

William Oh:

Hello everyone. My name is William Oh. I'm the Chief Medical Officer for the Prostate Cancer Foundation, and I'm happy to really welcome you to this webinar on Clinical Trials: What to Consider. Just an introduction to the Prostate Cancer Foundation, our 30-year mission has been to reduce death and suffering from prostate cancer. We really support transformational prostate cancer research accelerating towards this goal. We have funded over 2,200 projects around the world with hundreds of scientists and clinicians, and we also support the best and brightest of young investigators through our Young Investigator program. We also have a lot of resources for patients and families. Please go to our website, pcf.org. You can sign up for updates, download a lot of free guides, view some of our past excellent webinars. Our next webinar on May 16th is on genetic and biomarker testing. You can also join our online support group.

Also, we're really excited about the 27th year of the Home Run Challenge to support prostate cancer research. Major League Baseball and PCF have really partnered for many years on this very exciting initiative. You can sign up at the website noted for important announcements and learn about when we're coming to your hometown. You can also pledge a donation for every MLB home run hit between June 1st and Father's Day on June 18th. So this opens at the end of May, so please go to that website. So it's really my great pleasure to introduce our two speakers tonight, Isla Garraway from UCLA and the Greater Los Angeles VA Medical Center as Professor of Urology and Director of Research at the David Geffen School of Medicine at UCLA. She's a member of the Comprehensive Cancer Center there. She's a wonderful colleague, has received multiple funded awards from Prostate Cancer Foundation and has the research interests noted there and has been a leader in this space.

Our other speaker is Samuel Washington III. Dr. Washington is at UCSF and the San Francisco VA Healthcare System. He's an Assistant Professor of Urology and holds the Goldberg-Benioff Endowed Professorship in Cancer Biology. His research interests include looking at racial and ethnic disparities in prostate cancer and understanding how race and socioeconomic factors impact these outcomes.

Dr. Garraway, thank you for joining us tonight. We're really looking forward to an exciting conversation and interactive conversation around clinical trials, which is something that all of our patients are always very interested in. They don't always understand what they are. So could you give us an overview of what a clinical trial really is and the different phases and so on so that we can talk a little bit more and dig deeper?

Dr. Isla Garraway:

Yes. Well, thank you William. It's really always a pleasure to be here with the PCF family and to have the opportunity to talk about different topics related to prostate cancer. And this is definitely a very important topic, one that we try to make sure that all of our patients are aware of, both those that we serve in the academic centers like UCLA, as well as in the VA healthcare where I see most of my patients, and that's clinical trials and how as a patient to access clinical trials, figure out if you're a candidate for a clinical trial and navigate the whole clinical trial roadmap. So I just wanted to give a quick overview of clinical trials in general. So essentially, clinical trials are basically the endpoint or close to the endpoint of drug development. We're trying to develop new not only drugs, but new devices and new treatments for different diseases. And of course, what we're focused on here is prostate cancer.

So usually this starts in the laboratory. So scientists have ideas based on their laboratory studies about what might be a new target for our cancer or a new therapy. They do a lot of basic research in the lab and then bring that into generally an animal population to make sure that it's safe and something that can move forward into human clinical trials. And then you actually can start clinical trials formally where you're testing a new drug or therapeutic in a patient.

There are several different phases of clinical trials, which I'll go over in a minute, which finally, if everything goes well, will lead to a new therapy that's very promising, that has what we call efficacy or a really positive effect in treating that disease. And then we can apply for regulatory approval to have that drug approved and then be available to all patients. This whole process takes a really long time. So it's between 10 and 15 years from the time when the new drug is being developed in the lab until the time the regulatory approval process is complete and it's being offered to patients. It's a really long time, millions and millions of dollars and thousands of patients and investigators and clinicians collaborating together to make these new discoveries and make these new treatments available.

So what are the phases of a clinical trial? So as we discussed, everything starts in the lab, which is called the preclinical phase where you're doing all that testing to develop that drug and make it into a form that can be used either intravenously or through an oral medication or oral route to be given to our patients. So then you have the different phases of clinical trials. So phase one is really just the earliest phase. It's the first phase. The main point of the first phase is to really just test and make sure that medication is safe, so trying it out at different levels so it reaches different levels in the bloodstream and just making sure that there are no really adverse consequences of giving that drug. So it's not really looking to see if that drug is actually working or not on the tumor or on the cancer or on the disease process, it's more just to confirm that it's safe to give.

And then once that we really feel confident that it's safe, we can start a phase two trial. So that, again, is expanding to more patients. So you're having a wider group of patients, you're still looking at safety, but you're also now trying to get an idea about whether this drug may actually make a difference in terms of a treatment. And then if that goes well, you can move on to phase three. And so this is when you have many, many more patients that you're recruiting. Oftentimes you're recruiting them into two groups, so a group that you're treating with more standard of care therapies, and then one that is more of an experimental group that is getting that new drug treatment or new device or whatever it is. And so you can really compare the effects of the new treatment versus the standard of care treatment.

And then if that's successful, you can go on again and go to the FDA and say, "We have a new treatment. It works really well. It prolongs life or reduces suffering." And then hopefully that will be approved and then you can start using the drug and you can even do larger studies, but looking at thousands of patients to just confirm that the effects that you see with the drug really validate that it's working well and making sure there is no adverse effects that are arising in these larger populations of people.

William Oh:

So phase three is what really compares your new drug to the standard of care and leads to the drug being approved if it's positive. What's the usual reason why a drug would be considered better than the standard of care? Is it PSA declines? Is it-

Dr. Isla Garraway:

Yeah, that's a really good question.

William Oh:

Is it change on x-ray or is there something else that the FDA is looking for to get a drug approved?

Dr. Isla Garraway:

Yeah. Well, I think the gold standard, and you can correct me if I'm wrong, but I think the gold standard usually is survival. You're really looking for survival benefit, especially when we're talking about the

majority of prostate cancer drugs, which are given at a phase for systemic disease or more advanced disease. So you really want to see if that drug is having an impact in prolonging life, prolonging survival, overall survival is really the gold standard for whether that drug is going to move forward, but certainly there are other secondary endpoints that you can look at in these trials, as well as PSA response, pain reduction, quality of life. All of these things are important in potentially a drug being viable or useful, but mainly the gold standard is survival.

So what should you think about when you're considering enrolling in a trial? So the first thing is the details of the study that you're thinking about enrolling in. You want to know what type of trial it is. Is it a randomized trial, meaning that you don't know if you're going to be in the study group or in the control group receiving more standard of care? Is it basically an open label where everybody gets the treatment essentially and you know who's getting the treatment? That's pretty much anybody can enroll and get the experimental treatment. Is it an early phase, like a phase one or two where you're just looking mainly at safety or is it one of those later phases that we discussed where you're actually looking at the effect of the treatment? So you really want to understand what type of trial you're enrolling in.

Another thing related to clinical trials is they can add more time. It is a time commitment because you're going to be followed really closely, and sometimes you need to get extra testing done, like extra blood tests or extra imaging studies to monitor you as you're going through the investigatory phase. So you probably want to understand how much more of a time commitment you're going to need to be able to provide in order to be a participant in the study.

And then of course, you want to know the risk and the benefits of the study. So what are the benefits of the study? Of course, the main benefit is that you might have early access to a new therapy that could prolong your life or improve your quality of life. So you might be the first one treated with a new drug that actually may be a benefit and eventually become approved to treat all patients. So that's a potential benefit. You also, as I mentioned, there's a time commitment involved in a clinical trial, but sometimes that's a good thing because you really get maybe an elevated level of care. Everybody really wants to make sure that you're getting your treatments on time and you're getting your x-rays on time. So you really have that concierge service with all the study coordinators that are involved in the clinical trials to make sure you're getting the studies that you need done in a timely fashion.

So in some ways, you might even be getting a little bit better care because it's a little bit more personalized since you're involved in the clinical trial. And then of course, there's the altruistic benefit. So just the fact that this is something that you may feel good about doing because it's a service, it's a community service that may lead to more benefit in patients in the future in terms of allowing them to have prolonged life or quality of life. And so definitely all these reasons are potential benefits for why you might say yes and participate in a clinical trial.

But of course, there are risks involved as well. New treatments sometimes come with side effects, and some of those side effects can be serious or unknown. Sometimes we don't even know all the potential side effects before we start the treatment. So that's something that you need to understand is that you may experience side effects that are serious when you get this, if you're a part of a trial. And then sometimes the treatments don't actually work as much as we try to test in the preclinical phase in the laboratory and really try to get a good idea in our different tools and models that we have in the lab that this treatment is going to work against the cancer. Sometimes we're all disappointed and it doesn't actually work well or work any better than our current standard of care. So there's always a chance that yes, you'll get a new treatment, you'll get early access, but at the end of the day, it may not work well.

And then there's always a chance that, especially in the later trials, in the phase three trials, that you might not actually get the treatment because a lot of those trials, there's a control group that's getting more standard of care, and then there's the actual experimental group that's getting the new treatment.

And so sometimes you don't even know which group you're in. They're what we call randomized so that we don't bias against select patients who maybe the treatment is more likely to work in. We want to make sure that the it is going to work in all patients or most patients and not really biased against that. So there's a chance that you might not be in the group that gets the new treatment. And then, again, it's inconvenient. And again, going back to that time commitment, it may be adding on that additional time. It's just an inconvenience that you don't want to have to deal with or getting those additional testing that oftentimes need to be done as being part of a clinical trial.

So why should prostate cancer patients participate? First of all, I want to make a point that clinical trials are available through all phases of the disease. No matter what phase you're in, even if you're just screening for prostate cancer, there's probably a clinical trial that you could participate in. However, a lot of the trials are more weighted, of course, to advance disease because that's the disease that we cannot cure yet. So we need new treatments. So we have a lot of trials really focused on that population. And sometimes patients have exhausted all of their standard of care therapies and their tumors are now resistant. So clinical trials may be the best option in those cases. So that might be one reason to participate. But again, sometimes patients are worried about this whole concept of receiving a placebo or not being in the group that receives the experimental treatment because oftentimes, of course, you're excited about a new therapy that potentially could really help you, you want to be the one to get the therapy.

So you might be worried that, "Oh, well, what if I'm not in that group and maybe be getting a placebo or something?" Well, I think that's a little bit less of a worry nowadays because oftentimes in trials, the control group can cross over at some point in the trial and actually receive the experimental drug. So that means everybody has an opportunity to try the experimental drug. That's not always the case. But nowadays with clinical trials, they're really more innovative in the way they're designed to try to give as many people the opportunity to be treated as possible.

So the other reason to participate is sometimes patients may actually prefer the treatment in the trial over the standard of care treatment. So it might be a new, for example, there's a lot of interest in focal therapy for prostate cancer. So there's new focal therapy trials, and some people may prefer try that approach as opposed to the standard radiation treatment or surgical treatment. So these are just some of the reasons why you might want to participate, again, especially for patients who have prostate cancer, in addition to the purely altruistic reasons, which is it's a community service to fellow patients with prostate cancer you might help one day.

So how do I find out about clinical trials? The number one thing you should do is talk to your doctor. They know your situation the best. They know everything about you and your prostate cancer and what phase and stage of the disease you're in. And so what options are going to be available that are going to best suit you? So that's the first person to turn to. But of course, most of us really love to go online and do our own investigations and what might be available so that the next resource is probably clinicaltrials.gov, because that's an official listing of most of the clinical trials that are open right now, or what phase they are.

They list pretty much everything, some of them close, some of them are opening, some of them are enrolling, some of them not in different phases of analysis, but you can just do a lot of different types of searches going on the clinicaltrials.gov website. And then also there's other registries that you can join to hear about more clinical trials. And then of course, you can always go to the Prostate Cancer Foundation website, which is fabulous to hear about the newest data and the news and clinical trials and to get more information about how you can enroll. So that's pretty much all I have for now, and happy to take any questions.

William Oh:

Thanks, Isla. So there are a lot of questions, of course, but I wanted to ask a couple. One is, what does eligibility mean? Why are some people considered for a trial? Let's say their doctor or somebody at a university offers them a trial, but then they actually wind up not being able to go on the trial. What does eligibility mean and why does it even exist for these kinds of trials?

Dr. Isla Garraway:

Yeah, no, that's a really great question. So first of all, as we discussed, that a really important thing to do is talk to your doctor when you're thinking about going on a trial because again, a lot of trials are targeted at a very specific point in time of your disease process. Some are really only offered for advanced disease, some are offered for an earlier stage of disease. So you want to make sure that you fit that criteria for what phase of the disease the trial is actually hoping to show an effect and a benefit in.

But the other thing is that, again, a lot of times with new agents that potentially can have complications or adverse effects, we want to make sure that you're just as healthy as possible and minimize the chance that you're going to not be able to stay on the trial. So there are some conditions that you might have that might make it more likely that you might suffer an adverse event related to the new medication or treatment. And so we just want to make sure that that's not going to be an issue, so really trying to optimize the health of the patient and minimize the chance that you could have an adverse event related to the medication or treatment.

William Oh:

Yeah, so exactly right. So for example, your liver blood tests or your kidney blood tests have to be within a range or if you've had a heart attack in the past year, you might not be a good candidate for a specific drug, and it's really done for the safety of the people going onto the study. There are a lot of myths about clinical trials. One that I get all the time is that people don't want to get a placebo, that they're worried they're going to go on a clinical trial. And you brought this up, but I just wanted to get your sense of whether is that what we're doing most of the time we're always comparing to placebos?

Dr. Isla Garraway:

Yeah, no, I think you're right. I think you're right. I think that's always a concern. And no, that's not what we're doing most of the time. So most of the time, especially in the earlier phases, everybody is getting the treatment because the number one goal is to make sure that treatment is safe and then to see, just get a hint at, how efficacious it is or how effective that new treatment is. So in the early phases of the experimental process, of the clinical trial process, everybody's getting the drug. So it's only really in the later phases where you really need to try to prove that this drug effect is working that sometimes placebo will be considered in the control group to give them a placebo. But again, it's not everybody. And now trials are being designed so that you can cross over and if you were not getting the treatment at first, you can cross over and get it later on and see if it'll benefit you at that point.

William Oh:

What about the concept of being a guinea pig? Obviously there's unfortunately some examples in history of people having research done without full disclosure. What's the modern way of making sure that that kind of thing doesn't happen, and what's your opinion about that concept of research as experiments on people?

Dr. Isla Garraway:

Oh, absolutely. First of all, I think there's been so many things that have changed over the past couple decades to make sure that research is ethical and it's safe. And first of all, it's the level of training that you have to now undergo before you can even propose a research study, I think, is really important. And so any investigator or doctor or nurse or anybody who wants to be involved in a clinical trial has to go through a large amount of training and really almost become an expert in clinical trial design and ethics and going through different scenarios of what can happen and how to make sure that the patient is number one.

Everything is always patient-centered and always based on protecting that patient. And that's everything, from their privacy, protecting those to make sure that they're protected in terms of nobody's going to know that they even participated in a trial, it's up to the patient to disclose, not anyone else, to the actual physical safety of the patient with a new medication. And learning how to report all potential effects because when you go on a trial, anything that happens, you break your arm accidentally falling off a ladder, we report that as potentially an adverse effect from the trial. We report everything so that at the end of the day, we can really understand what are the risks of being on the treatment versus not being on the treatment. So I think the training has really changed and the level and the degree and seriousness of the training of everyone involved in the research program has really led to trials being a lot safer and hopefully can reduce that myth or concern that patients are just being treated like guinea pigs and that their safety and wellbeing is not being taken into account.

William Oh:

One question that people are asking is, can their local doctor help with the clinical trial? Do they have to come to Los Angeles or New York to go on a clinical trial?

Dr. Isla Garraway:

Yeah, no, that's a really great question. And something that's really important for me as a VA doctor is making sure that clinical trials are accessible to everyone. So I wish I could say that you never had to travel or you could always just get every trial through the site that you're at, the location that you're at or the doctor that you're with, but the reality is that clinical trials are not necessarily offered everywhere. So again, you do have to oftentimes be referred to the particular place where the trial is being offered. However, there are some trials you don't always necessarily require you to physically be there. There's different ways of offering trials now.

So for example, in the VA, we're looking at basically offering clinical trials remotely or through telehealth. For certain trials, it's amenable to that where we can enroll patients that way and follow them that way. And they only have to come in for very specific things related to the trial that don't require them to always be constantly coming in. But sometimes you do have to be in at least in close proximity of the institution where the trial is being performed.

As far as if you can continue to see your doctor, if your doctor can offer you the trial, so oftentimes the doctor who you see all the time is not the person who's offering the trial, and they're able to inform you of the trials that are open or available, but they aren't necessarily the one who's actually conducting the trial. And that's actually a good thing. It's actually good to have a little distance between no conflict, it reduces conflict between your doctor and the person who's running the trial and hopefully less coercion, nobody wants to feel like they have to do it because they want to please their doctor. But oftentimes you'll still see your doctor, your regular doctor, you'll just also see other doctors who are running the trial.

William Oh:

So one of the questions is, do you have to have advanced stage cancer to be on a clinical trial? And is there a point where your cancer's so advanced where you're no longer eligible for a trial? So on the one hand, do patients with localized prostate cancer, can they go on a clinical trial? And on the other hand, is there a point where you're no longer eligible for clinical trials?

Dr. Isla Garraway:

Yeah, no, that's a really excellent question. And yeah, pretty much everywhere along the spectrum, whether you're localized prostate cancer or PSA recurring prostate cancer, where you don't have any signs of any other spread besides maybe just your PSA has bumped a little bit to people who have advanced disease and have distant metastasis or involvement of other cancer, or have been treated with a lot of different medications and their cancer is recurring, everywhere along that spectrum there is most likely going to be a clinical trial. But of course, there are stipulations in terms of eligibility that sometimes, it doesn't guarantee that you're going to be able to be enrolled, but certainly there are offerings along the entire spectrum.

So for example, in localized prostate cancer, there are different ways of treating localized prostate cancer. So maybe there's a new type of radiation treatment or there's a new type of surgical treatment approach or there's an adjuvant therapy, meaning that there's like, "Oh, we're going to try treating you first with this medication before we do the surgery or before we do the radiation to see if that will benefit you." So there's just different ways along the whole entire spectrum where you could participate in the trial.

William Oh:

Let me ask you one more question. A lot of people they don't know how to go about this, their own doctor may or may not bring up a clinical trial option. So how should they talk to their doctors? Let's say they're in a community practice, they're on a treatment and that treatment's no longer working. What do you recommend as the question to ask next or the way in which they can find out the best clinical trial option for them?

Dr. Isla Garraway:

Yeah, so I think anytime you're having that conversation with your doctor about, oh, there's a fork in the road, so we're finishing this treatment, we're onto the next thing for whatever reason, either you can't tolerate that treatment or you're advancing, your tumor is progressing despite having that treatment, it's always an opportunity to raise a question with your doctor. Even if there's a standard of care treatment available, you can still make that decision. So your doctor might say, "Oh yes, now we've tried this particular treatment, which is our standard of care treatment. Now we have another one that is next in the line, next in the algorithm that we generally would offer you as a patient," but you could say at that point, "Oh, okay, well, I understand that this is a treatment that is a standard of care that would be next in line for my particular condition, but are there any clinical trials that I could consider?"

And even if your doctor doesn't even know, it might be that he's not aware of any or whatever, but he might say, "Oh, well, let me check and get back to you about it or I have a colleague that I might be able to refer you to or there's a research clinical care coordinator who we could have call you about any trials that might be available to you." So it's mainly just bringing it up with your doctor, and they might be very knowledgeable. They might say, "Oh, unfortunately there's nothing that we have in our area, in our

university, in our community setting at this time, but we could consider it later down the line." So at least you could get a sense of if it's not now, maybe it's something that I can consider later.

William Oh:

No, that's great. And there are questions about how people actually find these trials, and I think that's the biggest challenge. I always tell people second opinions. If your doctor's not able to answer the question, there's very little harm without hurting anyone's feelings, it's your life or your loved one's life, get a second opinion. Usually a lot of these clinical trials are more in bigger research hospitals, and if the trial's for you, then you may want to do it. If not, then you go back and get the standard of care treatments.