Conference Update: The Latest Updates from ASCO 7/21/2025

Dr. Phillip Koo [00:00:00] I want to thank everyone. We've had over 3,500 patients or supporters register for this webinar, which is amazing. And I think we could all agree when you sign on to one of these webinars and you learn something, it really can make a huge difference. So, let's continue spreading the word and making sure all those loved ones or friends or family, whoever around us, have the opportunity and are aware to sign on and listen to these great webinars. So, thanks, Zach, for joining us. We only have 30 minutes, so let's sort of go right into it. We talked last time about the importance of these meetings, and ASCO is one of the biggest cancer meetings that is hosted every year in Chicago. One of the major studies that was actually produced or presented was something called CAN-2409. So, this is for patients who have localized disease. Can you tell us more about this study?

Dr. Zachary Klaassen [00:00:53] Yeah, thanks so much, Phil. And I'll get into that study in a minute. Again, just thanks to PCF and for your time for hosting this. Again, everybody on the call, just a tremendous opportunity to learn and to educate each other. And the studies we'll be talking about tonight, Becky is also going to send out a UroToday link. So, we do coverage for these meetings for patients and providers as well. And so, everything we're discussing tonight, if you miss something you want to read about, the full write-up will be available as well, and it's already available online. But Becky will also provide that too. So just want to throw that out there.

The CAN-2409 trial was very interesting. It was one of the oral presentations. So basically, it's one of the big studies presented for prostate cancer at ASCO. And basically, what the study was, it was a phase 3 randomized trial, where everybody was planned to get radiotherapy as their primary treatment for localized cancer, and what they did was they randomized patients to this CAN-2409. This is a non-replicating adenovirus. Plus valacyclovir, which is an antiviral medicine, oral medicine. So, patients either received this three treatments, this was three injections of this adenovirus right into the tumor itself, into the prostate, plus 14 days of valacyclovir. The control group was patients that were receiving radiotherapy, valacyclovir and the placebo.

And what they found was really interesting. They found that this injection, compared to those that did not get the injection, had an improvement in the time from prostate cancer recurrence or death, a 30% improvement, as well as decreasing prostate cancer mortality by 38%. So, this is, it takes a long time to get this follow-up for these kinds of outcomes. So, there's something there in the boosting of the immune system with this non-replicating adenovirus injected directly into the tumor, plus this 14 days of valacyclovir, plus the radiation that just is creating an immunotherapy reaction. That clearly is producing important downstream outcomes. So really exciting results, somewhat surprising, honestly, but something we'll be keeping an eye on for sure.

Dr. Phillip Koo [00:02:56] Great, any comments, were there any adverse effects or things to be concerned about for patients who might receive this?

Dr. Zachary Klaassen [00:03:04] Yeah, nothing out of the ordinary, a little bit of, you know, we're injecting a virus, we're taking this valacyclovir, a little bit of antiviral reactions, flu symptoms for a few patients, all minor symptoms. This is also, everybody's getting radiotherapy, so the usual side effects you may get with radiotherapy may be some bowel

toxicity or urinary toxicity, but nothing out the ordinary that we would expect from radiotherapy and this cocktail of treatments. So, very well tolerated.

Dr. Phillip Koo [00:03:32] That's exciting to see these trials that, you know, for the listeners out there, you have the drug versus the placebo, and you see this effect, which we're seeing here with this drug called CAN-2409. So, this is very exciting that something like this up front can really have some improvements in the longer-term outcomes for patients. So very exciting, awesome. Thank you.

So now we're going to sort of move forward into patients who have recurrence. So, we've talked a lot about biochemical recurrence on our PCF webinars. And we've heard about this trial called EMBARK. A lot of excitement around this, it's a big trial, but they had new data they presented at ASCO as well. And this is something we see often, right? Where you have sort of different ideas or different things that come out of a trial at later time points. So, can you tell us sort of about that process and what we learned at this past meeting at ASCO?

Dr. Zachary Klaassen [00:04:25] Yeah, absolutely. So, one of our three big meetings, typically either ASCO or ESMO, which is the European equivalent to the American Society Clinical Oncology. And then also the third meeting is GU ASCO, which is just specifically on genitourinary cancer. Those are sort of what we call the big three meetings.

So, as you mentioned, EMBARK was presented now 18 months ago or so as a big plenary session. And then this gets approval. This gets published in the New England Journal Medicine. And then what happens is there's secondary analyses. There's extended follow-up. And so, we see these at subsequent meetings, often for years after the initial presentation.

And so, what they presented at ASCO, I think, it sort of supports this combination of enzalutamide plus Lupron or enzalutamide alone versus ADT. So, it's a three-arm trial. Basically, what this trial showed is if you have high-risk biochemical recurrence, which is a PSA doubling time less than 10 months after a primary treatment, and these patients had conventional imaging (CT scans or MRIs or bone scans), if those were negative, they were considered high risk, non-metastatic. They were then randomized to one of these three arms. And basically, what this showed 18 months ago is that if you get enzalutamide plus Lupron or enzalutamide alone versus ADT, both of those combinations led to improved metastasis-free survival. And so that was the big outcome, which was presented previously.

What they showed at ASCO, I thought was interesting and why I wanted to bring it up is: No matter what your type of primary therapy was, whether that was surgery alone, radiotherapy alone, surgery followed by radiotherapy, the outcomes were exactly the same. So, I think as a urologist who's sitting there seeing patients, that their primary therapy may have been one of those three combinations of surgery, radiation, or surgery and radiation, we know that this EMBARK protocol, which is nine months of treatment, so it's a very specific nine months of enzalutamide plus Lupron or enzalutamide by itself. And then we see if the PSA goes down to less than 0.2. If that happens at nine months, we give patients a break from treatment and then reinitiate if the PSA starts going up. So, I think this is a nice secondary analysis that tells us that no matter how you got to that biochemical recurrence standpoint where you're high-risk, this is the right treatment for you, regardless of whether you had surgery or radiotherapy.

Dr. Phillip Koo [00:06:45] Great, so for patients, I guess… the take-home messages are if you have biochemical recurrence, a lot of different options, but if it's high risk, based on a [PSA] doubling time of less than 10 months, really one of these options could improve your outcomes. So be sure to have that conversation with your treating physician. Alright, good.

So now let's move on to advanced disease. So, disease out, now that is metastatic, has spread outside of the prostate gland. And some of us may have heard of a study called ARANOTE. And I believe there were some new data presented around this study called ARANOTE, so can you help fill us in here as well?

Dr. Zachary Klaassen [00:07:27] Yeah, so this was in patients that had metastatic hormone-sensitive prostate cancer. And that means that they have metastatic disease outside the prostate. They may have had treatment previously, and we call that metachronous or recurrent metastatic hormone- sensitive disease. Or they show up to the clinic, they've had no treatment, and this is the first stage that they get is this metastatic disease. That's called de novo metastatic disease. So, both patients are kind of grouped into this metastatic hormone-sensitive prostate cancer umbrella.

We've had a number of what we call second-generation ARPIs [androgen receptor pathway inhibitors], which are pills that help in combination with ADT, which is the hormone therapy, improve outcomes in these patients, whether they're recurrent or they show up with metastatic disease. And ARANOTE was sort of a second study of darolutamide, which is one of the ARPIs, and there's now four of them, that was looked at in a previous trial where we combine darolutamide, plus Lupron, plus docetaxel. So, it's called triplet therapy, and we still use that in a number of high-risk patients for sure, hitting that tumor hard.

ARANOTE was the second study looking at: what's the combination of darolutamide plus ADT? Does that improve outcomes versus ADT alone? And so presented at ESMO in 2024 - was presented by Fred Saad- and showed a 46% improvement in recurrent [editor's note: radiographic] progression-free survival compared to ADT alone. And so, we kind of expect that result, but it was a nice take-home point that this combination by itself without the chemotherapy works better than ADT. And so, it now gives patients a very tolerable option with darolutamide plus ADT to bring their prostate cancer under control very quickly. And to your point, what was presented at ASCO and sort of why I wanted to lead into this is two important things. One, right at the end of ASCO, June 3rd, 2025. This was FDA approved. So, this was presented initially, September 2024. Fast forward to June 3, 2025, it's now FDA approved as a combination of darolutamide plus ADT for these patients.

Alicia Morgans presented some really interesting quality of life data. And so, when we have these patients, we're obviously thinking about the cancer control and what's the best option for them, but what's the tolerability going to be? How much of an impact on quality of life is this going to have? And so, there was two important end points she showed. There was a 24% improvement in time to pain progression. So, we know that patients that have disease that's in the bone, this can be painful. And so, this combination got better control of that pain compared to the ADT monotherapy by itself. And it also improved by 28%, time to deterioration in quality of life. So if you think about this on a high level, we're controlling the cancer better, we're decreasing their time to where they have pain, and we're decreasing the time to where their quality of life decreases, I think that's a triple threat because we have both the quality of the life aspect and we also have the cancer control aspect.

Dr. Phillip Koo [00:10:29] You know, that's great to hear, and I think it's wonderful because we often lose sight of some of the negative effects or adverse events that these drugs can cause, but it's great to hear some of these regimens and therapies improving quality of life, which we see here as well.
You know just to sort of take a side, ask a question here about, you know, oftentimes we hear about ARPIs. We know there are four, as you mentioned. It's easy for us to want to sort of group them all together or think, oh, one, they're all the same. And sometimes we try to compare different trials. What advice do you have for the listener on with regards to sort the scientific method and what we might think of just from a conventional wisdom perspective?

Dr. Zachary Klaassen [00:11:14] Yeah, it's a great question, Phil. I'm going to take a step back even further. I think we know in 2025 that if you have metastatic hormone-sensitive prostate cancer, aside from the odd patient, everybody should be getting ADT, which is the backbone, plus one of these four options. Unfortunately, in this country, we still see a lot of ADT monotherapy, and this is just treatment. This is not intensification; this is not standard of care. So, unless there's some really random reason why not to, everybody should be getting one of these four. So, if we take that as this is our goal, as patient education, as physician education, if you're on one of these four, it's way better than having ADT by itself.

So having said that, to your point, you know, these all work very well, and they all show improvement versus ADT alone. And so, it becomes sort of a bit of a nuance in terms of, you know, some work a little bit better in patients that have a history of seizures. Some work a little bit better in terms of other medications that somebody may be taking, such as cholesterol medicines or blood thinners and stuff like that. Some is just better covered by insurance companies. And so, I think there's a lot of aspects that go into it. Some of it is provider-dependent. Maybe they like one a little bit better than the other. That's fine. Some of is based on what's covered by insurance. And some of it's based on what's cover in terms of what the other medications the patient's taking. So, the take-home here is they all work very well. Everybody that has this disease state should be on it, at least a combination therapy.

To your point of comparing these trials, we…. from a scientific standpoint, we shouldn't compare these trials. We do in these conversations because this is what we have in the clinic, but there's populations, they're similar populations, but they're not perfect in terms of comparing head-to-head. There's never been a head-to-head of ARPI number one versus number two or number two versus number three. We have the individual trials. And so, from a scientific standpoint, not kosher to necessarily compare them, but when we're looking at the clinical data, we're looking at the patients in front of us, we certainly do that all the time in terms of how we're making treatment decisions.

Dr. Phillip Koo [00:13:19] Great, you know, I agree it's nuanced and I think for the listeners out there, every time you hear these types of headlines and you hear these new options, it doesn't mean you have to change, it's just sort of new information that helps us make better informed decisions. So, that was a great summary.

Dr. Zachary Klaassen [00:13:37] I'll just chip in really quick, so the patients know the name. So, this is darolutamide, this is apalutamide, enzalutamide, and abiraterone. So those are the four that they should be considering if they're looking at treatment intensification.

Dr. Phillip Koo [00:13:50] It's a mouthful. I actually had to practice a lot to pronounce those early on when I started getting into this, so good. All right, so now we're going to move on and stay in the advanced space and talk about this study called AMPLITUDE, which really had a lot of exciting conversation and buzz at ASCO. So, tell us about AMPLITUDE.

Dr. Zachary Klaassen [00:14:09] Yeah, so AMPLITUDE was another one of these big phase three trials where they took, again, with metastatic hormone-sensitive prostate cancer patients, and they took patients in this disease space, and they randomized them to a PARP inhibitor plus ADT, versus sort of standard of care plus ADT.

And the way…I just want to back up a little bit and talk a little bit about PARPs. So, PARPs are another oral medication. They've been approved in the mCRPC [metastatic castration-resistant prostate cancer] state. So, this is the more advanced state than mHSPC. So, the combination of niraparib plus abiraterone plus ADT versus ADT plus abiraterone which was what was looked at in this trial. And so niraparib plus ADT already is being used in mCRPC. Now they're looking at they can move that combination up into the metastatic hormone-sensitive setting. Now the difference with PARP inhibitors is that this opens another box of having tumor sequencing. So, there's different mutations that can happen, either in your blood, this is called germline, this is what you're born with, versus what's in the tumor, which is called somatic. So, to get into this trial, you had to have a certain [medication] called HRR mutations. And so, this is an entrance requirement. And so not everybody has these mutations, but this is what they looked at in this specific trial. And so, what they found was -- and PARPs go back a long ways in ovarian and pancreatic cancer, it's come into prostate in the last probably five to seven years or so. And we know that they work very well in these really advanced patients. So, the AMPLITUDE study looked at this combination and to see if there was a benefit of adding the niraparib plus abiraterone plus ADT in an earlier setting. They found that there was a 48% reduction in radiographic progression in the triplet combination, as we'll say, versus the control arm, abiraterone plus ADT in the patients that have a *BRCA*, which is a common mutation, *BRCA* mutation. Or, in the patients that had all of these other mutations (about 12 of them) there's a 38% reduction. So, it's kind of a long-winded way to say that this treatment, this PARP inhibitor, which breaks double-stranded DNA in the tumor, works very well for these patients if you have one of these 12. Specifically, if you have this *BRCA* mutation compared to just abiraterone versus ADT. So, what we're seeing here, and this is not uncommon, we start with testing these in the very advanced state. If they work, we try to move them up so that more people may benefit from them. And certainly, AMPLITUDE had a lot of buzz because of that. So, we're seeing this combination of niraparib and abiraterone moving up potentially in this disease space.

Dr. Phillip Koo [00:16:43] You know, that's great. And I agree. I think this is sort of the promise of precision medicine. And for the listeners out there, we have very specific webinars at where we talk about genetic testing. We talk about germline testing. We talk about somatic testing. And this is exactly how we see that be put into action. So for those, you know, have these conversations with your physicians if you have advanced disease and make sure you had the testing done, because that could help inform and get you into some of these different pathways that might have better improved effects compared to some of the other options that might be out there. So, this is really, really exciting.

After every one of these big meetings, we see all this wonderful data. Sometimes patients might go to their doctor and say, hey, why am I not getting this? Why am I getting that?

And there's a good reason why. So, let's sort of go through them and sort of explain or maybe predict when patients might be able to see this in the clinic. So, starting with CAN-2409, it was a phase three study. When will patients be able to access something like this in the clinic?

Dr. Zachary Klaassen [00:17:47] Yeah, it's a great question, Phil. I think, you know, when we look at this data, we get excited about it. We have these great discussions, and we see what's coming. The FDA takes this data, and they have to review it. And so, this is kind of an unpredictable timeline, and it depends on a lot of factors that are maybe beyond the scope of this conversation, but it's the quality of the data. It's how quickly the company files for the approval. They're very specific in how they want their approval data submitted. So, this can go back and forth a little bit.

The one thing I'll say, something brand new like CAN-2409, it may take a year or two, just because this is the first indication, first label of CAN-2409 in prostate cancer.

And so, what I mean by that is if you take, if we look at the ARANOTE approval, which was darolutamide plus ADT, the FDA already approved darolutamide plus ADT plus docetaxel. That's about three or four years ago now. And so, this was moving an additional label to something we already know something about. And so, I think that approval process likely is a little bit quicker than something that's brand new. So, we saw that ARANOTE was presented November 2024 by January, so that's what, excuse me, June, that's about eight months, we get approval for the doublet. Hopefully we get an approval that quickly for something like CAN-2409. Phase three, great trial, you know, the FDA looks at the quality of the trial, head-to-head, randomized, placebo-controlled, very well-designed trial that will help with hopefully approval. My guess is it may take a little bit longer just because this is the very first indication for something like that. So, I can't predict what the FDA is going to do, but probably I'm guessing a year or two down the road.

Dr. Phillip Koo [00:19:27] All right, good. You know, it's encouraging, obviously, because the data is great, and hopefully that leads to a smooth path to approval. You know since we have a little bit of time, can you talk about this concept of phase four type trials and sort of what that means?

Dr. Zachary Klaassen [00:19:42] Yeah, it's interesting. So, we start at phase one, which is making sure it's safe in humans and getting doses right. We move on to phase two, which gives us a little more of a signal. Phase two is kind of a broad topic. Often, it's a hundred or so patients. Sometimes it's randomized. If that's feasible, then we get onto a phase three, which we've talked about with CAN-2409. We've talked with ARANOTE, we've talk about with AMPLITUDE. And we've talk with EMBARK. And so that's really the big one that kind of gets approval.

Phase four is sort of this post-approval space of what happens when it's approved, what happens in the real world. Sometimes there's a little more leniency in who's eligible for phase four. It's a little more on the real-world side, how it's being dispersed in the early days after approval. So, it's not as, I don't want to say it's not as important as phase three. Phase three is often what leads to the label from the FDA. But it's great to see how these work in a fashion once we get approval, how they're distributed across the country.

Dr. Phillip Koo [00:20:46] So moving back on to EMBARK, you mentioned how it was first presented 18 months ago or so. Now we have continued data coming from it. Any changes

or what should patients expect now that they see this type of data presented at a big meeting?

Dr. Zachary Klaassen [00:21:05] Yeah, I think, you know, with these, what these sort of supplementary or secondary analyses do is just give us as providers a little more confidence that we're not seeing something different in patients that are in the real world. And so what I mean by that is, again, like, until they did this analysis, did we really know if a patient that started with radiotherapy or started with a prostatectomy, did their primary therapy mean they were going to act differently once we gave them the EMBARK protocol, you know enzalutamide plus Lupron or enzalutamide alone? And so, the answer is no, it's more of, the answer's no because it doesn't matter which one you get. So, it's a more of a confidence for us to be able to tell patients, you know, we know this data's been presented, it's great data, but now we have all these other little check boxes that help us with our confidence in saying, yeah, we think this is the right treatment for you.

Dr. Phillip Koo [00:21:52] You know, that's great. So, for EMBARK and this data, it really sort of solidifies its presence and its use as a great tool. All right, so for ARANOTE, interesting, that was presented before….you kind of talked about it. There was interesting news at ASCO, I think at the tail end of ASCO with regarding to ARANOTE. So, can you sort of walk us through that process?

Dr. Zachary Klaassen [00:22:10] Yeah, so as I mentioned, the FDA approval just kind of happened to be around the time of ASCO. So, there was a lot of excitement around that. There was some buzz that they were going to get it maybe in May. But again, we had an idea that darolutamide works great with metastatic hormone-sensitive prostate cancer in combination with docetaxel and ADT. And so, when that came down at a huge cancer meeting, obviously among providers, that's a huge deal. So, it was really exciting to know that we could go back to our clinic the next day literally and start giving the combination of just the darolutamide plus ADT. And I think it's important when we're thinking, we know that the triplet works great for a lot of patients. Perhaps people aren't chemotherapy candidates, whether it's they have kidney dysfunction, they have already neuropathy, they can't feel in their fingers or their feet or they have bad hearing, things that we may not want to give a chemotherapy to. We know that in those patients, now we can just give the doublet therapy of darolutamide and ADT. So, I think when we look at somebody who's a candidate for treatment intensification, it's still important to give chemo that to the patients that truly need it. And that's a discussion between the physician and their patient and their family members. But now we know that doublet therapy works excellent as well.

Dr. Phillip Koo [00:23:25] That's great. So, ARANOTE, the data comes and then all of a sudden it gets a change, and FDA approved and their label can be updated. AMPLITUDE sort of falls into a different space where we're seeing the data from AMPLITUDE. When can patients expect to see this available for them if they're in that metastatic hormone-sensitive space?

Dr. Zachary Klaassen [00:23:42] Yeah, I think, you know, it's taking the information we already know about niraparib and abiraterone in mCRPC. So, we know it works in mCRPC. We know that combination is safe. They'll need a new label for the metastatic hormone-sensitive disease space, which is what AMPLITUDE was. So, I'm hopeful again, because we already have a label in prostate cancer - advanced - that they'll be able to move it quickly into the metastatic hormone-sensitive space. And so, I think, again, I'm hopeful that's in that 6-to-12-month timeline, that we'll see that.

Dr. Phillip Koo [00:24:14] All right, so the last item or presentation we're going to talk about is a study on exercise and colon cancer, and it was published in the New England Journal of Medicine. Can you sort of give us a brief overview about that, and we'll get into some questions about exercise?

Dr. Zachary Klaassen [00:24:32] Yeah, absolutely. So, for the listeners, the New England Journal of Medicine is sort of the holy grail of publications when we're talking about, you know, when we do a randomized trial and we're looking at where we want it to get into, it's the Lancet, which is European, it's New England Journal of Medicine. So, this is a big deal when anything, a phase three trial, gets published in New England Journals. So, it means it's been rigorously reviewed. It's one of the top journals for publishing our research. So, it automatically, when you get the table of contents emailed every Wednesday, as a provider, you flip through and you're looking through it, when something in cancer hits that journal - because this is all medicine, it's not just cancer for that journal. When it hits that journal, it immediately is something that you're clicking on just to see what was published, even if it's not in the prostate cancer or bladder or kidney cancer space. And so this was a colon cancer trial where - and neither of us are colon cancer surgeons or physicians - but, the concept is very interesting because it was a colon cancer trial where patients had surgery, they had treatment after their surgery, but what they did in this study was they randomized these people to a very intensive three-year exercise regimen versus standard of care and support for the patients that were in the sort of control arm. And what they found was this three-year exercise regimen improved colon cancer-specific survival as well as improved overall survival. Compared to those that did not have the intensive exercise regimen. So, to my knowledge, this is the first very structured exercise, prolonged, you know, three years, a long time, the first structured long exercise regimen in any cancer that has shown not only benefits in overall survival, which we would kind of expect it's going to be better for your heart, everything else, but also improve cancer-specific survival as well. So, not specific to prostate, but very interesting to see them hit both of those endpoints in this trial.

Dr. Phillip Koo [00:26:25] And that's great. I think sometimes purists always want to say, you know, that it has to be studied in a very specific state. And yes, for drugs and whatnot, that makes a lot of sense. For exercise, I think, you know, we all in our gut and conventional wisdom know that exercise is good. Eating well is good. And then why are we investing all this time and energy into this three-year-long study that requires a lot of resources? In some ways, we're holding something that we know is so good for patients away from patients. So, what's sort of our takeaway when it comes to prostate? Do we just kind of assume it works?

Dr. Zachary Klaassen [00:26:58] Yeah, it's a great point. I think you're right; we know that it works for overall health for sure. I have a couple of patients on the webinar tonight. They hear me talk about cardiovascular health as much as I talk about prostate cancer, because at the end of the day, the number one cause of mortality in the US is cardiovascular disease. And I think we're all at risk of that. And so, I think to your point about do we need a prostate cancer trial to tell us that exercise helps. It'd be nice to have it, but it's a big lift. It's a five-to-ten-year trial. To get the three years of exercise, plus you wait for the long-term follow-up to see if those endpoints are beneficial. But I think if the take-home tonight, in my opinion, is if we are regimented about exercise, it's no question going to help our overall health, and it probably will help our overall survival like we saw in that trial, because it's going to help out heart, it's going to help our mental health, it's going to help everything. And if we're lucky, it may help our prostate cancer survival as well. And that's the question we don't know until we have a trial. I don't if there will be a trial, but I know that if we're

exercising, it can't hurt the prostate cancer, and it certainly will help our overall health as well.

Dr. Phillip Koo [00:28:08] That's great, you know, I've heard this before, but heart healthy is cancer healthy, regardless. So that's great. Well, thank you very much. Again, submit your questions for the next webinar we're going to have sort of an “ask me anything” type but we're going to get the questions beforehand and try to pick sort of the high-yield and those that seem to be entered in a little bit more frequently. So, appreciate all the feedback and just all your engagement across the globe for these wonderful webinars. And Zach, you make this possible, really, really appreciate the time.

Dr. Zachary Klaassen [00:28:38] Pleasure is always mine and thank you to over a thousand listeners that joined. Hopefully it was helpful and Phil, thank you and Becky as well. Thank you very much.