

Dr. Leslie Ballas: I'm going to just briefly talk to you guys about shared decision making, choosing the treatment, choosing a treatment for, you know, your primary prostate cancer. Prostate cancer risk stratification is very important in how we, as physicians, think about what options patients have. And I think, more than anything else, I want patients and caregivers to take away that you have options at any cancer risk stratification and that it's important for you to understand what your options are, and that will help you decide what is the best treatment that makes you the most comfortable with, you know, with, your diagnosis. When we talk about prostate cancer risk stratification, we generally break down the risk groups into low, intermediate, and high risk disease. This is based on your PSA, your Gleason score. As Dr. Klaassen said, how aggressive the cancer cells look under the microscope, as well as your digital rectal exam. Within these risk groups, things are broken down even a little bit further.

Within low-risk prostate cancer, there are some patients that have very low-risk prostate cancer based on things such as how many biopsies show disease. What is the relationship of your PSA to the volume of your prostate gland that can distinguish very low disease from low-risk disease. Similarly, within intermediate-risk disease, there is a breakdown into favorable-intermediate, unfavorable-intermediate.

And within the high-risk group we've got high-risk and very high-risk. Very high-risk includes, you know, mostly Gleason 5, which is the most aggressive under the microscope, as well as multiple cores with high-risk disease. And the reason, as I said, that this is so important, is that treatment options depend on risk stratification.

If you have low-risk disease, you have the option of active surveillance surgery or radiation. However, with low-risk disease, as you can see, you may have much more—it might be much more reasonable to undergo an active surveillance type treatment, and that's why I've enlarged that box here. With intermediate-risk disease, you have still the option of active surveillance.

You have surgery and radiation plus or minus the addition of hormone therapy. And I say plus or minus because intermediate-risk disease is a broad category. Favorable intermediate risk patients may not need hormone therapy. Unfavorable risk individuals may need hormone therapy. There's fairly, you know, robust data to say in the intermediate risk space, surgery and radiation plus or minus hormone therapy are equal in their cancer control of the prostate cancer, and so therefore when you're making decisions you need to understand, “okay, what are the side effects associated with each of these treatment options?” With high risk disease, you do still have options in terms of your treatment. Active

surveillance likely would not be recommended unless you have a lot of other, you know, comorbid diseases, other health concerns going on.

Surgery and radiation plus hormone therapy are options. In this setting, it is radiation and hormone therapy, not a plus minus, but definitely plus because we know that the hormone therapy adds to radiation. And while we don't have as robust data to say that surgery compared to radiation hormone therapy are equivalent, we do have very good data to say that there is equivalence there.

In the setting of high risk disease, which is a somewhat special situation, you may need more than one treatment. You may make that decision up front that you want surgery, but based on your surgical results, you may need additional therapy. And so you might—you should be at least open to the idea that high-risk disease is often a multi-modality treatment required for your disease, and even within radiation therapy, as we're going to get to in the next section, you may need a combination of radiation treatments.

And so I think that with high-risk disease, you need to be open to the idea that whatever you choose upfront may or may not, you know, be your only treatment that you receive based on either your pathology or your PSA results. And that's really all I wanted to share during this portion of the conversation, but welcome any of Dr. Klaassen's questions.

Dr. Zachary Klaassen: Yeah. Thank you, Dr. Ballas. Excellent. A great overview, a high-level overview. I just want to delve into a couple of additional questions. And one of them is what should patients be considering and what questions should they be asking if they're a candidate for both radiation or surgery? I think that understanding the side effect profile of each treatment is really important.

Dr. Leslie Ballas: I think most of us would consider that surgery and radiation, whether it's with hormones or without, depending on the risk stratification of your disease, is similar in its outcome in terms of your cancer care. And so when you're making decisions, understanding those side effects is really important. And so asking your physician, you know, "How is this going to affect my sexual quality of life?"

"How is this going to affect, you know, my urination, my bowel movements?" That's really important because that's what's going to, you know, be the day-to-day thing that you deal with as a patient and can help you make decisions.

Dr. Zachary Klaassen: Yeah, that's well said. I think, and when I opened with not panicking and really getting those questions answered, you nailed exactly. You have to understand and chat with both a surgeon and radiation oncologist, because having those opinions and having that information to make that shared decision is truly important. The other thing I want to talk about is certainly NCCN, which is the risk stratification you laid out so nicely, has been our go-to for decades.

And it's excellent. And there's that table on the side where it really breaks down the criteria. What are some of the other additional tests that patients may hear about? For instance Decipher or Artera AI prostate test, that are really shown, maybe even a little bit better than some of the NCCN or at least contributing to more information for the patient and the physician.

Dr. Leslie Ballas: Yeah. So thankfully—and a lot of this comes from PCF, honestly—we've had quite a bit of advancement in our ability to discriminate prostate cancer. beyond just those sort of three tests: PSA, Gleason, and digital rectal exam. And so, you know, one of the ones that you mentioned, the Decipher score, that is a genomic test.

And I always tell patients genomic is not necessarily genetic. It's not looking at, you know, you have blue eyes because your dad had blue eyes, right? It's looking at the tissue that was taken out of your body at the time of your biopsy and analyzing your patient's specific tumor for alterations, modifications in the tumor itself to help predict, you know, what your potential outcomes are going to be in the long term.

Very important to understand that this is prognostic. It tells patients sort of what to expect, but it's not necessarily predictive. It doesn't yet have the level of data to say, “because my Decipher is high, I must get this treatment.” There are studies ongoing within the radiation oncology community through the National Radiation Research Organization (NRG) looking at this exact question, “Can we use Decipher to dictate how we treat patients?” Artera AI, another thing that you mentioned, another incredible advancement in prostate cancer is using artificial intelligence to look at your specific prostate cancer biopsy under the microscope, and use that to predict how you're going to do in the future. That is, again, not able to discriminate treatment at this time. However, that is the direction we're going in.

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And there are studies looking to incorporate that into the treatment paradigm. So yeah, really exciting time for prostate cancer research and understanding more about personalized medicine.

Dr. Zachary Klaassen: That's great. In the last minute we have in this session, I want you to quickly hit on Gleason 6 a little bit. So, Matt Cooperberg, who's one of our colleagues up at UCSF and has been huge with active surveillance, and certainly there's been some debates within our academic societies about, is Gleason 6 prostate cancer, is it pre-prostate cancer? Certainly, this we could have a whole webinar on this topic alone, but maybe just delve into a little bit more about what Gleason 6 is and the implications for active surveillance.

Dr. Leslie Ballas: So Gleason 6 is in the low-risk prostate cancer group, oftentimes possibly very low-risk prostate cancer. And the issue around Gleason 6 is that it very rarely spreads beyond the prostate.

And so, very—due to some of the amazing work by Dr. Cooperberg and some of, you know, his colleagues, some of which are on this call today, have looked at, you know, active surveillance as a real treatment option for patients with low-risk and very low-risk disease. I think that, as you mentioned, during the opening of this conversation, people hear cancer and get very, very nervous.

And it's so natural for patients to want to take the disease out of their body, immediately go to treatment. And with Gleason 6 disease, sometimes there's overtreatment is what we're really afraid of is that patients are going to undergo treatments that have quality of life ramifications that maybe they don't necessarily need. And so that's really where the debate in Gleason 6 comes from.

Do we need to be treating patients? How can patients understand that, yes, it has the cancer name but doesn't have the same ability to spread beyond the prostate. And I'm not going to answer the question of whether it should be called cancer or not. I will leave that to some smarter colleagues than myself. But I think that, like you said, when you hear that word “cancer,” you need to take a minute, understand where in the spectrum of disease you are, and that active surveillance is a—like—a real option for so many patients.

Dr. Zachary Klaassen: Yeah. Excellent. Dr. Ballas, thank you for that session. I want to bring Becky back in to introduce our next session.