Transcript Details

This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/project-oncology/emerging-biomarkers-nsclc-adcs/49137/

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Emerging Biomarker Research for NSCLC Antibody-Drug Conjugates

Announcer:
Welcome to *Project Oncology* on ReachMD. On this episode, we'll hear from Dr. Christine Bestvina, who's an Associate Director for Clinical Operations for Thoracic Oncology at the University of Chicago Department of Medicine. She'll be discussing how biomarker research is evolving and what it may reveal about which patients with non-small cell lung cancer are most likely to benefit from antibody-drug conjugates. Here's Dr. Bestvina now.

Dr. Bestvina:
As we increasingly use antibody-drug conjugates in the treatment of non-small cell lung cancer, there are multiple different types of biomarkers that are generating interest. We have molecular alterations that can identify patients as candidates for certain antibody-drug conjugates. Right now, those include having an EGFR mutation for which patients are candidates for Dato-DXd. Additionally, we have HER2 mutations in lung cancer, which signal sensitivity to trastuzumab deruxtecan.

Outside of molecular targets, though, we can look at IHC expression to identify patients as candidates for certain treatments. Right now, c-Met overexpression identifies a group of patients that are able to receive talisoV for c-Met overexpression with 3+ at 50 percent or greater.

But then there are other biomarkers that are less clear, such as Trop-2 expression where expression doesn't directly correlate with sensitivity to certain treatments, and we need to do better at trying to use these biomarkers or potentially develop new biomarkers to better identify what therapies are best for each patient.

As researchers, one of the challenges that we probably didn't predict when determining what biomarkers were going to predict response has been that for multiple different antibody-drug conjugates and for what was thought to be the initial biomarker, things just didn't pan out the way that we thought. For multiple different targets of these antibody-drug conjugates, the IHC expression did not clearly identify which patients were most sensitive to the drugs. And so we've had to try to get smarter about using biomarkers because these simple IHC stains are just not going to be the answer for all of these different antibody-drug conjugates.

So there's been increasing interest in composite biomarkers. How can we include antigen expression, tumor subtype, prior therapies, payload sensitivity, and even resistance biology to better identify a biomarker, even if it isn't as clean as simple IHC expression?

As we try to advance biomarker research in parallel with the development of new antibody-drug conjugates, there has been increasing interest in how we can use artificial intelligence and other things to try to help us develop better biomarkers for each individual patient. And in lung cancer, some of the biggest strides and some of the most promising data that we've seen has been Trop-2 NMR, or Trop-2 normalized membrane ratio, that is measured by QCS, or quantitative continuous scoring.

So this is a complex process; I'm going to try to break it down as clearly as possible. But IHC staining is performed for the Trop-2 assay. Whole slide imaging is performed, and using AI, we try to understand how much Trop-2 expression is on the cell surface or on the membrane versus how much expression is within the cytoplasm. That creates a ratio to try to understand essentially how much internalization of Trop-2 is occurring, and that seems to be a better biomarker or a better predictor for response to Dato-DXd, which is a Trop-2 targeting antibody-drug conjugate.

While this was only done in a retrospective fashion, there are currently multiple clinical trials that are utilizing this in a prospective fashion to see if we can better identify those patients to benefit from Dato-DXd.

Announcer:

That was Dr. Christine Bestvina discussing how advances in biomarker research may help identify patients with non-small cell lung cancer who might benefit most from antibody-drug conjugates. To access this and other episodes in our series, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!