Padcev™ (enfortumab vedotin-ejfv) – New drug approval

- On December 18, 2019, the FDA announced the approval of Seattle Genetics' and Astellas Pharma's Padcev (enfortumab vedotin-ejfv), for the treatment of adult patients with locally advanced or metastatic urothelial cancer who have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor, and a platinum-containing chemotherapy in the neoadjuvant/adjuvant, locally advanced or metastatic setting.
    - This indication is approved under accelerated approval based on tumor response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.
- Bladder cancer is the sixth most common cancer in the U.S. and urothelial cancer accounts for more than 90% of cases. Urothelial cancer begins in cells that line the bladder and nearby organs. Platinum-containing chemotherapy, PD-1 and PD-L1 inhibitors are standard treatments for patients with bladder cancer.
- Padcev is a first-in-class antibody-drug conjugate that is directed against Nectin-4, a protein located on the surface of cells and highly expressed in bladder cancer.
    - Nonclinical data suggest the anticancer activity of Padcev is due to its binding to Nectin-4 expressing cells followed by the internalization and release of the anti-tumor agent monomethyl auristatin E into the cell, which results in the cell not reproducing (cell cycle arrest) and in programmed cell death (apoptosis).
- The efficacy of Padcev was established in EV-201, a single-arm study in 125 patients with locally advanced or metastatic urothelial cancer who received prior treatment with a PD-1 or PD-L1 inhibitor and platinum-based chemotherapy. The major efficacy outcome measures were confirmed objective response rate (ORR) and duration of response (DOR).
    - The confirmed ORR was 44% (95% CI: 35.1, 53.2).
    - The median DOR was 7.6 months (95% CI: 6.3, not estimable).
- Warnings and precautions for Padcev include hyperglycemia, peripheral neuropathy, ocular disorders, skin reactions, infusion site extravasation, and embryo-fetal toxicity.
- The most common adverse reactions (≥ 20%) with Padcev use were fatigue, peripheral neuropathy, decreased appetite, rash, alopecia, nausea, dysgeusia, diarrhea, dry eye, pruritus, and dry skin.
- The recommended dose of Padcev is 1.25 mg/kg (up to a maximum of 125 mg for patients ≥ 100 kg) administered as an intravenous infusion over 30 minutes on Days 1, 8 and 15 of a 28-day cycle until disease progression or unacceptable toxicity.
- Seattle Genetics' and Astellas Pharma's launch plans for Padcev are pending. Padcev will be available as a 20 mg and 30 mg lyophilized powder in single-dose vials.