Flince - Interview

All right. If you would start out by telling me a little bit about your practice, the setting that you re in, and a bit about the mix of patients you treat.
Okay. I am an adult urologist. I m in practice in a suburban area of a large urban center. It s a multispecialty group in which there are two practicing urologists and approximately 60 other practitioners, primary care, rheumatology, et cetera, and I mixes pretty much all adult general urology.
Okay. Good. Well, that s interesting. I talked to a lot of urologists that are in big urologist practices, not many that are one of two in a big mixed group. That s interesting. I wonder if that changes the mix of patients you see at all. Today we re going to be talking about metastatic castrate-resistant prostate cancer. If you think about that population, about how many of those patients would you estimate are under your care right now?
Metastatic castrate-resistant prostate cancer, somewhere between five and 10, I would say.
Okay. Perfect. Give me a sense, within that practice, what are the diagnostics and treatment options for these patients that you can offer right there at your practice and what are the kind of things that a patient has to go somewhere else for? Can they get an MRI right there or things like that?
Basically, we don t have a lot of options in that regard, certainly from diagnostic stuff but other than oral medication or injection, usually it would be like GnRH hormonal therapy, that would depend on what I can offer in the practice. We don t have it in-house. Radiology, I don t do infusion but primarily that s it.
Okay. Perfect. All right. Talk me through if a patient is under your care and let s say they re on they ve had resection, they re on adjuvant ADT therapy, and their PSA starts to rise. Talk to me about the things you want to do at that point and when you might think about referring that patient to someone else.
There s a lot more to that. Patient s age and how long they ve been a patient of mine but assuming that scenario and I have full knowledge of their underlying disease and their status and all that stuff, I

typically once patients become castrate-resistant, I almost always at that point just start including oncology and have them at least establish a relationship with an oncologist only because the disease is going to progress, and so it s better to have them onboard earlier rather than later. I d say 95% of patients will go. There s a very small group of people who won t go until more advanced stuff but that s really the onset of just castrate-resistant disease, much less metastatic castrate-resistant disease.
Okay. Sorry, I m blanking on words right now. The androgen receptor pathway inhibitors. Are you ever offering any of those? I m thinking about enzalutamide, any of those kinds of drugs?
Novel hormonal agent?
Exactly, the novel hormonals.
Yes, I will. Typically, in certain patients that I think they re low risk and don t have a lot of comorbidities, I would initiate treatment with something. Usually I use Erleada. That s one that I have the most comfort with in those patients as I send them along to oncology and that s usually about the extent of my comfort zone.
Okay. Why is Erleada the one you re most comfortable with? That s apalutamide.
There s so many of these agents out there. There s so much conflicting information. That s the one that has good performance, good tolerability. That s my interpretation of the available data.
All right. Are you using that in hormone-sensitive, as well as I guess you said you don t really treat somebody that s castrate-resistant, so using it in hormone-sensitive patients or M0, as well as M1 or what s your I guess where are you comfortable using it?
Again, generally it s pretty rare that I ll do it in hormone-sensitive patients unless they have really aggressive disease but I will start it in hormone-resistant patients with just biochemical recurrence. If someone presents a metastatic disease,
typically I might suggest it but I would also that really denotes a more aggressive disease situation and I would tend to recommend that they get with the oncologist because there s often more that they ll need if they have possible metastatics at that point.
Okay. There s something called PSMA PET scans. Is that something you re familiar with or have asked for in any of these patients?

I m familiar with it. I ask for it sometimes. I think a lot of us are still trying to figure out exactly what the best place is to try to use it. In these patients
Exactly.
In these patients, I m still not sure what exactly information that gives you and how valuable it is because that s occurred. My personal feeling is which is not really where it s indicated yet that it s better indicated in before treatment patients if it can be more if it can be better refined to be more sensitive there to determine if it was a better candidate for definitive treatment versus systemic treatment but that s not really the spot where it seems to be slotted out. Again, for some
Where does it seem to be slotted now? Where do you see other people using it?
Usually again, in the situation of is the recurrence biochemical, is there visible evidence of metastatic disease. The most common place that I would use it now would be where I think it actually has value would be in someone who has undergone surgical treatment and has biochemical recurrence and there s a potential consideration or for salvage radiation therapy, curative salvage radiation therapy.
Got it.
Again, if someone s already failed all the curative treatments then in my opinion, it doesn t really have a significant effect on my management whether he has identifiable disease on a PET scan or not. It s still hormonal therapy
Okay. Good.
with novel hormonal agent. I ll use it somewhat but not a super amount.
Got it. All right. I want to show you product description. I brought this up on screen and this is a new targeted radioligand therapy for the treatment of patients who are PSMA-positive with metastatic castrate-resistant prostate cancer and have been treated with at least one of these androgen receptor pathway inhibitors. Take a look at this product profile. Once you ve had a chance to review it, I want to talk about what your reactions are and what the value seems to be to you. [Activity]
Okay. I mean to me because it s an infusion, probably not anything that I would myself at this point in time be getting involved with.

Possibly oncology or cancer center type of thing but that s what I d say about it.
This is something that would be administered by radiation oncology or a nuc med. I know that s not clear here but I actually have a little bit of information about that here. It does require radioactive material licensure and all of that stuff. The question I have for you is is it something you would imagine referring for or not really that either, not getting involved in that way?
The efficacy doesn t seem super. Four months isn t great. That s the problem again with a lot of the products that are available and out there for down the line in prostate cancer, they all have somewhere in these months or so of results, there s very few that there s very little that separates them and again, to really deal with things like this type. I don t deal directly with this type of hormonal treatment. I can t tell you where this falls in.
Okay.
No, I would not be likely to be the one to push for this especially in this patient population but just again, my opinion of these results are that four-month survival, four-month progression-free survival is not a huge benefit.
Yes, okay. It s not looking like it s that impressive in terms of its efficacy and it s just that down the line enough that it s not something that you would be seeing yourself dealing with directly is what I m hearing.
Right. Again, I don t know where it would fall in line with these oral novel hormonal agents and then there s the chemotherapy agents and there s PARP inhibitors. There s all kinds of things now and so many different options for castrate-resistant prostate cancer and it is very difficult for me and quite frankly something that I don t really want to devote a lot of time to to try to figure out what is the best option because in this group of patients at this stage with these types of treatments, there is not one that I want to get super involved with. It s just not within the scope of my practice.
Absolutely. The patient that you re using Erleada is not yet metastatic and so if they transition to metastatic, you ll definitely be getting them a med onc consult at that time so that the med onc if it felt like it was the right time could bring this up. Is that how you see working

that would be the person who would be thinking about this or who would you imagine would be thinking about this?
Yes, the medical oncologist would be. Yes, correct.
Okay. All right. Fair enough. All right. I would like to, if you ll bear with me, I want to go through a couple of patient scenarios and just understand a little bit about as you read through the description of this guy, his history and his current status, first of all, I want to talk about if this feels like a realistic patient for you. Let s start there, so read it through. [Activity]
I mean I guess yes, there s no real ultimate surgical pathology, it s hard to know exactly and why
Well, tell me more about that. Without his surgical pathology, what s missing? What information about his surgical pathology would help you think about what comes next?
What the Gleason score was on his pathology, the extent of the disease, was there any extra prostatic disease at the time with positive margins, why potentially this individual when he had supposedly a good result from surgery, eight years of undetectable PSA after radical prostatectomy and then had a rising PSA, why wasn t he treated before initiating hormonal therapy? Why wasn t salvage radiation attempted as a curative option? That s a little out of the realm of typical that I ve seen.
Good. Okay. This idea that he got to PSA undetectable from his complete prostatectomy and then eight years later when his PSA began to rise, why go directly to ADT and not try some salvage radiation to try to again, get to a curative option at that point? Is that right?
Yes, why wait until his PSA is 3 if he s being followed carefully, salvage radiation with or without a neoadjuvant hormonal therapy. Again, a lot of that depends on his underlying surgical pathology. It s best to initiate at earlier points in time with PSA levels as low as .1, .5, certainly below one. It seems like that was totally missed here.
All right. That s really useful to help make these cases stronger. Talk to me about if this had been the way this guy was treated, where would you involve a medical oncologist here? At what point? They did put him on the ADT. His PSA levels stabilized and then began to rise again and at that point there were metastatic lesions to the pelvis and ribs and enzalutamide was added. Would you imagine that

might be a place where you might add treatment or a place where you would refer him off? Assuming that there s no symptoms associated with those mets?
Again, firstly, that s a very unusual presentation, at least in my opinion. That someone goes again, from surgery, undetectable PSA, rising PSA, hormonal therapy. I don t know what stabilize means but on hormonal therapy, the PSA should be undetectable and then rise again. I m not sure what stabilize means and that s probably not the best word, at least for his etiology and then how again, how high does it rise before follow-up imaging is done? Most of these people don t go from biochemical recurrence to metastatic castrate-resistant disease. They usually go to non-metastatic castrate-resistant disease before that s that, in my opinion, is another unusual step in just the disease process. In that situation, I would typically potentially be comfortable adding the novel hormonal therapy in that setting in the non-metastatic castrate-resistant disease but once and if the patient did progress and ultimately he didn t respond to it or developed metastatic disease, then I would send him. Or I just think there s a lot of steps
Okay. There s a lot of things that don t add up here. Okay. That s fair. All right. That s useful. Let s do the same thing with Ethan and see. I have a feeling in the early stages of his history, there may be gaps as well because I think the folks who
put this together were focused on the later stage stuff but let s take a look and see how it goes.
Okay. [Activity] Okay.
Anything that stands out as unusual here or does this feel like a fairly typical presentation?
Well, they don t say how old he was at diagnosis and I m not sure how to interpret image-guided radiation therapy, ADT initiated. Was this neoadjuvant hormonal therapy, for how long? He has high risk prostate cancer with a Gleason 8 and PSA 15, the current recommendations are two years of neoadjuvant hormonal therapy. It says two years later. Does that mean that he never responded? Something is off there and
Well, I think two years later, I would assume that he did respond to the ADT. He was able to stay on that for two years and then he started to have a consistent rise. No?

I don t know. I mean to me it s not clear whether that s again, the question is when was the hormonal therapy initiated? Was it initiated as part of a neoadjuvant protocol with ?
Yes, exactly. Let s assume that that was the case that the image-guided radiation and the ADT were initiated at the same time.
Exactly.
Basically, if he had it for two years where it says the moment he stopped hormonal therapy, his PSA rose which means that he didn t respond at all to treatment and so he never got off hormonal therapy and they I m not sure whether they added I guess
I see.
Darolutamide as opposed to something else but
Yes, with a non-metastatic castrate-resistant patient like this, what would you be offering at that point that will work with it?
With Erleada.
Okay. Then his PSA is rising for three years and nothing was done, they don t talk about his doubling time and then all of a sudden, they decided to look again and now he s got metastatic disease. It just seems that it doesn t all just add up. That s all.
Okay. I think it s just a language issue. I think we can assume that he was treated with ADT and darolutamide successfully for 36 months and then after multiple PSA rises, conventional imaging showed four mets in the pelvis and femur. I think the bullets do represent different points in time, and so at that point he was given a PSMA PET. Go ahead.
Right. If you re treated with darolutamide and hormonal therapy and your PSA is rising consecutively, multiple times, typically you re doing these in intervals of three months, so that s a lot of time. What change in treatment was done then before imaging showed multiple mets? What were people doing?
I think the question is what would happen next in treatment. This is confirmation that the darolutamide, he has progressed on the ADT plus darolutamide, so what would happen next? What would be the next course of action? If this patient did present to you with this current status, what would you be thinking to do for this guy?
He d be referred to the oncologist right away because there s nothing more
Right.

Because he already failed novel hormonal therapy, I think he s managed because he s already failed it. He hasn t had his treatment modified. He hasn t had a second-line treatment despite rising PSAs and that s come back to bite him because now all of a sudden, in addition to biochemical recurrence, he has metastatic disease. I would definitely understand how this goes. In my opinion, this guy has been mismanaged in his treatment.

Okay. Good. That s extremely useful. Typically, in a patient like this, nobody would be waiting that long if he had the the PSA rises, they d be changing therapies and the likelihood that he d have PSA rises along with mets showing up for the first time is highly unlikely. Is that fair?

I mean if he has PSA rises on multiple occasions and you re not responding to it either by initiating treatment yourself or by having taken some initiative in referring the guy to an oncologist then what do you ?

Do you see Provenge used much at all either by you or by other treating physicians for not for this specific patient but it just raised the question for me of other treatments that are out there.

I can t recall the last time I saw Provenge used at all.

Okay. What about Xofigo, same question?

I believe I ve had one patient who s probably on fourth or fifth line therapy with his type of advanced disease where I used Xofigo.

Okay. When patients are on those fourth or fifth line therapies, what are they coming to you for? What is your role in their care at that point?

Mostly it s maintenance with hormonal therapy and assessment of any underlying urinary issues. Again, if these people may be having radiation-related hematuria, et cetera or sometimes they ll have disease that can create obstructive uropathy, they would be requiring stents or even nephrostomy tube or something like that on top of everything.

Yikes. Do you feel that as you do continue to manage these patients, metastatic castrate-resistant, the care is fairly consistent among the medical oncologists that are treating them or do you see it all over the board and not really a lot of logic to it?

I d say 95% of the patients that I see, I work with one medical oncologist.

Consistently because it s one. Okay.
patients who go elsewhere but I have a good relationship with the medical oncologist, he s on the faculty of a large university hospital here with a cancer center, with a lot of resources.
In the area that I practice, there are a lot of tertiary care facilities with very strong worldwide reputation, so sometimes patients will go there as opposed to where I would recommend to this one tertiary care center but that s generally the place, the one oncologist that I tend to work with and again, we tend to have a very good relationship and I see a lot of consistency in his practice patterns and again, he s very good about keeping me in the loop and we have very open and clear lines of communication.
I m curious if the way you re practicing now where you ll contemplate or use Erleada and then pass along to him at that point, if that has changed at all in the last, I don t know, three to four years, are you passing patients earlier? Are you holding them a little bit longer or has that been quite consistent as the use of novel hormonal has evolved and as other treatments have come into play?
I m still referring them just as early when they become typically castrate-resistant but impressions and then with in understanding our practice patterns, we both agree that it s fine and he does to start Erleada while sending them over. I ll also send them at the same time but typically with Erleada on board.
Yes, exactly. All right. Coming back to the logistics for this product, this idea of having a product that would have to be referred out to radiation oncology or a nuc med, so the medical oncologist would have to be making this decision to refer out this patient during this period of time as well. Do you have any feeling about whether that makes sense during that time or whether there would be hurdles to patients or physicians wanting to get involved with a treatment like this in that point of time? Does it make sense?
I m not sure I understand the question. I m sorry.
This idea of having a product that would have to be the medical oncologist would have to refer the patient to a radiation oncologist or a nuc med department for six treatments that are six weeks in between and I m just curious during this course of time that we re talking about when a patient is metastatic castrate-resistant, if you see

any barriers to willingness to do that or do you feel like this would be pretty readily added into the treatment mix at that time?
I mean I don t know based on what I m seeing here that anybody can refer him. It doesn t have to be a medical oncologist. I suppose if there are urologists who are comfortable in treating these patients so far down the line then I guess they could refer them just as easily to the medical oncologist. It s just a matter of who is actively treating these patients and changing medications and treatments as they progress, in my experience with that I have, I d say 99+% of the time it is the medical oncologist then I don t think there s any barriers there but because they re the ones who have the contact within that and they re the ones who have their boots on the ground as it were.
Exactly. All right. Well, listen. I do think those are my questions for you today. I appreciate you taking the time. This has been really, really helpful. This has filled some gaps in my knowledge, so I appreciate it and enjoy the rest of your evening.
Thank you very much. You have a good evening as well. It s all good. Thanks.
Thank you. Bye-bye.