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<https://reachmd.com/programs/cme/biliary-tract-and-pancreatic-cancer-her2-targeted-adcs-for-gastrointestinal-cancers/16560/>

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Biliary Tract and Pancreatic Cancer: HER2-Targeted ADCs for Gastrointestinal Cancers

Announcer:

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

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Pant:

Survival rates for patients with advanced pancreatic and biliary tract cancers remain dismal, around 10% to 12% after 5 years; however, new HER2-targeted therapies are beginning to show promising treatment.

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

We've seen the success with HER2-targeted antibody-drug conjugates in HER2-positive breast and gastric cancers. The next logical step is to see what happens when trastuzumab deruxtecan, T-DXd, is used to treat advanced HER2-positive pancreatic and biliary tract cancers.

I'm going to discuss the results of DESTINY-PanTumor02, which was reported in ASCO 2023 and was updated in ESMO 2023. This was a basket trial for patients with unresectable and/or metastatic solid tumors who were HER2 positive defined as IHC 3+ or IHC 2+ and ISH [in situ hybridization] positive, except patients with breast, gastric, or gastroesophageal junction cancer or HER2-mutant non-small lung cancer.

Now, a meaningful response was seen with T-DXd across a range of HER2-expressing tumors. Specifically for biliary tract cancers, there was a response rate of 22% for all, which is IHC 2+ and 3+, and the patients who had IHC 3+ disease, their response rate was 56.3%. The median duration of response for all patients was 8.6 months. In pancreatic cancer, we saw lower rates of response, with only 4% of patients having a response to T-DXd in this basket trial.

Other drugs which are in development, SHR-A1811, which is an anti-HER2 [ADC] with trastuzumab, a cleavable linker, and a topoisomerase I inhibitor payload. This has shown efficacy in phase 1 study of solid tumors, also especially BTC, biliary tract cancers. Also ORM-5029, which is another HER2-targeted ADC being investigated in advanced solid tumors. Now this is comprised of Smol006, a highly potent G1 to S phase transition 1 degrader conjugated to pertuzumab. Study enrollment is ongoing, and we are looking forward to seeing results in the future.

I'm also going to discuss a bispecific HER2 agent called zanidatamab, which is also reported in biliary tract cancers in ASCO 2023; 80 patients with IHC 2+ and 3+ and ISH positive were reported. The overall response rate per investigator assessment and by independent central review was 41.3% with the duration of response of 12.9 months, and the median time to first response of 1.8 months.

So to conclude, HER2 is an oncogenic driver in biliary tract cancer, and targeting HER2 is associated with responses in these patients.

Well, that is all the time we have for today. Thank you for joining me.

Announcer:

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