Sacituzumab Govitecan: A Revolutionary New Treatment for Aggressive Breast Cancers

The new immunotherapy drug holds promise as a therapeutic option for patients with metastatic triple-negative breast cancer, who may not have responded to other treatments.

Since the 1980s, chemotherapy has saved the lives of millions of women diagnosed with breast cancer. But there are still many types of breast cancer that do not respond to chemotherapy. Moreover, chemotherapy targets all the cells in the body, regardless of whether they are cancerous or healthy. As a result, it can cause severe side effects, such as nausea, diarrhea, and low white blood cell counts (neutropenia), which can have a significant impact on patients' quality of life.

Thus, while the advantages of chemotherapy are undeniable, there is still an urgent need for precision-targeting therapeutics with improved efficacy and fewer side effects. One of the newer advances in breast cancer treatment is the immunotherapy drug Sacituzumab Govitecan. In a recent *Annals of Medicine* review, a global team of doctors collected and analyzed the clinical trial data on Sacituzumab Govitecan. The review highlights its anti-cancer potential, particularly for a rare and aggressive form of the disease called 'triple-negative breast cancer (TNBC)'.

TNBC is a type of cancer in which tumor cells lack or have low levels of estrogen receptors and progesterone receptors, and do not show high levels of human epidermal growth factor receptor 2 (HER2). Treating TNBC is challenging, because the cancer grows rapidly and has a high risk of recurring. It also does not respond to hormone therapy, which is frequently used to treat other types of breast cancer. "*TNBC accounts for 15–20% of all breast cancer cases*," explains Dr. Shivendra Shah from Nepalgunj Medical College, Nepal, who is the corresponding author of the review. "*Using Sacituzumab Govitecan to treat TNBC could constitute a paradigm shift in precision medicine.*"

Sacituzumab Govitecan is a three-part molecule that contains an antibody, an active anti-cancer agent, and a proprietary water-soluble linker connecting the two. The antibody portion consists of a 'humanized' monoclonal antibody (proteins produced by a line of identical cells, which are highly specific to certain antigens or receptors). Here, the monoclonal antibody is specific to trophoblast cell-surface antigen 2 (Trop-2), a receptor that is found only on cancer cells. 'Humanized' refers to the modification of non-human-derived proteins to make them similar to proteins produced by humans. The anti-Trop-2 antibody is linked to a molecule called SN-38, which is the active agent of the commonly known anti-cancer drug called irinotecan. "*Because the antibody only targets cells that express Trop-2, Sacituzumab Govitecan delivers its payload to only cancer cells, thereby minimizing collateral damage to surrounding healthy tissue and reducing severe side effects*," says Dr. Shah.

As a part of their review, the research team evaluated all the available literature on Sacituzumab Govitecan. They found two milestone clinical trials for the drug, the IMMU-123 trial, which was published in 2017 and 2019, and the ASCENT-05 trial, which was published in 2021. The IMMU-123 trial enrolled 108 patients with metastatic TNBC who had previously received a median of three anti-cancer therapies. It found that 34.3% of the enrolled patients responded to Sacituzumab Govitecan. The median progression-free survival (PFS)—a state where cancer is present in the body, but its growth is arrested—was 5.5 months and overall survival was 13 months.

The ASCENT-05 trial enrolled 468 patients with metastatic TNBC who had already completed at least two standard chemotherapy treatments. This trial compared the effectiveness and safety of a combination of Sacituzumab Govitecan and another immunotherapy drug, Pembrolizumab, to conventional treatment. The conventional treatment consisted of Pembrolizumab alone or a combination of Pembrolizumab and the chemotherapy drug Capecitabine). 33.3% of the patients on Sacituzumab Govitecan responded to treatment compared to 5.3% on conventional treatment. The median PFS and overall survival were also significantly higher for those on Sacituzumab Govitecan than those on conventional treatment (5.6 months and 12.1 months vs. 1.7 months and 6.7 months).

The impact of the treatment on patient quality of life was also a major concern for the research team. "*Decreasing the crippling side effects of traditional chemotherapy, such as vomiting, hair loss, and diarrhea, is critical to preserving a patient's self-respect and dignity throughout the treatment journey*," explains Dr. Shah. "*The literature indicates that patients taking Sacituzumab Govitecan experience significant reductions in pain and fatigue, as well as lower rates of severe adverse effects like neutropenia (10% vs 50%) and diarrhea (10% vs 18%) compared to patients undergoing traditional chemotherapy*."

Sacituzumab Govitecan has received both 'Fast Track' and 'Breakthrough' medication designations from the US Food and Drug Administration (FDA), which will accelerate the research on the drug and make it available to patients sooner. "*While more research is required to optimize treatment protocols and explore synergistic drug combinations*," concludes Dr. Shah, "*the effects of Sacituzumab Govitecan on tumor response, survival, and quality of life are remarkable, thereby offering hope to patients battling persistent breast cancer*."

By combining innovation with precision medicine, this new therapy embodies hope for patients and marks a pivotal moment in the evolution of breast cancer care.

Manuscript details:

Title: Revolutionizing triple-negative metastatic breast cancer treatment: sacituzumab Govitecan's role in advancing chemotherapy

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Journal: *Annals of Medicine & Surgery*

Publication date: September 2024

DOI: 10.1097/MS9.0000000000002347