

Dr. Zachary Klaassen: With that, I'm—we're going to keep the same folks on the panel. We're going to pivot a little bit to Q&A about treatment and recurrence. And we had some excellent questions that were sent in earlier for the discussion today from patients and their providers. And so we'll go through some of those. Again, as Becky mentioned, off the top, we obviously don't have time to get to everybody's question today.

What we're going to do is take the questions that are in the chat. Maybe those that were sent in that don't get answered, we're going to collate them into topics, and we're going to provide resources and answers to those questions so that even if your question doesn't get answered during this two-hour session, we will certainly do that after this event.

So, I think one of the questions that was sent in was after salvage radiotherapy, what PSA level would be concerning? So this is a patient who had the prostate removed, and then they've had radiation therapy. Maybe we'll ask Dr. Koo that question – when should we be thinking about additional imaging or additional therapy?

Dr. Phillip Koo: You know, at minimum I think if you have two rising PSAs, there is some consistency in that rise, you know, gives me more confidence that it's real.

But it's sort of goes back to what we talked about earlier. Is the multidisciplinary team ready to act if we see something? And, you know, the good news is we're learning a lot more about this topic of oligometastatic disease and mets-directed therapy. So if you do see some, you know, a smaller number of lesions that might have escaped out of the prostate, there is a clinical benefit to using radiation to sort of treat those sites of disease. And it's really promising. And hopefully as imaging gets better, maybe we could actually have the potential to cure patients who have this type of recurrence.

Dr. Zachary Klaassen: Yeah, absolutely. Another great question that was sent in. And I'll ask Dr. Ballas this, is options to manage recurrence after radical prostatectomy. How do you decide whether you're going to radiate just the prostate bed? Or maybe the pelvic lymph nodes as well? What's sort of that decision-making process look like?

Dr. Leslie Ballas: I think that obviously it's, you know, patient-specific. We think about, were pelvic lymph nodes evaluated at the time of surgery. If they were never evaluated, most radiation oncologists would include the pelvic lymph node fields with their—with the prostate bed.

Or if there were only a minimum number of lymph nodes evaluated, we might also include the pelvic lymph nodes with the prostate bed. Additionally, the radiation field is determined by what the PSA is when we meet the patient to discuss salvage radiation. Higher the PSA, more likely we are to include pelvic lymph nodes with the prostate radiation.

And then, of course, depending on the post-operative PSA, we may involve PSMA PET if there is evidence of disease in the lymph nodes following surgery on PSMA PET, typically we include—we would radiate the prostate bed, the pelvic lymph nodes, and then give a little extra what we call “boost dose” to those to...lymph nodes that are involved or shown as involved on the PSMA PET. And so all of these things come into the decision making by your radiation oncologist.

Dr. Zachary Klaassen: Excellent. Here's a question from the Q&A online. Dr. Koo, how could PSA rise be differentiated from a PSA bounce after salvage radiation therapy?

Dr. Phillip Koo: Good question. You know, I think there's always variability in lab tests. You know, ideally you go to the same lab, you know, and you have consistency. And I think this is where you want to sort of make sure there's—that it's not just a blip. So, you know, at least two sort of showing a trend in a certain direction provides that confidence.

Dr. Zachary Klaassen: Yeah.

Dr. Leslie Ballas: I could add just one thing about that, is that PSA bounce is a phenomenon that is seen after primary radiation because the prostate is still in your body. And what it basically means is that because the prostate is still in your body, you know, the PSA may go up on one draw, maybe two draws, but then comes back down. That's why initially I said it's about trend over time, not just one drop. But after you've had a prostatectomy, there's very rarely a PSA bounce. And so in the way that the, you know, patient or caregiver worded the question, I just want to make sure we understand that you don't usually get a PSA bounce after salvage treatment unless it's salvage after prior radiation. In order to have a bounce you really need to have the prostate still in your body.

Dr. Zachary Klaassen: Yeah. Great. Great clarification. Doctor Ballas, there's another great question online. Please discuss options after brachytherapy as the initial treatment that the patient received.

Dr. Leslie Ballas: So this is very much based on where recurrences happen. So brachytherapy, external beam radiation in the definitive setting are very successful treatments.

And I think that patients commonly think that if they have recurrence after radiation that it's going to be in the prostate. And most commonly actually the recurrence is outside of the prostate. It's in the pelvic lymph nodes. Maybe it's in the bone. And so, it's only in those very few patients, probably in 10% or less that have a recurrence in the prostate gland, where treatment options become a little bit more limited, but more commonly after brachytherapy, if you are to have a failure, it would be a recurrence in a lymph node.

At that point, we would recommend an external beam radiation treatment option to the lymph nodes because they weren't previously treated. And we have excellent ways of making sure that we don't overlap the radiation to the lymph nodes with the brachytherapy or prior radiation to the prostate. And so you do have options certainly after brachytherapy or external beam radiation for recurrences if they happen.

Dr. Zachary Klaassen: Yeah. Great answer. Dr. Koo, this will be probably our last question for this session. So this is a gentleman that had radiotherapy and two years of hormone therapy, androgen deprivation. PSA initially went down. Now it's slowly going back up. What are the options in this situation where they've already had radiotherapy. They've had two years of hormone deprivation. Hormone deprivation certainly is another option. Is there other options out there for a patient in this situation?

Dr. Phillip Koo: You know I won't speak too much on the treatment options because that's not my area of expertise. I will say though, you know, getting a PSMA PET in those clinical scenarios, I think, could be very helpful because it helps define the landscape and what we're dealing with.

And obviously, after we obtain those results, I turn it back over to Dr. Ballas to see if there may be radiation options, and to use that to see if there are other options available. Or perhaps, you know, there's needs, depending on what we see. Maybe a medical oncologist needs to get involved here as well.

Dr. Zachary Klaassen: Yeah, I think I'll add a little bit to that too. I think there may be a situation in this specific scenario where intermittent ADT is also a potential option to sort of decrease some of those side effects of continual therapy. Take a course of additional maybe 6 to 9 months of ADT, PSA comes back down. There's some good data that's you

know, 10 or 15 years old you know, that intermittent hormone therapy can also be a safe option and maybe minimize some of those side effects as well. So.

Dr. Leslie Ballas: And for that patient, I think as Doctor Koo said, like figuring out where the disease is, where that—what's causing that PSA rise if there are just 1 or 2 sites of disease, that, you know, where maybe radiation could target it, something Dr. Koo mentioned before, metastasis directed therapy, these are all options, and they may be delivered with hormone therapy. They may be delivered without. But understanding where that disease is coming from is important.

Dr. Zachary Klaassen: Absolutely. Thank you both a great discussion. We got a few more of the patient questions. So thank you for sending those in and for typing a few online. I'm going to bring Becky back in to introduce the next session.