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Comparing First-Line TROP2-Directed ADCs in Metastatic TNBC: Latest Clinical Evidence

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Dr. Cortés:

Welcome. This is CE with GLC. I'm Dr. Javier Cortés, and today I'll review the latest clinical data on anti-TROP2-directed antibody-drug conjugates for the first-line treatment of patients with metastatic triple-negative breast cancer who are not eligible for immunotherapy.

As we all know, 3 antibody-drug conjugates have been entered in randomized phase 3 clinical trials: sacituzumab govitecan, datopotamab deruxtecan, and sacituzumab tirumotecan.

Sacituzumab govitecan has been explored in 2 trials in the first line with or without immunotherapy. Today I'll review the data in those patients who are not eligible for immunotherapy, patients who are not candidates for pembrolizumab, atezolizumab, because their tumors did not express PD-L1, or because the patients were not candidate because of any other reason.

Patients were randomized in the ASCENT-03 trial to SG or chemotherapy, including either paclitaxel, nab-paclitaxel, or carbo/gem. The primary endpoint was progression-free survival by BICR. And of interest, patients in the control arm were able to cross to SG, and this crossover strategy was provided by the sponsor beyond progression.

The primary endpoint was met, and progression-free survival was clearly improved. The hazard ratio was 0.62 in favor of sacituzumab govitecan. Overall survival was immature at the time of this analysis.

The second study, TROPION-Breast02, explored another antibody-drug conjugate against TROP2, Dato-DXd. Similar strategy, Dato-DXd versus chemotherapy in a similar patient population with some differences. Crossover was not there. Monotherapy was allowed in the control arm, but not doublets, and some differences in inclusion criteria, including patients with a very short treatment-free interval of less than 6 months, was also allowed here.

Two primary endpoints: PFS and survival. Both PFS and survival was met. Hazard ratio of PFS was 0.57 and hazard ratio for OS 0.79.

However, adverse events were different between SG and Dato-DXd. The most important and well-known adverse events with SG were neutropenia and diarrhea. Grade 3 or higher neutropenia was reported in 43% of patients. Grade 3 diarrhea was reported in 9%.

On the other hand, with datopotamab deruxtecan, the most important adverse events were stomatitis in roughly 60% of patients, being grade 3 or higher in 8%, and ocular toxicity in the range of 47%, grade 3 or higher in the range of 7% to 8%.

All grade 3 or 4 treatment-related adverse events were slightly higher with SG, 61%, than with Dato-DXd, 33%, based on hematological toxicities.

So, dear friends, the most important question that we have in the clinic, how to select the first-line anti-TROP2 antibody-drug conjugate

for our patients? Well, we have 2 drugs, 2 good approaches to treat these patients, both of them showing improvement benefit in PFS.

We don't have survival data with SG based on the impact of crossover and also the immaturity of the data. So how to select this in the clinical practice, in my opinion? We have to discuss about toxicity. We have to take into account the shorter or longer duration, the schema, the schedule, the strategy. But at the end, all these aspects to discuss in detail with our patients. What is better for them is something that we'll have to discuss in detail.

Dear friends and dear colleagues, again, thanks very much for listening. Has been a great pleasure, but unfortunately, that's all the time we have today. Thanks for listening.

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