Becky Campbell: Next we're going to move into a Q&A, and I'd like to invite Dr. Neal Shore to join back in to help moderate. We're going to be focusing on hormone therapy, hormone sensitive prostate cancer. You can type your question in the Q&A box at the bottom of the screen. And we did receive many excellent questions in advance, so we'll try to cover as much as we can.

Dr. Shore, we all got together for a little prep call to plan this session out a couple weeks ago, and we talked about the question of testosterone replacement. I'm just going to kick it off with that.

Is that an option? I know we received a number of questions in advance about how to balance the levels of testosterone and feeling well.

Dr. Neal Shore: Yeah, it's an exceptionally important and very contemporaneous question that I get asked all the time, especially in patients who are metastatic hormone-sensitive, some patients who are receiving androgen deprivation therapy for localized disease, particularly if they're getting radiation therapy.

The description that Dr. Holick gave was really very accurate. So many of these times, it can lead to, you know, to terrible depression and all the other somatic issues of bodily function, negative things that he talked about. Patients will oftentimes ask, “Can I get a holiday? Can I interrupt this treatment?” and sort of baked into your question as well, “Okay. if my numbers are still really suppressed, can I add supplemental testosterone?” And it's a very controversial area because so much of it really just depends upon the stage of one's disease. In the setting of advanced cancer, the worry always is, is that we're proverbially adding “fuel to the fire.” But these are really important questions that we deal with all the time. So, let me ask you, Alicia, do you ever stop the therapy that, whether it's parenteral or oral, that lowers testosterone suppression, monitor the testosterone level and sometimes see even a benefit? Even if the level doesn't come up because you're not administered therapy, maybe there's some feeling that there's a psychological benefit from avoiding therapy?

Dr. Alicia Morgans: Yeah, actually, we certainly we do this in the setting of medical challenges that sometimes people face, and we have to pause therapy. And we also do it when we sometimes even patients with metastatic disease, when they have an undetectable PSA for some period of time and for whatever the reason is. Often quality of life. Sometimes because they just don't want to keep taking medicines. They have good control. We stop the therapy. This is something that, if we're stopping an injection, is expected to actually not necessarily lead to very rapid recovery of your testosterone level, because it does take time for the body to kind of wake up after it's been suppressed for so long. But it's interesting that even when testosterone levels are still in the low range, even a very marginal incremental difference in testosterone, and perhaps it is just feeling well because you've been able to stop your injections, seems to be associated with people feeling better.

And it's not uncommon that I'm seeing someone in clinic and we've taken a pause and I say, “How are you doing?” And they talk about actually feeling

quite a bit better. And then the testosterone level comes in while we're chatting and I say, “Wow, well, it's actually still in a kind of low range. But I'm so happy you're feeling better.” And I can't necessarily say for one individual or another why they're feeling better. But if they feel better, to be honest, that's all we're really shooting for.

I would say that when it comes to metastatic disease, we would always, before we would stop something like hormonal therapy, have a discussion around “when do we restart?” Because this is something that I presume for most people, especially with larger amounts of metastatic disease, is going to be inevitable. And so I think those conversations with doctors around both “when do I stop” and “when would I probably have to restart?” our kind of the important way to keep that conversation complete.

Because if you're stopping and your doctor's expecting that you're going to restart treatment, but you don't know or realize that you're going to be restarting treatment, I can imagine that that would be a really stressful conversation.

If the doctor says, “Okay, we have to go back on treatment,” and that's not really something that you've thought was going to be necessary. So having both sides of that discussion are going to be really key.

Dr. Neal Shore: Yeah, I think that's really great. Later on, I think we're going to talk about some of the clinical trial work. You know, in prostate cancer, that we oftentimes--we regularly pay homage to Huggins and Hodges back in the 1940s. And that's been the quote “cornerstone foundation mainstay” of prostate cancer for over 70 plus years.

But now we're trying to think about using the ARPIs, you know, radio pharmaceutical therapies to try--SBRT as Dr. Sartor was asking earlier--to try to delay, mitigate, ADT initiation. And we're all trying to do this in a very thoughtful way.

I want to just go back for a second to Dr. Holick’s wonderful presentation about the importance of exercise. I mean, gosh, even throughout the arc of my career and in my medical school and residency, no one talked about this. But now we have, PCF has dedicated areas on its website, Maple Tree Cancer Alliance, IRONMAN, the importance of regular exercise, aerobic, cross resistance, owning what you want to do. You may not be able to run a marathon like Dr. Holick, which congratulations, that's amazing! But let me ask you: exercise is absolutely vital, vital to aging, whether you have cancer or not. What about nutrition? Let’stalk about nutrition. In addition to the vitamin D and calcium, do you have any nutrition recommendations? And in the spirit of being proactive to dealing with your cancer rather than taking the therapies that doctors prescribe?

Dr. Michael Holick: So one of the areas that is really not looked at carefully, but is incredibly important, is making sure you have a good source of protein intake. Many elders have a low protein intake and that definitely has a negative impact on their health. So I've started taking protein shakes with whey protein. Milk contains whey protein, which is--has all the essential amino acids. And so to me, that's one of the most important. I've increased my protein intake by almost 50g a day, just by

some of these protein bars and protein shakes. I think that those are very important. I think that, you know, having a healthy diet with green leafy vegetables, minimal red meat, all can add to your health.

Dr. Alicia Morgans: I agree…I would just say, Dr. Holick was giving examples of lean, lean kind of approaches that were lean protein, and I think that's the piece that I want to emphasize. So, we're not talking about protein, and, you know, red meat--obviously that contains protein--but red meat is not necessarily healthy for your heart health. Fried meats, fried foods, not necessarily healthy for your heart health.

So lean sources of protein might include fish, chicken, tofu, legumes like beans, and certainly these protein shakes and powders and things. But it's important, I think, also to pay attention to what's good for your heart, because this is going to be one of the main challenges as we age as well.

Dr. Neal Shore: Yeah, wonderful. In the final minutes, sorry to put this on you, Alicia, but a lot of questions coming up on the choice of ADT. So now we have typically intramuscular, subcutaneous agonist as well as antagonist. Now we have an oral antagonist. Tell us about the oral antagonist relugolix vis a vis parenteral administrations. How do you frame the decision if you're going to invoke ADT with all these different choices.

Dr. Alicia Morgans: So I think it's important to actually talk to your doctor about both of the options, because there are pros and cons for any individual to choose one or the other.

The relugolix oral pill option can be nice if you don't mind taking a daily pill, and I think a lot of people don't mind because they already are taking pills. And they also like the control of having the ability to start and stop that treatment, of course, under the direction of their doctor, if that's the decision that they're making. The other thing that's really, I think, beneficial about the oral pill option is that there seems to be faster testosterone recovery when you do stop your treatment.

It does take, it seems, less time for the testosterone to rebound or to come up to whatever level it will achieve, at less time than it would with a shot option. The other thing that may be the case is that there may be a better cardiovascular risk profile for the pills. What does that mean in English? There may be fewer effects in terms of heart risk.

And I would say, I say “may” because there's not been a definitive study that uses that outcome of heart attacks or strokes as the main thing that it's looking for that has been able to really successfully complete and show that benefit. But there has been a large amount, actually, of data in smaller studies and with other endpoints that suggest that that's the case. However, there are some patients who do seem to like and prefer the injectable option with one injection every number of months, whether it's three months or four months. This can be more convenient for some people, and from a coverage perspective, injections are typically covered with no out-of-pocket costs, whereas sometimes the pills can come with an out-of-pocket cost.

One piece about that, just so everyone's aware, Medicare is making changes in 2025 such that the out-of-pocket costs for anybody enrolled in Medicare Part D is capped at $2,000. This is for all medicines that they take, not just the medicines that they take for prostate cancer. So really important. And there's a thing that you can opt into called “Smoothing” that actually makes that $2,000 extend over the entire year. And you do that at enrollment. And if you do that, I think it's around $160 - $768 a month that you'd have to pay over that whole year for all prescriptions. Anyway, that was a little off topic, but just a public health announcement that I wanted to put out there for anybody on Medicare.