FDA Approves Padcev for Advanced Bladder Cancer

Novel antibody-drug conjugate shrank tumors in more than 40% of people previously treated with immunotherapy.

December 18, 2019 By Liz Highleyman

On December 18, the Food and Drug Administration (FDA) granted accelerated approved Padcev (enfortumab vedotin-ejfv) for the treatment of adults with inoperable locally advanced or metastatic bladder cancer and other urothelial cancers who were previously treated with checkpoint inhibitors and platinum-based chemotherapy.

Padcev, from Astellas and Seattle Genetics, consists of an antibody that targets nectin-4, a protein found at high levels on most urothelial cancer cells. The antibody carries a chemotherapy drug (monomethyl auristantin E) that disrupts cellular structures known as microtubules and prevents cell division.

“Antibody-drug conjugates are strategic tools in the targeted treatment of cancer,” Richard Pazdur, MD, acting director of the FDA’s new Office of Oncologic Diseases, said in a press release. “These conjugates combine the ability of monoclonal antibodies to target specific receptors on cancer cells and then deliver a drug to the cancer cell.”

Urothelial cancer affects the lining of the urinary tract. In most cases it involves the bladder, but it can also occur in the urethra, ureters (the ducts from the kidneys to the bladder) and part of the kidneys.

The recommended initial treatment for metastatic urothelial cancer is cisplatin, a platinum-based chemotherapy drug. Those who cannot use cisplatin can try PD-1 or PD-L1 checkpoint inhibitor immunotherapy. The PD-1 blockers Keytruda (pembrolizumab) and Opdivo (nivolumab) and the PD-L1 blockers Bavencio (avelumab), Imfinzi (durvalumab) and Tecentriq (atezolizumab) are all approved for advanced bladder cancer. Most people do not respond, however, and at that point there are limited options for further treatment.

Approval of Padcev was based on findings from the Phase II EV-201 trial, which enrolled people with advanced urothelial cancer who were previously treated with checkpoint inhibitors, with or without platinum chemotherapy. Participants received Padcev monotherapy by IV infusion on three days in a 28-day cycle.

As reported at this year's American Society of Clinical Oncology annual meeting in June, among the 125 participants previously treated with both cisplatin and a checkpoint inhibitor, 44% had an overall response, meaning complete or partial tumor shrinkage. Of these, 12% had complete remission. Another 28% had stable disease with no further cancer growth. The median duration of response was 7.6 months, the median progression-free survival time was 5.8 months and the estimated overall survival was 11.7 months. Evaluation of people who previously received only a checkpoint blocker is ongoing.

Padcev may work even better when combined with immunotherapy from the outset. Another study (EV-103), presented at the European Society for Medical Oncology Congress in the fall, evaluated Padcev plus Keytruda in people being treated for the first time who could not take cisplatin. In an analysis of 45 participants, 71% experienced tumor remission, including 13% with a complete response. Another 22% had stable disease.

Padcev is generally safe. The most common adverse events include fatigue, peripheral neuropathy (nerve damage in the hands and feet), decreased appetite, skin rash, hair loss, nausea, dysgeusia (altered taste sensations), diarrhea, dry eyes, dry skin and itching. Potential serious adverse events include severe hyperglycemia (high blood sugar), severe peripheral neuropathy, eye disorders and severe skin reactions.

A full course of Padcev is expected to cost around $100,000, according to Seattle Genetics.

"The FDA approval of Padcev is welcome news for patients with bladder cancer," Andrea Maddox-Smith of the Bladder Cancer Advocacy Network said in a company press release. "Though new medicines for bladder cancer have been approved in recent years, most people living with advanced stages of this disease face a difficult journey with few treatment options."

A Phase III study comparing Padcev versus chemotherapy for people with previously treated locally advanced or metastatic urothelial cancer is currently underway (EV-301; ClinicalTrials.gov number NCT03474107).

Click here to learn more about bladder cancer.
