Transcript Details

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Testing for Solid Tumors: Tissue and Liquid Biopsy Approaches Using NGS Technologies for cfDNA and ctDNA Analysis

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Moore:
HER2 antibody-drug conjugates are emerging as potential new treatment options for patients with advanced solid tumors, which begs the question: What's the best way to identify these tumors and who might benefit from this new class of agents?

This is CME on ReachMD, and I'm Dr. Kathleen Moore.

I think we can all agree that testing for HER2 alterations outside of breast and gastric cancer is not currently standard but is rapidly becoming so. And the studies that have been reported to date are currently relying on use of immunohistochemistry, either from new tumors or from archival specimens, which has generated some very promising data, but does come with limitations. Biopsies are invasive. Outside of breast and gastric cancers, we really don't know the temporal heterogeneity of HER2 expression, so if we're relying on archival specimens, sometimes from many years ago, does that really represent the state of the tumor now? So there's a lot of interest in developing these blood-based or liquid biopsies that we can do in real time at the time we're thinking about a new therapy for a patient to really identify who will benefit from these exciting new drugs. And we did see some data come out in the past year trying to get us there, looking both at cell-free DNA, as well as circulating tumor DNA [ctDNA].

And so from the HERALD study, this was an enormous screening study. Almost 5,000 patients were screened to find the 252 that were amplified by cell-free DNA. And of those patients who were identified, the response rate was quite high and very durable. So this did look like a very good way to identify patients who were highly likely to respond, in this case to trastuzumab deruxtecan. So that was exciting news.

We then saw a couple of smaller studies, the HERB study and then a correlative analysis out of DESTINY-PanTumor that looked at patients who were enrolled on clinical trials of trastuzumab deruxtecan by IHC, but it also looked, at the time of enrollment, at ctDNA to see how well it correlated. And these are small studies. HERB was just done in biliary tract, and of course, DESTINY-PanTumor in all solids. But very consistent lack of concordance. So only about 35% to 36% of patients who met eligibility for both of these studies, which was 2+ and 3+ gastric scoring by IHC, were found to have ctDNA.

Now, if they had ctDNA, there was a signal that those tumors responded better than those that did not have ctDNA, but those tumors that did not have ctDNA that were otherwise IHC expressing still responded. So it wasn't a sort of yes/no. We'll pick based on ctDNA just may enrich for patients who are going to do better. So at this point, it's not quite ready for prime time.

In my practice, what we do is, when we're sending a tumor specimen out for next-generation sequencing, we use an assay that has IHC as an option and so we're adding on HER2 IHC, in this case to all of our cervix, endometrial, and ovarian specimens, but we're also

getting amplifications. We're getting both, so we can assess for either biomarker and access clinical trials and now NCCN listed agents for our patients. Hopefully in the future, these blood-based biomarkers will get a little bit more sensitive and so they may be able to some day replace tissue-based screening. But for now, that remains the standard of care.

And that's all the time we have for today. Thank you so much for joining me.

Announcer:
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