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

Pivotal Data on Targeting HER2 in HER2-Expressing Solid Tumors

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

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Dr. Pant:
This is CME on ReachMD, and I am Dr. Shubham Pant. Today I'll review some of the pivotal data on targeting HER2 and HER2-expressing solid tumors.

And I'll start with the latest data that we have on DESTINY-PanTumor02. Now the study design had patients with advanced solid tumors not eligible for curative therapy. This was a second-line patient population that have HER2 protein expression by IHC 3+ or 2+ and prior HER2-targeting agents were allowed. Patients also were required to have an ECOG 0 or 1. T-DXd, which is a HER2-targeted antibody-drug conjugate, was given at the dose of 5.4 mg/kg once every 3 weeks, and there were different cohorts: cervical cancer, endometrial cancer, ovarian cancer, biliary tract cancer, pancreatic cancer, bladder cancer, and other tumors.

Now the overall response rate and the duration of response, when you look at the overall response rate across all patients, it was 37.1%, but this was really pronounced amongst the patients who had IHC 3+, which was 61.3%. Of note, patients with bladder cancer and IHC 3+ had an overall response rate of 56.3%. In the other cohort, they had an overall response rate of 44.4%. In patients with IHC 3+ biliary tract cancer, it had an overall response rate of 56.3%. Whereas in pancreatic cancer, it was a 4% overall response rate, but no patients who were HER2 3+ had a response.

The median duration of response for all patients was 11.3 months, with the patients with IHC 3+ had the best median duration response of 22.1 months.

Now in these DESTINY-PanTumor02, we did see a robust best percentage change in target lesion from baseline in multiple tumor types. According to the safety, now this an antibody-drug conjugate, patients do see some treatment-related adverse events, which are similar to chemotherapy like nausea, vomiting, fatigue. So in this trial, any drug-related treatment-emergent adverse events were in 84.3% of patients and greater than or equal to the grade 3 were in 38.6% of patients.

Of note, one of the main side effects, which is rare but can be very serious, is ILD or pneumonitis, which was, again, which can be T-DXd related. Some patients did also had left ventricular ejection fraction, with about 4% of patients with a grade 2 left ventricular ejection fraction decrease.

Now we are coming to another study called HERIZON-BTC-01. This is the biggest study of its kind in patients with biliary tract cancers where HER2 2+ or 3+ and they were ISH positive, in situ hybridization positive. Patient received zanidatamab once every 2 weeks. This was a global trial of 80 patients with biliary tract cancers. The zanidatamab was given on day 1 and day 15 with a primary endpoint of overall response rate. And 42% of patients had confirmed overall response rate by independent central review. The patients with HER2 IHC 3+ had an overall response rate of 51.6%. And the median duration of response for these patients, that means the patients were responding, the median duration of response was 14.9 months.

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Now again to summarize key points of the discussion based on the DESTINY-PanTumor02 data, trastuzumab deruxtecan was approved in the setting after frontline therapy in patients with HER2 3+ positive disease, which was a tumor-agnostic approval.

Well, this was a brief but hopefully useful overview. My time is up. Thank you so much for listening.

Announcer:
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