New Treatments Show Promise for Advanced Cervical Cancer

A checkpoint inhibitor combination and an antibody-drug conjugate may offer new treatment options.

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Two experimental checkpoint blockers and a novel antibody-drug conjugate demonstrated promising activity in people with recurrent or metastatic cervical cancer, according to presentations at the recent European Society for Medical Oncology's ESMO Virtual Congress 2020.

In mid-stage clinical trials, the new PD-1 checkpoint blocker balstilimab plus the CTLA-4 blocker zalifrelimab had an overall response rate of 22%, while the investigational antibody-drug conjugate tisotumab vedotin showed a response rate of 24%.

Cervical cancer is caused by the human papillomavirus (HPV). Although a vaccine can prevent cervical cancer, and precancerous cervical cell changes can be detected early using Pap smears and HPV tests, advanced cervical cancer is difficult to treat. More than 4,000 women in the United States are expected to die of cervical cancer this year, according to the American Cancer Society.

Checkpoint Inhibitors

David O'Malley, MD, of the Ohio State University Comprehensive Cancer Center in Columbus, presented findings from a pair of Phase II studies evaluating balstilimab, with or without zalifrelimab, in more than 300 people with recurrent or metastatic cervical cancer.

Balstilimab is a monoclonal antibody that blocks PD-1, an immune checkpoint on T cells that regulates immune function. Drugs that block the interaction between PD-1 and its binding partner, known as PD-L1, can release the brakes and restore T-cell activity against tumors. Tumors with higher PD-L1 levels tend to respond better to this type of treatment. Zalifrelimab blocks CTLA-4, another immune checkpoint that suppresses T-cell multiplication. Both drugs are being developed by Agenus.

In the first study, 160 patients (median age 53), most of whom were previously treated with platinum-based chemotherapy, received IV infusions of balstilimab alone every two weeks for up to two years.

The overall response rate (ORR) was 14%, including three people (2%) with complete responses.

The ORRs were 18% for patients with squamous cell carcinoma—by far the most common type of cervical cancer—and 8% for those with adenocarcinoma or other types.

In the second study, 155 patients (median age 50) received balstilimab every two weeks plus zalifrelimab infusions every six weeks.

The overall response rate was 22%, including eight people (6%) with complete remission. The ORRs were 27% for squamous cell carcinoma and 5% for other types.

In the balstilimab monotherapy study, the ORR was 19% for people whose tumors tested positive for PD-L1 and 10% for those with PD-L1–negative tumors. In the combination trial, the ORRs were 27% and 11%, respectively. That is, the response rates for PD-L1–positive tumors were about the same as those for squamous cell carcinoma overall. But some people with PD-L1–negative tumors were responders. Another checkpoint inhibitor, Keytruda (pembrolizumab), is currently approved for advanced cervical cancer, but only for patients with PD-L1–positive tumors.

The median duration of response was 15.4 months with balstilimab alone, but it was not reached with the combination regimen because most patients were still responding.

Treatment was generally safe, with side effects similar to those of approved PD-1 checkpoint inhibitors. These drugs work by restoring immune responses against cancer cells, but they can also activate the immune system more broadly, leading to excessive inflammation that can damage organs. People taking the combination regimen were more likely than those taking balstilimab alone to have immune-related adverse events, including gastrointestinal and endocrine problems.

“These two studies represent the largest trials of immuno-oncology therapies in relapsed cervical cancer to date and show that balstilimab and zalifrelimab may present meaningful new therapies for patients with cervical cancer,” O’Malley said in a press release. “Advances in these agents offer renewed hope for patients who have limited treatment options. This is especially important because this disease disproportionately affects younger women.”

Tisotumab Vedotin

Robert Coleman, MD, of U.S. Oncology Research, presented findings from a Phase II study of tisotumab vedotin, an antibody-drug conjugate from Seagen (formerly Seattle Genetics). The novel therapy 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 study included 101 people (median age 50) with relapsed or metastatic cervical cancer who had previously received chemotherapy with or without the targeted therapy Avastin (bevacizumab); about half had undergone radiation therapy. Two thirds had squamous cell carcinoma and about a quarter had adenocarcinoma.

The participants all received tisotumab vedotin by IV infusion once every three weeks until they

experienced disease progression or unacceptable side effects. There was no placebo or comparator treatment arm in this mid-stage study.

The overall response rate was 24%, including seven people (7%) with complete remission. Another 49% had stable disease without further progression. People with squamous cell carcinoma and other cancer types had similar response rates (23% and 25%). The ORR was somewhat higher for patients who had not yet tried Avastin (32%).

After a median 10 months of follow-up, the median duration of response was 8.3 months, the median progression-free survival 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%.

Treatment was generally safe. The most common side effects were hair loss (38%), nosebleeds (30%), nausea (27%), conjunctivitis (26%), fatigue (24%) and dry eyes (23%); 7% developed severe neuropathy, and 2% each had severe bleeding and severe eye problems. Most people discontinued treatment because of disease progression, but 13% stopped due to adverse events.

“The results of the tisotumab vedotin Phase II clinical trial are encouraging as they demonstrate clinically meaningful, durable responses with a manageable side effect profile,” Coleman said in a Seagen press release.

Click here to read the checkpoint inhibitor abstract.

Click here to read the tisotumab vedotin abstract.

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