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Bladder Cancer: HER2-Targeted ADCs for Genitourinary Cancers

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

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Dr. McGregor:
Treatment of advanced bladder cancer remains challenging. We've had a lot of success and revolution in the frontline therapy, but we know for those few patients who progress on platinum or now combination of enfortumab vedotin and pembrolizumab, we really have limited treatment options and a dearth of targeted agents. But HER2 is overexpressed, and bladder cancer is not looking at IHC in upwards of 20% to 30% of patients, and HER2-targeted antibody-drug conjugates, or ADCs, may be the path forward for certain populations.

This is CME on ReachMD, and I'm Dr. Brad McGregor.

So HER2 ADCs and HER2-positive breast cancer and gastric cancer have shown treatment success and are now really a standard of care. But what about other solid tumors? Particularly ones that are difficult to treat, such as urothelial carcinoma. What happens when we start looking at the role of HER2 ADCs in those patients, specifically drugs such as maybe trastuzumab deruxtecan, or T-DXd.

So DESTINY-PanTumor02 was a trial that was tumor agnostic, looking at the role of T-DXd given every 2 weeks in those patients who overexpressed HER2 by IHC. This is in contrast with PanTumor01, which looked at the role of the drug in those patients who had a mutation. And so this was a trial of the drug in patients with endometrial, cervical, ovarian, bladder, as well as others including biliary tract cancers and pancreatic – patients that had HER2 overexpression as defined by IHC using the gastric assay, so not the breast cancer assay.

And research specifically looked at those with bladder cancer. They had 41 patients enrolled. The objective response rate overall was 39% with a median duration response of close to 9 months. But we start looking at those who had increased HER2 expression, IHC 3+, that response rate went up to 56%. And I will comment that investigator-assessed IHC, there was some discrepancies between investigator and central review. So I think learning better how to directly assess and best assess the HER2 expression is going to be critical.

So this is obviously exciting results, but what about toxicity? So, there's really no new safety concerns identified in this trial versus all the other trials. The most common grade 3 or higher treatment-emergent adverse events were neutropenia, anemia, fatigue. And the one that everyone cares about the most, obviously, its interstitial lung disease. So we saw that in about 10% of patients, with the majority of those low grade, with only one grade 3 event.

So really exciting early data, you know, across tumor types, specifically in bladder cancer. And there's also studies where we can maybe combine this with immunotherapy. So there was a trial presented by Dr. Galsky where they combined T-DXd with nivolumab, and we saw some, sort of, exciting responses with an objective response rate of 37%, again, higher in those who were HER2 3+. And then

there's other ADCs out there. The one that's furthest along RC48, or disitamab vedotin, which is another HER2 ADC that's linked to MMAE [monomethyl auristatin E]. So we had very early data from China looking at the role of RC48 alone in patients as second-line therapy with intriguing results. And then we had another trial where they combined RC48 with immunotherapy on 36 patients. And the objective response rate was close to 40%. So really, really exciting data and really suggests that as we move forward, HER2 can be a viable target in urothelial carcinoma. It's definitely maybe something within these variant cells like micropapillary, where we see overexpression of HER2 by IHC. And while right now, HER2 ADC isn't a standard of care unless you're looking at going to clinical trial, I think in the future, as we get further development and these drugs are approved, it will be a standard, of care and I really look forward to how we can incorporate this into our treatment armamentarium to improve outcomes for our patients.

Unfortunately, that's all the time we have for today. I want to thank you for joining me.

Announcer:
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