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What's Next for TROP2-Directed ADCs in TNBC?

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Dr. Traina:

Welcome. This is CE with GLC. I'm Dr. Tiffany Traina. Today, I'll review emerging strategies for managing triple-negative breast cancer using TROP2-directed ADCs.

So first, let's talk about ASCENT-04, which was the sister trial to ASCENT-03. This is studying sacituzumab govitecan with pembrolizumab in patients who have PD-L1-positive tumors in the first-line setting for metastatic triple-negative breast cancer, defined as having a CPS score of 10 or higher.

And this trial met its primary endpoint. Median progression-free survival with sacituzumab and pembro was superior to that of chemo, with a median PFS of about 11 months compared to 7.8 months, and that was highly statistically significant.

So let's talk a little bit about what other ongoing studies are there. Well, we have TROPION-Breast05, which is looking at a very similar patient population: first-line metastatic triple-negative breast cancer patients who have a PD-L1-positive tumor.

This study is randomizing patients to either standard of care chemotherapy with pembro or datopotamab with durvalumab, the checkpoint inhibitor, and interestingly, this trial has a third arm, datopotamab monotherapy. And I think, importantly, looking at answering that question of whether checkpoint inhibitor is of benefit when patients are potentially progressing with a short disease-free interval after having seen early-stage treatment.

There is also the TroFuse-011 study. This is a first-line study in metastatic triple-negative breast cancer. It's asking the question, also, can antibody-drug conjugate combination with IO potentially expand the benefit of checkpoint inhibitors even beyond those tumors that are PD-L1 positive alone?

So in this study, patients have PD-L1-negative tumors, CPS less than 10. They are in the first-line setting for metastatic triple-negative breast cancer. They have at least a 6-month disease-free interval, and they're randomized to sacituzumab TMT [tirumotecan] versus sacituzumab TMT with pembrolizumab or treatment of physician's choice, choosing between either taxane or gem/carbo combination.

And then lastly, let's think about earlier-stage disease.

In the neoadjuvant setting, we have the TROPION-Breast04 study examining datopotamab with durvalumab compared to KEYNOTE-522.

There is TroFuse-032. In this trial, patients receive Sac-TMT with pembro versus the KEYNOTE-522 regimen.

And then we have ADAPT-TN-III. This is a phase 3 study looking at sacituzumab versus sacituzumab/pembro in patients who have

stage I triple-negative breast cancer.

There are a portfolio of trials in the adjuvant setting after patients have received neoadjuvant therapy and have residual disease. So, for example, TROPION-Breast03 is examining datopotamab deruxtecan versus dato/durvalumab versus standard of care therapy.

We have the ASCENT-05 trial looking at sacituzumab with pembro compared to treatment of physician's choice.

And then finally, TroFuse-012 is using sacituzumab TMT with pembro versus standard of care such as pembro, capecitabine.

So with that, thank you so much for listening. Thank you for spending time with us. I hope that brief overview was helpful.

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