

Novel Approaches in Triple Negative And HR+/HER2- Metastatic Breast Cancer - Anti-Trop2 ADC And Future Development

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Patients with metastatic triple-negative breast cancer (mTNBC) and endocrine-refractory hormone receptor positive HER2-negative metastatic breast cancer (HR+/HER2- mBC) have relatively poor survival outcomes among all breast cancers. Though the emergence of innovative agents, such as checkpoint inhibitor, CDK 4/6 inhibitor, has transformed the treatment paradigm in first-line settings, limited option other than conventional chemotherapy remains for patients after failure of frontline treatment.

However, chemotherapy provides low response rates and PFS in later lines of both mTNBC and HR+/HER2-mBC, along with the intolerable adverse effect to bear. Antibody-drug conjugates (ADCs) are a rapidly growing class of potent anticancer drugs, allowing targeted delivery of cytotoxic agents to cancer cells and/or the tumor microenvironment, which it to enhance the cytotoxicity at tumor site but reduce the potential off-target adverse effect. Sacituzumab govitecan (SG) is a first-in-class TROP-2-directed ADC with an anti-TROP-2 antibody conjugated to SN-38, a topoisomerase I inhibitor via a pH-sensitive hydrolysable linker. The novel design permits intracellular and extracellular release of the membrane permeable payload, enabling the "bystander effect" to contribute a greater potential for improved clinical activity in heterogeneous biomarker expression.

The U.S. FDA has granted approval of SG in the treatment of metastatic triple-negative breast cancer (mTNBC), locally advanced or metastatic urothelial cancer (mUC) and unresectable locally advanced or HR+/HER2-metastatic breast cancer (HR+/HER2- mBC) successively. SG is also under evaluation in several ongoing clinical trials including in earlier setting, in combination with different novel agents, and across different tumor types. Simultaneously, several Trop-2 targeted ADCs have also been under investigated at current stage, demonstrating the potential of Trop-2 targeted therapy to address more unmet needs in the future. Dr. Amy Krie will walk us through the current state of art about Trop2 as a therapeutic target in breast cancer, with a particular what impact anti-Trop2 ADC can and will bring to the patients from her clinical experience and perspective.