Newly Approved Treatment Shows Promise for Advanced Cervical Cancer

The antibody-drug conjugate Tivdak led to remission in 24% of cervical cancer patients.

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On September 20, the Food and Drug Administration (FDA) granted accelerated approval of Tivdak (tisotumab vedotin), an antibody-drug conjugate for the treatment of recurrent or metastatic cervical cancer that has progressed despite chemotherapy.

In a Phase II clinical trial, Tivdak used as monotherapy led to complete or partial remission in 24% of patients. A follow-up study, presented this week at the European Society for Medical Oncology (ESMO) Congress 2021, showed that combining Tivdak with chemotherapy or immunotherapy boosted overall response rates.

Cervical cancer, caused by human papillomavirus (HPV), can be prevented with a vaccine, and precancerous cervical cell changes can be detected early with regular Pap smears and HPV tests. But if it goes undetected, advanced cervical cancer is difficult to treat. More than 4,000 people in the United States are expected to die of cervical cancer this year, and it is a leading cause of cancer death among women worldwide.

“Once recurrent or metastatic cervical cancer progresses, there is a need for more options for these patients,” study investigator Robert Coleman, MD, chief scientific officer of U.S. Oncology Research, said in a SeaGen press release. “This is an important development for patients with recurrent or metastatic cervical cancer.”

Tivdak (formerly know as HuMax-TF), from SeaGen and Genmab, is an antibody-drug conjugate that uses a monoclonal antibody that targets tissue factor, a protein found on many types of tumors, to deliver a potent chemotherapy drug directly to cancer cells.

The approval was based on findings from the innovaTV204 trial (NCT03438396), which included 101 patients with relapsed or metastatic cervical cancer. Most were white, and the median age was 50 years. Almost all had cancer that had spread beyond the pelvis. They had previously received no more than two prior systemic regimens, including platinum-based chemotherapy; about two thirds had also tried Avastin (bevacizumab), and about half had undergone radiation therapy.

The participants all received Tivdak as monotherapy by IV infusion once every three weeks until they experienced disease progression or unacceptable side effects. There was no placebo or comparison treatment arm (typical of Phase II studies).

As previously reported at last year's ESMO Congress and in The Lancet Oncology, the overall response rate was 24%, including seven people (7%) with complete remission. Another 49% had stable disease without further progression.

After a median 10 months of follow-up, the median duration of response was 8.3 months, the median progression-free survival (PFS) time was 4.2 months and the median overall survival time was 12.1 months. At six months, 30% had not yet experienced disease progression and the survival rate was 79%.

At this year's ESMO meeting, Ignace Vergote, MD, PhD, of Catholic University of Leuven in Belgium, presented results from the Phase I/II trial innovaTV 205 trial (NCT03786081), which is testing Tivdak in combination with chemotherapy, Avastin or the checkpoint inhibitor Keytruda (pembrolizumab).

Among the 33 patients who received Tivdak plus carboplatin chemotherapy as first-line treatment, the overall response rate was 55%, including four (12%) with complete responses. Here too, the median duration of response was 8.3 months, and the median PFS time was 9.5 months. Among the 34 people treated with Tivdak plus Keytruda as second- or third-line therapy, the overall response rate was 38%, including two (6%) with complete responses; the median duration of response was 13.8 months, and the median PFS time was 5.6 months.

Treatment with Tivdak is generally safe with manageable side effects; 13% of patients in innovaTV204 stopped therapy due to adverse events. The most common adverse reactions to Tivdak include nausea, diarrhea, peripheral neuropathy, hair loss, rash and dry and irritated eyes. The package insert includes a warning about more severe eye problems that can lead to vision loss. The drug can cause depletion of red blood cells (anemia), white blood cells and platelets (thrombocytopenia), which can lead to fatigue, infections and easy bleeding.

Drugs that receive accelerated approval based on overall response rate are expected to undergo further testing to confirm whether they provide clinical benefit such as improved survival, and the FDA can rescind the approval if they fail to measure up.

"We are thrilled to see this new treatment approved by the FDA," said Tamika Felder, founder of the cervical cancer advocacy group Cervivor (one of this year's Cancer Health 25). "We are grateful to have another option for this devastating disease."

Click here for full prescribing information for Tivdak.

Click here for more news about cervical cancer.
