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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Innovations Shaping the Future of Antibody-Drug Conjugates in NSCLC

Announcer:
You're listening to *Project Oncology* on ReachMD. On this episode, we'll explore the evolving development landscape for antibody-drug conjugates in non-small cell lung cancer with Dr. Christine Bestvina. She's an Associate Director for Clinical Operations for Thoracic Oncology at the University of Chicago Department of Medicine. Let's hear from Dr. Bestvina now.

Dr. Bestvina:
As we continue to design next-generation antibody-drug conjugates, there are multiple different characteristics of these ADCs that can be modified and hopefully optimized compared to the earlier agents. One of the things that has been modified is the linker and particularly its stability. That will frequently affect how much drug is delivered, where, and when, as well as the toxicity profile.

We're also looking to try to optimize the drug-to-antibody ratio. I think that is something that certainly has improved as we've gotten more familiar with these antibody-drug conjugates. Loading as much as possible to each specific antibody is probably not the right answer, and instead, we need to optimize that DAR, or drug-to-antibody ratio, for each particular molecule.

As far as how we're going to continue to optimize the use of antibody-drug conjugates in our clinic in the next several years, we're going to be using a variety of clinical trials that try to move antibody-drug conjugates into the first-line space. A good example of this is a trial looking at trastuzumab deruxtecan in the first-line space for patients who have HER2-mutated non-small cell lung cancer.

We also have a variety of clinical trials that are utilizing antibody-drug conjugates in the first line in combination with immunotherapy as doublet treatment and even in triplet combination with immunotherapy and more traditional chemotherapy agents. How these will pan out from both an efficacy and a toxicity perspective still remains to be determined.

Additionally, we need to answer the question of rational antibody-drug sequencing. And that may include not just clinical characteristics such as efficacy and toxicity, but also trying to understand for each individual patient what is the best target and what is the best payload to try to optimize patient response.

We need to continue trying to modify these ADCs to allow for minimal toxicity. One of the things that I certainly have noticed in my clinic in using antibody-drug conjugates is that the cumulative toxicity of these drugs can be difficult for patients. The fatigue and the cytopenias over time can be very challenging because oftentimes with ADCs, there's not a set duration of therapy. We keep it going for as long as the patient is tolerating it and as long as the patient is having clinical benefit. But I think there's a lot that needs to be individualized to each patient about what is even considered tolerable. That is certainly an individualized patient decision about when that side effect burden may outweigh the potential clinical benefit.

And so I think this is a very exciting field. I'm very excited to see how we're going to evolve in the next several years, and I'm also excited that we have this drug class to help extend patients' lives and improve their outcomes.

Announcer:
That was Dr. Christine Bestvina talking about how innovation is shaping the next generation of antibody-drug conjugates for 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!