Transcript Details

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Targeting HER2 in Advanced Solid Tumors: A Comprehensive Understanding of the Rationale and Potential Benefits

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

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Dr. Pant:
HER2 antibody-drug conjugates [ADCs] are emerging as potential new treatment options for patients with advanced solid tumors. But how do HER2 antibody-drug conjugates work, and why is targeting HER2 in these tumors a good idea?

This is CME on ReachMD. Hi, I'm Dr. Shubham Pant.

Now first, let's start out by looking at how HER2 antibody-drug conjugates work. The mechanism for action – first, we have an antibody and it's designed such that immunogenicity is minimized while maintaining a high target affinity. And what that means is that we really want the drug to bind to the target in the cancer cell. Now the linker which is there must be stable in circulation to avoid premature release of payload and to decrease any side effects because of early release of payload, so that linker must be stable. And also, you have the cytotoxic payload. For example, the topoisomerase I inhibitor and trastuzumab deruxtecan, and that goes inside the tumor cell and kills the tumor cell. So it's really like a smart bomb attaching to the surface of the cancer cell and really releasing its payload inside. Now ADCs have been successful in HER2 tumors in breast, lung, and gastric cancers, and now they're being tested in other tumors.

The clinical rationale from HER2-targeted ADCs comes from DESTINY-PanTumor02, which is a phase 2 study of trastuzumab deruxtecan for HER2-expressing solid tumors. This was presented in ASCO 2023 and updated in ESMO 2023. Now, the key eligibility criteria were that patients needed to have advanced solid tumor that were not eligible for curative therapy, the HER2 expression needed to be IHC [immunohistochemistry] 3+ or 2+, and prior HER2-targeting therapy was allowed. And on the results we saw objective response and duration of response across a wide variety of tumor types, including endometrial, cervical, ovarian, bladder, and biliary tract cancers. And this response was durable. The progression-free survival of all cohorts was 6.9 months, with the patients with HER2 IHC 3+ had a median PFS of 11.9 months. All patients had an overall survival of 13.4 months, and patients with IHC 3+ had a median overall survival of 21.1 months.

And interestingly, in a recent publication, it was found that HER2-low expression, that was IHC 1 or 2+ for IHC, was common across many solid tumor types, about 41% of patients. And a significant number of patients without HER2 alterations, that was 35.7%, had HER2 expression which is greater than or equal to 1+. And what that means is potentially in future studies we could use ADCs to target this HER2-low expression just like has been done with breast cancer in the past.

This is an important part of drug development because, historically, treatments have been limited to traditional cytotoxic chemotherapy and radiation, and they sometimes are not well tolerated and potentially have less efficacy in these really specific tumor types with these amplifications.

To conclude, HER2 antibody-drug conjugates certainly sound like viable treatment options for HER2-expressing solid tumors. Please check out the other episodes where results for some of those specific tumor types are discussed.

Thank you for joining me today. I'm Dr. Shubham Pant, and this has been CME on ReachMD.

Announcer:
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