy. And certainly if you're going to a level four epilepsy center, a center that is used to participating in the latest clinical trials and participating in specialty meetings for epilepsy, many times these individuals are very knowledgeable about clinical trials that are available that for which you might be interested and eligible for.

Dr. Darcy Krueger: [04:49](#) The last, I wouldn't discount in any way, shape, or form, is through the internet. Particularly there's Facebook groups that many individuals who share the same diagnosis are able to communicate back and forth about what they've heard or what their experience has been in a clinical trial. And this is a certainly a useful place to find out about information trial, but I would not consider it as the authoritative to know all of the requirements and eligibility, and procedures of [inaudible 00:05:18] that study. You would still want to find out from either clinicaltrials.gov or contacting a site that's participate in the study to get the official information, but it's often a good place to hear about trials that could be of interest.

Kelly Cervantes: [05:30](#) Okay, so a patient knows now where to go to find the trials. So let's say they have now found one that they think that they

would be a quality candidate for, what are the questions that they should be asking the investigator before agreeing to participate?

- Dr. Darcy Krueger: [05:48](#) I think the first question is, is to find out or just verify is there anything major that you should be aware of that you don't qualify for the study? So, upfront information about eligibility, there'll be more details later to confirm that, but it's important to find out upfront before you get too far down the pathway whether there's any major things that could have indicated whether or not the conversation needs to go forward.
- Dr. Darcy Krueger: [06:17](#) After that, I would ask about how often you're going to need to be at study visits, and whether those study visits need to happen in person in a particular place, because there may be travel involved. And if there's frequent visits and the distance is far, that needs to be calculated into your enthusiasm and availability to participate in a specific study.
- Dr. Darcy Krueger: [06:40](#) The other thing is to ask about, well, okay, when I do come to study visits, what is I or my child have to do? There may be blood tests. There may be electroencephalography, or EEG tests. There may be other study procedures have to be done, and you want to have a general sense of how much is going to be asked of you or your child during the study. And then finally, I find it useful at least to start, if the family doesn't already have understanding about what the trial is about, I like to tell them about, is it a safety trial? Is it an efficacy trial? And what is the reason why we think the trial is important to be done at this time? And so what are our goals of the trial? I think that's very helpful to make sure that everybody is fully engaged in what the trial's purposes are.
- Brandon: [07:31](#) Hi, this is Brandon from CURE Epilepsy. An estimated 3.4 million Americans and 65 million people worldwide currently live with epilepsy. For more than 20 years, CURE Epilepsy has funded cutting edge, patient-focused research. Learn what you can do to support epilepsy research by going to cureepilepsy.org. Now back to Seizing Life.
- Kelly Cervantes: [07:54](#) So now I want to go back to sort of the legal, and the consent, and all those aspects of agreeing to participate in a trial. So we have the questions answered, we know that we're a good candidate, but what do we need to watch out for on the consent side?
- Dr. Darcy Krueger: [08:13](#) So the consent is a process that has been worked out now extending decades to make sure that all research that is done

with patients is done in an ethical way, and done in a safe way. And so the consent is the legal aspect that we make sure that that is indeed the case.

Dr. Darcy Krueger: [08:30](#)

So there are key things on every consent form. Number one is, who is doing the study and who's paying for it? So that we can know that if there's any potential biases or other reasons why the trial may not be as clear or straightforward that anybody participating knows who's behind it.

Dr. Darcy Krueger: [08:50](#)

The second thing is, is what to do if anything is unclear or seems to be done in a way that is not consistent with what was explained to you as far as starting the trial. So there's always numbers to call and people to contact to that are either involved in this study, if it has to do with something occurring during the study itself, or even outside the study, so that they're independent regulators and overseers that you can contact and talk to if there's concerns there.

Dr. Darcy Krueger: [09:18](#)

The third thing that's in any trial is it has to explain in very plain language, so this is not really convoluted language that is allowed to be inserted into these agreements, about what is expected of you and what is being expected of the team that's conducting the trial. Who covers what? What is paid for? What is not paid for? If you have something go wrong, what is to be done? What are the reasons why you could be exited from the study, even if you didn't want to be? Those should all be spelled out very clearly, as well as those earlier things I talked about as far as knowing how often, what's involved, and what is the purpose of the study. That's all outlined in the consent.

Dr. Darcy Krueger: [10:00](#)

The other thing about a consent is, is to make sure that nothing seems coercive. It has to be total voluntary on both the part of the investigator and the participant that the participation is voluntary. And that has to be witnessed, so that this document can also be reviewed as being officially saying, yes, I want to be in this trial, and I understand what is known and what is not known, and I'm still okay with it.

Kelly Cervantes: [10:26](#)

Now, if there are any concerns regarding this legal document, I imagine that there is an organization that oversees this sort of thing. What is that organizing body?

Dr. Darcy Krueger: [10:38](#)

Yeah. So every human study has to be reviewed by what we call an institutional review board, or IRB. Outside the United States they may be called an ethics board, but it's the same body. And these are certified, in the case of United States, they are certified by the Food and Drug Administration to act in this

capacity on their behalf. And the rules are very clear on who makes up this body and what their responsibilities are. And so before we can enroll a single patient into any clinical trial, the IRB has to determine whether or not this study can move forward according to the rules that the FDA has outlined. In addition, we are required to report back to them under circumstances if there's unexpected events in the study, we have to report back to the IRB when they happen. And every year that a study is ongoing, we have to give them a full update every year of the progress of the study as it pertains to its objectives, its enrollment, and any unexpected findings.

- Kelly Cervantes: [11:40](#) I know that there are research studies that aren't always focused on a new treatment. Can you explain what other kind of research studies are being done that may not be treatment focused?
- Dr. Darcy Krueger: [11:54](#) The biggest ones that we have, if they're not a specific treatment, and to be clear, treatments can be a new drug or they can be a new therapy, they could be a new device. So what we call those, those are called intervention trials. Meaning that the study team is introducing something new to the patient, and we want to know either how safe it is or how does it work.
- Dr. Darcy Krueger: [12:14](#) Aside from intervention trials, there's probably two major categories. One is called a natural history study or observational study. And these are the types of studies where we need to find out more about the disorder or the disease itself before we can move into treatment ideas. This is particularly important for rare epilepsies in genetic disorders where numbers are relatively few, and there may be unique aspects about, in this case, epilepsy in individuals with that specific condition that's different from general epilepsy. So those are what we call observational studies for natural history, and they identify when and how, and we should potentially design a future study to intervene with a potential treatment or device.
- Dr. Darcy Krueger: [13:02](#) The second type of non-interventional study are where we're evaluating a diagnostic method. This could be like a blood test that we've not used before. We want to know how good this blood test works. It could be looking at MRIs for clues about how to use MRIs better to make other decisions related to a patient's treatment, or to understand the disease better mechanistically. So those are really how I divide the trials into either interventional or non-interventional, and they all have immense value. If we don't do the earlier studies without treatments, then the treatment trials don't come later.

- Kelly Cervantes: [13:39](#) So let's focus for a moment just on the intervention or the intervention treatment studies that you were talking about before. I have to imagine that most of the people who are signing up for a study of that nature are still actively having seizures. Otherwise they probably wouldn't be interested in going into these studies. So they're probably already on medications. Are they expected to come off of those medications in order to participate in the study? What is expected of them treatment wise?
- Dr. Darcy Krueger: [14:14](#) It depends on the study. Most studies will be designed so that you stay on your current treatments, and that we ask you, as much as possible, during a portion of the study to not change those, and not to have your other doctors change those. That's not always possible, or some studies are designed to allow changes to occur, but that should be clarified upfront as the study is being explained to you. The reason for that is that we need to know whether the new treatment or intervention is what it's doing on its own, but for most studies we don't have to have you change medications.
- Dr. Darcy Krueger: [14:50](#) The one thing to be aware of is that eligibility requirements for some studies will require you to be on or off certain medications as the study is designed. And so there could be a situation where you're interested in the study, you find out more about it, and you find out that a particular medication is not allowed in patients who want to participate in that trial. And so you work with your clinical doctors to change it so you're no longer on that medication, and then you go through eight observation time period. That can be as short as a week. It sometimes can be as long as six months, that you're not on that medication that has been specified as non-compatible for the study. And in which case, then you can enroll in the study at that point. But most of the time, you should just think that whatever I'm on going into the study, I will stay on at least for a period of time.
- Kelly Cervantes: [15:41](#) So I imagine that it becomes incredibly crucial to, you know, if you're going into a study, if you are adding a new drug to your regimen, this is clearly something that you should be speaking about with your neurologist or epileptologist.
- Dr. Darcy Krueger: [15:58](#) Absolutely, absolutely. And also, I would think that they're a trusted source for you to know whether or not the trial, if they've heard of it, what they know about it, or what they think about it. I think both making sure that it's safe for you to do so, to have their support, I think is pretty important.

Kelly Cervantes: [16:14](#) Now what happens, heaven forbid, if there is, you know, you have an adverse reaction to the treatment that is being tested?

Dr. Darcy Krueger: [16:25](#) The first step is always to contact the study team and they will give you that information from the first day that you enroll saying, "Hey, if you have any questions or concerns about the medicine. If you have any adverse events, you can call this person and let them know what's what's going on." They may be give you some instructions that if it's not worrisome, or pretty mild, or just something you note, they may ask you just to record it in some sort of diary or recording app on a phone, and then they will talk to you more about it either by contacting you directly, or by waiting to your next visit and reviewing all of your notes from what may have happened. It really depends on the type of adverse event, and the type of study on whether they want instant feedback on any concerns, or whether you can hold onto those and share them later. So always contact your study team if there's an adverse event that you're either not expecting or is concerning to you.

Kelly Cervantes: [17:17](#) Now, let's say, a drug goes through trial and it doesn't get approved, but it helped a handful of patients. Are those patients still able to access that drug?

Dr. Darcy Krueger: [17:31](#) Only under very limited circumstances. So if a particular trial is unsuccessful, but the company that is working on getting that drug approved by the FDA has other protocols open, or they have a strategy in which they plan to continue the investigation of that drug in similar patients, but with a slightly different trial design, it's possible that the FDA may give them permission to do what we call an open-label compassionate use type access to a drug. That does require approval from the FDA, and it does require approval from the managing IRB for that study. So there are people that are making sure that this is not used inappropriately as a mechanism to give people access to a drug that the FDA has not approved.

Kelly Cervantes: [18:24](#) Okay. So, the study is concluded, and are the final results, and the findings, are they shared with the participants of the study? Do they get to see what they were a part of?

Dr. Darcy Krueger: [18:41](#) It really depends on the study design and the study team, but that should be disclosed to you upfront on whether you would have that information or not. I participate in trials with all of the above. So some of those trials, either the design, or because of legal, and financial considerations, that the trial data is not available to the patients in any way, shape, or form other than what's publicly available.

- Dr. Darcy Krueger: [19:09](#) That said, I can tell you in the trials that I've tried to design, if there is a justification and reason to share those results with the family, then we do so. For example, if we have a study that's collecting genetic information, but the study is not a genetic study. We just have that so we know how to apply the results to them. We will often share the genetic results if those were obtained during the study, because it doesn't influence the results at all, and that's useful to the family. So the important message here is know that sometimes there's very legitimate reasons why you can't have that information, but you should ask upfront if and what could be shared with you during the study or when the study is done.
- Kelly Cervantes: [19:47](#) So let's say you have a child with a rare disease, and you cannot find any studies available for your child, or for yourself, or you don't actually have a diagnosis, which was the case with our daughter is that we didn't have a genetic diagnosis. She didn't have a sort of slot that she could fit in for a lot of trials. What are the options out there for these patients and their families?
- Dr. Darcy Krueger: [20:21](#) Sometimes there are studies that don't require you to have a definitive diagnosis if the studies are designed around your situation or your own symptoms. So there are studies that look for just seizure types, that aren't dependent on a specific confirmation of the type of epilepsy you have as from a genetic standpoint or a syndrome standpoint. So look for those types of studies that are designed around symptoms that you might qualify for that don't require a specific diagnosis.
- Dr. Darcy Krueger: [20:50](#) The second, particularly for rare diseases, is to look for studies that may provide that opportunity to get to a diagnosis. There's these undiagnosed diseases network studies that the NIH has sponsored for multiple years, and many large epilepsy institutions may have even their own institutional versions of this type of study that could maybe offer a route towards getting to a specific diagnosis. But even then, that still will be an unmet need for somebody who has a particularly rare diagnosis for which there are no studies.
- Dr. Darcy Krueger: [21:27](#) In which case I find it useful to start to do searches, and put on kind of your internet savvy shoes to try to find a like-mind. And that like-mind may come through patient organizations, epilepsy foundation, infantile spasms, advocacy groups, oftentimes are dealing with this very scenario. And they may know either individual researchers that would take interest in your situation. And/or I know that we are working on a clinical trial design for a disorder that we thought there were only about 20 individuals in the entire world. And then when we

started working with the first family, they formed a Facebook group, and lo and behold, we're up to somewhere around 50, and we're working on the trial design for them in that scenario. And it all started with that family coming to our center and asking these types of questions to us. And we started, saying, okay, yeah, maybe there's no trial right now, but what would it take, and what would we be able to do in a trial that would be of direct interest to you.

- Dr. Darcy Krueger: [22:35](#) Now sometimes the science isn't far enough along we can do that, but that's where I would start the conversation, because if we don't have that information, then how do we get to that stage where we can get that information?
- Kelly Cervantes: [22:46](#) I want to end on that incredibly powerful point that patients and their families that we hold so much power in terms of advocating for ourselves and advocating for research to be done that we need. And that research doesn't happen unless we're willing to take the time and volunteer and be a part of these studies that are pushing science forward.
- Kelly Cervantes: [23:14](#) What are your words of motivation or your thoughts for a family or individual that might be on the fence and isn't sure about whether they feel comfortable participating in a trial? Why is it so important?
- Dr. Darcy Krueger: [23:29](#) It's hard for me to really top what you just said. Know that every effort starts with one. Our clinic here, that we deal with a rare disease that has high rates of epilepsy called tuberous sclerosis complex, or TSC, started when family asked my predecessor, would you start a clinic for TSC patients at your hospital? And he said, sure. And now we've grown that into a very, very significant research program for patients with tuberous sclerosis. That's how we've started with our Smith-Kingsmore Syndrome Foundation. Like I said, it started with a family who just said, can you guys do this? And if we bring the families or we talk to the families, will you guys work with us? So the power is immense there.
- Dr. Darcy Krueger: [24:19](#) The other thing about starting clinical trials is that while we all want that clinical trial to help me right now, some of these studies, we need pioneers, where maybe we can't do everything that we would want to do, but we won't get there for future generations and future parents that are dealing with these same issues without people taking that first step now. So it can be daunting. It can be nerve wracking about whether you should or shouldn't participate in a clinical trial, but if you're at all inclined to do so, and any concerns that you might have can

be addressed, then you should really do that and know that every individual, whether you're the first person to start this process off, or you're the first person for this new study, or this is first for you, all of it has immense value, and it's the only way we move forward.

Kelly Cervantes: [25:14](#)

Dr. Krueger, thank you so, so much for sharing this vital information. And I really hope it encourages people to hunt down those trials that make sense for them or for their loved one. I just, I appreciate you so much, the research that you do and the care that you provide for our community. Thank You.

Dr. Darcy Krueger: [25:33](#)

Thank you for having me.

Kelly Cervantes: [25:37](#)

Thank you, Dr. Krueger for your insights on participating in clinical trials. As Dr. Krueger emphasized, epilepsy patients have a crucial role to play in developing new treatments. Researchers cannot make discoveries and create new medications without the participation of patients and families impacted by epilepsy. The mothers who founded CURE epilepsy knew this, and for over 20 years, CURE epilepsy has supported patient-focused epilepsy research by raising over \$70 million to fund more than 240 research grants in 15 countries. There have been wonderful advances in understanding and developing new therapies, but we won't stop until we realize our goal, a world without epilepsy. To help us achieve this goal, please visit cureepilepsy.org/donate. Your support and generosity are greatly appreciated. Thank you.