Ask Me Anything About Prostate Cancer– 8/26/25

Dr. Phillip Koo [00:00:00] Pleasure and honor to be here today because this - you know this type of format really comes from all of you know - given all the various webinars we've done over you know the years, we see so many wonderful questions come in. And unfortunately we don't have the time to get to all of them and just given the engagement that we've had from the entire community, we thought it made a lot of sense to put it all together, find certain common themes and be able to address them for of you.

What we're seeing is a very clear shift in how care is being delivered. You know, we really like the fact that care is more patient-centered today, but what's even more important is that patients are now in control of their care. And it's important in order to make sure that goes well, that patients be informed and educated about the various disease states so that they can make the best decisions. And there are a lot of resources out there, and obviously this is one of them, but we're going to hopefully empower all of you through this type of education.

So, before we get started, I know there's lots of resources out there. There are a couple of resources and sort of a couple certain ways in which I think patients can get information. And Zach, I did want you to highlight something called Prostate Cancer Patient Voices. So, could you tell us a little bit about what that is?

Dr. Zachary Klaassen [00:01:16] Yeah, thanks so much, Phil. Great to be on with these great panelists, and again, for all the phenomenal questions that are rolled in from the patients and their caregivers.

Prostate Cancer Patient Voices has been around for a couple of years. It's essentially hosted by Prostate Cancer Foundation, and with generous industry support, we've been able to put together a really, really important website. We often battle in the clinic with sending people to reputable websites, and there's plenty of them out there. NCI, American Cancer Society, but really something focused for patients with prostate cancer and not only focused on that but written for the patient level. So, we have several sorts of iterations on this website. There's sort of a written content, which is written at the level of a patient or their family member, such as what is a PSA, what is a Gleason score, what's a multi-parametric MRI, all the way up to advanced prostate cancer.

And then what's really interesting and really important is a video series from the patients and their caregivers. And I think people can listen to all of what we have to say about what they're going to go through, but to hear it from people and caregivers that have actually gone through it, whether it be radiation, surgery, hormone therapy, etc., the side effects of treatment, that resource from the patient side and the video content is just incredible. So that's a little brief highlight of what that website is. I use it all the time. And I've been fortunate and maybe some of my patients are listening to, they've contributed to that as well. And it just is a valuable resource.

Dr. Phillip Koo [00:02:48] Great, thank you, Zach. So, Angela, what's sort of your approach to being able to educate patients in your clinic?

Dr. Angela Jia [00:02:55] Yeah, absolutely, thanks so much. So, you know, as a radiation oncologist, most of the time when a patient comes and sees me, they don't know what radiation is. It's very much a black box and it's a great opportunity to teach, not just how we treat prostate cancer, but what is radiation. And so, a lot of our kind of patient

teachings are done in clinic at the time of me meeting the patient. I have a really good team. My nursing partner does a lot of teachings of how do you prepare for radiation, you know, your bladder, your bowel, etc.

We also, so I'm in Cleveland, Ohio, and in Ohio, we have something called The Gathering Place, which is a lovely community center. It's several different locations in Cleveland. Completely free. It's for patients with cancer and their caregivers. There's a large prostate cancer population there, and they're always hosting kind of webinars, seminars, where faculty come and chat to answer any patient questions. And so that's a resource that we have as well. That's kind of specific to my region. And I actually refer them to Prostate Cancer Foundation, the website. There are great videos there for patients to see, you know, everybody, we all have similar questions, and you can see what's been asked before. So, to summarize, in my clinic when I meet them, The Gathering Place and also PCF.

Dr. Phillip Koo [00:04:32] That's great, you know, radiation often comes, you know, with a lot of sorts of preconceptions, preconceived ideas on what it is. And I think it is really important to learn about that. So, Karine, you're a medical oncologist, oftentimes we associate medical oncologists with chemotherapies that sort of has a certain, you know, ring to it or people have thoughts about that. But there's also other types of drugs. How do you approach educating patients in your clinic?

Dr. Karine Tawagi [00:04:57] Yeah, that's a great question. And thank you for having me today. So, I think, you know, one of the misconceptions like you talked about is that as medical oncologists we're the chemo doctors, but you know really we are, in prostate cancer, there are a lot more therapies beyond chemotherapies. So, you know hormone therapy - which we're going to dive into more during the course of this webinar - is our mainstay of prostate cancer treatment when we think about drug treatment for prostate cancer. So, it's one of the resources, actually PCF has a lot of really great patient resources, and then Chemocare.com has specific info per drug. Although some of the drugs are not chemo, as we mentioned, a lot of them are hormone therapies and then the American cancer society.

But you know, I always print out documents in terms of the medication, how it's taken, is it an oral, is an injection, is it IV? And then the main side effects for patients when they start a new treatment. And if you are seeing your provider and you're not clear, you can absolutely ask them to print out information on the drug. That is definitely something that any oncologist can do for you when you see them in clinic.

Dr. Phillip Koo [00:06:07] Great, so lots of resources online. Make sure you go to credible resources online because we don't want any patients to be misinformed.

All right, so once you get a diagnosis of prostate cancer, oftentimes you're thinking about prognosis. How many days, how many years, months? What's sort of my timeline look like? I think it's a really tricky question, but I think each of you sort of has a different perspective on this because your approach, and your perspectives on this obviously are going to be very different.

Zach, I'm going to start with you as a urologist. You know, you often do surgery, you get this question all the time. What advice do you have patients regarding prognosis?

Dr. Zachary Klaassen [00:06:41] Yeah, I think, Phil, it's a great question. If we look at diagnosis of prostate cancer, nobody wants to hear that diagnosis. No matter whether it's low grade, intermediate grade, high risk, you have time to get the information. I think that's a really important take home point. You know, when we think about even aggressive prostate cancer compared to pancreatic cancer or really aggressive lung cancer, even bladder cancer, even in its aggressive form, prostate cancer is not as fast moving as some of the other ones that are sort of common out there. And I think I say that to the patient just to say, let's take a deep breath. Let's step back. Let's get the information. Are you a candidate for surgery or radiation? We need you to go talk to Dr. Jia and her colleagues. Get the information so you understand not only what the options are, what the side effect profile is. And so, we really focus that first discussion on taking a deep breath, taking a step back, meeting with all the people, making an educated decision with your patient, your family. And oftentimes that's followed up with a follow-up within two to four weeks once those consults are done. I think with prostate cancer, it's easy to jump right into a treatment option. But when there are multiple options, I think it's important to have those discussions so that the patient and their family is really informed about not just cures, but also side effects.

Dr. Phillip Koo [00:07:59] So a follow-up question, you know, cure is obviously someone who doesn't have the disease anymore, and at least from my perspective, has no chance of having the disease down the road as well or recurring. Do you use, because this question has come up a few times, do you use the term cure in your clinic? And if so, in what situations do you say cure?

Dr. Zachary Klaassen [00:08:18] Yeah, it's a great question. Everybody wants to have the word cure associated with their prostate cancer diagnosis. I think in localized prostate cancer, we can cure prostate cancer. Having said that, we still follow their PSAs for many, many years, even on an annual basis. And then every occasionally we'll see a PSA start to go up a little bit after five or 10 years. I think there's a possibility of curing prostate cancer in the localized setting. I think we have to have additional follow-up over periods of a long time to get to that point. But I basically tell them once we're done the treatment and we get PSAs that are undetectable, whether that be surgery or whether they're decreasing with radiation, we want to put this in the rear-view window. So, it becomes like a chronic thing that you're checking your blood pressure every six months. You're checking your sugar, you're checking your lipids. I want it to be part of the story, but not the forefront. I think cure is always a tricky term to use. We have to be a little bit careful with that, but certainly that's our goal. In that localized setting.

Dr. Phillip Koo [00:09:17] Great, so Angela, for you, obviously you use radiation to treat it and oftentimes it's definitive, you know, hopefully you eradicate the disease. So how do you deal with the question of prognosis, what advice do you have for patients? And same question, how do approach using the word cure?

Dr. Angela Jia [00:09:34] That's a fantastic question. I agree with everything Dr. Klaassen just mentioned. In prostate cancer, it's such a wide spectrum of disease. I tell my patients about one in eight men get it. And oftentimes, you die with the disease, not of the disease. And so, there are many diseases, low risk setting, where we're advocating for active surveillance. It doesn't mean I never see you again. It means we watch that PSA. You're following with urology like Dr. Klaassen, making sure you get another prostate biopsy that you're following appropriately, but that many of those men don't ever need treatment for the rest of their lives. And then so you're essentially, are you cured of the cancer even though you're living with it, but it's never going to do anything? So, I agree that the word

cure is a little bit tricky, the way I kind of described my patients exactly as Dr. Klaassen said, you know. Cure, I think of, you know, getting a urinary tract infection. You're cured of it, meaning you took the antibiotics, you never have to think about it again, and you never have to check it again.

Prostate cancer, even after you treat it, you're still monitoring, you're checking that blood work, that PSA, right? And when it is no longer localized, say it has spread, you, know, spread to the lymph nodes or spread somewhere else. Just like Dr. Klaassen said, fortunately, this is not. You know, a GBM, a glioblastoma of the brain or pancreatic cancer, cancers that go at a very rapid pace. Even if it has spread a lot of times, I tell my patients, you know, we're managing this. It doesn't mean I can cure you, doesn't mean I completely get rid of it, but you, you may be on systemic treatment and we're managing it. Like kind of like how I can't cure you of your diabetes, but you're going to take metformin for it, or I can't cure you of your high blood pressure, but you're going to take something for it and we're managing it, right?

Dr. Phillip Koo [00:11:28] Great, so, Karine, you know, you often see patients when they're diagnosed with metastatic disease, when the disease gets outside of the prostate, they might come see you. And in that space, you know, there's a lot of decisions that need to be made, a lot of different options. How do you, what advice do you have for patients with regards to how they should make decisions on their treatment?

Dr. Karine Tawagi [00:11:52] So, that's a great question. I think the first step is, you know, do they have symptoms from where the cancer has spread? So metastatic means the cancer spread from where it started, whether it's to lymph nodes or to another organ.

So, the first question is, are they having symptoms? The second question is, is this new cancer, meaning it presented as a stage four or metastatic cancer, or is it a cancer that was initially treated and now has come back?

The fourth thing that we think about is what is the volume of the cancer? Is it in a lot of places in the body? Is it in a lot bones? Bones being the most common place that the cancer can spread as far as another organ.

And then we really have to think about other medical problems that a patient might have. Do, you know, what's their activity level? Do they have diabetes, do they have heart disease? And all of those things go into the consideration of someone with a new diagnosis of stage four prostate cancer.

So, I think first and foremost, hormone treatment is sort of the baseline of all stage four prostate cancer treatment. And I think we'll dive into that in more detail, but that might be the first step. And then for some patients, adding chemotherapy makes sense. And we can talk more about what kind of patients may need chemotherapy. And then there are, of course, clinical trials. And then, there are some patients with stage four or metastatic disease where they only have a few spots. And so, for some of those patients, they're called oligometastatic, meaning a limited number of metastatic or spread to other organs or sites. And some of those patients can be treated with a combination of surgery or radiation, and it really involves a multidisciplinary team like we have on this webinar here today.

Dr. Phillip Koo [00:13:39] Great. So, thank you. So, you know, I think it gets pretty complicated. Sometimes being informed, educated will go a long way towards being able

to write, make the right decision. So, we're going to dive sort of straight into some more specific questions and one question that comes up is, you, know, the use of PSMA PET. And this is something I think we've spoken a lot about PSMA PET. But this is an interesting question about PSMA PET and its ability to detect the primary lesion, you know, perhaps if the MRI is negative.

Zach, your thoughts on that. How often have you ordered that in that setting and what are your thoughts on getting a PSMA PET to localize the primary lesion?

Dr. Zachary Klaassen [00:14:17] Yeah, it's interesting. I think there's some really fascinating trials going on right now looking at correlations between MRI, PSMA PET, lesions in the prostate and then corresponding those with what it looks like after we take the prostate out. So, I tend to think in 2025, I still think of it as PSMA is telling me a little bit more about what's going on outside the prostate, lymph nodes, bones, etc. Can you sometimes see prostate cancer in the prostate on PSMA PET? Sure. But I think MRI is really at this point still a little bit better in my opinion, of really getting the localization of those lesions. But I think this is a very active field. I think we're going to see a lot of activity in terms of what is the best and how we can use them together probably in localizing prostate cancer in the prostate itself.

Dr. Phillip Koo [00:15:07] Great, so that's really helpful. So just sort of to tack onto that, let's say you get a patient who has an elevated PSA, they get an MRI of the prostate, and the MRI shows nothing. What do you do then? Do you still recommend the biopsy because of the elevated PSA?

Dr. Zachary Klaassen [00:15:24] Yeah, this is something we see quite often, Phil. I think, you know, when you look at the data that's almost seven, eight years old now, some of these trials were published in the New England Journal of Medicine, really informing how we use multi-parametric MRI in the localized setting. And the consensus sort of wrap all that together is even if the MRI is perfectly normal and the PSA is indicative of a prostate biopsy may be needed, there's still a 10, 15, maybe 20% chance that there's clinically significant prostate cancer, which means prostate cancer that probably will need treatment.
So, I tell them, listen, it's good that we didn't find anything. Your PSA is still, let's say, 8 or 10 or 12. I think we should still do the biopsy. It may mean we're not targeting anything specifically, but we're going to do our systematic sort of 12- to 16-core biopsy regardless. So, I think the take home is, it's good news that it's not, there's not a lesion, but, you know, there's still 10 to 20% of patients will have prostate cancer that needs to be treated even without the MRI showing something.

Dr. Phillip Koo [00:16:21] Great. Angela, you do a lot of your research in the biomarker space. It's a really complicated topic regarding biomarkers, whether blood, urine or whatnot. In the pre-diagnosis space, what advice do you have for patients regarding those biomarkers?

Dr. Angela Jia [00:16:42] Yeah. So, you know, before a diagnosis is made, meaning before you have confirmation that there indeed is cancer in the prostate, the best we have is the PSA. That's the prostate specific antigen. And I like to tell my patients that's like your canary in the gold mine. Like when you go down to the goldmine, you bring the little yellow bird with you. And if anything's going on, that's wrong. The bird, something will happen to the bird first. So, the PSA, that's our indication. And it's a relatively, you know, straightforward blood test. It's not terribly invasive. And so just to tag on to, you know, what

Dr. Klaassen was saying, you know, if let's say the PSA was up and the MRI didn't show anything, I would not move to a PSMA PET right away. I would ask for urology to please do a prostate biopsy. You should have a diagnosis first because, you know, there are also reasons sometimes a PSA is high because of an infection of the prostate, right? That's not cancer. And so, that was my specific point on that question, but in general, it's the PSA. In the localized setting, it's the PSA that you're looking at

Dr. Phillip Koo [00:17:58] So, you know, now we have a patient who's undergoing, who needs a biopsy and gets a biopsy done. There's always this question of, how should the biopsy be performed? There is a way to go through the rectum and sample the prostate. Then there's a way to go the perineum and sample of the prostate, then the question comes up, how many samples do they need to get? Really confusing for all of us. Zach, break it down for us as a person who does these biopsies.

Dr. Zachary Klaassen [00:18:22] Yeah, I think there's a lot of interest in how to do this and patients certainly ask a lot of questions about it. There's no perfect answer, but the way I'll summarize it and how I think about it and how I do it in my practice is, historically, we've done transrectal biopsy. It can be done easily through a rectal probe showing us the prostate. The prostate sits right adjacent to the rectum and we're able to pass a needle through a guide and obtain 12 or so cores in sort of a systematic fashion. And at most, there's a lot of prostate cancer diagnosed from that type of biopsy.

There's always reasons that transperineal has had some uptake. And I think the two main ones are that there's always an infection risk passing a needle through the rectum. Now that infection risk is not super high. It's probably about one in 300 patients may need IV antibiotics after a prostate biopsy, but it's still there. I think the transperineal aspect, you're not going through the rectum, you are going through the area between the bottom of the scrotum and the anus, which is right where the prostate also sits, and you're going directly through the skin into the prostate. So that virtually eliminates any risk. Now there's more setup and there's a more involvement to get a transperineal biopsy than maybe a transrectal biopsies, so there's logistic issues sometimes perhaps for doing that. Equipment wise, it's a little bit different.

The other reason to do a transperineal biopsy is if you've had a transrectal biopsy, maybe there's no cancer on that, but there's an MRI that shows maybe there is a tumor at the apex of the prostate. And this is right close to the urinary sphincter. We think of the front of the prostate. That's easier to target from a transperineal approach perhaps than a transrectal. So, it's a difficult question. It's a relatively quick answer, but hopefully that gives a little bit of guidance on the differences and why we do them.

Dr. Phillip Koo [00:20:13] So, would you say, you know, one is better than the other? Would you recommend patients sort of look for one technique?

Dr. Zachary Klaassen [00:20:20] I don't think so. I think you want a physician who's going to more so guide you when you need a prostate biopsy. I think that's more important of a discussion. I think most people these days will offer both and they'll have their reasons for doing one or the other. And so, I think it's more important to find somebody that knows when to do one and what the risks are and explain that - rather than just saying, I need to find somebody that does it this way because most of us do it both ways.

Dr. Phillip Koo [00:20:44] That's great advice. So, sticking on the topic of biopsy. You know, 12 cores, you often sort of do them in just very, you know, regimented areas. And

then there's something called mapping biopsies or whatnot. Sort of, can you explain just quickly what that means and when one might be indicated versus the other?

Dr. Zachary Klaassen [00:21:03] Yeah, so I think one of the reasons we have data and why we try to get an MRI before prostate biopsy, we talked a little bit about what happens when it's clean, there's no lesions. Let's say there's a spot in the prostate, let's say the right side, it's one centimeter. We know that that's an area we want to get a little more tissue. So, we're still going to do our sort of what we call a systematic biopsy where we're hitting all those areas in sort of a segmented way. But we're going to focus on that one spot on the right side and maybe do three or four additional biopsies to that lesion. Because that's telling us that we have an idea what is going on outside that spot, but we're also going to target that spot because the MRI suggests maybe there's prostate cancer in that area.

Dr. Phillip Koo [00:21:45] Great, so we're going to move on to the topic of active surveillance. And for everyone out there, we're not ignoring Karine, but we're going to get to her heavily once we start talking about advanced disease. So, we'll get to Karine. So active surveillance, you know, I think when patients get diagnosed with a Gleason 3 + 3, I think active surveillance is a great option. I think a lot of questions come up when someone might have a 3 + 4 or whatnot. So, Zach, we'll start with you with regards to your recommendations for patients in active surveillance in that sort of 3 + 4 setting.

Dr. Zachary Klaassen [00:22:20] Yeah, we spent a lot of time talking about active surveillance in my clinic. I'm a big fan of active surveillance in appropriate patients because we know the side effects of overtreatment. Overtreatment being we're treating you today with a high risk of side effects with really a low potential benefit of treating the prostate cancer in that moment. And so, I think I'm big fan a 3+3. I think that's something we monitor. We can always intervene at any time. But if we give you three or four years of... Good sexual function, no urinary incontinence, etc. That's a win.

To your question of 3+4, I think this is a really interesting area of active surveillance because there's some men that will be candidates for active surveillance and some that won't be. And I think we use additional tools to sort of figure that out. One of them is if you're 50 years old and excellent health, that may be not an attractive option for a 3+4. If you're 75 or 76 and you've got several comorbidities. Lung issues or heart issues, that may be a reasonable option because the likelihood of that prostate cancer being a problem down the road is a lot lower. So, I think that's one thing we look at, comorbidities, age, goals of care, etc.

The other one we can use, and there's some interesting biomarkers in this space. One of them is called Decipher, and this is a genomic marker. So, we take your biopsy tissue, and it'll tell us, is it low, intermediate, or high risk, and that gives us an idea of what's going on at the tumor level. If it's a low risk Decipher with 3+4, maybe we can watch this with active surveillance for a period of time. If it is higher risk, maybe that's something we don't need to treat necessarily immediately, but it's something that will trigger a treatment a little bit sooner.

And then I think we've got another one as well. Artificial intelligence, we could have a whole webinar on that, but I'll just briefly mention the Artera AI prostate test, which also is kind of in this space and gives us some information from a digital capture of the tumor. And sort of plugging that into an algorithm that tells us whether it's low or intermediate risk. We have genomic markers, which is the genes of the tumor with Decipher, and we have

artificial intelligence, which takes other information, which can be very helpful in this setting of 3+4, should we or should we not do active surveillance.

Dr. Phillip Koo [00:24:29] You know, I think that really reinforces this concept that it's really personal and it's personalized. And, you know, depending on your age, your comorbidities, how you sort of, you're just your overall health, it really informs the decisions, yeah, that you make regarding how aggressive you are. And I think, that's a great take home message. There was a question about, you now, what are the signs that prostate cancer might be spreading in someone who has a Gleason 3 + 3? And I the take home messages there is: just because you're on active surveillance doesn't mean you shouldn't see your doctor. You need to make sure you're following up, getting PSAs and perhaps other testing if needed and being followed closely. You know the term “watchful waiting” is often out there, but I think active surveillance is a better term because it's much more involved. It's not just sitting there and waiting; it's actually monitoring and being followed closely so make sure all the patients on there remember that.

Dr. Zachary Klaassen [00:25:23] So, really quick, I love that way you said it. I think of active surveillance as almost a treatment in a way of we're not, you're on a very strict program. So, it's a form of, I don't want to say treatment because we're doing something, but it is an aggressive monitoring plan. Usually for me, it's PSAs every six months, it's MRIs every two to three years. It's a confirmatory biopsy within about a year after that first biopsy. And then anytime that MRI or PSA gets a little out of what my comfort zone, we may do additional biopsy. So, you're absolutely right. It's much different than waiting for symptoms. It's a very active process.

Dr. Phillip Koo [00:26:03] So, patients who then are diagnosed with prostate cancer, let's say it's a higher grade and they need definitive treatment. They need either the surgery or radiation for the prostate. Oftentimes patients will get radiation. So, Angela, radiation, there's always, there's multiple different types and there's different courses. Just sticking to external beam, SBRT, whatever we want to call it in terms of the number of treatments you should get. What advice do you have there? And how can patients know that it's actually working or not?

Dr. Angela Jia [00:26:33] Fantastic question. So just so everybody's same vocab, external beam radiation means the source of radiation is external to the body, so it's outside of the body. You're not radioactive when you go home. You don't glow in the dark and you don't have special powers. This is different than brachytherapy, right? Brachytherapy is where a radioactive - there's two forms - but the most common form would sometimes people refer to a seed therapy or brachytherapy seeds. That means the radioactive material is actually, it's an invasive procedure, where it's inserted into the prostate itself. It's another way to treat prostate cancer. You would be radioactive right afterwards.

But sticking to the EBRT or external beam that you talked about, when in radiation, the reason we can't do it all in one treatment is that it's too toxic. So, we break it up into bite-sized pieces. We call each piece a fraction. So, you may hear we say, oh, daily fractions. That just literally means daily treatments. And radiation is an outpatient treatment, so you're not hospitalized or anything. It's a non-invasive treatment. You're lying on the table, you're wide awake, and the machine kind of rotates around you while shooting x-rays. That's what radiation is. It's x-ray, so it's high energy light. That is different than protons, which I can talk about. The radiation that's broken up into daily treatments, traditionally what we call conventional fractionation is usually given over like 40 to 44 daily treatments. And so that's coming out to be around maybe nine and a half weeks. We've since then had

many trials and studies to show with better technology now that we have that shorter treatment times. So more on the order of maybe like four to five weeks can produce just as good results with no more added toxicity. And then in these days, we're also having studies showing, you know, in you mentioned 3+4, so kind of intermediate risk group, you can do five treatments, as low as five treatments, we call that ultra hypofractionation.

So conventional fractionation, original nine weeks. Moderate hypofractionation is more like four to five weeks. And then you have the ultra hypo-fractionations which is just five days. And those five days are typically every other day. So, it's not like five weekdays, it's usually comes out to be a week and a half, right? And all of these different regimens are things that your radiation oncologist would kind of describe to you to see which is most appropriate for the patient, depending on you know, the size of the prostate or what are his current baseline symptoms. And then in terms of, sorry, go ahead.

Dr. Phillip Koo [00:29:25] No, no, please, please finish.

Dr. Angela Jia [00:29:27] In terms of how do you know it's working? Well, radiation takes time to work. When Dr. Klaassen puts the prostate in a bucket, you know, it worked because it was removed and then you will check the PSA and the PSA's going to be zero or undetectable because you know prostate's gone.

I previously mentioned the PSAs are canary in the gold mine and there are only two things in the body that make it, right? Your prostate and your prostate cancer. So, after surgery, it's easy to monitor. It ought to be undetectable. And if it's coming back up, it's not that you're growing another prostate, it's that there's likely prostate cancer. Whereas radiation, the prostate still is inside the body. And so oftentimes, and I know we'll talk about hormone therapy, but in the absence of hormone therapy, if it was just radiation on its own, that PSA is going to slowly mosey its way down. Often over like a course of a year, to a year and a half before it hits what we call the lowest point, which is the nadir, the PSA nadir. So, you're simply checking the PSA, like every four to six months after treatment and you're just watching it. As long as it's going down, that's the correct direction. We wouldn't need any more biopsies. We would not need any more imaging. You're just using that blood test to inform you. So, I also like to say radiation is a gift that keeps on giving. So even though you finish your treatments, it doesn't mean the moment you finish all those treatments, everything is done. It actually keeps working inside the body.

Dr. Phillip Koo [00:30:57] So if you could answer this question yes or no, and it may not be possible, but are protons ready for prime time?

Dr. Angela Jia [00:31:03] Great question. It already is kind of in prime time in prostate cancer. So, you know, proton is a different way to deliver that radiation and in certain disease sites, like in children in pediatrics, it is, we use it a lot, because it's very...

Dr. Phillip Koo [00:31:21] But in prostate, is it ready for prime time?

Dr. Angela Jia [00:31:22] In prostate, however, I would say it has not shown to be superior. It has not shown to be better than the photons or the x-rays that I have just been describing. It is a fine modality, it is a fine other option to treat prostate cancer, but it is not any better than x-ray treatment.

Dr. Phillip Koo [00:31:45] Great, that's really helpful. I think that's a great take-home message for all our listeners.

So, we're going to shift to surgery as a definitive treatment. Zach, you know, in the OR, we often talk about, we think about just taking the prostate out surgically is something easy, but what are some other techniques you do to minimize complications like nerve sparing or things like that?

Dr. Zachary Klaassen [00:32:05] Yeah, I think, you know, the prostatectomy or removal of the prostate, it's a very technical procedure. There's a lot of intraoperative steps that can lead to better outcomes for patients. I think you mentioned one of them, nerve sparing. So, we can't typically see the nerves, but we know which course they run along the prostate. And so, we can be very gentle in those areas. We can move them off the prostate and that typically helps with erectile function recovery. When we think about continence, you know urethral length's a big deal. So, when we get to the apex and we're doing the final steps to remove it, we're making sure we're getting a long urethra so we can help with the continence as well. So those are two just sort of basic things we're thinking about in terms of battling those side effects of sexual dysfunction and incontinence. I will say though that this takes a hit on both, no matter how good the operation is. So, if you finish your operation, you have your catheter in for say seven days, you're going to have a little bit of leakage for a period of time, and that may be three or six months. You're going to have a hit to your sexual function as those nerves heal. So, even a perfect technical operation still affects both of these. You're just hoping in the long term that the recovery is better because of a good operation.

Dr. Phillip Koo [00:33:13] Great, so oftentimes we use what we call adjuvant treatments. We might give patients hormones with these different treatments. What's sort of your approach from the surgical perspective with regards to hormones? So, I'll start with you, Zach, and then Angela we'll turn to you.

Dr. Zachary Klaassen [00:33:30] In terms of hormones and surgery, the relationship's not very strong. I think the goal for surgery is, we talked about cure, and we were careful with that term. The goal, at least from my standpoint, and this is a bit controversial amongst the urology colleagues and even radiation oncology, is to try to get that PSA to zero with just surgery alone. And so, we have good imaging with MRI, we have a good staging with PET scans. If I think you're a candidate, I want to take your prostate out if I feel as confident as possible. That we can get your PSA to zero just with an operation. So, I think there's some trials going on in higher risk patients. Can we give hormones up front and other treatments to help that ability to get the PSA to zero? It's not ready for prime time yet. So, it's currently the relationship, I think, between hormones and surgery is pretty weak. We might see it in some high-risk patients as we see data come out.

Dr. Phillip Koo [00:34:17] Great. And in the radiation space, it's a little different. So, Angela, sort of, help clarify that space.

Dr. Angela Jia [00:34:23] Yeah. So, in radiation, we really like to divide people into buckets of risk. So, we would say, you know, when you're speaking to your radiation oncologist or the providers, they may say favorable intermediate risk or unfavorable intermediate risk or high risk. And the general concept is if, you know, surgery alone can cure, cure meaning the PSA doesn't come back up again, and you wouldn't need any other treatment. that's great.

But if there's going to be a high likelihood, you're going to need something afterwards, then we think about, well, maybe not going through the whole surgery and the potential side effects of surgery and just proceeding with radiation [and] hormone therapy. Usually, we

add on hormone therapy as that level of risk gets higher. So, the riskier the disease, kind of the more intense the treatment we do. There's that kind of a distinction between short-term hormone therapy versus long-term hormone therapy. Short- term typically four to six months, long- term, typically 18 months and on, you know, 18 months to maybe even two to three years. And again, that duration depends on the patient's specific risk category. But in general, when we're combining it with radiation, it will be given, you usually start the hormone therapy, you do the radiation kind of in that beginning. And then you'd be on a hormone therapy for a longer time after radiation. So, it's a concurrent, it's at the same time approach.

Dr. Phillip Koo [00:36:00] So we're going to shift gears a little and talk about focal therapy. So, I think there's a lot of, if you Google this, there's lot of different techniques, microwaves, ultrasounds, a lot of different ways to do focal therapy, Zach, really quickly, what's sort of the big picture on focal therapies and just briefly, who should be getting them?

Dr. Zachary Klaassen [00:36:18] Yeah, it's a really important topic, Phil, because there's a lot of, there's a clear indication in sort of who's a good candidate and there's a lot of people doing it for, probably not the best indications. I think to answer your question, the best candidate for focal therapy is somebody who has an MRI, it shows a spot, a lesion, on the MRI that's then targeted with the biopsy confirming typically 3+4 Gleason or 4+3, and then just that spot is treated with exactly what you said. Freezing, heat, electricity, lasers, you can pick your one that you want to go with. And then that spot is very carefully evaluated with MRIs and additional PSA follow-up.

I think the one thing I'll add to that, too, is we think of focal therapy as well as bringing somebody back down to an active surveillance candidate. So, let's say you have that spot on the prostate, but maybe there's a couple of cores of Gleason 3+3 on the other side. We treat that spot, we know those 3+3 spots are still there. But now you're an active surveillance candidate. So, I think in the right hands, the right patient selection, focal therapy is great. I think from a marketing standpoint, it's been a little bit out of the box quicker than maybe we expected and maybe used sometimes not in the most appropriate ways, but that's sort of the quick answer to the appropriate patient.

Dr. Phillip Koo [00:37:33] There was a question where if you treated one side with focal therapy and then something pops up on the other side, could you do focal again? Is that something you would recommend?

Dr. Zachary Klaassen [00:37:42] You could. I mean, I think it comes back to the same thing. I know if you treat that one side and let's say two years later you get an MRI, there's a new spot on that other side and there's nothing high risk in the prostate. I think you could easily treat that spot. I think where you get into a bit of a gray zone and probably need a different modality is once you hit that Gleason 4+4 and higher, I think focal therapy really is not appropriate.

Dr. Phillip Koo [00:38:06] So we're going to shift gears a little and talk about biochemical recurrence. So now you treated the prostate, whether you've got radiation or surgery, the PSA goes down and all of a sudden it starts creeping back up. So, we talked about the definition of biochemical recurrence and it's different for someone who's gotten surgery versus someone who has gotten radiation. So, Karine, from your perspective. You know, most of these patients will get or - I would say - all these patients, if they're biochemical

recurrent should get a PSMA PET. What's your approach to this patient and do you sort of have an approach at what level PSA you would order a PSMA PET?

Dr. Karine Tawagi [00:38:45] So I think a few factors, you know, go into the, so I do agree that we would get a PET PSMA, but the decision at which cutoff level, I mean, we know at like very low levels, like under 0.5, it's really hard to detect much on the PET scan. So, I the cutoff upon which to order it really depends on how fast the PSA is going up. And to the points that have been made before it, and to the point that you made, it really depends on whether someone has had radiation or surgery. So, I don't think there's a specific cutoff. I think I take into account the whole history, how high risk was the prostate cancer initially? Did they have surgery or radiation with those cutoffs being different? And then how fast, is it going up? What's their age? Are there other things to consider as far as other medical problems?

And then when we have the PET-PSMA result, it really comes back to a multidisciplinary discussion. So, I know we're here in a multidisciplinary discussion, but really, it's the three teams of us, the medical oncologists, our urology colleagues and our radiation colleagues, to really talk about what's the best option here. If they had radiation - is surgery an option? if they had surgery - is radiation an option? Is hormone therapy indicated? And I know, we're going to talk about more specifics in terms of what hormone therapy is and how long it should be given.

Dr. Phillip Koo [00:40:06] You know, this is interesting. It's already 43 minutes past the hour and we're not even halfway done all the things that we want to talk about. And that's a good thing. So, we're going to keep going. Angela, in these patients who have biochemical recurrence, in the past, people will get a PSMA PET, and they would actually want to see a lesion before they went after it. But I think the tides have changed and the approach is different today. Can you help explain to all of us what it is, how it's approached today?

Dr. Angela Jia [00:40:34] Yeah, a hundred percent. So, I always like to remind my patients - and this is to Dr. Klaassen's point in the very beginning, when he was talking about PSMA PET, how he's looking for something outside of the prostate. So typically, I see these folks, they've had surgery and now their PSA is coming up, right? And like we said, PSA ought to be undetectable, but now if it's creeping up, we may get a PET.

And at that point, I tell my patients not seeing anything on the PET would not change my recommendation of proceeding with salvage radiation. And we use the word salvage meaning we're salvaging the situation and that radiation is typically of the prostate bed itself. Most of my patients say, what are you radiating? I don't have a prostate anymore. And I say, you know, by anatomic boundaries. I know where the prostate once lived. And that's kind of the region we are giving radiation to. So, if there is nothing on the PET, the PET I'm really getting to see if it's already spread, because if it already spread then the management is different, right? There are different kinds of hormone therapies that we're going to have to be thinking about, and maybe radiation to wherever it's spread to. But if there's nothing on the PET, it tells me, ah, it hasn't spread. And so, to me, I still know there's disease because your PSA is the canary in the gold mine. That already told me that there is disease. So therefore, nothing on the PET means I am still treating. If there is something on the PET, then that, depending on where it is in the body, that will affect what the next steps are.

Dr. Phillip Koo [00:42:20] That's great. And I think that's a really important take home message for everyone. You know, not seeing on the PET is fine. PET isn't perfect. And then treating that, you know, and sort of shooting blind is, as someone has said in the past, you know, will help patients in that salvage setting.

So, Karine, you talked about oligometastatic disease. So, it's sort of maybe three or less than five metastases. First question is, does it matter where those metastases are and what does that inform you with regards to prognosis? Let's start there.

Dr. Karine Tawagi [00:42:53] Yes, it absolutely matters where they are. So most commonly we'll see cancer spreading to lymph nodes. Next would be bone and then third would be other organs, lungs, liver, things like that. So, I think knowing where the sites are and whether radiation is appropriate for all those sites or in some select cases, actually surgery could even be considered if there's like three or less and really, it's in the area of the prostate with some lymph nodes. So, it absolutely matters. And I think if we think that we can capture all of the spots, whether it's with radiation or with surgery or combination, then we can think about a more reduced timeframe of how much hormone therapy a patient may need rather than our metastatic, meaning stage four, meaning spread to more than five places. Those patients may need longer-term hormone therapy to keep their cancer controlled or other systemic therapies as well.

Dr. Phillip Koo [00:43:56] All right, so let's sort of take that patient with less than five metastases. When do you initiate ADT and when do you initiate something more aggressive on top of that, like what we call an ARPI, like an abiraterone, enzalutamide, darolutamide, a drug like that.

Dr. Karine Tawagi [00:44:13] So for most patients that have oligometastatic disease, as long as they don't have any severe medical conditions that would prevent them from receiving hormone therapy, we recommend hormone therapy. And what I mean when I say hormone therapy is androgen deprivation therapy, which the way I explain it to patients is testosterone, the male hormone is the fuel to the cancer. And so, our goal is to reduce the testosterone to take away the fuel from that cancer. So, I would say, as a rule of thumb, all patients with oligometastatic or metastatic disease need this androgen deprivation therapy where their testosterone is going to be lowered. And for most patients, we will also consider these second generation or newer treatments that help decrease testosterone in other parts of the body, and those are pills. There's four different kinds. They're called abiraterone, enzalutamide, darolutamide and apalutamide. And I'm sure some of our listeners here are on some of these treatments. But if they're oligometastatic, you know, I think we can consider, for some patients, maybe a two-year duration of these treatments. Or let's say they had a history of prostate cancer and it came back - an even shorter period of time on these treatments depending on how they can be treated as far as radiation and things like that. But for other patients, the same way that Dr. Jia mentioned, it's a chronic condition like diabetes. For some patients that have more sites of disease, we need to keep them on their treatment long-term, the same way that you do for diabetes, to keep the cancer controlled.

Dr. Phillip Koo [00:45:43] Great, so, you know, patients are started on ADT, and they might get an ARPI, one of those other drugs. Are there ever instances in which you would just keep them on an ARPI and not have them on ADT?

Dr. Karine Tawagi [00:45:57] Very infrequently. There are some studies showing, for example, for the biochemical recurrent prostate cancer, where we see that there was

some efficacy for enzalutamide, one of the pills by itself, compared to in combination, the combination of the androgen deprivation therapy, so the hormone shots or pills with these newer generation pills is still superior in terms of the risk of the cancer coming back. But for some patients, as far as side effects, things like sexual dysfunction, other side effects from hormone therapy, there are some cases where maybe you would consider one of the pills alone. In the metastatic setting, very rarely. And it's not, the trials as far as in the metastatic settings are not, haven't studied this as far as these pills alone. But for some patients, I do talk about it because if the side effects of their other hormone therapy is too much, perhaps we can consider the pill by itself. It's better than not being on anything.

Dr. Phillip Koo [00:47:00] And that's another great point, is you need to tell your physicians what you're feeling, what you are going through, because again, what the recommendation might be, might be outside of what they did in the trials, but again, it's probably what might be best for you, but they won't know unless you talk to them and tell them. So, whether it's you or your caregiver, make sure you share all that information.

So, hormone therapy, there's lots of different formulations, I myself, I am so confused. Some are injected, some are long-acting, short-acting. Some are oral. They all have their pros and cons, agonists, antagonists. We've had webinars based on that, just covering that topic itself. Zach, is there sort of just, oh, let's focus on the cardiovascular side effects, because that question comes up. If someone has cardiovascular disease, is there a preference that you might have?

Dr. Zachary Klaassen [00:47:46] Yeah, I think to your point, there's a great webinar, I think it just happened recently, that people can go back and look at this. I think in short; somebody has significant cardiac side effects. The antagonist, which is a different mechanism of how this is lowering the testosterone, seems to have less side effects. So one that the patients may be on is Orgovyx, or relugolix, that's the new pill, which is quite commonly used in patients with side effects versus maybe Lupron or one of these other injections that is an agonist. And so, without getting into too much of the mechanism, the antagonist a little bit better for people with cardiovascular disease (and severe cardiovascular disease) versus the agonist, which and maybe just the usual patient doesn't have those risk factors.

Dr. Phillip Koo [00:48:33] Great, so anyone want to chime in? I know it's a really complicated topic, but if not, go ahead, Karine.

Dr. Karine Tawagi [00:48:40] Oh yeah. I mean, I'll just add, I think as far as the decision of which hormone therapy to go on, it's not that there's a best one. I think it's really patient preference, also insurance sometimes dictates what somebody can be on. But as far as the one that Dr. Klaassen just mentioned, if someone has side effects, there's a quicker “off” from the side effects. Some of our other injectable hormone therapies are given once a month, or every three months, or every six months, those last the amount of time upon the frequency of which they're given. So, if it's a three-month injection, the side effects may take three months to wear off.
So, for patients that have a lot of pills or have pills that interact with some of these, the oral version of this, I think that can come into consideration. Or if you're a forgetful person, then the shots might be a better option. So, I don't think there's a one size fits all. I think it's really individualized and it's important to explore those options with your doctor.

Dr. Phillip Koo [00:49:35] So this question comes up is hot flashes in particular. Do you have a preference for those who really want to avoid all those hot flashes?

Dr. Karine Tawagi [00:49:44] I will hear from my peers, but I don't know that there's any evidence that one over the other causes less hot flashes, at least in my experience. I would say as far as hot flashes - if patients have hot flashes, which happens of course very frequently with these hormone treatments as we lower testosterone - we can have behavioral modifications in terms of wearing layers, carrying a fan. Many of my patients do that, but there are also medications that we can give to reduce the frequency and severity of hot flashes that can be quite effective. And there is a lot of emerging data in terms of additional pills or even shots that can be given to decrease the severity and frequency of hot flashes. So, if it's really impacting your quality of life, I would definitely talk to your doctor and explore what options there are to help with those.

Dr. Phillip Koo [00:50:34] Great, anyone else want to add anything on this? Oh, Angela.

Dr. Angela Jia [00:50:39] I was only going to briefly say: some of my patients, patients who've had radiation treatment, sometimes there are some obstructive symptoms, meaning that the prostate is a little bit more swollen and the stream may be a little weaker for the first three months. Sometimes something I have seen is that every time that there's a bit of an obstructive symptom that can trigger a hot flash. And the vice versa can sometimes also happen when you have a hot flash, and you feel like the stream is worse. So, there's also a low-hanging fruit is just addressing the obstructive symptoms, like put you on Flomax or, you know, a medication like that. And I have had quite a few patients who tell me, oh, yeah, when my flow is good, I have less hot flashes. That's just anecdotal.

Dr. Phillip Koo [00:51:25] And again, this is another great example, ADT hormones are really complicated, there's nuances between all the different formulations, so make sure you talk to your physicians about this.

So, alright, so this is an interesting question that came in about bone health. We talk about bone health often, if you're metastatic, they might put patients on Denosumab, but they get a DEXA scan that shows they're not osteopenic, don't have osteoporosis, so why are you putting them on a bone health agent? So, Karine, what are your thoughts there?

Dr. Karine Tawagi [00:51:56] That's a really great question and something that sort of, when we have our checklist of all the things that we need to go through when you have a new diagnosis or existing diagnosis of prostate cancer, bone health is absolutely really important. So, in the localized setting, even for patients on more than 18 months of hormone therapy are at increased risk of lower bone density, which can be called osteopenia, or in the more severe form, osteoporosis. The way that we identify this is with something called a bone density scan, also known as a DEXA. And so, if those patients have evidence of bone density loss, even if they're localized and are on hormone therapy for more than a year and a half, we may consider some of these bone-strengthening therapies.

And then in the metastatic setting, the same paradigm is there. And then if you have what's called castrate-resistant prostate cancer, meaning the cancer is growing beyond the suppression of testosterone, all of those patients should be considered for bone strengthening therapy. And those are usually infusions, and we do require that all patients get a dental clearance before proceeding with these treatments because it can lead to necrosis of the jawbone, which can be very serious if it happens. So, we want to make sure there's no tooth decay or anything like that.

Dr. Phillip Koo [00:53:14] So yeah, dentists, so the dreaded dentist visit, but it's good for you, you have to do it. How often, Karine, do you see brain metastases in your patients with prostate cancer? We'll start there.

Dr. Karine Tawagi [00:53:28] It's very uncommon. So, in terms of cancer in the brain itself, it's extremely, extremely rare. In terms of cancer in the skull bone, that can be a little bit more prevalent. So, I have seen that, you know, in terms of what we talked about, metastatic spreads to other organs, including the bone, including the bones and lining of the skull, I think it's important to have systemic therapy, meaning cancer that's going to treat the entire body. Usually, at that stage, you would definitely recommend chemotherapy, and if the cancer is not responding to chemotherapy, I think we're going to dive into some of the other treatments that are available. And then radiation is an option too, if there is pain in the areas where there is spread of the cancer.

Dr. Phillip Koo [00:54:11] Great. And Angela, I think oftentimes we hear brain, but it's truly not in the brain. It's sort of in the skull, as Karine said, or maybe along the dura. So, but do you have anything to add here? Cause I know you would.

Dr. Angela Jia [00:54:22] Yeah, I completely agree with what she said. Oftentimes they're pretty amenable to radiation treatment. And so, we see them, it's both for disease control, controlling the disease and to palliate symptoms, to help with pain.

Dr. Phillip Koo [00:54:37] So you know we're not going to have enough time to go through everything. One interesting question came in regarding Pluvicto and using radiotherapy and when it was first approved it was for patients post-chemotherapy who were CRPC. Now we're seeing it being approved earlier and earlier, but let's sort of stick to those who received it sort of more as a later line therapy. Karine, what advice do you give patients or what options are there for patients who receive that in the third, fourth line setting?

Dr. Karine Tawagi [00:55:05] So the first step is that you need to have one of those PET PSMAs that we've talked about. So, the way that Pluvicto works is also called lutetium. It basically targets PSMA, prostate-specific membrane antigen. Think of it as a little flag on the cancer cells. And this radioisotope will bind to that flag on the cancer cell and emit radiation. So, patients can have radioactive risk after these treatments. So, there are isolation precautions for patients that receive these treatments. It's given through an infusion every six weeks for up to six cycles. And because these flags are specific to cancer cells, there's much less toxicity to other healthy cells.

However, one of the areas that it's expressed are in the salivary glands. So, patients can experience dry mouth, which can sometimes be problematic. And we have, you know. Substitutes for saliva and other medications to help with that. Other side effects that can happen with Pluvicto, it can lower blood counts. Patients can need blood transfusions in order to get this safely. And the precautions as far as isolation in terms of how far you need to be from someone for the first three days, and then it spaces out after a week. Um, you know, there's a lot of really great patient information guidelines, including from the company itself, Pluvicto. They have very specifics with diagrams in terms of precautions that patients need to take, trying to use a separate bathroom if that's available to you. We're very happy that we have new newer therapies that have been around, you know, widely available in the last two years or so beyond chemotherapy for patients with refractory stage four prostate cancer.

Dr. Phillip Koo [00:56:46] Great, you know, we're at the top of the hour. We're not able to get through everything. One last question, if patients are looking at clinical trial options, where do you direct them to? Because I think there's a variety of resources out there. Angela, let's start with you because you're first on my screen.

Dr. Angela Jia [00:57:02] There's clinicaltrials.gov, you can always go there. There are some others, like Primr, P-R-I-M-R, they have really patient-friendly videos that show you what the trial is about. Uro Times [UroToday] is great at reporting on, you know, trials that are up and coming, because they report on large conferences like ASTRO and ASCO and such.

Dr. Phillip Koo [00:57:32] Yeah, I think you meant UroToday, but yes.

Dr. Angela Jia [00:57:34] Sorry, UroToday.

Dr. Zachary Klaassen [00:57:39] Yeah, no, I agree with all of that. I think, you know, just being proactive, I think Googling MD Anderson, the big cancer centers typically will have good websites, but I agree everything Dr. Jia has said as well. I think just getting online and being proactive and seeing what's out there, clinicaltrials.gov, UroToday, big cancer center is probably a great place to start. PCF.

Dr. Phillip Koo [00:58:00] And then, Karine, for you, advice for patients thinking about clinical trials, just in like 10 seconds.

Dr. Karine Tawagi [00:58:08] It's extremely important to ask your physician about clinical trials. This is the only way that we advance the treatment. So Pluvicto is approved because patients went on trials to get these new therapies approved. There's a lot of really exciting trials in metastatic prostate cancer. So, ask your doctor. And I know there's navigators through PCF and other places that can help patients identify trials for them.

Dr. Phillip Koo [00:58:28] Great. So, you know, this was wonderful. I think we went through a lot. Clearly, we couldn't get through everything. So, if the listeners out there found this valuable, please give us some feedback whether we should, you know do something like this on a regular basis. We take your feedback very seriously and it really helps inform what we do next. So, we really appreciate any information that you give us. And we have a ton of questions that were submitted during this webinar, and we'll try to incorporate that into future programming as well. But lastly, I really want to thank all three of you. It was great to talk to all of you and really learn. Again, I always learn so much from this. So, thank you, thank you very much and enjoy your evenings.