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Integrating Guideline Updates in Squamous Cell Carcinoma of the Anal Canal

Announcer:
You're listening to *Project Oncology* on ReachMD, and this episode is sponsored by Incyte. Here's your host, Dr. Charles Turck.

Dr. Turck:
This is *Project Oncology* on ReachMD, and I'm Dr. Charles Turck. Here with me today to examine how we can integrate the updated NCCN® Clinical Practice Guidelines into our management of squamous cell carcinoma of the anal canal is Dr. Stacey Cohen. Not only is she a Professor in the Clinical Research Division at Fred Hutch Cancer Center, but she's also a Professor in the Division of Hematology and Oncology at the University of Washington School of Medicine. Dr. Cohen, welcome to the program.

Dr. Cohen:
Thank you so much for having me today.

Dr. Turck:
Well, to get started, the NCCN® guidelines now include chemoimmunotherapy among the preferred first-line options for eligible patients with unresectable, locally recurrent, or metastatic squamous cell carcinoma of the anal canal. From your perspective, what practical implications does that have for clinical care?

Dr. Cohen:
It was a really big change to include immunotherapy with chemotherapy or, as you said, chemoimmunotherapy, as part of our guidelines, because historically, we've really managed anal cancer with chemotherapy. We know that in localized disease we use chemo and radiation. In metastatic disease, we were largely using chemotherapy or reserving immunotherapy for later lines. So this was practice-changing when we finally had randomized data suggesting that the combination of chemotherapy and immunotherapy led to better survival. So that was a very exciting change to see.

Dr. Turck:
Now, the guidelines also note that first-line therapy selection should take into account patient-specific factors like performance status, organ function, autoimmune history, and HIV status. So how do you conduct individualized assessments when applying guideline recommendations in practice?

Dr. Cohen:
I think this is part of our regular workup that we would do for any patient, which is that you have one idea for what the on-paper answer is supposed to be for how you treat a patient, and then you need to adjust that treatment plan according to many different factors, including patient goals, patient characteristics, and desire for treatment or not.

And so, with immunotherapy, we are opening up a whole new drug class for which we have to be careful about any potential autoimmune-type reactions. So, even when these guidelines came out, and even when the POD1UM-303 data came out, I was not able to use this regimen on every patient, because we certainly do see patients for which immunotherapy is not the right choice.

For example, I had a patient who had a previous exposure to immunotherapy and had a very bad reaction with a bad skin rash. And so I knew that when she recurred with metastatic disease, that for her, the risk/benefit really did not favor chemoimmunotherapy, and instead, our classic chemotherapy alone was the better choice.

And so I think, fundamentally, while we have changed the standard, preferred first-line therapy, preferred does not mean it's right for every patient.

Dr. Turck:
I think it's important to call out that in prior guideline iterations, single agent PD-1 inhibitors were positioned after progression on platinum-based chemotherapy. But now that immunotherapy is included within preferred first-line combination regimens, how are you thinking about treatment sequencing across the disease course?

Dr. Cohen:
I think it's a lot more complicated now. So, with every good change in first-line therapy, you ask the best question, which is, what do we do next? Because, unfortunately, we are not curing most patients with first-line therapy, and so they are going to need to be exposed to subsequent therapies. And so I would say, if someone did not get immunotherapy in the first line, as in previous times, I absolutely would try to give them immunotherapy in the second or subsequent line. If they get immunotherapy with chemotherapy in the first line, then we're in a much stickier situation, and so I think I would first pause and try to ask myself, why do I think that person could no longer be on first-line therapy?

Because if it was a toxicity based on their chemotherapy backbone, for example, maybe continuing with immunotherapy made sense. On the flip side, if they had a clear immune toxicity, maybe chemotherapy made sense. But if they just had standard disease progression, then we really don't know the right answer.

But I think the guidelines suggest to us that maybe going on chemotherapy alone is the best choice, and I would say, as with some other targeted therapies, maybe we would do chemotherapy alone in the second line and consider immunotherapy alone in the third line—for example, if your patient was fit enough. But truly no one knows the answer to that question.

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 Dr. Stacy Cohen about integrating updated NCCN® guidelines for the management of squamous cell carcinoma of the anal canal into clinical practice.

So, Dr. Cohen, when using platinum-based chemotherapy in combination with immunotherapy—which, again, are regimens currently reflected in the preferred first-line options—what practical steps do you take to monitor and manage both chemotherapy-related toxicities and immune-mediated adverse events?

Dr. Cohen:
We have standard labs that we follow with every cycle of chemotherapy. And when we use just chemotherapy alone, we're more focused on blood counts and liver and kidney function. Now, we're going to add in a wider panel of labs, including looking for hormonal-based disruption by the immunotherapy. And so I think that that would be part of our screening.

We're, of course, going to be talking to patients about how they are feeling. And you have to have a slightly different ear for potential toxicities. So, what I mean by that, is that you can get inflammation of any body part, really, from immunotherapy. And so one such example would be that you could get pneumonitis, or inflammation of the lungs.

And so in another disease, I have a patient who's on immunotherapy and she called in complaining of some shortness of breath. And it could be an asthma exacerbation, it could be an upper respiratory infection, but we can't forget that that could be the early signs of a potentially very severe reaction to her immunotherapy drugs. And so I think we just have to be careful about dismissing minor symptoms as being not something to worry about, and think about if that could actually be the early sign of a problem. Because we know that immune-mediated adverse events are rare but serious, and they can get even worse if you continue to expose someone to an immune-based agent after they've already started to develop that symptom.

And so I think that it takes an education of yourself and of your team members—because, often, our first line of defense are very valuable nurses who are talking to patients—so educate everybody on the team, including the patient themselves, that we really do need to know the variety of symptoms that they may be experiencing. And then, from there, we can try and decide, is this something to worry about? Is it not? Do we just follow it up closely? But I just caution everybody, because it's not necessarily the classic side effects that you might expect.

Dr. Turck:
If we look beyond the guidelines for a moment, real-world implementation of the preferred regimens may be influenced by access and reimbursement factors. In your experience, how can prior authorization requirements or coverage variability affect the use of these therapies?

Dr. Cohen:
Well, when a new drug comes out, often it's not accessible to many individuals, whether it's because they haven't put it through their institution's formulary yet, because they have it on formulary but insurance is denying it, or because maybe a provider doesn't even

know to be using a new regimen. Because the dissemination of data is a feat in and of itself. And so, I think that there are a lot of barriers between data coming out, guidelines being updated, and that actually getting to the patients that require those treatments. And so, thankfully, when you're at a bigger institution, they may have pathways for prior authorization for counseling and patient access. But we know that there are simply delays that can happen.

However, usually when there is a guideline update and when there is phase 3 data, often that does trickle down, and we do see insurance coverage. We do see providers being able to get the drugs more, and sometimes we see instances where someone may choose to adapt the approved regimen based on what they do have on formulary, such as swapping out one PD-1 inhibitor for another, because maybe they either have more comfort with it or maybe they have more access to it.

And so I think, while there are some issues that are beyond our power, sometimes it also goes to a provider's comfort level about what drugs they know and what they feel comfortable giving. Because if the provider doesn't feel good about the therapy, they certainly can't deliver that effectively to their patient.

Dr. Turck:
Now, even with these guideline recommendations, treatment selection ultimately involves shared decision-making. So before we close, Dr. Cohen, how do you use these updated recommendations to guide conversations with patients about goals of care, quality of life, and expectations for therapy?

Dr. Cohen:
So I think the guidelines allow us to show that even in a rare cancer, we've made some progress. And what an exciting thing, because so often, rare tumors do not have specific trials being evaluated in that space, and so we have to borrow data from other types of cancer treatments. And so, how exciting now that we have a specific trial being done for metastatic anal cancer that has allowed us to change standard of care. And so I think that as we talk with patients, we can let them know that there are some changes being done. I think it encourages both excitement in the treatment itself, but then patients may also be more willing to enroll on clinical trials in that space, knowing that we really are seeing that level of change.

So I think it's an exciting time, because care hadn't really changed in a number of years, so to be able to do that is great. And then, as I said, with that, we need to make sure that all team members know about that. So, in the multidisciplinary space, everybody is aware that we talk about changes in prognosis, updates, and what we might anticipate for prognosis.

And so I think with every new trial, it really adds to our knowledge and hopefully improves our ability to take care of patients.

Dr. Turck:
Well, as those comments bring us to the end of today's program, I want to thank my guest, Dr. Stacey Cohen, for joining me to discuss how we can apply the updated NCCN® guidelines for the management of squamous cell carcinoma of the anal canal in clinical practice. Dr. Cohen, thanks for being here today.

Dr. Cohen:
Thank you so much.

Announcer:
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