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Significance of HER2 Expression in Solid Tumors

Announcer:
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Dr. Pant:
This is CME on ReachMD. Hi, I'm Dr. Shubham Pant.

Dr. Salani:
And I am Dr. Ritu Salani.

Dr. Pant:
Now, HER2 alterations are associated with the development of a wide range of solid tumors and poor prognosis. So, Dr. Salani, what is the significance of HER2 expression in solid tumors?

Dr. Salani:
From a gynecologic malignancy standpoint, HER2 expression has classically been associated with poor prognosis, and we've seen that in cervical cancer, ovarian cancer, and endometrial cancer, where we have the most data. And it seems like this is something that we can now exploit, so I think we have some exciting updates.

What do you see in GI cancers?

Dr. Pant:
Yeah, same thing. So I think about, what, 3 decades back it came into breast cancer, and I think it's really interesting that now we're incorporating it into multiple, multiple GI malignancies and really looking at different things. Again, the HER2 IHC, different ways of categorizing it in GI cancers versus breast cancer. How you do the immunohistochemistry, utilizing FISH and other ways to kind of look at the protein overexpression. So I think it's a really exciting part here in GI cancers and in gynecological cancers, obviously, that we can use these agents that we use in other cancers, especially breast cancer, into now GI and gyn cancers.

Dr. Salani:
Yeah, and I think we've learned a lot from our colleagues such as you, who've been using it for a lot longer. And one of the things that we haven't really understood in gyn cancers and still are kind of developing and understanding is kind of what the right testing is. There's protein overexpression, gene amplification, and actually HER2 mutations. And so there's a variety of different kind of HER2 changes that you may see and understanding how each of those may impact cancer treatments is really important.

What are your thoughts about the significance of HER2 expression?

Dr. Pant:
Yeah, thank you, Dr. Salani. You're exactly right. So interesting. HER2 expression, again, you really, for me, we really have to go to our

pathologists, but it's kind of different again in different malignancies. So sometimes in, let's say, gastric cancer, you have these little pockets that you have to really look at multiple pockets to look at HER2 expression.

The other important thing is, most of the recent tissue-agnostic approval, let's say for trastuzumab deruxtecan, is for HER2 IHC 3+. Remember, because in the trial was done in IHC 2+ and 3+, so we really need to know that expression level. And I think that expression level really matters when you come to the efficacy of these drugs. So it's really important.

The other important things are tumor heterogeneity. As we know, primary tumors can have different expression than metastatic tumors, so I like to get a good core biopsy from the metastatic sample to see the expression. But they can be intratumoral, like even different metastatic areas you can have different biopsies, different HER2 expressions, so it's inherently complicated in a way. But the main thing is, for our listeners, is that they really need to do that biopsy of that metastatic sample and test it out because they can be different things.

The other thing is the lines of therapy. So I'm going to, again, take an example of gastric cancer. So more than a decade back, trastuzumab was approved in the frontline setting based on a trial called the ToGA trial, which I thought was a really cool name by the way. So they brought trastuzumab in the frontline, but now we have trastuzumab deruxtecan in the second line for gastric cancers. However, we want to retest these patients because there is a percentage of patients, when they have been treated with trastuzumab, they lose the HER2 expression. So if you don't have that expression, if you don't have that target, then that targeted therapy is not going to work there. So it's very, very important, I think, to retest HER2 overexpression, because I think that really matters. Because in the patients who've lost that expression, that targeted therapy is not going to work.

So what do you think, Dr. Salani, similar things in gyn cancers?

Dr. Salani:
Yeah, our experience with HER2 is kind of still emerging but we do see that there is that same, exactly like you described, temporal and kind of also that intratumor heterogeneity, and so I do think kind of testing multiple specimens. I worry a little bit, just kind of anecdotally, about patients who may have a negative HER2 expression in one area, but 2 or 3+ in another area. Those are the patients where you may get a mixed response, and maybe combination therapies will be the next kind of opportunity for those patients. So I think it's really important to enroll patients in clinical trials so we can just help optimize the right treatment strategies for our patients.

Dr. Pant:
Yeah, and I think, to end, I think HER2 has emerged as a valid target in GI cancers and gyn cancers and lung cancers, also in bladder cancers. So it's amazing to see where the field is going.

And with that, great discussion, but our time is up. Thanks to our audience for also tuning in.

Announcer:
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