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Application of guidelines-recommended broad molecular profiling to patients with NSCLC

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

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Dr. Paz-Ares:
This is CME on ReachMD, and I am Dr. Luis Paz-Ares.

Dr. Gubens:
And I'm Dr. Matt Gubens.

Dr. Paz-Ares:
The NCCN Guidelines recommend broad molecular testing for patients with advanced non-small cell lung cancer. So, Matt, when you see a patient diagnosed with metastatic non-small cell lung cancer, how do you approach your biomarker testing today?

Dr. Gubens:
Well, lung cancer has such a proliferation of actionable genomic targets that it's essential, especially, non-squamous patients, but even in selective squamous patients, to do broad molecular profiling from the get-go. This is faster than the old piecemeal approach. It conserves tissue. It gets us the answer we need.

Generally, I approach this as a single next-generation sequencing, or NGS, test. It can be either DNA or RNA based. Our group favors RNA, a little better fusion capture, but really either technology is adequate. And at a minimum, you want to test for the set of mutations and fusions for which we have targeted therapies: EGFR, ALK, ROS1, BRAF, NTRK, MET, RET, KRAS, HER2. Really, any of the modern NGS panels are going to catch all these.

Another question is, do we do this based on the tissue from a biopsy or from a liquid biopsy technology? And I think these can be complementary. Certainly, the gold standard over time has been the tissue biopsy, and that's still what I will send. But if a patient has a high burden of disease and symptoms, or if we have the opportunity to do a liquid biopsy even as we're waiting for the biopsy results to come back, I'll send that as well. That can be complementary, and it can be quicker. But the key thing to remember there is that the liquid biopsy, while when it's positive, you can trust and act on the results, if it doesn't show results, you still want to wait for that tissue biopsy because sometimes you can have things that are below the level of detection for the liquid biopsy.

And of course, PD-L1 is essential, too. The assay probably doesn't matter so much, but you want that to also choose, if there's not a targeted opportunity, which of the immunotherapy or chemoimmunotherapy options you're going to go with. That comes back faster. So especially in non-squamous, it's important to wait for the NGS as well, even though you have that PD-L1 in hand.

Luis, what about early-stage non-small cell lung cancer? How do you approach molecular testing in that setting?

Dr. Paz-Ares:

So I have to say that today I'm not differentiating very much the information that really I would like to have for the late-stage as compared to early-stage. And also, on the being pragmatic, having an NGS test with a wide panel is going to really shorten the time we have the information and also is going to provide more information today. Of course, the minimum thing I could need is EGFR and ALK profiling.

For that reason, typically, at my institution, we typically do default testing. So when my pathologists see a biopsy, regardless it's advanced stage or early stage, they typically do the NGS testing. Liquid biopsy is somehow of less, let's say, utility here because less often we got ctDNA enough to do the testing in early stages, particularly in stage 1. But as you said, it could be complementary.

Secondly, of course I'd like to have PD-L1 expression on the tumor. That is helping me to decide also if that particular patient could go to chemo/IO before surgery or maybe to chemo and then IO after surgery. So I think molecular testing and molecular information is really essential to guide the treatments today.

Dr. Gubens:
I completely agree. And again, I think that you're right, that when you can get your pathologists to do reflex testing, that can really shorten the time frame and get a patient to adequate appropriate treatment as soon as possible.

One emerging interesting extra testing we're thinking about these days is with the tumor agnostic approval of trastuzumab deruxtecan. Separate from the HER2 mutation we look for in NGS, I also now look for HER2 expression, because if we do happen to find 3+ expression, even without the mutation, we have another treatment granted in the second line and beyond.

Dr. Paz-Ares:
Absolutely. I'm pretty sure that in the coming years, we will add on a number of other biomarkers to really guide the treatment for our patients. But the bottom line is without proper molecular information, I don't think we will be able to do the right variety of the treatment of our patient.

Well, this has been a brief but a great discussion, I think. So I hope we have given you something to think about. And thank you very much for tuning in.

Announcer:
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