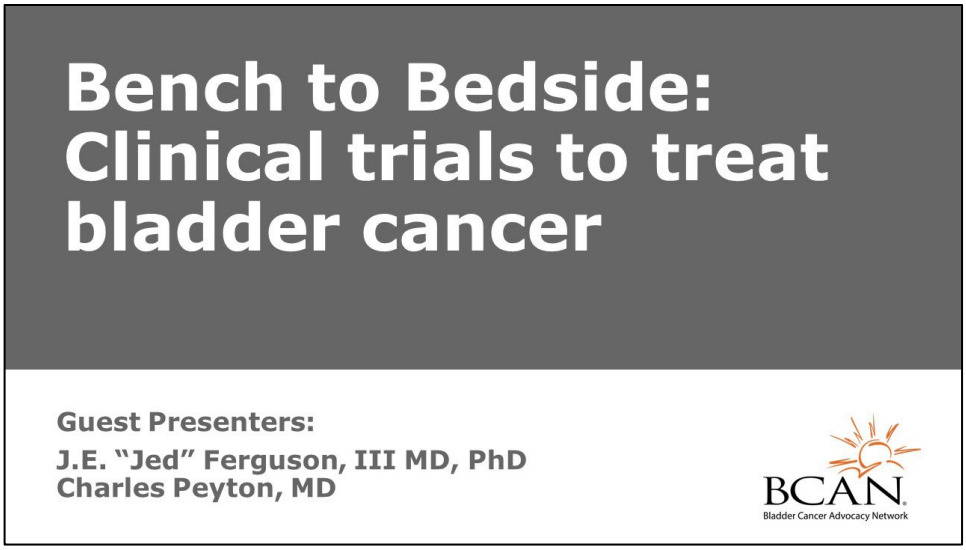

Patricia Rios

Great. Thank you both for an excellent presentation and for covering what happens in the lab and then what happens at the clinic or bedside. So Dr. Peyton, you mentioned the timeline from bench to bedside is around 10 years at least. You also went through the different phases, phase 1, phase 2, phase 3, phase 4. I'm curious to know how many of the trials actually make it? What percentage make it to that phase 3, phase 4? There's a lot of investments in these trials. Do all of them make it to the end?

Dr. Charles Peyton:

Good question. I don't know the exact answer to that question, but it's very limited. And Jed, you can comment on this more than I can. Most investigational drugs in the labs don't even make it to the phase 1 trial and then it is attrition thereafter. I don't have an absolute number for you, but there's a lot of great ideas in the lab that don't pan out in humans, and that's repeatedly..

Dr. James Ferguson:

I think we should be a little bit specific about that timeline. I think what you're talking about is discovery of a drug, testing the drug in vitro, in the cells, and in animals, moving to clinical trials, and then de novo, a brand new drug. That takes a long time.

Dr. Charles Peyton:

Right.

Dr. James Ferguson:

But for example, the study where I was talking EZH2 inhibitors and PI3 kinase inhibitors, those are medications that are already being used for different indications. So that's a little bit different. They're already FDA approved and being used in humans. So if you find a new indication for them in

bladder cancer, the timeline is a lot quicker. I don't want to paint a bleak picture like everything is going to take decades. In some cases, it's a little bit quicker than that.

Patricia Rios

Thank you for explaining. I think that speaks about the complexity and that it's not a linear process necessarily and just so much that there is to learn about this. You talked about different clinical trials at UAB and there's a question from one of the participants who's interested in knowing how the clinical trial findings at UAB are shared with other bladder cancer researchers.

Dr. Charles Peyton:

That's a good question. The three bladder cancer trials that I mentioned are national trials. They are not my trials, I'm just the leader at UAB, right? There's a national PI as well, like the BRIDGE one where I was talking about the upfront BCG versus... It was a phase 3 randomizing. The lead PI on that is Max Kates. He's at Hopkins, I know him and he asked me to open the trial, so I opened. Urology is not that big of a group. Urologic oncology is not that big of a group. And then the people that really like bladder cancer in the country, we all know each other. We go to meetings annually and then we get updates on these big trials on how they're doing, how they're accruing. I get periodic emails from the leads on these nationally as far as how well they're enrolling and whatnot. It's constant communication.

And when you're talking about big clinical trials that have a lot of money invested in them, a lot of dollars, the sponsors who are paying for it are monitoring that data very closely. There's constant communication on what the results are. Now, if you have a local trial, which can be done ... an investigator initiated trial, which is a local trial in your own institution, that's something that we always want to do and strive to do with something like what Jed is talking about. That data would be kept here. We would not necessarily make it public until we understand more of what our data means because no one else is looking at it. That's a very different scenario than what I had described.

Dr. James Ferguson:

Then ultimately, you share your findings at conferences, national conferences, and BCAN think tanks and publications and get the word out there to get on the stump and share to the world what you've learned.

Patricia Rios

Thanks for answering that.

Dr. Charles Peyton:

Any more questions?

Patricia Rios

There was a question that we... You mentioned the cost on the researcher's side. Are there any costs for the clinical trials for participating for patients? Do insurance cover them? What is the patient's financial responsibility, if any, if participating in a clinical trial?

Dr. Charles Peyton:

Usually they're completely covered. With any clinical trial, there's standard of care and your insurance in and of itself will cover standard of care. They'll cover that. But drug expenses and all that stuff, the insurance companies are never going to pay for, are not paid for by the patient in general. For instance, that trial I discussed with the company that was sponsoring is Janssen. I mean, Janssen has invested millions and millions of dollars in this and it's paid for. The cost of the patient shouldn't be any more than standard of care. In fact, it's less and a lot of times because for people that are traveling a lot of ways, there's ways to petition the company to give you stipends for travel and various other ways to get reimbursed for some expenses that may be out of the ordinary for some folks if you're coming a long way, for instance.

Patricia Rios

Thank you for answering that.

Dr. Charles Peyton:

A couple other questions we can address if you want us to. Rose was asking about radiation before surgery. Not usually would be the answer there. And then they asked about EV, which is a new nectin-4 inhibitor that is a new type of chemotherapy and it has been doing very well. Results have been good with a lot of that. Neither Jed and I are medical oncologists. Our colleagues in medical oncology are the ones who give those medicines. We get to see the results of them a lot of the times. The results from the EV medicine when it's combined with immunotherapy has been very robust so far in my experience. There's a big trial ongoing right now that will be the updated results from GU ASCO, which was done several months ago, was very encouraging but not conclusive.

Oh, good. So your husband was on trial at Penn, so he probably gets treated by Phil Pierorazio, and we all know each other there.

Patricia Rios

One of the questions that we got during the registration process was around bladder transplant research. Is there anything around that that you can share with us today?

Dr. James Ferguson:

That worked very well, but I could tell you that just off the bat, the challenge with bladder transplant is going to be every transplant needs vascular supply. And in order to make vascular anastomosis with the small and multiple blood vessels that go to the bladder is going to be the major barrier there or one of the major barriers. So I think that's something that people are trying to get around and address.

Dr. Charles Peyton:

There's work in the mid to early 2000s on, not necessarily bladder transplant, but scaffold matrix bladders that have been seeded with people's own stem cells to grow urothelium. That was done in the early 2000s and it was well investigated and not particularly robustly successful.

Dr. James Ferguson:

Again, because of blood supply.

Patricia Rios

Good to understand that. And then there was also a question about tumor genomics profiling. At what point should that be done for a patient, and should a patient request that?

Dr. James Ferguson:

Yeah. That's a great question. I love doing these because the patients on here are so smart and so well informed.

Dr. Charles Peyton:

Yeah, that's right.

Dr. James Ferguson:

It's great. But it's a moving target. It's not always covered by insurance currently. I don't think we have enough data in each decision point to support it for the payers. So that's fairly variable. You can pay for it out of pocket. Now, let's just assume that money grows on trees and we could get it done for everybody. We don't always understand how to interpret the data and act on the data. That's the next big thing is trying to make sure that we understand how we can act on the data. I think we're a little bit further along in that process in the stage IV setting. And as we get more knowledge from stage IV, we'll be able to hopefully trickle that down to earlier stages as well.

Dr. Charles Peyton:

Jed is right on the money. I mean, oncology just in general has grown tremendously. Then this is what precision oncology will be. We're not there in every cancer, but that's the idea is to tailor the treatment to the patient's genomic profiling of those tumors. Because a lot of times, we over treat patients. A lot of times, we under treat patients. And understanding that is what he's commenting on. It's not there yet, but within our lifetime, it will be hopefully commonplace. But again, like anything else, getting it paid for is hard.

Dr. James Ferguson:

So the short answer to your question, I think if you had the means to get it done and can afford it, I think you're not going to lose much by it. But I think at some point in the near future, we'll have a better idea how to use that data.

Patricia Rios

Related to clinical trials, do they often cover the cost for profiling?

Dr. Charles Peyton:

It's often incorporated in many clinical trials, yes, because that data is really important to see how medicines or therapies will react with some genetic mutations and not others. So it's very common to have that.

Dr. James Ferguson:

And it's getting cheaper and cheaper and quicker and quicker. So it used to be when they sequenced the human genome initially, it took years and years and years and years and billions of dollars. And now it costs about a thousand bucks and takes a couple of weeks. So it's just amazing the technological advances with next generation sequencing.

Patricia Rios

That is very true. I think about when the genome project got started, but it also reminds me of a conversation we were having before the webinar started about research in bladder cancer and how many advancements there have been in the past five, 10, even a year. So as we reach the end of the webinar, I wanted to ask from both of you, what is the single most important message you want our participants today to leave with?

Dr. James Ferguson:

Chas, you want to start?

Dr. Charles Peyton:

Sure. I mean, we were talking about clinical trials today. I guess my most important thing to say is that, as a patient, you should be open to those opportunities and talk with your treating provider about them, if any are available to you. Sometimes you're not right for the trial or you won't... And that's okay, too. But first step is at least asking.

Dr. James Ferguson:

And I would just say keep the hope and keep plugging, and there are amazing possibilities in the near future and in the pipeline. So stay involved with BCAN and ask your providers for information and be an advocate for yourself and just keep the hope up. I mean, we can all beat this.

Patricia Rios

Those are great words to bring us to close. I want to thank both of you, Dr. Peyton, Dr. Ferguson. Thank you so much for taking the time to share information about clinical trials and answering questions from our participants. I also want to thank our sponsors, Merck and UroGen, for making this webinar possible. And of course, to our participants. We hope to see you next time. Have a great evening, and thanks again for joining us.