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Coordinating Care for mCSPC Patients Receiving Androgen Receptor Pathway Inhibitors

Dr. Turck:
This is *Project Oncology* on ReachMD, and I'm Dr. Charles Turck. Today, we'll be discussing strategies for managing tolerability, comorbidities, and care coordination in patients receiving AR pathway inhibitors for metastatic castration-sensitive prostate cancer. And joining me in this conversation are Drs. Daniel Geynisman and Jonathan Henderson.

Dr. Geynisman is an Associate Professor in the Department of Hematology and Oncology and the Chief of the Division of Genitourinary Medical Oncology at the Fox Chase Cancer Center in Philadelphia. Dr. Geynisman, welcome to the program.

Dr. Geynisman:
Thank you. Great to be here.

Dr. Turck:
And Dr. Henderson is a board-certified urologist at Arkansas Urology in Little Rock. Dr. Henderson, thank you for being here today.

Dr. Henderson:
Thank you for having me.

Dr. Turck:
Well, I'd like to open up our conversation by looking at the big picture. Dr. Henderson, when you think about long-term management in this setting, what defines success beyond that initial response to an AR pathway inhibitor?

Dr. Henderson:
Thank you for the question. I think it's a very important one, because if you think about it, in this patient population, we're looking at a long time on drug—ideally, anyway. And rather than making a big splash with a medication that's rather toxic and that is going to have an important impact upfront, what matters more to me is having a patient-tolerated, long-term approach to this. So while PSA 90 is important—the percentage of patients that we get a 90 percent PSA decline in within the first three to six months is an important metric that we follow—what matters more to me is how long I can keep a patient on the therapy for the long run.

And ARPIs are fairly well tolerated, but they do have a number of side effects—things like fatigue, some glucose abnormalities, and some cognitive problems. And some of these can shorten the ability of the patient to stay on the medication for the full duration of response. And so, when we're looking at having somebody on this for maybe up to a decade even, what matters is having a good quality of life, having access to the medication, and having a patient who's willing to comply and take the medication on schedule.

Overall, again, I think the patient's ability to stay on medication and have a good quality of life is what matters most, rather than a big impact right up front.

Dr. Turck:
Turning to you now, Dr. Geynisman, how do tolerability considerations shape your decisions to adjust, interrupt, or continue AR-targeted therapy?

Dr. Geynisman:
It's a great question. First, we have to understand that men will be on this therapy, potentially, for many years. And so they really have to balance treatment with, as you've already heard, quality of life and their multiple, sometimes, other comorbidities. And all of the drugs that we use for metastatic hormone-sensitive prostate cancer—which, by the way, has recently been renamed APMN, Androgen

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Pathway Modulation Naïve, or APMS, Androgen Pathway Modulation Sensitive in the news by Prostate Cancer Working Group 4, but it's a mouthful, so I'll just keep saying castrate-sensitive prostate cancer or hormone-sensitive prostate cancer—these men will be on drugs for a long time. There's many of them. They're oral. They have a lot of interactions with other medications.

And so it's really important to talk to patients up front that this is a process, and there's going to be a lot of adjustments—dose adjustments and breaks, potentially. Sometimes you have to change medications depending on what other comorbidities they have and what some other doctor may put them on. And this is an ongoing chronic disease. I think of it as diabetes or congestive heart failure, right? We can't cure this, but we can manage this for a long time, and we have to work together to do that. And we have to have open lines of communication, so we know what they're doing, they know what we're doing, and we don't make mistakes.

Dr. Turck:
Dr. Geynisman, I'd like to dig a little bit deeper into some of what you were just saying. We know that many patients have multiple comorbidities, so how do you approach polypharmacy and manage potential drug-drug interactions when initiating or maintaining AR pathway inhibitors?

Dr. Geynisman:
So I think that's very important. And first of all, you have to look at the other medications the patients are on, and you have to sometimes enlist help: help, for example, from our wonderful pharmacists. I work closely with our advanced practice providers and nurses in the clinic, and we have to make sure that we understand exactly the other medications that the patients are on—frankly, run them through programs, whichever one you like to use, to make sure there are no drug-drug interactions.

And there's some very common ones that exist. For example, interactions between the ARPIs and blood thinners are very common, or calcium channel blockers, or diabetes medications. And you have to make sure and look particularly at that so that you choose the correct drug or the drug that, at least, is least likely to have potential for side effects.

Dr. Turck:
For those just tuning in, you're listening to *Project Oncology* On ReachMD. I'm Dr. Charles Turck, and I'm speaking with Drs. Daniel Geynisman and Jonathan Henderson about navigating the complexities of AR-targeted therapy in metastatic castration-sensitive prostate cancer.

Coming back to you now, Dr. Henderson, let's zero in on CNS-related effects. How do you assess and monitor for cognitive changes and neurologic risk, and how do those factors influence your choice of therapy?

Dr. Henderson:
That's an important question, and it’s top of mind in this patient population. So the first thing that I do is I see these patients at least every three months. That gives me the ability to personally gauge their cognitive abilities and any impairment. I rely heavily on family to weigh in on that as well.

I do not use a dedicated survey of any sort. It's basically just a physical exam and discussion. But the category of cognitive impairment is huge in the ARPIs, and frankly, it is the number one reason—that and fatigue—for decreasing dose, changing medications, or cessation completely.

Some of the newer ARPIs have less affinity to cross the blood-brain barrier, so that potentially modulates some of these effects. And that's something that I think most of us have already seen in practice; not just theoretical. And that's a very important impact on quality of life.

Patient-reported outcomes are important, again, more so to me with fatigue than cognitive impairment, because generally, the patient's a little too subjective in that situation to really understand that they're experiencing that cognitive impairment. And that's again why I rely on family input as much as I can.

Dr. Turck:
Now, cardiovascular health is another major consideration. So sticking with you, Dr. Henderson. And how does cardiovascular risk shape your treatment decisions upfront? And then how do you incorporate ongoing monitoring into your planning?

Dr. Henderson:
Yeah, cardiovascular risk in the mCSPC patient population is huge—really anybody with advanced prostate cancer—because the last thing we want to do is take a relatively indolent disease and, through treating that disease, create a bigger risk factor by accentuating cardiovascular toxicity. And ADT alone does that, but that's even more heightened when we are adding an ARPI to it. So we're disrupting multiple hormonal pathways and inducing metabolic syndrome for these patients.

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Prior to initiating therapy, I think it's important to assess the patient's cardiovascular risk, and I will contact the patient's cardiologist if they already have one and be sure. I don't get a formal clearance. I don't have an oncologic-cardiology associate in our vicinity. But for those people that do, I think that's an excellent resource. But I think involving the cardiologist is key for these people. And monitoring blood tests, along with symptomatology, is important. Again, the last thing that I want to do is treat somebody for a disease that has years and years of life expectancy with a medication that's going to cripple them from a cardiovascular stance.

Dr. Turck:
Before we wrap up, Dr. Geynisman, let's put this in the context of everyday practice. How do you coordinate across oncology, urology, pharmacy, and primary care to support adherence over time?

Dr. Geynisman:
Adherence is, obviously, very important. If you're not taking these medications, most of which are oral, you're obviously not going to get the benefit. And so it's exactly as you point out: you have to engage your colleagues and have a team approach.

For example, our pharmacy team will call the patients on a monthly basis to check in and make sure that they're not having new side effects that we're not hearing about, to make sure that they're receiving their medications, and to make sure that they're able to afford their medications. And if there are any issues, they will alert us. That's in addition, of course, to us seeing the patients as well. So working with pharmacists, once again, is critical from the very beginning.

I think that working with our urology colleagues is also fundamentally very important, because a lot of times we share these patients, and they go back and forth between our practices. And so we have to be aligned on what the goals are. We have to, obviously, be seeing each other's notes and documentation. And we have to be clear with the patients upfront that this is, in fact, the team approach for us—not always, but a lot of the times.

And then I think we just have to empower our patients to talk to us and report side effects so that we can work with them to do dose adjustments, which is okay. We have to remember that in all the clinical trials that got these drugs approved, dose adjustments, dose reductions, and breaks were allowed. So the great benefits that these drugs bring us comes with all of these breaks, interruptions, et cetera. So it is okay. I'd rather patients know that and talk to us, rather than not say anything and keep it to themselves. And then this occasionally happens: I find out months later, they say, listen, honestly, I haven't been taking my ARPI at all.

And so, again, I'd rather have this open communication, and I say that upfront to them. So it's really complex. As you heard Dr. Henderson say, we have to work with our colleagues. We have to work with cardiologists, we have to work with endocrinologists, nephrologists, and primary care physicians. It really takes a village to take care of these patients.

Dr. Turck:
That's a great comment for us to think on as we come to the end of today's program. And I want to thank my guests, Drs. Daniel Geynisman and Jonathan Henderson, for sharing their insights on how we can optimize the long-term patient-centered use of AR pathway inhibitors in metastatic castration-sensitive prostate cancer. Dr. Geynisman, Dr. Henderson, it was great having you both on the program.

Dr. Henderson:
Thank you, Dr. Turck.

Dr. Geynisman:
Thank you. Pleasure.

Dr. Turck:
For ReachMD, I'm Dr. Charles Turck. To access this and other episodes in our series, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.

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