Trodelvy Improves Survival for Patients With Metastatic Breast Cancer

Treatment-experienced people who received the antibody-drug conjugate lived three months longer than those who got more chemotherapy.

September 15, 2022 By Liz Highleyman

The antibody-drug conjugate Trodelvy (sacituzumab govitecan) improved overall survival for women with HER2-negative metastatic breast cancer who had received extensive prior treatment, according to study findings presented at the European Society for Medical Oncology (ESMO) Congress 2022.

Participants in the Phase III TROPiCS-02 trial who received Trodelvy lived 3.2 months longer than those who received another round of chemotherapy, a statistically significant improvement.

“It is outstanding to see a clinically meaningful survival benefit of over three months for patients with pretreated HR-positive/HER2-negative metastatic breast cancer,” presenter Hope S. Rugo, MD, of the University of California San Francisco, said in a Gilead Sciences press release. “Nearly all patients with HR-positive/HER2-negative metastatic breast cancer will develop resistance to endocrine-based therapies even in combination with targeted agents, so these data are welcome news for the breast cancer community.”

Breast cancer is classified according to the types of receptors it expresses. A majority of breast tumors carry estrogen or progesterone hormone receptors (known as HR-positive). Others express the HER2 receptor and can be treated with HER2 inhibitors such as Herceptin (trastuzumab), but these drugs don’t work for people with HER2-negative tumors. Triple-negative breast cancer doesn’t express any of these receptors.

The TROPiCS-02 study included 543 patients with HR-positive/HER2-negative metastatic breast cancer who were previously treated with endocrine (hormone) therapy, a CDK4/6 inhibitor and at least two prior lines of chemotherapy.

The participants were randomly assigned to receive Trodelvy or another course of chemotherapy selected by their physician (capecitabine, eribulin, gemcitabine or vinorelbine). Treatment continued until patients experienced disease progression or unacceptable side effects.

Trodelvy is an antibody-drug conjugate uses a monoclonal antibody that targets Trop-2 to deliver

an active form of a potent chemotherapy drug that is too toxic to administer on its own. It is currently approved for previously treated advanced triple-negative breast cancer and for advanced bladder cancer, but it is not yet approved for HR-positive/HER2-negative breast cancer.

Rugo reported that patients treated with Trodelvy had a median overall survival time of 14.4 months, compared with 11.2 months for those who received another round of chemotherapy, a 21% reduction in the risk of death.

Trodelvy previously demonstrated improved progression-free survival (the study's primary endpoint), as Rugo reported at this year's American Society of Clinical Oncology (ASCO) Annual Meeting in June. The median progression-free survival time was 5.5 months with Trodelvy versus 4.0 months with chemotherapy, a 34% reduction in the risk of disease progression or death.

The overall response rate was also significantly higher for Trodelvy versus chemotherapy (21% versus 14%). What's more, patients who received Trodelvy reported less fatigue and delayed deterioration of quality of life.

Treatment was generally safe, although side effects were common. No new safety signals were seen compared with previous Trodelvy trials. Patients assigned to Trodelvy had more severe (Grade 3 or higher) adverse events than those who received more chemotherapy, but rates of treatment discontinuation due to side effects was similar in both groups (6% versus 4%).

These results come on the heels of data presented at ASCO showing that another antibody-drug conjugate, Daiichi Sankyo and AstraZeneca's Enhertu (fam-trastuzumab deruxtecan), improved progression-free and overall survival for patients with metastatic breast cancer with low HER2 expression. Enhertu was already approved for HER2-positive advanced breast cancer, and it received an additional indication for HER2-low breast cancer in August.

In early September, Gilead announced findings from a post hoc analysis from TROPiCS-02 showing that Trodelvy also improved progression-free survival in patients with HER2-low breast cancer who had initially been classified as HER2- negative.

Commenting on the TROPiCS-02 findings at ESMO, Meritxell Bellet-Ezquerra, MD, PhD, of Vall d'Hebron Institute of Oncology in Barcelona, said that, in her opinion, they should lead to regulatory approval of Trodelvy for this patient population. Gilead has requested the new indication and, if granted, women with advanced breast cancer will have new treatment options regardless of their HER2 status.

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