

ADC Combination Outperforms Standard Treatment of Advanced Triple-Negative Breast Cancer

Patients who received Trodelvy plus Keytruda were more likely to survive longer without disease progression.

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In patients with advanced triple negative breast cancer, treatment with the antibody-drug conjugate sacituzumab govitecan [Trodelvy] plus pembrolizumab [Keytruda] led to durable responses and improved progression free survival compared to the current standard treatment, according to results of the ASCENT-04/KEYNOTE-D19 study, published [January 21] in the [New England Journal of Medicine](#).

Results from the study, which was led by Dana-Farber's [Sara Tolaney, MD](#), will soon be submitted to regulators and could change clinical practice for first-line treatment of patients with advanced triple negative breast cancer that tests positive for the immune checkpoint PD-L1.

Triple-negative breast cancer is an aggressive and difficult to treat form of breast cancer that accounts for about 15% of all breast cancer cases. The five-year survival rate for patients with metastatic triple-negative breast cancer is just 12%.

"There is a huge unmet need for new therapies for patients with triple-negative breast cancer," says Tolaney, chief of the Division of Breast Oncology at Dana-Farber Cancer Institute. "It is important that we work toward shifting these very effective novel drugs to the first line of therapy to move the needle and improve outcomes for these patients."

The global, open-label ASCENT-04/KEYNOTE-D19 study enrolled 443 patients who were randomized to receive either sacituzumab govitecan plus pembrolizumab or chemotherapy plus pembrolizumab. Patients were followed until their disease either worsened or they experienced unmanageable side effects.

After a median follow-up of 14 months, patients who received the sacituzumab govitecan combination were more likely to survive longer without progression, with an 11.2-month median progression free survival compared to 7.8 months among those who received the chemotherapy

combination. Nearly 60% of patients responded to the sacituzumab govitecan combination. Those who responded experienced durable responses with a median of 16.6 months compared to 9.2 months among those who responded to the chemotherapy combination.

Sacituzumab govitecan is an antibody-drug conjugate designed to direct a potent chemotherapy drug into cancer cells by targeting a protein called TROP-2 that is found on triple-negative breast cancer cells. It is currently approved as second line or later therapy for advanced triple-negative breast cancer. However, approximately half of the patients who receive the current standard first-line treatment for advanced triple-negative breast cancer do not survive long enough to receive a second line of therapy.

Pembrolizumab is an immune checkpoint inhibitor that targets PD-L1, an immune checkpoint that can help cancer cells evade immune system attack.

“We hope these data will result in approval of sacituzumab govitecan plus pembrolizumab for first-line treatment in our patients with metastatic triple-negative breast cancer with tumors that are PD-L1-positive. Currently we sometimes see patients experience deterioration in their health during first-line treatment and they don’t always have an opportunity to benefit from these sacituzumab in later lines,” says Tolaney. “We need to move these agents up front so more patients can benefit.”

The safety profile of sacituzumab govitecan in combination with pembrolizumab was consistent with the established profiles of each agent and treatment discontinuation due to side effects was less frequent among patients taking the sacituzumab govitecan combination.

Today’s NEJM publication of ASCENT-04 results follow a data presentation at the 2025 ASCO Annual Meeting, as well a simultaneous presentation at the 2025 European Society for Medical Oncology Congress and publication in NEJM of primary results from the ASCENT-03 trial of sacituzumab govitecan monotherapy in patients with first-line metastatic TNBC who are not candidates for PD-1/PD-L1 inhibitors.

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