New horizon of TNBC: clinical outcomes and perspective of a novel Trop-2 antibody-drug conjugate

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Patients with metastatic triple-negative breast cancer (mTNBC) have poor survival outcomes. Although immunotherapy has shown effective 1st-line clinical activity, single-agent chemotherapy remains standard for previously treated mTNBC. However, chemotherapy is associated with low response rates and short progression-free survival (PFS). A novel targeting agent, Sacituzumab govitecan (SG), is an antibody–drug conjugate composed of an antibody targeting the human trophoblast cell-surface antigen 2 (Trop-2), which is expressed in the majority of breast cancers and urothelial cancer, coupled to SN-38 (topoisomerase I inhibitor) through a proprietary hydrolyzable linker. The U.S. FDA has granted approval for the treatment of metastatic triple-negative breast cancer (mTNBC) and metastatic urothelial cancer (mUC) in 2021 successively.

In phase III ASCENT trial, a total of 468 mTNBC patients without brain metastases were randomly assigned to receive SG (235 patients) or chemotherapy (233 patients). The median PFS was 5.6 months (95% confidence interval [CI], 4.3 to 6.3; 166 events) with SG and 1.7 months (95% CI, 1.5 to 2.6; 150 events) with chemotherapy (HR for disease progression or death, 0.41; 95% CI, 0.32 to 0.52; P<0.001). The median overall survival (OS) was 12.1 months (95% CI, 10.7 to 14.0) with SG and 6.7 months (95% CI, 5.8 to 7.7) with chemotherapy (HR for death, 0.48; 95% CI, 0.38 to 0.59; P<0.001). The percentage of patients with an objective response was 35% with SG and 5% with chemotherapy. The most common AEs associated with SG were neutropenia (63%), diarrhea (59%), nausea (57%), alopecia (46%), fatigue (45%), and anemia (34%). SG is an effective and generally well-tolerated agent that represents a promising novel therapy for patients with mTNBC. The most common adverse effects observed in patients with mTNBC treated with SG parallel those of chemotherapy and can be manageable with early, proactive intervention.

The FDA and EMA consider SG to be a first-in-class medication and approved for medical use in the European Union in November 2021 and in Singapore in January 2022 respectively. There are several other ongoing clinical trials involving SG in the treatment of mTNBC as part of a combination therapy and in the neoadjuvant setting. SG is also being studied in the treatment of HR+/HER2- mBC and other cancers.