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Treatment Updates in Nonmetastatic Castration-Resistant Prostate Cancer (nmCRPC)

Announcer:
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Dr. Saad:
Hello. So I'm Fred Saad, Professor and Chairman of Urology at the University of Montreal Hospital Center and Director of GU Oncology, and I'm very happy to be with my friend and colleague, Dan George. So Dan, can you do a brief introduction?

Dr. George:
Yes, sure, Fred, thanks for having me. I'm Dan George. I'm a GU Medical Oncologist, Professor of Surgery and Urology and Medical Oncology at Duke University, and Director of GU Oncology here, and happy to join you, Fred.

Dr. Saad:
Great. So, you know, I think the theme here is that ASCO was a huge meeting, over 40,000 participants this year, nice to see it back into full force. And there's been a lot of great stuff presented at ASCO. But there's some things that, you know, with all that was presented that might be under the radar, but some really interesting stuff coming out, where we're trying to learn from the real-world experience, it's one thing phase 3 studies, but in the real world, what's going on? And what can we expect?

And so, there's the DEAR study that I think you were a part of, and very involved in trying to get some idea in the real world how these drugs, apalutamide darolutamide, enzalutamide are working when used in the real world. So maybe you can share some of your insights in that study.

Dr. George:
Yeah, Fred, you know, I mean, I think this is where real-world data can be really helpful in kind of filling the gaps. You know, we have 3 large phase 3 studies demonstrating the clinical benefits in metastasis-free survival and overall survival in nonmetastatic castrate-resistant prostate cancer. The ARAMIS trial, the SPARTAN trial, and the PROSPER study, all of them, you know, showed robust time – you know, improvements in time to metastasis-free survival and in early signals and overall survival benefit as well. So, it's clear we need to treat patients. But what's not so clear is, is there any difference between these agents? And, you know, when we just look, you know, within each study at its own, you know, interventional agent versus placebo, there are some differences. We do see, you know, proportionately less toxicity in the ARAMIS study, versus, you know, darolutamide versus it's placebo, versus, say, the SPARTAN trial, and apalutamide versus it's placebo and enzalutamide versus it's placebo in the PROSPER study. So there's reason to suspect that there could be differences in the tolerability of these agents in real-world practice.

And so the DEAR study was really to look just at that, at darolutamide, enzalutamide, apalutamide, in real-world evidence; hence the name. And it was a retrospective look at a really a national database of urology practices around the country where we looked at, you know, around 600 or so patients with - who were treated in the nonmetastatic castrate-resistant prostate cancer setting with these agents. And they had 6 months of lead-in data, they had treatment on drug in this space up until either disease progression or

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discontinuation because of toxicity. And it was interesting, because, you know, darolutamide was the last to be approved in this setting, but it's actually increased in its use in utility in this space recently. So we have relatively equal numbers of enzalutamide, darolutamide, less so with apalutamide.

But the real signal here was a composite endpoint of both stopping therapy because of either treatment discontinuation for toxicity or disease progression. And when we look at that, there was a clear signal for a longer time to discontinuation with darolutamide than with either the other two agents. And when we break it down by the different composites of that endpoint, just looking at the time to treatment discontinuation, or the time to disease progression, it's significant. It's about a hazard ratio, you know, of 0.7. So there's about a 30%, longer a treatment effect. And, in fact, the median is not reached in the darolutamide group versus the other two. So and the other two are around, you know, 22, 24 months, median time to progression shorter than what we see in our clinical trial population.

But these patients are different. They're older, you know, the average age was median age was 80. And I think that's really reflective of our real-world population of patients. And to being able to see that maybe in that population of patients, we do see a little bit better tolerance, and maybe a little bit better, you know, dosing. We don't have insights into dosing but, but one of the reasons we might see a difference in efficacy could be because of the dose intensity in those populations with daro versus the other agents. So interesting data, really the only comparative data we have, between these agents and in this nonmetastatic castrate-resistant disease setting.

Dr. Saad:
Yeah, well, that's really interesting. I think, outside of clinical trials, we need to learn from the real world of what's going on and try to - and this is really, really important across the field, to learn what we're doing well, and what we can improve on.

So there was another study looking at darolutamide, more specifically the DAROL study, that addressed some - that was reported earlier, and now this is an update. So maybe you just bring us up to date on this trial that maybe people aren't very much aware of.

Dr. George:
Yeah, you know, DAROL, in many ways is kind of a complement to DEAR, because the DEAR was a retrospective analysis. This was a prospective analysis of outcomes in kind of an observational registry type format of patients with nonmetastatic castrate-resistant prostate cancer starting on darolutamide. And so it's exclusive darolutamide.

The patient characteristics though were similar to what we saw in DEAR. The median age was 80, the median PSA coming on was relatively low, somewhere around 3 or so. And the median PSA doubling time was about 5.5 months, or a little bit longer PSA doubling time than what we saw on our clinical trials. And yet, we still see that median, you know, time to progression around 24 months. So it suggests that, you know, in the real world, our expectations around our patients outcomes might be a little bit different than what we see in our clinical trial practice. But again, we saw really well tolerance, we saw, you know, less than 5% toxicity rates from most toxicities associated with darolutamide. So even in, again, this older population in this prospective study, we're able to really document you know, good overall tolerance. Again, maybe a little bit, you know, shorter, you know, time to disease progression, but sort of in line with what we expect to see in this older population of patients.

Dr. Saad:
That's great. And like I say, whenever I go around to the centers as a visiting professor, is when you're doing things now, registries are a great source of information. You know, and whether we're looking at all oligometastatic treatment with radiation and all the rest, I think it's going to be very hard to do trials in a lot of settings. And these registry type prospective studies really includes patients that are often not in clinical trials.

So congratulations to both of these trials and thanks for sharing that insight, Dan.

Dr. George:
My pleasure.

Announcer:
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