FDA Approves Padcev Plus Keytruda for Advanced Bladder Cancer

The combination regimen improved overall survival by more than 50% compared with chemotherapy.

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On December 15, the Food and Drug Administration (FDA) approved Padcev (enfortumab vedotin) plus Keytruda (pembrolizumab) for people with locally advanced or metastatic urothelial cancer, which affects the lining of the urinary tract, usually involving the bladder.

"Despite advances in the treatment of advanced bladder cancer, there remains a need for therapies that extend patients' lives," Andrea Maddox-Smith, CEO of the Bladder Cancer Advocacy Network, said in a Pfizer and Astellas news release. "Our network is thrilled that the FDA has approved a new treatment option, and we are excited about the hope it will provide to members of the bladder cancer patient community."

The standard of care for first-line treatment of urothelial cancer is platinum-based chemotherapy such as cisplatin. In April, the FDA granted accelerated approval of Padcev plus Keytruda for patients who are ineligible for cisplatin-containing chemotherapy.

Padcev, first approved for bladder cancer in 2019, is an antibody-drug conjugate, a monoclonal antibody targeting nectin-4 (a protein found on most urothelial cancer cells) that carries a potent chemotherapy drug that halts cell division. A prior study showed that Padcev alone works well for people with advanced bladder cancer who had already received a checkpoint inhibitor with or without chemotherapy. Keytruda, a PD-1 checkpoint inhibitor that restores T-cell activity, also is effective alone for bladder cancer patients who either are ineligible for platinum chemotherapy or progressed despite using it.

But combining Padcev with Keytruda appears to work even better. The new indication is supported by data from the Phase III KEYNOTE-A39/EV-302 trial (NCT04223856), which evaluated Padcev plus Keytruda versus chemotherapy as first-line treatment for people with locally advanced or metastatic urothelial cancer. The study enrolled 886 patients who had received no prior systemic therapy for advanced disease. Padcev, Keytruda and chemotherapy were all administered via intravenous infusion.

As recently reported at this year's European Society for Medical Oncology Congress, the

combination regimen improved overall and progression-free survival by more than 50% compared with chemotherapy. Overall survival was 31.5 months for patients who received Padcev and Keytruda versus 16.1 months for those assigned to chemotherapy. Likewise, the progression-free survival time was twice as long (12.5 months versus 6.3 months, respectively).

Treatment was generally safe, though side effects were common in both groups: 56% of people who received Keytruda plus Padcev and 70% of those who received chemotherapy experienced severe treatment-related adverse events. The most common adverse reactions in patients receiving the combination include rash, peripheral neuropathy, fatigue, nausea, diarrhea, hair loss, low red and white blood cell and platelet counts and various laboratory abnormalities.

“Advanced bladder cancer is a common cause of cancer-related death,” primary investigator Thomas Powles, MD, of Barts Cancer Centre at Queen Mary University of London, said in news releases from Pfizer and Astellas (makers of Padcev) and Merck (maker of Keytruda). The overall survival benefit seen in the trial “demonstrates the potential for [Padcev] in combination with [Keytruda] to impact the first-line treatment of patients with locally advanced or metastatic urothelial cancer. In my opinion, this is a meaningful advancement over platinum-based chemotherapy in the systemic treatment of these patients.”

Click here for full prescribing information for Padcev.

Click here for full prescribing information for Keytruda.

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