The Landscape of Advanced Prostate Cancer

Phillip Koo, MD [00:00:00] So let's go right into it and talk about prostate cancer from a high level. So, Dr. Sartor, when we hear prostate cancer, it being so many different things, obviously we need to know a lot more, but give us a high-level overview of what that means to you and how you sort of look at the disease in different buckets.

Oliver Sartor, MD [00:00:21] Yeah, thank you very much, Phil. And, you know, it can be a little bit complicated, but I'd like to keep it simple. So first of all, when you're diagnosed, you're typically either localized disease or potentially the cancer spread beyond the prostate. Now, when we look at metastatic disease today, we often need to understand the type of imaging that is compatible with the metastasis. It used to be we'd use a lot of bone scans and CAT scans. Today, we use a lot of PSMA PET scans. And actually, I like to kind of classify the metastatic patients into those that are oligometastatic and those that are polymetastatic. And there are different definitions, but typically one to five is gonna be the oligometastatic, and more than five is going to be the polymetastatic. What you decide to do in that initial phase after the treatment, is very dependent on the risk stratification as well as the comorbidities and age of the patient. When I talk about risk stratifications, I'm thinking about things like the PSA, the Gleason score, the clinical stage, and we stratify the patients in accordance with fairly worked out algorithms. And yes, those algorithms can be augmented by certain genomic testing, at times transcriptomics, which is looking at the type of RNA that might be produced. But the basics are pretty straightforward. What type of cancer do you have? What sort of patient are you? And then come into the proper decision, often in consultation with the multidisciplinary team. It turns out that urologists, medical oncologists, as well as nuclear medicine physicians, radiation oncologists may all have a particular perspective. Now, when we take this initial patient, diagnosed with either localized or metastatic disease, and we initiate therapy, or not, for instance, we use surveillance in many of the patients with localized prostate cancer that's low risk, like with Gleason 6. The patients are either gonna be in remission if they're treated in the traditional sense for hormonal therapies for metastatic disease, or maybe even cured. But not everyone will stay in remission, not everyone will be cured, and so we have to worry about the relapse patient, and those relapses can be categorized in a variety of different ways. If you had a local definitive therapy, such as radical prostatectomy or radiation, and then recur, you can often recur only with what we call about chemical recurrence. Today we try to understand that biochemical recurrence in terms of things like the PSA doubling time and now we begin to introduce molecular imaging, things like PSMA PET, in order to try to find the metastatic disease and make good treatment decisions. If in fact you've been diagnosed initially with metastatic disease and you're treated with hormonal therapy and then relapse, then we have the large disease state. That we call castrate-resistant prostate cancer. And this is simply the cancer that has progressed after the hormonal therapy has been used. And despite the hormonal therapy being utilized, that there is progression. Now, one of the things we'll talk about is the fact that hormones today and hormones yesterday are not necessarily the same. It used to be that we would use the Leuprolide-type therapies suppress the testosterone with the use of injections being the most common way. And then a few of the older ways that were oral would be things like flutamide and bicalutamide, but those are not that often used today because we have better hormonal therapies and we have a generic term for them, the ARPIs, androgen receptor pathway inhibitors. And the androgen receptive pathways inhibitors include things like abiraterone, enzalutamide, apalutamide, darolutamide. And that augments the effects of the traditional hormones. But the recurrences after the use of an ADT and an ARPI is a little bit distinct from what it used to be. In the old days, we would typically use those ADT-treated patients and then add an ARPI at relapse. But today, we're often bringing that back

and to use in the setting of hormone-sensitive disease. Bottom line is we're going to get a tour on this. And we have a terrific group of lectures, going to concentrate on these individual disease states, take us through one by one, and then of course we'll have some Q&A at the end to try to answer any questions. Phil, that's kind of a high-level overview, and of course, we can talk a lot more, but that's why we're here tonight, is to hear from the good people who are going to be classifying and helping people understand their disease states.

Phillip Koo, MD [00:05:07] Absolutely. So today we're focusing just on advanced prostate cancer. So those with metastatic disease. So, Oliver, just quickly, what is different about advanced prostate cancer today and what is so exciting that patients need to sort of recognize? Because I think oftentimes, they'll say, oh, I'm stage four and they just, you know, creates a lot of anxiety. But the landscape is different today. So, can you sum that up for us?

Oliver Sartor, MD [00:05:35] Sure, I think there are a couple of things that are really distinct. Number one is the imaging that we do in order to classify the patient as being metastatic has changed dramatically. It used to be, as mentioned, CAT scan and the bone scan. And that typically when it was positive would be a fairly large lesion, often multifocal and much more difficult to treat in comparison to today's metastatic patient. Many of whom may have PSMA-PET-positive disease and may or may not even have conventional imaging positivity. So, number one, we've changed the way we diagnose using imaging and that's very important. The other critical factor is that we have more tools at our disposal. For instance, for the oligometastatic patient, we can use focused radiation on the metastatic disease. Sometimes we call it SBRT, or stereotactic body radiotherapy. I think Jason will be talking about some of that. But we also have better therapies. I mentioned the ARPIs and darolutamides, abiraterones, et cetera. And these are really quite effective, and they've changed the natural history. You know, it used to be somebody with metastatic disease may only have a two-to-three-year life expectancy. And when I started my career back in the 1990s, that was a very true statement. Now, the expected survival, and I can just look at it in ADT Abiraterone Trial, published out of the UK. We're talking about six and a half, seven years, and I think that we can even have further improvements by using some of the more modern therapies that have been introduced since that STAMPEDE trial. So, the bottom line is, what was true yesterday, what's true today, are distinct. Not only the imaging, but the treatment is variable.

Phillip Koo, MD [00:07:14] That's great. And I think that's a great message. Patients are living much, much longer today with metastatic disease than they did in the past.