FDA Approves Trodelvy for Advanced Bladder Cancer

The antibody-drug conjugate shrank tumors in 28% of people with locally advanced or metastatic urothelial cancer.

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On April 13, the Food and Drug Administration (FDA) granted accelerated approval of Trodelvy (sacituzumab govitecan)—an antibody-drug conjugate that delivers potent chemotherapy to tumors—for people with previously treated advanced urothelial cancer. This malignancy, originating in cells lining the urinary tract, is the most common type of bladder cancer.

The medication is indicated for adults with locally advanced or metastatic urothelial cancer who previously received platinum-containing chemotherapy and either PD-1 or PD-L1 checkpoint inhibitor immunotherapy.

Trodelvy was developed by Immunomedics, which was acquired by Gilead Sciences last fall. It consists of a monoclonal antibody targeting Trop-2, a protein commonly found on urothelial tumors, which carries an active form of the chemotherapy drug irinotecan.

Trodelvy was approved last year for the treatment of triple-negative breast cancer; it is also being studied as a treatment for several other had-to-treat malignancies. Another antibody-drug conjugate, Padcev (enfortumab vedotin), from Astellas and Seattle Genetics, was granted accelerated approval for previously treated advanced urothelial cancer in December 2019.

The accelerated approval of Trodelvy was based on results from the Phase II TROPHY-U-01 trial (ClinicalTrials.gov NCT03547973), which enrolled people with inoperable locally advanced or metastatic urothelial carcinoma. The participants were grouped according to their prior therapy.

At last years European Society for Medical Oncology's ESMO Virtual Congress, Yohann Loriot, MD, PhD, of Institut de Cancèrologie Gustave Roussy near Paris, presented findings from Cohort 1, which included 113 people whose cancer had progressed despite platinum-based chemotherapy and checkpoint inhibitors. (Other cohorts had received platinum chemotherapy or checkpoint inhibitors, but not both.)

More than three quarters of participants in Cohort 1 were men, most were white and the median age was 66 years. They all received Trodelvy administered via IV infusion on days 1 and 8 of each

21-day cycle until they experienced disease progression or unacceptable side effects. There was no comparison regimen or placebo group.

Loriot reported that the overall response rate, meaning complete or partial tumor shrinkage, was 27%, including 5% with complete remission, and the median duration of response was 5.9 months. According to updated results from the FDA, the response rate rose to 28% and the duration of response to 7.2 months. The trial is ongoing; at the time of the ESMO report, the median progression-free survival time was 5.4 months and the median overall survival time was 10.5 months.

Treatment with Trodelvy is generally safe and well tolerated. The most common adverse reactions include nausea, vomiting, abdominal pain, decreased appetite, diarrhea, constipation, fatigue, hair loss, skin rash and anemia. The drug can cause depletion of white blood cells (neutropenia), which leaves patients prone to infections; one person in the trial died from sepsis, or severe infection. Ten percent of patients stopped treatment due to adverse events.

Drugs that receive accelerated approval based on response rates in early studies are expected to undergo further testing in larger randomized trials to confirm clinical benefits such as improved survival. A global Phase III trial dubbed TROPiCS-04 (NCT04527991) is currently underway. (Trodelvy recently received full regular approval for its breast cancer indication.)

“Only a fraction of patients derives long-term benefit from previously approved cytotoxic therapy or immunotherapy, leaving a great unmet need for treatment options for patients with advanced urothelial cancer who have progressed on first- and second-line therapies,” TROPHY principal investigator Scott Tagawa, MD, of Weill Cornell Medical Center, said in a Gilead press release. “The response rate and tolerability seen with sacituzumab govitecan-hziy may provide physicians an effective new treatment option for patients whose cancer continues to progress even after multiple therapies.”

Click here for full prescribing information for Trodelvy.
Click here to learn more about bladder cancer.
