Patient Advocates: Their Role and Benefits in Clinical Trial Groups

September is Prostate Cancer Awareness month and we are talking to patient advocates to get a better insight into their roles in major clinical groups. Mike Scott is talking to Tony Crispino, patient advocate to the Genitourinary Cancer Section of the Southwest Oncology Group (SWOG) and a long time prostate cancer advocate on his role and address matters like training available, learning about evidence based medicine and funding of clinical trials. Tony will also explore the role of SWOG in recent major clinical trials (like the CHAARTED trial and pivotal trials for enzalutamide, radium-223, abiraterone acetate, etc.) Mike Scott is joined by prostate cancer advocates Paul Carpenter, Jan Manarite, and Allen Edel.

Full Transcript:

Priya Menon : Good afternoon and welcome to CureTalks. I am Priya Menon, your host, joining you from India; and we are talking about prostate cancer this afternoon on our 92nd episode. Our prostate cancer talks are conducted in association with Prostate Cancer International and the Prostate Cancer Foundation. September is prostate cancer awareness month, and we are talking to patient advocates to get a better insight into their role in major clinical groups. We will also be addressing matters like training available, learning about evidence-based medicine, and funding of clinical trials and also explore the role of SWOG in recent major clinical trials. My co-host for the show is Mike Scott. Mike is Co-founder and President of Prostate Cancer International, a prostate cancer-specific, not-for-profit educational and informational organization based in Virginia. Mike works for Calcium, a privately held healthcare communication company based in Philadelphia. He is also a member of the Board of Directors of the National Organization for Rare Diseases and the International Myeloma Foundation. Mike is today talking to Tony Crispino, patient advocate to the Genitorurinary Cancer Section of the Southwest Oncology Group. An advanced disease survivor himself, Tony has run online discussion for live support groups and is currently the President of UsTOO Las Vegas and a member at the America Society of Clinical Oncology. Supporting Mike on the panel, we have prostate…, prostate cancer advocate, Paul Carpenter. Paul has contributed to dozens of online groups and forums, and he co-founded a Los Angeles support group for gay and bisexual men living with prostate cancer. Allen Edel, Allen is a member of two prostate cancer support groups as well as online groups and often acts as a patient advocate in the Los Angeles area. Jan Manarite is the Vice-President of Advocacy and Education at PAACT, a prostate cancer advocacy organization founded in the early 80s. I extend a hearty welcome to everyone. Before I hand over to Mike to begin with the discussion, I would like to remind our listeners that you can send in your questions to me, priya@trialx.com, or post it on curetalks.com website. If you would like to ask a question live, please press 1 on your keypads to let us know. With that, Mike, its over to you. You are on air.

Mike Scott : Thank you, Priya. I appreciate it and welcome everyone. Tony, can you hear me?

Tony Crispino : – I can hear you fine.

Mike Scott : Excellent! So, I want to spend as much time today as possible giving the panelists and also the audience time to ask you questions, but perhaps you would like to take sort of 5 to 10 minutes just to tell us little bit about your own prostate cancer and how you ended up becoming involved in so many of the different advocacy roles that you now have.

Tony Crispino : – Certainly, Mike. I can… I can relate back to the fateful day back in 2006, just a few days before the Christmas season, and I was told at that time that I had prostate cancer; and I went through, of course, all of the preliminary things that were available in 2006 and early 2007, breaking down what it was

that we wanted to do with my prostate cancer. Its important to note that it appeared at that time destined for treatment because I was 4-way of course positive and it was Gleason 7, so it was that in February of that year I had robotic surgery and that time bilateral seminal vesicle invasion and bilateral seminal vesicle invasion, of course, was stage IIIB. So, we wanted to take some more precautionary steps. I went ahead and had hormonal therapy for a 28-month period; and about 120 days after the surgery, we began a protocol 38 fractions of radiation therapy. I will say that from the moment that I was first detected with my PSA in August of that same year of 2006, I had a 20 PSA. The next test was 18. The next test was 17, and at that particular point I had the surgery. I have never had a rise in PSA in my life from the moment it was detected. Of course, it must have risen drastically in order to get to 20, but at that particular point, I had never had a rise in PSA and that includes after all therapies and today I am in remission. What I started to do right after diagnosis, though, is one of the things that changed my…, my route in dealing with prostate cancer; and the first thing I figured out to do was to find online support groups, talk to my peers, get with people who have been on the road ahead and tell me what they saw coming back; and that was very helpful to me in being able to deal with my own disease and it made me interested to continue to stay in that role as a mentor to others and in, you know, having as many treatments as I did. That would make me a mentor that at least had experienced a good number of treatment types, and HealingWell.com represented an outstanding forum for me. I stood there and moderated it for about five years, eventually leading to my meeting you yourself, Mike but also leading to working more, trying to find ways to work with alive patients; and when the local man out here had retired, he came to me and asked me to start dealing with the live meeting situations and _____[00:06:11]_____ who is one of the top researchers whose name might pop up more than once in this call, had come to me and asked me if I wanted to also participate in the Southwest Oncology Group as a patient representative. That was a little bit daunting to me when I first heard it because I didn't know what that person did. He told me I would be fine. He told me that if my knowledge was good and that my willingness to accept information was good, that he thought that that might be a great role for me. At that particular point, I was doing SWOG, I was doing CDMRP. I was doing a number of different programs that are out there, that's the Congressionally Directed Medical Research Program; and other types of advocacies I have been involved with included going to Capitol Hill, speaking on Capitol Hill and in addition to that representing NASPCC for the State of Nevada. So, as it is, I have done pretty much just about all aspects of advocacy, but the one I find the most interesting is the Southwest Oncology Group I am working on clinical trials.

Mike Scott : So, before we move on, just for the audience's benefit, I should point out Tony also somehow manages to hold a full-time job. I am not quite sure how he damn manages to do that too, but, you know, maybe we can get into that later. Tony, I have got a couple of quick questions myself before I…, I start opening it up to the rest of the panel. The first one is, how do you go about making sure in all of these actions that you take, that you aren't just expressing your opinion but you are doing everything you can to represent the community as a whole?

Tony Crispino : It didn't start out that way. Its very easy to fall under the trap of believing in what you believe in, but it didn't take me too terribly long to realize that the physicians that I was working with recognized that they themselves followed the same trial and understanding that you have to open up the doors to a more broader point of view than your own leads you to kind of believe that, you know, some of the initial encounters I had and some of my initial physicians that I took, they needed to be questioned and I had to learn how to question them and that's when I…, when on healthcare evidence-based medicine and that made a substantial mark in how I can decide what I can still feel, but understanding that what I feel is not necessarily going to be helpful in this as much as it is going to be that what does everybody feel and what do we feel as a group that we can make a difference and properly move ahead without my opinions getting infirmed.

Mike Scott : And what exactly are your responsibilities as the patient advocate for the GU section at SWOG?

Tony Crispino : You know, this was a piece that I didn't know exactly how to expect when I…, when I first went on into the first group meeting. They were very, very wonderful to me. They were very helpful to me in

letting me know that we understand you understand a lot of our prostate cancer. We understand you have a lot of connections in the networking capabilities of reaching on out to a lot of survivors. What do you see us doing in trials and stuff and, I immediately had a backup and…, and be overwhelmed by the question because I didn't know how to answer that question, but in time I learned to adapt within the group. Now, not all patient advocates can do this. Many patient advocates have had difficulty in integrating into their respective groups, be it breast cancer or multiple myeloma or whichever of the many different communities that are available at SWOG, not all of the prostate… I am sorry, of the patient advocates were integrating into their group, but I found myself slipping right on in and integrating very well into the group and my counterpart in the GU community is Ric Banks who is a bladder cancer survivor. He also has the same approaches that I do and we both agreed that we are fully integrated. Now, what are our responsibilities? Our responsibilities are to be attentive and paying attention to each of the offered clinical trials that are coming down the pipe, making sure that the proper protocols are placed, and facing the patient. When we get to facing the patient, we have to say, okay, is this test reasonable? Is…, is it something that would be easy for somebody to do? Or, is the ICF or the informed consent form worded in an easy enough way to understand and there are protocols that are in place to establish those things, but even with those protocols in place, they can get complex and get difficult for a patient to understand them. So, it is that we, as the patient advocates, get on in there, get involved into the ICF portion of it. We do get involved into the trial design, but as much as that is a lot of that is handled outside of the Southwest Oncology Group and handled by the National Cancer Institute. So, understanding how those processes work, they expect me to understand those processes. They expect me to understand what the trial is trying to accomplish, what is the key question in the clinical trial, and are we getting to where we are not including enough people or we are including enough. Those are the kinds of things they would like us to participate in.

Mike Scott : So, one more question. I…, I know you can't talk about trials that are in development or ongoing because you can't promote those, but are you able to give us an example of somewhere where you feel you have been able to help to make a trial better from the patient perspective?

Tony Crispino : Yeah. Over the last two years, we have heard of different callouts for screening and doing baseline testing for men at the age 40. Screening maybe in the 40s but not necessarily at 40. There was a trial that came on down. I immediately took a look at it, said I don't like the trial because it said its inclusion criteria would be men starting at the age of 45 and I…, I had suggested to them we should include right on down to where we can detect these people and that includes the age 40 as they do in baseline screening and they fall under that criteria. The principal investigator agreed with me a 100%. He made the change to the trial.

Mike Scott : Excellent! So, let's…., let's start with…, with Paul because I know Paul had spent a lot of time looking at different clinical trials and wondering why people were doing and were not doing them. So, Paul, what would you like to talk to Tony about?

Paul Carpenter : Yes, indeed. Thank you, Mike. Thanks, Tony. Thanks. Umm… I find that clinical trials are very hard to…, to explain to the laymen and I struggle with explaining why the criteria are in place, what the criteria mean. I wonder if there is any…, any kind of effort for helping the laymen understand what the criteria are and why they are for some of the clinical trials that they may be considering enrolling in?

Tony Crispino : I think the best way, you know, to get back on over to a patient is to explain why the trial is being done, what is it trying to accomplish. We see a lot of people look at clinical trials or in clinical trials with the thought that this might be another form of treatment, but the…, the whole point of a clinical trial is not to be another form of treatment. It is to answer a question and you need to explain to the individual what the question is that's being asked and how the trial would be run from there. So, for example, if you have a trial that's going to be comparing one drug against another, that is typically a new experimental drug against a standard of care, so if the standard of care has already been established, we don't want to go back to the placebo level of doing the trial. We want to be able to do the trial with the standard of care, so either way the patient is still being helped. That is one aspect of doing it and that would be in the drug-related type trial. In a trial maybe that's not drug related, but for example, there was a trial on out about eating healthier and

being able to follow a certain diet guideline, we have to be able to explain to them why the other trial is being done and after a diagnosis, does eating healthier make you have a better fight against cancer.

Tony Crispino : Now, most people will say that's not too terribly difficult to understand, but you are right, Paul. As soon as you read the…, the clinical trial, in other words, it…, it can get a lot…, very confusing to somebody very fast who has no experience in dealing with it. That's where we go back on over as an advocate and ask them to, you know, make sure that language is very, very easy to understand in the informed consent form but also give proper instructions back on over to those who present that ICF to the patient on making sure that they understand each point of it. That's where we are with advocate. There's also one other point to add. The NCTN has an advocacy network and that's the National Clinical Trials Network. They have a group that's been together right now, that's working right now on trying to standardize how that language should be presented to the patient.

Paul Carpenter : Oh, very good! That's exactly what I was hoping to hear. I did not know about that initiative.

Tony Crispino : Yeah. That…, that is currently going on and that will be going on through the remainder of this year. I think that probably by 2016, end of 2016, that we will have set standards that must be applied in all of the forums and the NCI in order to try to standardize the language because that…, that is a major problem, getting a standardized language on…, on how to explain things.

Paul Carpenter : Yes, indeed. Well, thank you.

Mike Scott : Thank you. If I may interject quickly, Paul, I think also its important for us to remember that most of the trials we see information about are…, are through things like clinical trials.gov and those have not been written for patients.

Paul Carpenter : Yes. Yes.

Mike Scott : They have been written for the professional community. The material that was actually handed to a patient in order to seek his informed consent is usually at least a little more intelligible.

Paul Carpenter : I agree and actually I was thinking about bridging of that gap when you have a patient saying, well, I think I might be interested in enrolling in a clinical trial. What could I do with and then all of a sudden they are faced with a 150 possible things, they can't possibly look at all of the informed consent forms for each one. So, they are.., they are picking and choosing but often without the ability to understand.

Tony Crispino : Well, I think its also important to note on that, Paul, is that the physicians that are working with this patient need to be properly selecting the clinical trial. I don't think that its appropriate for a patient to look at a shopping list of clinical trials and then go back on over and choose which one they think might be best for them, but rather have the consensus from your medical team to go back on over. Is this trial appropriate for you at this time and here's…, here's what's involved into doing this particular trial. Now, that stated, you bring up an interesting point in that at any given time there might be more than one trial that fits a particular patient and, of course, they always want to go with which one is best for them and getting through that menusha and trying to figure out which one to select is very difficult to do. You can get a hold of the trial coordinators any time you want. There is usually a phone number that is included in the clinical trial and that phone number brings you to the trial coordinator and can help you also discuss with the trial coordinator what is this trying to accomplish? Does… Do I really fit this criteria? Am I properly in the inclusion criteria? And what is the hypothesis based upon?

Paul Carpenter : Right. Yeah. Thank you.

Mike Scott : Anything else come to mind immediately, Paul?

Paul Carpenter : I am sorry. I didn't get that.

Mike Scott : Anything else come to mind immediately as a followup?

Paul Carpenter : Umm… The criteria for inclusion, I know, I think this is also relating to a question that we got from a listener. Sometimes its unclear how soft they might be and there are rumors out there saying well, I might be able to get you in through the back door and I have not encountered that myself, but I would be interested in hearing what Tony's experiences are, whether things can be modified just a little to get someone in who doesn't quite meet the inclusion criteria.

Tony Crispino : Yeah and I can give you a really solid example as well. We have, for example, this one I can mention because I am published on this trial, but on S1216, there is a trial from SWOG that is comparing orteronel to the standard of care. Now, orteronel is the TAK-700 component that many of us have probably read about it in the past. Its being tested in a different setting than the previous trials which didn't fare so well and in that setting including men with…, presented with metastatic disease at…, at their…, at their onset and at this point it would be a good trial to continue with or is there another one that's out there that's better. Well, at last ASCO, the American Society of Clinical Oncology, at the presentation from Chris Sweeny, they came on out on the ECOG trial which was done with SWOG by the way and it was called the charted trial and the charted trial, of course, was comparing the early years in the same patient set with chemotherapy and presenting in…, in that way showed that men with poor metastatic lesions or visceral disease benefited highly from the early chemotherapy. Now, that affected our trial directly, so would be that patient who hears about that and then hears about this trial, should I not just go straight to the chemotherapy. Well, what SWOG did was we went back on over and changed our inclusion criteria so that there are patients who can still follow that because that is now a standard of care and we have to subset them, but we are now including those patients that would qualify for that…, that charted setting and they can still stay within the setting of the 1216 trial. So, yes, its important to ask that trial coordinator, can I do this if I do this and its important to say the inclusion criteria are not always set in stone. For example, again on 12/16, we started out with the…, the need for the electrocardiograms every year on a patient. Well, that was too tasking for many patients. So, we changed the criteria and we have reduced it to the number of occurrences of that particular event and that is the kind of thing that everybody has to remember. There are things that can be modified in a trial on the fly as long as we get the proper okay from the National Cancer Institute and everybody agrees in consensus that it will not harm the results of the trial, then we can make those modifications and we can make exceptions for individual patients.

Paul Carpenter : Oh, thank you. That gives me some insight into the process that I was completely unaware of. So, what I would say to someone who is not sure whether they could be…, whether they meet the inclusion criteria would be ask and maybe keep asking because sometimes it does change, sometimes the criteria evolve every time.

Tony Crispino : The key to asking probably includes who is doing the trial and can you get to the person that's coordinating the trial. Typically, yes. The answer is yes and typically if you look at clinicaltrials.gov, you will see who the principal investigator is and you will typically find out who the trial coordinator is as well.

Mike Scott : So, moving along… Thank you, Paul. Allen, what sort of questions do you have for…, for…, for Tony with the immediate acknowledgement that SWOG does not do vast numbers of radiation therapy trials.

Allen Edel : – Actually, what I was going to ask Tony about is, I have a little Tony Crispino living on my shoulder at all times. You don't know anything until we have a randomized controlled trial. It was very influential on healing well and putting that across. So, Tony, I was wondering if you could explain for listeners what do we mean by the term "level of evidence" and why are randomized controlled trials so important?

Tony Crispino : Yeah. Well, I think its…, you know, there is…, there is important piece of this is the understanding the level of evidence that's out there and typically a level III level of evidence is not… Its basically considered more of an expert opinion and many retrospective works at hospital records or clinical

records and such are typically a level III type of trials where you go ahead and you develop a hypothesis based upon what you found in your set. The problem with that particular level of trial is that it…, it can be done on a sliding scale. It can include the criteria towards which the investigator makes into it and that is not really a trial. Its just basically a study. Now, level II is a little bit tighter in that it…, it contains a lot more closely related information and even multi-level peer reviews that give the level II information a lot more foundation to arrive to a hypothesis that might be able to be presented into a level I trial and a level I trial, we call it fact. Whether or not its fact with which everybody would be looking for in the form of a fact, a level I trial is one with which has been stripped of bias as much possible. Of course, I don't think that we could ever strip a 100% bias in this industry, but its been stripped off bias and a randomization of not just the patients but a randomization as to the institutes as well. So, at SWOG, we are a 24-institute organization and all of our institutions are pretty much IRB approved for SWOG trials, but any other locations which might want to do it, try and prove a point for a specific drug, you know, I think that we have to make…, try our best to make sure that a level I trial is what's in place. Now, what are some of the examples of a…, a level III hypothesis not proving well. There are so many of them. I mean there are so many of them in the Vioxx world. Vioxx was being was being put out there, but…, then when it finally went to level I clinical trial, everybody found out that we were creating more heart conditions than…, than we were solving with the Vioxx. And that can happen in prostate cancer world just the same way. I think that its important to know for a level I trial versus a level III opinion that at SWOG, we believe that about 90% of the level III conclusions are not a 100% correct and some of them are just not correct at all and that led to the selenium and the SELECT and PCPT trials which showed the hypothesis that were on out there on study at level III, none of them passed.

Mike Scott : Hello! So, do you have any followup to that, Allen?

Allen Edel : Yeah. So, from the patient's point of view and the patient typically when they read about a study in the media, they…, they don't know if its level I evidence or level II or level III. All they know is some media said, for example, that taking soda and molasses will cure cancer or last year media were saying things like it was pomegranate juice will do it. What…, what do you say to…, to patients who want to try some therapy or…, or a diagnostic test just because they read about it on the internet?

Tony Crispino : Oh, I'd say, my…, my…, my thoughts about the internet and the gathering of information is very cautious. As you already know, Allen, as you mentioned even now that I believe if its not a level I trial, its more susceptible to error. Its…, its a major issue, but when we get to start talking about the media, we are not even talking about level I, II, or III. We are talking about somebody doing the reporting and that somebody doing the reporting is typically not even a physician. Sometimes it is, but typically its not even a physician. You know, if you can make something sound better than it was or something that might catch your people's interest, that's what the media is after. They are not after the same thing that we are over in the clinical trial side where we are trying to…, to prove that molasses has an effect on somebody or…, or deferring back to the SWOG trial, selenium and vitamin E in the SELECT trial where it was…, it was stated and reported back in the early 90s, that taking higher arms of selenium and vitamin E will prevent you from getting prostate cancer. Not only when it was put into trial was it not true, but it also showed an example of where you may be doing more harm than good and at that particular point, we ended that trial and said that, we don't need to go any further because we know we are doing more harm than good. Well, that didn't get as much press as it was getting before that when the press was reporting that selenium and vitamin E were great ways to help avoid prostate cancer, but we know that's not true now. We know that there are reasons that maybe somewhere suggesting it, such as maybe a reduction in the number of detections, but reality was that those who were taking high amounts of vitamin E were actually having higher rates of aggressive prostate cancer.

Mike Scott : I think so its worth mentioning that in defense of the media that many very respectable institutions spend a great deal of time publicizing the results of very early stage research as part of their strategy to raise the next round of money to do the next round of research and so there's an awful lot of material that gets out on to the internet and even into the New York Times and the World Street Journal, that is really hypothesis generating and it is not actually a study designed to prove whether something works or not, but it may get presented in a way that makes it look as though its clinically

meaningful and…, and this is…., this is one of the complexities of…, of, you know, having access to the internet for all of us. You…, you…, you can't…, you can't look at what's on the internet and assume that its true anymore than you can look at, you know, somebody's review of.., of a film and say that he must be right. He may like that film. You may go to see it but think its terrible and…, and there's a large element of that in…, in how one understands and dissimulates scientific information as well.

Tony Crispino : Yeah, Mike, I… I agree with that. I think that lot of our…, our own bias gets into the equation and when our own bias gets into the equation, it makes it easier to digest what we hear in the media if its what we want to hear and if its not necessarily so much, it makes it harder to push it back and say, I don't… I don't believe that. I think that a lot of people have to remember that the biggest enemy to evidence-based medicine is always and typically biased and it happens not just at our patient levels, which we talk about all the time at healingwell.com, about, you know, if you…, if you talk to a radiation oncologist, he is going to do radiation; if you talk to a surgeon, he is going to do surgery. The…, the medical professionals have the same issue and they have to deal with their own biases as well. So, when they develop these hypotheses, they release into the media. It gets into conversation generating. The fact is that there is really no way to come back on over until that level I trial is done to state whether or not the entire statement is true. In fact, it could be entirely false. Sadly, it could also be true and so many years we have done the rejection in the cancer industry about complementary alternative medicine approaches to dealing with cancers and physicians for many years wrote them off, that basically there is no such thing as integrative oncology. Well, that's changed too over time. We have seen that that has changed because as what was mentioned earlier about eating well and doing physical therapy, physical exercising, you build up your body's immune system and you create that opportunity to go ahead and fight the cancer better, but for many years if you walk into Harvard University and you said, "I think that exercise and diet are going to play an important role in this patient," they would have…, they would have lost jobs.

Mike Scott : So, with that we will move…, move to Jan. We have got a couple of questions because Jan spent more time trying to simplify all of this for patients than the rest of us put together, I suspect. Jan?

Jan Manarite : Thank you. (Laughter) Yeah. You know me, Mike. I… Because I lived in the space like… Hi, Tony! Like Tony has for so long, you know, I…, I kept hitting brick walls and feeling overwhelmed and confused and so my passion has always been to just help people with clear information and I use phrases like, if we are going to share the decisions, we must share the information. So, with clinical trials, well, let me back up. I want to go back to a comment about the internet for patients in case there are any patients or caregivers listening. It is hard to find accurate information. There are a few flags you can look for, like if somebody is selling something. They are trying to make a case that they are unbiased is just unreasonable, but I am going to go so far, Mike, as to say that I found the Prostate Cancer InfoLink to be a consistent source of understandable valid information. So, I don't know if you are allowed to give that out, but I would be happy to give out the new Prostate Cancer InfoLink as a good source of information. I wonder if…, if the other panelists will agree.

Tony Crispino : I can say from my perspective, yes.

Jan Manarite : – Yeah, I agree too.

Mike Scott : We… We try hard because I am very conscious that sometimes I am biased about things. I have opinions and they get in the way of…

Jan Manarite : So, that's a good….Yeah. Well, that just says right there that you are probably less biased than other people, but I would like to at least give listeners instead of telling them, you know, what the internet cannot do, give them one place that maybe they could go. I mean let's face it, right now we are on the internet, you know, and we are trying to give good information, so…Let's give them something good and in addition…

Paul Carpenter : And also, Jan, I would like to follow up on one of the things that Mike does. He says, yes, I

know, I have some biases sometimes and when he writes something and he knows he has a bias, he says, my bias is as follows, but that's what my bias is. …presents as a fact……is evidentiary fact, but one can track down where he got that information from. So, yes… It keeps you as what you are doing right.

Jan Manarite : Yes. So, you should go to the new Prostate Cancer InfoLink and just search that site. If you have an issue that you want to try and…, try and find some clear information on and for the most part, its really vast and usually understandable and fairly unbiased. I think that's really fair, so…Yeah.

Mike Scott : Well, thank you folks. I appreciate that….so does, Tony. So…, so does Allen too because he happens to be dealing a lot.

Jan Manarite : And then moving on to, you know, understanding clinical files, Paul, you were addressing that and I… One perspective, I think that helps, is not focusing on the clinical trial but focusing on the patient and all they really want to know is, is this a clinical trial for me and with good direction, I found it takes that as a simple risk versus benefit perspective in discussion and the risks in the trial may be, you know, does it have placebo and people still think that all clinical trials have placebo and they don't. So, you need to ask or you need to find out and we are in an age now where a lot of placebo-driven trials have two-thirds of the man on the drug and only one-third on placebo. So, that lessens the risk for the patient. In addition, some of those trials have an actual crossover provision and that's the key word, crossover. What that means is if you get the placebo and you don't even know it and your disease progresses, if there is a crossover provision, they cross you over either to standard of care or the trial drug or something else. So, obviously this risk column becomes minimized and that's what the patient wants to know. So, those are some of the key questions I think that help and second, if they know what they have as far as their cancer, if they have their medical records, they are going to have better questions and be able to evaluate risk and benefit better. So… So, they are trying to convince him that the trial is this so that I want to help them understand their risk versus benefit so they can make a decision. So, just some thoughts on that.

Mike Scott : Tony, which brings us to an interesting question, Tony, is…, is that something that gets specifically discussed during the trial design phase and how that is going to get presented to the patient.

Tony Crispino : Absolutely, it does! It can sound…, you know, there are a couple of aspects of what Jan pointed out there, being, you know, there is…. A trial sometimes is comparing with a placebo, minimizing the effect of the placebo that will improve the trial outcome and then also to do something else that's very important to a trial. When you include a placebo into a trial, often invariably, its going to run the risk of that trial failing and the failure of a trial is not that it didn't prove a drug was working or drug was not working, that is a successful trial. The trial that ends with accrual and in the accrual we have met the criteria of all of the…, of all the vital statistics that had to be accomplished and we arrived at an answer. No, this drug does not work. That's not a failed trial. That's a successful trial. A failed trial happens when you have an inclusion criteria that is tough to meet or…, and then you can't make the accrual criteria and therefore you won't be able to arrive at…, at the…, at the desired…, at the desired answer or a failed trial can also be towards which it was flawed by design and by design the trial itself had to be pulled back off of the table. Now, we see clinical trials fail and those are the worst kind. Those are the ones that cause the medical industry a lot of money, so there…. and being in there and if they can take that standard of care and substitute it with a placebo CTEP which is a very important arm of the National Cancer Institute, must review it and CTEP is the clinical trial evaluation program and if they go on through and they agree that they can substitute a placebo with a standard of care, it will help a trial be successful because the accrual rate will be much higher.

Mike Scott : I…, I have one more question before we move on and open this up to the audience. We are now in the situation where we have multiple drugs already available. Many of them are being tested earlier in the disease and there are literally dozens of other drugs coming down the pipeline which is going to have to go through the phase 2 and phase 3 trial process. How much effort is made to be quite sure we are going to be able to enroll enough patients into those trials before SWOG is willing to get involved because SWOG is the…, SWOG is the group that does the…, the majority of the prostate cancer trials. ECOG is much more involved in other disorders as are some of the other trial groups.

Jan Manarite : May I comment on that or is that for Tony?

Mike Scott : Well, its for…, its for Tony, but if you have got a comment, go right ahead.

Jan Manarite : Yeah, I would like to because I… You know me, Mike, I write about this. I take clinical trials. I sort of hand pick a few and then I pull out what I call basic eligibility criteria and I have been blogging about them on the PAACT website. Am I allowed to mention our website?

Mike Scott : Sure, while you just did do that.

Jan Manarite : That's not really fair because I mentioned, you are putting me on the spot.

Mike Scott : I am teasing you. Yes, of course, you are.

Jan Manarite : Okay. Its P-A-A-C-T-U-S-A.org, paactusa.org. On that website, you will find our blog and I have right now three different clinical trials on there in plain English that I thought were very interesting. One is ProstVac immunotherapy trial for newly diagnosed or active surveillance, which I think is super interesting. Again, two-thirds drug only, one-third placebo. There is the Artemis trial and the Spartan trial also, which are for men who are on hormone therapy, rising PSA, and no metastasis. So, there…, on there in plain English right now, you can go there and find information that helps you and takes you to the official site. So…

Mike Scott : So, to go back to my question, Tony, how much effort does trial groups themselves make to make sure that they think they will be able to enroll people?

Tony Crispino : It is almost imperative, but that's decided before we can calculate it and send it on over to CTEP. We… We have to feel that we can make the trial work or its not going to go and whatever has to be done and this is where those bio statisticians, the people who think with numbers will be on the calculus. Going back on over and looking at what the population would require for in that to get an answer, what kind of variance can get involved into that? We have to get into those levels of discussion in order to make sure that we are going to reach the accrual. If we don't think that we are going to reach the accrual and it does not appear that we are going to reach the accrual, we may be able to go back to the manufacturers and figure out what we need to do to maybe make the accrual happen. But you are right. With so many of the different drugs that are coming on down and the more drugs that come on down, the more competition that's going to be in various settings for clinical trial and that, of course, is going to make it more and more difficult as time moves on to define which is the appropriate trial. Is it the red one for me and if not, I am not going to do it and if everybody else feels the same way, the trial that might actually be better than some of the others is going to fall because we can't reach the accrual numbers and that is a failed trial and we have to do everything within our means to meet the inclusion criteria and meet the accrual criteria and that is how our meetings go. I mean, we will sit around and we will talk about that and say, well, you know, what is it going to take in order for these people to participate in this trial when in fact it competes maybe with active surveillance and most people would rather do nothing.

Paul Carpenter : I am curious, Tony. I am sorry. Go ahead.

[Mike Scott : No. Go…, go…, go ahead, Paul, but can we keep it quick because I want to get this out to the other audience as soon as we can….

Paul Carpenter : Of course. I… I was just curious how do you get the word out to physicians and clinics to say, hey, let's recruit. Let's recruit harder because we are failing to meet the accrual goals?

Tony Crispino : Well, a lot of the problems that make that happen, Paul, are not the smell or taste of the trial from the patient standpoint. Everybody has to understand that any institution that is going to offer the clinical trial has, what they call, an investigational review board, an IRB. Many times we are not hitting on

numbers because the IRBs are…, are sitting on it and they are not making the decisions that say, okay, we will clinically do this trial or okay, John Hopkins will do this trial. Each of these investigational review boards will have to then work with our group which has an investigational review board and with CTEP which has an investigational review board and take out the concerns that are preventing them from accepting the trial and offering the trial at their institution and then you have to get back down to the physician level. At that particular point, do they have the physicians at that institution that maybe are conflicted by another trial and would be more likely to participate in that particular trial with their institution. There are a lot of little things like that that get involved into making the number happen for accrual. The… The key to accrual is a very simply and well stated and outlined trial and has significant benefits to the patient himself and if can get all of the description done in that way, usually participate if its just their need and if not, they will go ahead and move on and we will need to hear why they selected no.

Mike Scott : So, at this point, Priya, what I would like to do is…, is hand this back over to you so you can help patients who are listening to the call to ask their questions.

Priya Menon : Thank you, Mike. We have a list of questions actually sent in via mail and posted on our website right now. Tony, I will just quickly go over them. You may have to repeat some of the things that we have actually already discussed, but I will try to keep that to the minimum. We have a listener asking, what are the challenges you face as a prostate cancer advocate. He says, what were they…., were there incidences of some tough emotional circumstances where you wish you could help the person you are dealing with but felt helpless?

Tony Crispino : Oh, many times over. You know, I can't…, I can't… I can't state enough the prostate cancer patients with that feeling of helplessness that I had when I got started out. It took an education to get myself to be able to come to grips with it. By then, I had to find out how to educate myself, which starting from the ground up, it was very difficult. To every patient that I would say that one goes through the experience of a diagnosis of cancer, discussion with your peers is very helpful, but…, and all of the courses that I run for the UsTOO group or anywhere online, it is…, education is the key. You don't want to make emotional decisions. You want to make educated decisions and if anybody is diagnosed with prostate cancer, don't feel alone. Go out and find the people that aren't alone and enjoying them in the conversation and then it will definitely help ease some of the fears that you might face.

Jan Manarite : This is Jan. Can I interject? I think what we have found really helpful is men are trying to make treatment decisions, but they don't know what they have because every prostate cancer is different. So, go backwards before you go forward and get your medical records, get a basic understanding of them and then you will know what type of prostate cancer you have, which helps you decide the type of research and conversations you need.

Paul Carpenter : The toughest challenge I have faced is that I am so much into evidence-based medicine, becoming informed, knowing what the risks are down to two decimal points if I can and when I am faced with someone who honestly doesn't want to become educated, they want some charismatic person to just tell them what to do and I feel helpless in the face of that because I just think that's a wrong way of proceeding, but I am not about to tell them, well, choose wisely whom you trust. Sorry, I can't help you. I feel helpless.

Allen Edel : If I may as a patient advocate, but my goal is not to tell the…, the patient what his course is, although I may give him a lot of options to discuss with his doctor, but my goal is to empower the patient to…, to get him to a point where he can talk to the right doctors and ask the right questions and if he…, if the patient advocate sees that as his goal rather than curing the patient, I think he would be a lot less frustrated.

Paul Carpenter : I am with you on that, Allen. I am…

Tony Crispino : I agree with everybody.

Paul Carpenter : What I was talking about was the situation where a patient who doesn't want to learn,

they want to be instructed to…, by someone they trust.

Allen Edel : Yes, Paul, I wasn't responding to you.

Paul Carpenter : Oh! Okay.

Priya Menon : Thank you, everyone. The next question that is thrown out to the panel, we will start with Tony and I wish…, I hope everybody can give in their thoughts on this. The question is, many trials fail to enroll enough patients leading to increase in cost or even cancellation of the trials. Being a patient advocate for many years, what changes would you like to see in the patient recruitment process or efforts?

Tony Crispino : Umm… And its a terrific question. The first part of that question is, you know, cost. I… I… We didn't get any time to talk about that, but like everything else in this world, it seems like the top three layers of decision making to go ahead and move forward with something is preferential, political, and financial with financial typically being at the top of the list. Clinical trials are very, very expensive. Its very difficult to put out a trial that studies active surveillance over a 15- to 20-year period and be able to have it as a phase I trial, you are typically going to have to always go back on those trials because nobody is going to fund it. Its going to be very expensive to come back on over and follow patients for 15 to 20 years to be able to arrive at a conclusive answer in the trial that this person was better than this person for active surveillance, yet they were both the same at diagnosis. I think that a lot of this stuff is also going to continue to change as we move forward. How that changes the complexity of funding for trials is still yet to be seen, but I know in my heart, saying this on this show, specifically talked about what is the next phases of what we got to accomplish in the research side and its translational medicine which is the process of taking the genomics, assigning it to a targeted approach through individualized care to each patient. That is great. Its novel, but its very, very, very expensive.

Tony Crispino : I would like to see a change that the funding from the federal government considers going back on it. I mean the federal government funded the SELECT and the PCPT trials because of where they were at the time and that funding from them make two of the largest trials in…, in, you know, cancer research history, be able to be completed and if it wasn't for the 134 million dollars that was dumped into those trials, it would never have happened. So, where do you come back on over and get the funding for a trial that is really, really necessary to get done such as the following of the active surveillance core or the…, the following of early detection and did we need to treat this guy, did we not need to treat this guy. Those are the types of things that I would like to see included in the future and help us provide a more definitive answer so that, here's your Gleason score, here's your PSA, here's the number of cores positive. What do you want to do? That I am not happy with.

Mike Scott : Tony, do you think that the development of registry systems is really going to help with this or is it a…, a step in the right direction that's not going to go far enough?

Tony Crispino : I think a little of both, probably leaning towards your latter part because we don't have a criteria that was established by that database and its gathering of information. We…, we definitely don't want to end up in a scenario with which we trip everybody into a bucket and then depending on how you fit your sliding scale, these are the results, but yes, I think that it will help a great deal to have a…, a database, that database also coming to recognize the direction that we are going. Its also going to need to include tissue banking for that individual that's in the database so that we can get a retrospective view of what he was looking like when he was diagnosed and what he is looking like today, 20 years later.

Priya Menon : Jan, would you like to…

Mike Scott : Anybody else want to comment on that question? Okay, Priya. On you go.

Priya Menon : Hi… Yeah, okay. The next question is, what is the biggest fear of a patient about participating in a clinical trial that you have come across during practicing advocacy?

Tony Crispino : The biggest fear I see coming across patients entering a clinical trial is the uncertainty. Simply put, if they understand the trial well and they are in a trial that's for late-stage prostate cancer, you know, their…, their fears are probably a lot different than if its a trial examining early-stage prostate cancer and taking a look at the use of some of the novel new hormonal therapies that we have out there being used in that setting. I think the biggest…, the biggest fear I see in a prostate cancer patient entering a clinical trial is the disease progression itself and is it going to progress, is it not going to progress. What do I do, what do I not do? Some people don't like the idea of being randomized. Most people like control and they would like to be in control of their decision making processes; however, that said, a patient that would like a test… I am going to go backwards in time here so I don't step on anything that we are currently working on. XL184, I know many guys that were going on into that trial, but what they had to fear was far worse than the trial itself. Their disease was progressing and this was the disease… This was a drug being tested in the very late stage of the disease and, you know, their fear is that they…, they will never know if it helped them or not and then the second part of it is, is that the moment it starts to fail, they…, they feel the need to get out of that trial and do something different.

Priya Menon : Thank you, Tony. Just one more question. The listener wants to know that, I want to help the prostate cancer patient community by becoming a prostate cancer advocate. Where do I start and do I need special training for becoming a patient advocate?

Jan Manarite : May I interject?

Priya Menon : Sure, Jan, sure.

Jan Manarite : Yeah. Because of what we are, advocates here, but I would say the best way to be advocate is to just be yourself and I would say also that whatever caused you the greatest amount of pain, that you overcame is probably exactly where you need to advocate and that's what I mean by being yourself. For me, it was misinformation, incorrect information, and missing information. So, that's where I focused. That causes a lot of stress. So, I tried to make a difference right there. It can be as big or small as you want, just find a way to be yourself in your own space from where you struggled and conquered.

Mike Scott : I… I think that's a very good point, Jan, and I mean its interesting because you raised the whole question in partialness, in partiality before. I mean the…, the…, the thing I felt that I got involved was because I felt that the…, the information being presented to patients nearly always seemed to represent somebody's point of view……than it was just representing the factual evidence that was available and I…, I…, I know that, you know, others of us have also sort of come with this from the areas that we…, we felt under served by, but the other thing…

Jan Manarite : That caused you frustration. Right. Right. Yeah.

Mike Scott : The other thing I would say to somebody who wants to learn to become an advocate is find yourself a mentor, find somebody who has already taken steps like us. We have, as others have, the easiest place to start might well be with your local support group leader but find somebody who you can talk to and who you can discuss things that you don't understand with and things as you learn so that you have another…., another sounding board to work with.

Tony Crispino : But, I am going to interject. I know we are running at the last minute here. The…, the one key trait that I found was very valuable to me was the evidence-based medicine one and it was taught by another advocate, Musa Mayer who is with the CARE network and also with The Cochrane Collaboration has put together a series of training videos with which teach you how to compare the information that you are hearing and be able to go ahead and decipher between it and ask the right question. I think a good patient advocate will always be following that kind of criteria and, Mike, I will forward to you that information because its open to the public and if you want to get…, get that on the InfoLink site, I think that would be a great idea, but…It is.., it is a very intense training course. They say it takes a couple of months to do it. I was able to do it in less than a month. I was able to do it in a few weeks, but that was only because I…, I didn't

start at the…, at the go line.

Mike Scott : Well, thank you, everybody, for your time this evening. I think we have covered a lot of ground, and I really appreciate everybody's help. Priya, perhaps you would like to do wrap up.

Priya Menon : Yeah. Thank you, Mike. I feel over the hour we have shared valuable information regarding training, learning, clinical trials, and how to become an advocate, and I think this was very helpful. Patient advocates are a great resource to connect with for patients and caregivers who are looking for information. Thank you very much, Tony, Paul, Allen, Jan, Mike, for sharing all this great information with our audience. This talk will be made available on CureTalks' website along with the transcript. Please visit curetalks.com for details of upcoming talks. Thank you very much.