Trodelvy Improves Outcomes for Breast and Bladder Cancer

The antibody-drug conjugate nearly doubled survival time for people with triple-negative breast cancer.

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Trodelvy (sacituzumab govitecan), a recently approved antibody-drug conjugate, delayed disease progression and improved overall survival for women with hard-to-treat triple-negative breast cancer (TNBC) and shrank tumors in about a quarter of people with metastatic bladder cancer, researchers reported this week at the European Society for Medical Oncology's ESMO Virtual Congress 2020.

Trodelvy, from Immunomedics (soon to be acquired by Gilead Sciences), uses a monoclonal antibody to deliver a potent chemotherapy drug. The antibody targets Trop-2, a cell surface protein found in more than 90% of triple-negative breast tumors and at lower rates in many other types of cancer.

Triple-Negative Breast Cancer

Aditya Bardia, MD, MPH, of Massachusetts General Cancer Center and Harvard Medical School, presented the latest findings from the ASCENT study, a randomized Phase III trial comparing Trodelvy versus chemotherapy for TNBC. Based on an earlier Phase II study, the Food and Drug Administration (FDA) granted accelerated approval of Trodelvy for this indication in April.

Breast cancer is classified according to the types of receptors it expresses. A majority of breast tumors carry estrogen or progesterone hormone receptors (HR-positive) and can be treated with hormone therapy. Others express a receptor called HER2 and can be treated with HER2 inhibitors such as Herceptin (trastuzumab). Triple-negative breast cancer doesn't express any of these receptors and is more difficult to treat.

ASCENT (ClinicalTrials.gov NCT02574455) enrolled 529 people with metastatic TNBC in seven countries. Almost all were women, most were white and the median age was 54 years. They had received at least two and a median of four prior therapies. All had used various chemotherapy drugs, and about a quarter had tried checkpoint inhibitor immunotherapy. The most common metastasis sites were the lungs (44%), liver (43%) and bones (22%); a small proportion of participants with brain metastasis were not included in the main analysis.

The participants were randomly assigned to receive either Trodelvy by IV infusion on days 1 and 8 in each 21-day cycle or a physician's choice of a single chemotherapy drug (eribulin, vinorelbine, gemcitabine or capecitabine). Treatment continued until they experienced disease progression or unacceptable toxicity.

More than a third of Trodelvy recipients (35%) experienced tumor remission compared with just 5% of chemotherapy recipients; 4% and 1%, respectively, had complete responses.

Trodelvy reduced the risk of disease progression or death by 59% compared with chemotherapy in the subgroup without brain metastasis; the median progression-free survival time was 5.6 versus 1.7 months, respectively. The benefit was somewhat less when those with brain metastasis were included. The benefit was consistent across racial/ethnic groups and regardless of prior treatment regimens.

Overall survival time was 12.1 months in the Trodelvy group versus 6.7 months in the chemotherapy group, a clinically meaningful 52% improvement. At the time of the analysis, 15 Trodelvy recipients, but none of the chemotherapy recipients, were still taking their assigned treatment.

Trodelvy was generally safe, and side effects were usually manageable. The most common side effects were neutropenia, anemia, diarrhea, nausea, hair loss and fatigue. About 5% of people in both treatment groups stopped treatment due to adverse events.

"The randomized Phase III study results confirm that sacituzumab govitecan should be considered as a new standard of care in patients with third-line metastatic TNBC," Bardia said in an Immunomedics press release.

The ASCENT study was halted in April after a data safety monitoring committee found that Trodelvy demonstrated "compelling evidence of efficacy." Based on these findings, the company intends to seek full FDA approval for this indication later this year.

Bladder Cancer

Trodelvy for bladder cancer is further back in the pipeline. Yohann Loriot, MD, PhD, of Institut de Cancèrologie Gustave Roussy near Paris, presented findings from the global Phase II TROPHY-U-01 trial (ClinicalTrials.gov NCT03547973), which enrolled people with inoperable locally advanced or metastatic urothelial carcinoma, which arises from cells lining the urinary tract and is the most common type of bladder cancer.

Participants were grouped based on prior therapy. Loriot presented findings from cohort 1, which included 113 people whose cancer progressed despite platinum-based chemotherapy and checkpoint inhibitors. More than three quarters were men, most were white and the median age was 66 years. The most common metastasis sites were the internal abdomen (62%), lungs (40%) and liver (28%).

All participants received Trodelvy on days 1 and 8 of each 21-day cycle until it no longer worked or they experienced intolerable side effects. There was no comparison regimen or placebo group.

The overall response rate was 27%, including 5% with complete remission. Loriot noted that the response rate for chemotherapy is generally around 10%. The median duration of response was 5.9 months, the media progression-free survival time was 5.4 months and the median overall survival time was 10.5 months.

Again, treatment was generally well tolerated, with side effects similar to those seen in the breast cancer study; 6% stopped treatment for this reason. One patient died of sepsis related to neutropenia, or depletion of infection-fighting white blood cells.

These findings, the researchers concluded, support a randomized Phase III trial of Trodelvy for metastatic urothelial carcinoma. Accordingly, the TROPICS-04 study is now underway (ClinicalTrials.gov NCT04527991). Immunomedics plans to seek FDA accelerated approval this year based on the Phase II results.

Another antibody-drug conjugate, Padcev (enfortumab vedotin), from Astellas and Seattle Genetics, was granted accelerated approval for the same indication last December based on promising Phase II findings; a Phase III trial was recently stopped early based on good interim results.

In addition to TNBC and bladder cancer, Trodelvy is also being studied alone or in combination regimens for other malignancies, including HR-positive/HER2-negative metastatic breast cancer (TROPICS-02; ClinicalTrials.gov NCT03901339), metastatic non-small-cell lung cancer and glioblastoma brain cancer.

Click here for full prescribing information for Trodelvy.

Click here to learn more about breast cancer.

Click here to learn more about bladder cancer.
