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Data Updates in the Treatment of Hormone Sensitive Prostate Cancer (HSPC)

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Dr. George:
Welcome. I'm Dr. Dan George, Professor of Medicine and Surgery from Duke University Medical Center. I'm happy to talk with you today about hormone sensitive prostate cancer management with my good friend and colleague, Dr. Fred Saad. Fred, do you want to introduce yourself?

Dr. Saad:
Sure, Dan. So, I am Fred Saad, Professor and Chairman of Urology and Director of GU Oncology at the University of Montreal in Montreal, Canada.

Dr. George:
Fantastic. Well, welcome Fred, and, uh, what a great GU ASCO '23 we just finished. And I thought we could jump right in with some of the latest updates from – in this hormone sensitive space. Fred, do you want to lead us through a couple of, I think maybe some of the key presentations there?

Dr. Saad:
Right, so, I think one of the key presentations which was an oral presentation was some of the updated data on ARASENS. So I guess everybody knows ARASENS. Almost 1,500 patients randomized to one-to-one, to getting ADT and docetaxel, which was, for a long time, considered the standard of care for hormone sensitive metastatic disease and patients were randomized to get that standard of care, plus or minus darolutamide, to see if we can prolong survival if we do a triplet approach versus a doublet approach, and that study was clearly positive, with more than 32% reduction risk of death. The question that keeps coming up was, how do patients with high volume versus low volume, or high risk versus low risk perform with this triplet? Is there a difference, and do we really – should we really limit this triplet approach to a certain population of patients?

And so, we were both at that session. I think it stimulated some discussion. The bottom line is, we see the same kind of overall advantage survival, whether patients were high risk or low risk, or whether they were high volume or low volume. Now, when we get into statistics, the low volume patients were a small group of the patients, who came in because, you know, because patients have to be both eligible, or considered needing chemotherapy, there was a bit of a selection for the higher risk, higher volume patients. But the bottom line is we're seeing the same kind of survival advantage if we look at the hazard ratios – around 0.68, 0.7 hazard ratio.

Dr. George:
Yeah, it's really interesting, Fred. I think with that point you just made about they had to be patients who were otherwise docetaxel-eligible, so their treating physician felt that docetaxel was appropriate. Because remember, you know, this was being done in an era when we also had, now, novel hormonal therapies like abiraterone available, and for patients that feel like, you know, that chemotherapy

was really the appropriate, you know, treatment regardless of randomization. And then, obviously, you know, concerned enough to say would we want to offer these patients a triplet? So, this was probably patients in general that we felt, you know, kind of needed intensification, or maybe what we might term dual intensification, with chemotherapy and a novel hormonal therapy, and I think this is really kind of amazing, to be honest with you. I mean, granted that the numbers are small in terms of the low risk and the low volume patients, but they were, you know, still trends very much in favor of this, particularly in the low risk patients. You know, when you actually look at some of the breakdowns, in the low risk patients they got as much, and in some cases maybe even more benefit, in terms of preventing skeletal events and things like this, than we saw in some of our high volume patients. So it really suggests to me that risk – that is, although it's important, you know, it's really determined by that Gleason score, and volume, you know, is probably the real driver there, and so to me, anybody that has sort of multiple bony metastasis, that we really should be thinking about docetaxel chemotherapy and darolutamide therapy, or dual intensification in that population of patients.

Dr. Saad:
Yeah, absolutely, and I think the patients really have to be part of this discussion. It's unfair that it's only us that would decide you can benefit and other can't. I mean, in terms of docetaxel versus NHT, we have heard docetaxel is not used anymore, or very rarely used. That's true, because we have always had to choose one of the four – one of the three novel hormones, or docetaxel. So obviously, the results are very similar, so why would you choose docetaxel? But now that we have the option of combining, I think we have to look at our patient and say, is novel hormonal going to be enough on the long term? And if you think that patient might have clones that might be hormone-insensitive, we really need to consider that triple approach up front, you know, and what's amazing – and like you said, in the low risk, low volume, we're seeing some really tremendous long-term responses. And, you know, we're talking more and more about de-intensification. How are we going to de-intensify if we can't get as close as possible to cure, up front? So this very aggressive approach might actually allow us – with more research, in two or three years – to say, "Well, we'll stop everything. There's no trace of disease." I think our biggest opportunity is up front, so I think we really have to just avoid saying only the very worst are going to benefit from triplet. You might actually be many more patients than the very worst that will benefit from the long-term benefit, of having an aggressive, up front approach.

Dr. George:
Well said, Fred. Well said, and I like that idea of at least offering to patients, you know, more broadly now that we're not competing one therapy against another. I want to switch gears now, because there was something new presented at GU ASCO '23, in the salvage space with radiation therapy, and we've all known that, you know, salvage radiation therapy and hormonal therapy has been kind of a standard of care, but intensification in this space has – you know, we haven't seen a tremendous amount of data. And there was a new, really investigator-led, multi-center effort, that showed some fairly provocative results. You want to walk us through that?

Dr. Saad:
Yeah, so very briefly, I mean, it – we're talking about intensification in the metastatic hormone sensitive, but maybe if we can attack the patients that are not yet metastatic, and do the very best, and we've seen results from STAMPEDE in the very high risk patients, localized, getting ADT plus abiraterone, for only two years. Well here, these are patients that are recurring after surgery, with relatively low PSA's, and they got six months of ADT plus or minus APA and abiraterone. And what they saw is the patients that got the intensification with only six months, obviously a subgroup – but the patients with PSA's above 0.5, with only six months of ADT and apalutamide – I don't think we really need the abiraterone – had longer time to metastases. So, metastases-free survival, long term, recurrence-free survival was much improved. So really, a step in the right direction, that maybe with intensification we can avoid all these long-term needs for systemic therapy in these patients, that we might still have an opportunity to truly control their disease, if they've gone through surgery and had a recurrence.

Dr. George:
Well, really exciting data. It's an area we need to make more progress in, and obviously we would like to see, you know, a more definitive, larger powered study for metastasis-free survival. But seeing that signal, particularly in that kind of higher risk population, as you define by PSA, I think is super exciting, and really suggests it's going to be even more opportunities for intensification early in the disease course. Well, thanks, Fred. This has been a great discussion. I appreciate it.

Dr. Saad:
Thanks, Dan.

Announcer:
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