New Targeted Antibody Treatment for Bladder Cancer Shows Promise

More than 40% of people treated with enfortumab vedotin experienced complete or partial remission.

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The investigational targeted antibody enfortumab vedotin (EV) yielded good response rates in a Phase II trial among participants with urothelial cancer who were previously treated with chemotherapy and checkpoint inhibitor immunotherapy.

Daniel P. Petrylak, MD, a professor of medicine and urology at the Yale Cancer Center, presented findings from the trial at the American Society of Clinical Oncology annual meeting in Chicago.

Urothelial cancer involves cancer of the bladder in 90% of cases and can also occur in the urethra, ureters (the ducts through which urine passes from the kidneys to the bladder) and a few other nearby organs.

Typically, those who are diagnosed with metastatic urothelial cancer—meaning the cancer has spread from its original site—are first treated with platinum-based chemotherapy. Should their disease then progress, they may be treated with a PD-1 or PD-L1 checkpoint inhibitor. However, those who receive such second-line treatment still see progression of their cancer in about 75% of cases. At that point, there is no subsequent approved treatment for this cancer.

Enfortumab vedotin, from Astellas and Seattle Genetics, is an antibody-drug conjugate that targets nectin-4, an antigen expressed on almost all urothelial cancers. The antibody delivers a chemotherapy drug that disrupts cellular structures known as microtubules and prevents cell division.

A previous Phase I study of EV yielded evidence that the treatment was safe. In March 2018, the Food and Drug Administration designated EV a breakthrough therapy for those with locally advanced or metastatic urothelial cancer that has progressed after checkpoint inhibitor treatment.

In the new Phase II study, which is ongoing, Petrylak and his colleagues enrolled individuals with urothelial cancer and divided them into two groups. One group included participants who had received both platinum-based chemotherapy and a checkpoint inhibitor. The second group included those who were ineligible for the platinum drug cisplatin and had received only a

checkpoint inhibitor.

The ASCO presentation concerned only those in the group treated with chemotherapy and a checkpoint inhibitor. A total of 128 people were enrolled in this group between October 2017 and July 2018; 70% were male, and the median age was 69 years old. About a third had cancer in their upper urinary tract, which is an uncommon site for urothelial cancer; the rest had cancer in the bladder or elsewhere. The cohort members had received a median of three prior systemic treatments for locally advanced or metastatic urothelial cancer. None had received cancer treatment for at least two weeks prior to entering the EV trial.

The 125 participants who were ultimately treated received intravenous infusions EV at 1.45 milligrams per kilogram of body weight on days 1, 8 and 15 in 28-day cycles. At the time of this report, the maximum time participants had spent on EV was 15.6 months.

EV led to a response in 44% of the cohort members, meaning their tumors shrank. Fifteen people (12%) experienced a complete response to treatment in which there was no detectable sign of cancer. Another 28% had stable disease with no further cancer growth. The estimated median progression-free survival time was 5.8 months, and the overall survival time was 11.7 months.

Of the participants whose cancer had not responded to a checkpoint inhibitor, 41% experienced a response to EV. Additionally, 38% of those whose cancer had spread to the liver responded to EV.

EV proved well tolerated. The most common side effects included fatigue (reported by 50% of participants), hair loss (49%) and decreased appetite (44%), which in most cases were mild or moderate. About 12% discontinued treatment because of treatment-related adverse events, most often peripheral neuropathy.

A Phase III trial of EV is under way. Meanwhile, investigators are still enrolling participants into the second study group in the Phase II trial. Another trial is currently examining treatment with EV in combination with platinum-based chemotherapy for those who are newly diagnosed with advanced urothelial cancer.

To read an ASCO press release about the study, click here.

To read the conference abstract, click here.
