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Current Unmet Needs in First-Line Treatment of Metastatic TNBC

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Dr. Cortés:

Welcome. This is CE with GLC. I'm Dr. Javier Cortés, and today I'll discuss the current unmet needs in the first-line treatment of patients with metastatic triple-negative breast cancer.

As we all know, metastatic TNBC is a critical unmet need. Patients with metastatic TNBC who are candidates to first-line treatment, about two-thirds of these patients will be unable to receive immune checkpoint inhibitors. The 2 out of 3 patients, the standard of care today continues to be chemotherapy-based therapy. However, unfortunately, between 30% to 50% of all patients who start first-line chemotherapy will be unable to proceed into the second line, and if we count these patients who started second-line treatment, about 50% of them will be unable to proceed to a third-line setting. So in total, approximately 1 out of 4 patients will start third-line treatment or beyond.

So what are the treatments our patients received in second, third line, or of course in first line? In the first-line setting, according to a paper published by Kevin Punie in *The Oncologist* in 2025, he observed that a majority of patients start with chemotherapy as either monotherapy or in combination. As I said before, only 1 out of 3 patients will be able to combine these chemotherapeutic strategies with immune checkpoint inhibitors, those ones whose tumors do express PD-L1.

In the second-line setting, we have seen a clear change over the last years. Many patients still continue to receive chemotherapy, but more and more patients have started to use antibody-drug conjugates, with sacituzumab govitecan being the preferred option in this tumor type.

In the third-line setting, patients will receive the treatment depending on the treatments the patient received before. If not an ADC, SG is the standard of care. If patients received SG already, chemotherapy continues to be the standard of care. In some countries, sequential strategies with different antibody-drug conjugates are also discussed.

What about the prognosis of patients with triple-negative breast cancer? Unfortunately, the median overall survival continues to be poor, and the median progression-free survival with first-line chemotherapy rarely exceeds 6 months. Over the last years, a very modest improvement has been seen basically in the tail of the Kaplan-Meier curves, but the median overall survival has changed very, very modestly.

And as I said before, median PFS continues to be very poor in the first-line setting, with median PFS ranges from 5 to 6 months at best. We will combine chemotherapy plus pembrolizumab, or atezolizumab. This is slightly longer in the range of 8 to 9 months.

So among these patients with this scenario, new drugs are clearly needed, and anti-TROP2 antibody-drug conjugates have appeared as one of the most exciting drugs to be used in the clinical practice. TROP2 is expressed in tumor cells compared with normal cells, and

this glycoprotein is associated with worse prognosis. Antibody-drug conjugates have shown an improvement in long-term outcomes in the second line and beyond. And recently, sacituzumab govitecan, SG, and datopotamab deruxtecan, Dato-DXd, have shown also improvements in the first-line setting.

Well, my time is up. I hope you found this brief overview helpful. Thanks for listening.

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