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Early Treatment Intensification in the Continuum of Prostate Cancer Care

Announcer:

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Dr. George:

Hi, I'm Dan George, GU Medical Oncologist, Professor of Medicine Surgery, and Director of GU Oncology at Duke Cancer Institute. And I'm joined by my good friend and colleague, Dr. Fred Saad from Montreal. Fred, you want to introduce yourself?

Dr. Saad:

Sure. So I'm Professor and Chairman of Urology, and Director of GU Oncology at the University of Montreal Hospital Center, and glad to be with you again, Dan.

Dr. George:

Fantastic, fantastic. Well, we are post ASCO, just trying to unpackage all the fantastic data that was presented. And of course, we have our top-line oral abstracts and all. But there was some interesting findings as well, buried in those poster sessions. And for those of you either not present there or who were there, but missed it, there were some – I think, really some really interesting findings there that I think help frame some of the ongoing studies of the day.

I want to talk, Fred, about surgery, about prostatectomy, and about the work that's going on around neoadjuvant therapy for prostatectomy. We've been at this game for a long time, docetaxel and other things. But in this era of novel hormonal agents and AR pathway inhibitors in particular, it seems like we're re-evaluating every paradigm of the past. Walk us through some of the – a couple of the abstracts there that we saw and posters that we saw that I think really caught your eye in terms of what we might be able to expect now in treating patients with these potent hormonal inhibitors pre-prostatectomy.

Dr. Saad:

Right. So like you said, we've been at this for over 20 years, trying to improve our outcome with surgery through neoadjuvant, but we're basically giving only standard ADT with relatively low chances of reaching that P0, or pathological complete response when we do the surgery. And although we looked like we were improving surgical margin rates, the outcomes in terms of PSA recurrence didn't look like it made any difference whether or not patients got a few months of ADT prior to surgery. But this was in an era where we only had ADT. And now we're in an era where we can do much better, where we see tremendous PSA declines to undetectable, even in metastatic disease when we start combining ADT with these novel hormonal therapies like apalutamide and others that have been tested.

And so that is being tested in a very large randomized study, the PROTEUS study, looking at 6 months of ADT plus or minus apalutamide, followed by 6 months of ADT plus apalutamide after surgery in very high-risk patients. And we're still going to be waiting for that data for some time.

But we've got some data that was presented at ASCO looking at, you know, this intensification approach prior to surgery, plus or minus

18 months of therapy. And we're seeing that, you know, when you really give intensive therapy prior to surgery, you might not need to give much more. And so that's really been interesting. And it's forcing us to revisit the concept of whether or not we can do better than surgery alone in an era where we have therapies that are much more effective. And I think it's building on a wealth of work that's been going on in trying to do better in these patients that historically we would maybe only send to radiation therapy where they would get 2 or 3 years of ADT, and maybe we can do even better through surgery. Not to say surgery is better than radiation therapy.

Dr. George:

Oh, come on now, you can say it.

Dr. Saad:

Or radiation resistant, Dan, and we need to maybe sometimes get that out.

Dr. George:

Yeah, I think you're absolutely right. And look it, I mean, I think surgery is still the gold standard for local control. And the truth is, is that if we can get by with 6 months of therapy, hormonal therapy, get people off of treatment, and be able to have that kind of clear pathologic reading and, you know, undetectable PSA to follow, that's attractive to a lot of patients, particularly our younger patients. And so the sort of definitive nature of that treatment is it's nice to have options for these people.

And, you know, I think, you know, radiation can learn from surgery, and maybe we won't need 2 years of hormonal therapy in everybody with radiation therapy. There was actually a nice oral presentation by Andy Armstrong from the NRG Group, showing an AI approach to predicting who needs 2 years of hormones versus a shorter course. And so there may be some tools in the future for, you know, who needs, you know, not just intensification but long-term intensification versus short-term intensification.

And this sort of story showing that the post-surgery adjuvant didn't necessarily make that big a difference is really interesting, that that wasn't randomized, that was sort of patient, you know, personal preference and whatnot. So, I think we have to be, you know, careful. There was some randomization, but there wasn't, you know, enough numbers, a lot of patients opted out of that. So I think we will need some future studies.

But there is a phase 3 study going on that is looking in this space around neoadjuvant and adjuvant hormonal therapy and surgery. Tell us about the PROTEUS study.

Dr. Saad:

Yeah, so this is taking, you know, patients that historically would really have little chance of curing with surgery. You know, these are not just simply high risk, these are very high-risk patients. And patients are randomized to getting ADT alone versus ADT plus apalutamide 6 months prior and 6 months after the surgery. And I've got several patients on those, and not a single one has failed yet, even though we're in the follow-up phase. So I'm very impressed. I'm very, you know - I'm being cautious. I don't know who's getting a placebo, because the added adverse events of apalutamide over the ADT is very hard to figure out who's on a placebo and who's on ADT in the early setting. And so it's encouraging in terms of adverse events.

But it's extremely encouraging in terms of what I'm seeing in terms of pathological response and what I'm seeing in terms of PSA control, now that patients have completed and are still being followed, and testosterone has recovered. As long as it hasn't recovered, we can't really claim success. And so this is interesting, and we're very much looking forward to that.

And we saw some inklings of control with more intensive, shorter treatment with the with the FORMULA-509 study that was presented few months ago where patients failing surgery that are high risk, getting 6 months of apalutamide and ADT and radiation, were doing really, really well. Very comparable to the 2 years that the RADICALS study had to give to patients with salvage radiation. So I think the field is moving towards less but more intense.

Dr. George:

Yes, less and more. I like it. All right. Well, thanks so much for the interesting discussion, Fred, as always appreciate it.

Dr. Saad:

Great stuff.

Announcer:

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