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/adc-nsclc-how-they-work-candidate-selection/49133/

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Antibody-Drug Conjugates for NSCLC: How They Work and Who's a Candidate

Announcer:
You're listening to *Project Oncology* on ReachMD. On this episode, we'll hear from Dr. Laura Alder, who's an Assistant Professor of Medicine at Duke University School of Medicine in Durham, North Carolina. She'll be discussing the evolving role of antibody-drug conjugates in the non-small cell lung cancer treatment landscape. Here's Dr. Alder now.

Dr. Alder:
So ADCs, or antibody-drug conjugates, are an exciting new treatment option. They're unique because they combine the precision of targeted therapies while also retaining the cytotoxicity of chemotherapy.

How I describe them to patients is they're more of a 'targeted chemotherapy,' like a smart bomb. And so it has this monoclonal antibody that is directed across something that the cancer cell expresses. And then once the ADC gets there, it releases the chemotherapy payload, and it's linked through a very unique chemical linker. A lot of these are designed to specifically release when they get to their intended location in that tumor cell environment, and a lot of these are even sucked into the tumor cell to maximize killing effect. And so what's nice is unlike standard chemotherapy, they deliver the highly potent payload or the cytotoxin directly to the cancer cell. And so the benefit of that is that really expands the therapeutic window. We can deliver these really effective chemotherapy payloads directly to where they need to go.

Another interesting thing with ADCs is they have this bystander effect. So not only are they targeted exactly where that tumor cell is, but they can also kill the neighboring tumor cells that may or may not express that same target. We know that the target or biomarker expression differs a bit even within the same tumor. And so that bystander effect of ADCs is really powerful because even if that ADC doesn't get exactly where it needs to be at every location, it seems like it even has benefit beyond where it's targeted.

So it's an important question to choose the best candidates for antibody-drug conjugate therapies. We know the best candidates are patients with any biomarker-defined tumors. So when they match an ADC's target antigen—we have a few of these already out that we use in everyday clinical use—trastuzumab deruxtecan is the HER2-mutant non-small cell lung cancer treatment, we have Dato-DXd for EGFR-mutant non-small cell lung cancer after prior targeted therapy and platinum-based chemotherapy, and we have TalisoVi for c-Met overexpressing non-squamous non-small cell lung cancer. Usually when we use these ADCs, they're for patients who have already progressed on the frontline treatments, such as immunotherapy, TKIs, and chemotherapy, and these can provide a really valuable option for the next line of treatment.

One thing that I want to emphasize is as we're thinking about how we can best treat our patients when the previous therapies have failed them, it's really important to make sure that they have comprehensive biomarker testing. And so like I mentioned, that includes HER2 mutation or expression via IHC. Since trastuzumab deruxtecan is also approved in HER3+ by IHC, TROP2 expression can be useful, and c-Met IHC is needed for TalisoVi. So it's very important that as we're thinking about next-line options, we make sure that these patients already have that testing available.

Announcer:
That was Dr. Laura Alder talking about the expanding impact of antibody-drug conjugates in non-small cell lung cancer. 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!

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