High Impact News in Prostate Cancer with Dr. Phillip Koo & Dr. Zachary Klaassen

Phillip J. Koo, MD: Great. Thank you very much, Becky. It really is a pleasure to be here. Can't think of anyone better than Zach Klaassen to be talking about these topics. Zach is really just an amazing educator who really understands these topics and can boil it down for all of us to be able to learn from this. So thank you, Zach, for joining us.

Zachary Klaassen, MD, MSc: Phil, thanks so much, and to Becky as well, and PCF. It's always fun to be on these webinars, and I appreciate the invite, and for all the listeners that are eager to learn about what we've been discussing at some of our recent conferences.

Phillip J. Koo, MD: Great. So you know these medical conferences, you know, we get to travel across the country, sometimes across the world, going to a lot of these medical conferences. And my kids think, “Oh, I'm going on vacation.” But as you and I both know, these are hardly vacations. Tell us, and tell the viewers, why these medical conferences are so important.

Zachary Klaassen, MD, MSc: Yeah. Great point. I mean, you're right. We go to some nice places, but it's often very rigorous. We're having conversations with each other. We're presenting research. We're listening to research being presented. And I think that's really the key. If we are at the head of our field and really wanting to understand what the cutting edge research are–what the cutting edge research is, what's being presented in these big trials with some of the topics we're talking about today. We don't get this information firsthand unless we're there.

Certainly, websites like UroToday are good for keeping up on all the sessions if we can't reach all of them. But it's all about the collaborations between you and myself and the rest of our colleagues, and really the goal here is to keep educated so that we can bring back to our clinics every Monday through Friday, and be offering our patients not only the cutting edge care, but understanding what's coming down the pipeline as well.

Phillip J. Koo, MD: Yeah, that's great. So we recently had two major conferences in the urology space - European Association of Urology, that was held in Madrid, and then American Urology Association, which was in Las Vegas, and lots of data, lots of discussions, lots of great work that was presented. And we're going to try to highlight some of these. So some of these, you know, data presentations or whatnot that benefit patients directly.

So, number one, at AUA this year, there was a large discussion about this caregiver survey that was presented. Can you tell us a little bit more about this survey?

Zachary Klaassen, MD, MSc: Yeah, absolutely. Before I get into that, I just want to bring one more point up about these meetings.

This is, you know, they're urology meetings, and 15 years ago, it was all urologists at these meetings. But now we have urologists, nurse practitioners, radiation oncologists, medical oncologists, nuclear medicine physicians. And so it's really become multidisciplinary around these meetings as well. Not just those meetings, but certainly upcoming meeting next month or later this month at ASCO, which is the big American Society of Clinical Oncology. So our listeners, I think it's important to understand that this is multi-specialty. Even at these quote unquote “urology meetings.”

So yeah, I think, Phil, this paper, I happen to be the author on it. I was delighted to be involved with it. And it really is important when you look at caregivers and what their needs are, there's decent amount of literature in breast cancer, and some of the other cancers, but for some reason prostate hasn't had as much looked at in terms of what are the needs? What is the role? What is the stresses?

All these things that come into play with caregivers, and I'm sure we have several on the line with their patients listening right now. So this study was a 528-caregiver survey; 57 questions given to 538 *[editor’s note, 528]* caregivers of prostate cancer patients. There's a lot to unpack here, and I know we'll send the link out to this video to sort of look at all of the many nuances and research that was sort of pulled out of this study.

But some of the highlights were, about half of these caregivers are females. The mean age is about 47, and about two-thirds of the caregivers live with the patients. And when we look at some of the stresses on the caregivers, about 50%, especially in patients with metastatic disease, either had to change their job or quit their job to help with their–with the patient. This may be driving to appointments. This may be activities of daily living, such as getting to the bathroom, cleaning, etc. But it really can be a huge, not only time commitment, but, you know, from a financial standpoint, as well.

You know, looking at some of the other things that were pulled out of this survey, a lot of the caregivers come to these appointments because they want to hear things that the physician, saying that the patient may miss. They want to advocate. What's one of the most interesting points was that the caregiver is 4 times more likely to talk about adverse events taking a medication than the patient is themselves.

And I think, so, this is really showing that as the patient, we may be shy to talk about it. But the caregiver is going to be right there. And really, you know, telling the healthcare provider what's really going on. I think the other interesting thing is that [the] majority of caregivers and patients have a very beneficial relationship. I think that was important, as well. You know, there's a lot of stress in these relationships. But it's very mutually rewarding, I would say.

And I think the final point on this survey–and again, there's a lot more information than what I'm just talking about right now– but is, how do caregivers want to get their information? Number one is getting to the doctor's appointment. Then there's a big push for social media. So Youtube, Facebook, they're doing their own research. And really, another really important take-home is

how to deal with stress and mental health in their own lives, associated with all this stuff going on. So I was delighted to be a part of this study. I think the link will be very helpful for people to look additional stuff we looked at, but you know, sort of a jumping-off point as to where we go from here for sure.

Phillip J. Koo, MD: You know, I think those are all great points. And we know it, but being able to sort of identify the impact that it has on, you know, not just the patient. But, you know, the community and the people surrounding the patient really helps us identify ways in which we can then start impacting care more effectively.

So I really appreciate, you know, the time and effort that it took to sort of conduct this survey and then analyze it more scientifically. So then, from your perspective, where do we go next? What's sort of the next step to this to sort of maximize that impact?

Zachary Klaassen, MD, MSc: I think it's it's all about implementing, getting information and resources to the caregivers. Now, whether this is support groups at cancer centers–I know PCF has some additional resources as well, which I know we'll link to this, too. But also, you know, every little nugget of information is another opportunity to intervene.

You know I talked about that, caregivers are 4 times more likely to discuss adverse events, and so I think, empowering caregivers and having that information, and also understanding that the physicians need to know this, too, they need to ask the caregiver what's going on. So there's a lot of implementation just at the grassroots level of both from the patient, the caregiver, and the healthcare provider to make this all work, because I think there's a lot of interesting and important stuff that came out of this study.

Phillip J. Koo, MD: Great. So you know, as Zach mentioned, we'll have an email that goes out with more links to more information and also resources for those who are looking for more resources to help with caregiver support.

So we're going to shift gears a little. So oftentimes when patients get diagnosed with prostate cancer, or they're undergoing treatment, we focus a lot on the actual treatments themselves, but a question that I guess get asked very often is, “What can I do besides that, to help improve my outcomes?” And there was some data presented on this idea of “prehabilitation.” So what is prehabilitation? And what does that mean for patients?

Zachary Klaassen, MD, MSc: Yeah, it's interesting. It's kind of a new word. It comes from rehabilitation. And so we think of rehabilitation as what do we do after something's been done, such as a surgery, or going through chemotherapy or going through hormone therapy. How do we get better after that's done? That's the rehabilitation.

So there's been a lot of great work, a lot of it led by Sarah Psutka, who's a urological oncologist and a dear friend of mine up at the University of Washington, and she spoke about this at the European meeting. And a lot of this comes out of the bladder cancer literature, because when

we take out bladders and we put patients through treatment, it's really debilitating. That whole aspect and certainly prostate cancer is no different in terms of some of the surgeries and the chemotherapies and the hormone therapies that people are on, and really what it comes down to prehab is getting yourself at your best, as you're getting ready for a big intervention. Whether that be surgery, chemo, hormonal therapy, radiation, etc.

And there's a lot of different ways we can sort of put this together. I think that the main things for the listeners is exercise is absolutely important. Whether that is going for a walk for ten minutes, moving it to twenty minutes whether–if you're already in shape, going for a twenty-minute run or thirty-minute run, sort of taking what your baseline is and starting to build on that. I think exercise, and Sarah definitely reiterated this in her presentation as well, there's no substitute for exercise for both the patients and everybody in general.

I think the other thing is, you know, some more actionable things, you know, smoking cessation is very, very important. And that's key for anybody undergoing anesthesia, anybody getting chemotherapy. All these things have more complications in people that are actively smoking.

You know, there's some really fancy stuff looking at digital tools to sort of track this, I think that's cool. But for the majority of patients, we don't need digital tools. We just got to have a plan. This may be resistance training, especially for people that are starting hormone therapy. We know there's bone mineral density issues, muscle loss with hormone therapy. So any resistance training, whether that's band workouts or light weights, weights, or swimming, aerobics, all these sorts of things to get yourself to where you're going to be at your peak performance, and that's different for everybody, before this intervention happens.

Phillip J. Koo, MD: That's great. So this idea of getting you into peak performance and ready to sort of deal with what might lie ahead. You know, can you talk a little bit about nutrition? Any sort of quick advice that you have with regards to nutrition, when it comes to sort of this idea of “prehabbing.”

Zachary Klaassen, MD, MSc: Yeah, absolutely. I think, you know, water intake is always key. I think, you know, the more water we drink, the better we feel. That's certainly part of the nutrition. But I think when we talk–when I talk to patients in the clinic about upcoming surgeries or upcoming interventions, and they say, “What can I do?” I always mention exercise, but to your point with diet, I think if we all focused on a heart-healthy diet, if we're lucky, that helps our prostate cancer treatment, maybe helps our prostate cancer prognosis.

But without a doubt it helps our heart health. And I think I never take a minute to not mention cardiovascular mortality is still number one in this country. It's still the number one cause of mortality among prostate cancer survivors. So anything we're doing that's good for our heart, lean meats, vegetables, fruits, water, etc, is going to be good for our overall health, and hopefully, even our prostate cancer health as well.

Phillip J. Koo, MD: You know. That's a great message. And patients and their caregivers. You could–you can control that diet, that exercise, nutrition. So you know, do your best, and I think you'll set yourself up for the greatest degree of success afterwards.

Zachary Klaassen, MD, MSc: Yep.

Phillip J. Koo, MD: All right. So you know–and also I just want to highlight, I love the fact that you talk about your friends. We talk about other institutions. And that's important, you know, in the world of medicine, it's a community. And when we go to these meetings, we're able to interact with long, dear friends who are also passionate and mission-driven, where we can share common interests around, you know, ending the pain and suffering and death around prostate cancer. And it really leads to a lot of meaningful work and raises sort of the level of purpose that we all have, which I think continues to drive us in this very collaborative environment. So I really appreciate that comment.

Zachary Klaassen, MD, MSc: Yep.

Phillip J. Koo, MD: All right. We're going to shift gears a little. So Pluvicto is a new–is a drug that's been around for a couple of years. It's a radiopharmaceutical. We've seen ads about it on television. Most recently, the pool of patients that are eligible for this drug have increased, which is great.

But obviously it's not meant for everyone. It's meant for certain populations. But it's nice to see data continuing to come out regarding this treatment. And one of the pieces of data–one of the areas is around quality of life. What impact does this drug have on quality of life? Because that's, in many ways, just as important as that drug has on the disease. So can you tell us a little bit more about what we learned about quality of life? First off, how do we define quality of life? And what do we learn about quality of life with this drug?

Zachary Klaassen, MD, MSc: Yeah, absolutely. I think–just to give you a little more background–as you mentioned, Pluvicto has been around for a couple years based off the VISION trial. And this was men with mCRPC. So metastatic castration resistant prostate cancer, who had received an ARPI *[editor's note: Androgen Receptor Pathway Inhibitor]*. So this may have been darolutamide, apalutamide, abiraterone, enzalutamide, as well as a chemotherapy, so either docetaxel or cabazitaxel, who then had a PSMA PET scan that had lesions that were visible, they were then eligible for Pluvicto. The most recent data was presented at ESMO 2024, called the PSMAfore study, and that was exactly the same type of men, but without chemotherapy beforehand. So we're sort of moving it a little bit more upstream in that mCRPC disease space.

And so what's exciting is that, as both of us know, and we'll share with our listeners, and they probably know as well, that at the end of March, we now have FDA approval in that new disease space of pre-chemotherapy for mCRPC for Pluvicto. And what's important, as you mentioned, quality of life is a huge aspect of my practice, because we all want to extend quantity of life.

But we also want to do that with the highest degree of quality of life. And so a lot of these big trials will certainly look at oncological efficacy of the treatment, but they'll also collect different metrics of what the patient's reporting, and I think this is important to sort of balance out. How much are we gaining? But at what cost to the patient's quality of life?

And so Dr. Neal Shore, at AUA a couple of weeks ago, presented the quality, some of the quality of life data for PSMAfore, which was that second trial we talked about. What's interesting is that in this pre-chemotherapy space, not only are we having improvement in radiographic progression-free survival, which means the disease is not progressing on imaging, but it also improved time to pain–and also improved people that had pain, it got better. And I think that's important.

Another aspect in terms of that is the time to symptomatic skeletal-related events. And this is something that is a devastating event if it happens, and this is fracture, spinal cord compression, along those lines, from bone metastases. And this treatment also delayed time to that as well.

And so we're seeing that on top of people living longer and having disease–less disease progression, it's also improving pain in the people that have pain and decreasing the time to pain in those that don't have pain at the time of the trial. So we're seeing that combination, which is really encouraging, because, again, we want to improve quantity of life. But we also want to keep or improve quality of life as well.

Phillip J. Koo, MD: You know, that's a real encouraging message, and I think it provides, you know, even more optimism. You know, if a drug is actually becoming more effective, it's actually helping you live longer, helping you, you know, delay the time to which the disease progresses, and you–the way in which you can go about your life and go about your normal daily living is real encouraging. So just, you know, for the listeners out there, how is it measured? How is it sort of studied? And how do we know that it, you know, it is a real finding?

Zachary Klaassen, MD, MSc: Great, great point, you know, when people get enrolled in these trials, they do it–they do a baseline collection of data. So this is everything from all the demographic stuff, the prostate cancer aspects, but also they'll give them surveys. And these are validated tools to sort of assess quality of life.

And this would–this ranges from, you know, pain, physical activity, emotional, spiritual, sexual. All of these metrics are collected at baseline, and then they're collected at certain time points throughout the trial, usually every three months, give or take, on the trial. But then these are compared between the treatment groups and the control groups, and sort of delineating what changes are happening, not just at baseline, but over the course of that trial.

Phillip J. Koo, MD: Yeah, that's great. So you know, if there are any listeners out there who have been involved in trials, and even if you're not involved in trials, I think it's, you know, this is really good message. To be honest and open with your provider team with regards to what you're

feeling and what's happening. And as you mentioned earlier, the caregivers are often the ones who bring this to light. But you know, patients need to sort of be honest and upfront as well, because this really has an impact on your treatment course.

All right. So we're going to shift gears now to talk–a little earlier, from CRPC, so now we're going to talk about patients who are still hormone-sensitive. You know, their disease is still reacting to the hormones and being treated by it. And we heard a lot of data being presented about drugs in this space.

First off, can you talk a little bit–just boil it down for us at a simple level about what this metastatic hormone-sensitive space is, and what we learned about how we treat patients in that space.

Zachary Klaassen, MD, MSc: Yeah. Great great jumping off point, Phil. You know, there's sort of two buckets that metastatic hormone-sensitive prostate cancer falls into. The most common one is, people come in for a first visit, and they're diagnosed with prostate cancer that spread outside the prostate cancer. We call that de novo metastatic hormone-sensitive prostate cancer. Roughly, about three quarters of the patients are in that bucket. Roughly, about one quarter of those patients are what we call “recurrent” or “metachronous,” another word for recurrent metastatic hormone-sensitive prostate cancer. These are patients that have had therapy to their prostate gland, whether it was removed for surgery, treated with radiation therapy, etc.

And they've now recurred, and they now have disease outside the prostate, or where the prostate used to be in other organs, such as the bone or the lymph nodes. So when we look at those patients, they all kind of grouped under this umbrella of metastatic hormone-sensitive prostate cancer, which means they have not seen ADT, such as Lupron, Orgovyx, some of the patients may be on these medicines that are listening.

And so the story of mHSPC, is what we call it, is really the last ten years has been remarkable. We started with just giving ADT. And then we had trials in 2015 and 16 that said if we add docetaxel, which is chemotherapy, to ADT, that does better than ADT alone. Fast forward another five years, sort of late 2018, 2019, we start getting these what we call “second generation androgen receptor pathway inhibitors,” such as enzalutamide, apalutamide abiraterone, combining those with ADT did better than ADT alone. So we have what's called “the doublet therapies.”

And then fast forward another three years to about two years ago. We now have what we call “triplet therapy.” So this is combining ADT, another ARPI called darolutamide plus docetaxel, which is better than docetaxel plus ADT.

And then another study looking at ADT, docetaxel, and abiraterone did better than the ADT plus docetaxel alone. So we have gone from monotherapy, which is ADT, to doublet therapy, to triplet therapy, and really the conversation is, who's a candidate for doublet versus triplet, and that's really what we've been looking at the last couple of years. And so what was presented first at

the European meeting last year was this new trial called ARANOTE. And ARANOTE is sort of the fourth study looking at that doublet of darolutamide plus ADT versus ADT alone.

And not surprisingly, it was a 46% improvement in radiographic progression-free survival. And so now we have several options in doublet. We have several options in triplet, and it's kind of figuring out who fits what profile, whether they're chemotherapy fit, whether they should benefit from chemotherapy or not.

Phillip J. Koo, MD: You know, that was a great explanation, and I think it really, you know, shows that in patients who have metastatic disease, whether it was de novo or recurrent, whatever path it comes from, that we need to be more aggressive and sort of this idea of treating patients with more drugs actually will lead to better outcomes for those patients. What's a little concerning, though, is when you look at real world data is, you actually see how it's being implemented in the, you know, at various sites.

There's still a lot of patients who might be on just one treatment–only ADT. And we know now that that is not the optimal care. So can you talk to us a little bit about that and what's going on? Why aren't people, you know, getting the appropriate care?

Zachary Klaassen, MD, MSc: Yeah, it's a really tough question. We could probably spend another 30-minute webinar on that topic alone. But I'll synthesize it down to this, I think, for the majority of patients, 98%, 99%, ADT plus something else is the standard of care. There may be that 1% where they have really bad comorbidities. They're really elderly where that doublet therapy may not be the right option, but for the majority, overwhelming majority, treatment intensification is important.

To answer your question about why it's not happening, I think there's a lot of factors. I don't think anybody's fully put their finger on how to fix all of this. But it's gone from about 50% of patients getting treatment intensified about 5 years ago. Some of the more recent data is up to 70% to 80%, so I think we're getting better. That 20% is that gap that's really difficult.

Whether this is, you know, payer-related, coverage-related may be part of it. Whether it's just somebody that's not keeping up with the literature as much as, you know, the people on the line and folks that go to all these meetings. There's a lot of potential hypotheses as to where that 20% still is falling through the cracks, but I think, encouragingly, it is getting better. [Clears throat] Excuse me, it's not perfect yet, but certainly it is getting better.

Phillip J. Koo, MD: You know, I think that's a great take home message for patients is, you know, patients becoming educated and taking power and being informed about their care really can make a difference. And yes, there are going to be exceptions. But you know, patients who have metastatic disease–disease outside the prostate should be getting more than just one anti-hormonal drug. So that's great to know.

You talked about sort of these doublets and triplets. Even within these doublets and triplets, we have multiple different options for the type of what we call “ARPI drugs” that you could use. You know, abiraterone, enzalutamide, darolutamide, and whatnot. How do you decide which one gets combined?

Zachary Klaassen, MD, MSc: Yeah, it's a great question. There's never been a head-to-head trial. So when we look at these options, we can't say one's better than the other, what it typically comes down to–and they all work very well. So I think the message is, the doublets work great, no matter which one you're on. There's a few nuances in terms of side effect profiles with some of these, so that may come into it a little bit.

There's some drugs that are a little bit better or easier to use in combination with other medicines, that many of these men are on, such as antithrombotics or blood thinners or cholesterol medicine, so that may come into a little bit as well, too.

And then it's probably a little bit just what the physician's preferences are. I think that's fair as well. They have more experience with one versus the other, they may be a little more apt to use it. The answer is, there's no head-to-head trial, so we can't say one's better. But there's nuances to say, “Maybe this patient's a little bit better for this treatment versus this treatment.”

Phillip J. Koo, MD: Great, and I think that's a conversation that you know patients should have with their physician. And then, you know, there's always a lot of debate about who gets a doublet versus who gets a triplet. And you know there's data. But it's interesting. When you hear these debates, you could hear both sides, and even for physicians who are discussing this, I walk away, and I'm like, “there's no clear answer here, and no simple answer.”

Kind of boil it down–sort of make it easy for us, you know, who in general might get a triplet who might get a doublet?

Zachary Klaassen, MD, MSc: I think in general, you know, there's this conversation we haven't touched on yet about high-volume or low-volume disease, and there's a lot of different ways to measure that, probably beyond the scope of this conversation. But in a patient, say they had their prostate removed or they had radiation.

They've now ten years past that, and they've got some disease outside the prostate. That's a low-volume recurrent patient. That patient's probably going to do just fine with doublet therapy, whichever one you want to choose.

I think that as we look at deciding between the two, one–the patient has to be chemotherapy fit. What that means is that their performance status has to be adequate to undergo chemotherapy. This is six cycles of chemotherapy. This is not chemotherapy forever, or chemotherapy till the disease progresses. It's six cycles, but it's still a hard four or five months of treatment.

So to be fit, you have to be active enough and have the performance status. The kidney function has to be adequate. You have to have adequate hearing. You know, the heart has to be in good shape. All these things that medical oncology team will look at before they think about chemotherapy.

I think the triplet therapy patient, especially in my practice in the Southeast, is still that young patient that shows up–PSA of 3 or 400–that has high-volume disease. That patient we want to hit–that we want to hit that cancer as hard as we can, and we hit it three different ways. We hit it with the hormone therapy. We hit it with the darolutamide, that second-generation ARPI, and we hit it with the docetaxel. And I think that we saw, especially at EAU and AUA, and to summarize some of that sort of post-trial data that was presented, is we want to get that PSA as low as possible as quickly as possible.

So if we're starting at 300, we don't want that PSA to go to 5. We want it to go to less than 0.2, and, in fact, Neal Shore presented at AUA, less than 0.2 even makes a difference. So the goal is hit it hard. Get that PSA down as low as possible, as quickly as possible. And that means that we're hopefully going to be able to stay on these medications and have benefit for a long time.

Phillip J. Koo, MD: You know that's great, and hit it hard for those right patients. And then it sort of ties back to what we talked about earlier. If you are going to undergo some of these treatments, you know that prehab, being in the best shape possible eating well, really will make a difference in how you can tolerate and get through those treatments, because we know, if you get through it, you have this benefit that we've shown in these different studies.

So this is wonderful. I really think it helped explain a lot of things for our listeners, and what's exciting is, now we have ASCO coming up. You know, the largest oncology meeting multidisciplinary at the end of May and June in Chicago. And then we have other future meetings where we're going to be able to continue to fill in these gaps and learn even more and more about how we best treat these patients with all these different treatments that we have now available. So really appreciate your time, Zach, and we look forward to having you back to help educate us more and see where we're going next.

Zachary Klaassen, MD, MSc: Pleasure is mine, as always, Phil, and Becky, and the PCF group. It's always fun having 453 people listening as well. It shows that they're interested in what's going on. We certainly get excited. ASCO is one of the best meetings. It has a lot of big trial data that always comes out. So we're excited to learn about it and talk about it and bring it back for our patients.

Phillip J. Koo, MD: Wonderful. Thank you. Zach.

Zachary Klaassen, MD, MSc: Thank you.