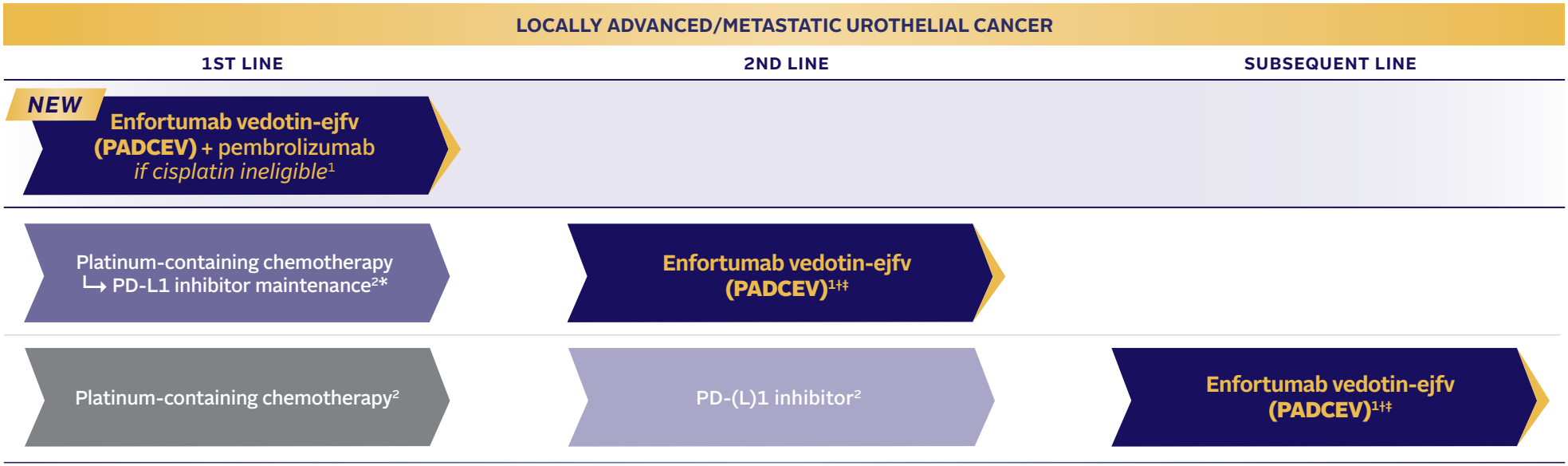
WHEN IS THE EARLIEST OPPORTUNITY TO USE PADCEV® (ENFORTUMAB VEDOTIN-EJFV) FOR YOUR ELIGIBLE PATIENTS?

PADCEV®
enfortumab vedotin-ejfv
Injection for IV infusion 20 mg & 30 mg vials

There are multiple settings in which PADCEV is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer (la/mUC)[1,2]



- PADCEV is also an FDA-approved treatment option for cisplatin-ineligible adult patients with la/mUC who have previously received one or more prior lines of therapy[1]

These are specific treatment scenarios for illustrative purposes only. Please visit NCCN.org for the full set of treatment recommendations.

*Maintenance therapy with avelumab only if there is no progression on first-line platinum- containing chemotherapy.[2]
†Patient should have already received platinum and a checkpoint inhibitor, if eligible.[2]
‡Appropriate for patients who have received a first-line platinum-containing chemotherapy followed by avelumab maintenance therapy.[2]

INDICATION

PADCEV, as a single agent, is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer (mUC) who:

- have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor and platinum-containing chemotherapy, or
- are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy.

PADCEV, in combination with pembrolizumab, is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer (mUC) who are not eligible for cisplatin-containing chemotherapy.

This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

BOXED WARNING: SERIOUS SKIN REACTIONS

- **PADCEV can cause severe and fatal cutaneous adverse reactions including Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), which occurred predominantly during the first cycle of treatment, but may occur later.**
- **Closely monitor patients for skin reactions.**
- **Immediately withhold PADCEV and consider referral for specialized care for suspected SJS or TEN or severe skin reactions.**
- **Permanently discontinue PADCEV in patients with confirmed SJS or TEN; or Grade 4 or recurrent Grade 3 skin reactions.**

Please see Important Safety Information and full Prescribing Information, including BOXED WARNING.

To learn more about PADCEV for your patients with la/mUC, visit **PADCEVhcp.com**

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Skin reactions Severe cutaneous adverse reactions, including fatal cases of SJS or TEN occurred in patients treated with PADCEV®. SJS and TEN occurred predominantly during the first cycle of treatment but may occur later. Skin reactions occurred in 56% (all grades) of the 753 patients treated with PADCEV as a single agent in clinical trials. Twenty-four percent (24%) of patients had maculo-papular rash and 33% had pruritus. Grade 3-4 skin reactions occurred in 12% of patients, including maculo-papular rash, erythematous rash, rash or drug eruption, symmetrical drug-related intertriginous and flexural exanthema (SDRIFE), bullous dermatitis, exfoliative dermatitis, and palmar-plantar erythrodysesthesia. The median time to onset of severe skin reactions was 0.7 months (range: 0.1 to 6 months). Among patients experiencing a skin reaction leading to dose interruption who then restarted PADCEV (n=59), 24% of patients restarting at the same dose and 16% of patients restarting at a reduced dose experienced recurrent severe skin reactions. Skin reactions led to discontinuation of PADCEV in 2.6% of patients.

When PADCEV was given in combination with pembrolizumab, the incidence of skin reactions, including severe events, occurred at a higher rate. Skin reactions occurred in 72% (all grades) of the 121 patients treated with PADCEV in combination with pembrolizumab in clinical trials. The majority of the skin reactions that occurred with combination therapy included maculo-papular rash, macular rash and papular rash. Grade 3-4 skin reactions occurred in 20% of patients (Grade 3: 19%, Grade 4: 0.8%), including maculo-papular rash, bullous dermatitis, dermatitis, exfoliative dermatitis, pemphigoid, rash, erythematous rash, macular rash, and papular rash. A fatal reaction of bullous dermatitis occurred in one patient (0.8%). The median time to onset of severe skin reactions was 2.6 months (range: 0.3 to 16 months). Skin reactions led to discontinuation of PADCEV in 6% of patients.

Monitor patients closely throughout treatment for skin reactions. Consider topical corticosteroids and antihistamines, as clinically indicated. For persistent or recurrent Grade 2 skin reactions, consider withholding PADCEV until Grade ≤1. Withhold PADCEV and refer for specialized care for suspected SJS, TEN or for Grade 3 skin reactions. Permanently discontinue PADCEV in patients with confirmed SJS or TEN; or Grade 4 or recurrent Grade 3 skin reactions.

Hyperglycemia and diabetic ketoacidosis (DKA) Hyperglycemia and DKA, including fatal events, occurred in patients with and without pre-existing diabetes mellitus, treated with PADCEV. Patients with baseline hemoglobin A1C ≥8% were excluded from clinical trials. In clinical trials of PADCEV as a single agent, 14% of the 753 patients treated with PADCEV developed hyperglycemia; 7% of patients developed Grade 3-4 hyperglycemia. Fatal events of hyperglycemia and diabetic ketoacidosis occurred in one patient each (0.1%). The incidence of Grade 3-4 hyperglycemia increased consistently in patients with higher body mass index and in patients with higher baseline A1C. Five percent (5%) of patients required initiation of insulin therapy for treatment of hyperglycemia. The median time to onset of hyperglycemia was 0.6 months (range: 0.1 to 20 months). Hyperglycemia led to discontinuation of PADCEV in 0.4% of patients. Closely monitor blood glucose levels in patients with, or at risk for, diabetes mellitus or hyperglycemia. If blood glucose is elevated (>250 mg/dL), withhold PADCEV.

Pneumonitis/Interstitial Lung Disease (ILD) Severe, life-threatening or fatal pneumonitis/ILD occurred in patients treated with PADCEV. In clinical trials of PADCEV as a single agent, 2.9% of the 753 patients treated with PADCEV had pneumonitis/ILD of any grade and 0.8% had Grade 3-4. The median time to onset of pneumonitis/ILD was 2.7 months (range: 0.6 to 6 months). The incidence of pneumonitis/ILD, including severe events occurred at a higher rate when PADCEV was given in combination with pembrolizumab. When PADCEV was given in combination with pembrolizumab, 9% of the 121 patients treated with combination therapy had pneumonitis/ILD of any grade and 3.3% had Grade 3. A fatal event of pneumonitis occurred in one patient (0.8%). The median time to onset of pneumonitis/ILD was 6 months (range: 0.6 to 26 months). Monitor patients for signs and symptoms indicative of pneumonitis/ILD such as hypoxia, cough, dyspnea or interstitial infiltrates on radiologic exams. Evaluate and exclude infectious, neoplastic and other causes for such signs and symptoms through appropriate investigations. Withhold PADCEV for patients who develop Grade 2 pneumonitis/ILD and consider dose reduction. Permanently discontinue PADCEV in all patients with Grade 3 or 4 pneumonitis/ILD.

Peripheral neuropathy (PN) Peripheral neuropathy occurred in 53% of the 753 patients treated with PADCEV as a single agent in clinical trials including 40% with sensory neuropathy, 7% with muscular weakness and 7% with motor neuropathy. Thirty percent of patients experienced Grade 2 reactions and 5% experienced Grade 3-4 reactions. Peripheral neuropathy occurred in patients treated with PADCEV with or without preexisting peripheral neuropathy. The median time to onset of Grade ≥2 peripheral neuropathy was 4.9 months (range: 0.1 to 20 months). Neuropathy led to treatment discontinuation in 7% of patients. Of the patients who experienced neuropathy who had data regarding resolution (N = 319), 14% had complete resolution, 46% had partial improvement, and 40% had no improvement at the time of their last evaluation. Of the 86% of patients with residual neuropathy at last evaluation, 51% had Grade 2 or greater neuropathy at the time of their last evaluation.

The incidence of peripheral neuropathy occurred at a higher rate when PADCEV was given in combination with pembrolizumab. When PADCEV was given in combination with pembrolizumab, 65% of the 121 patients treated with combination therapy had peripheral neuropathy of any grade, 45% had Grade 2 neuropathy, and 3.3% had Grade 3 neuropathy. The median time to onset of Grade ≥2 peripheral neuropathy was 6 months (range: 0.3 to 25 months).

Monitor patients for symptoms of new or worsening peripheral neuropathy and consider dose interruption or dose reduction of PADCEV when peripheral neuropathy occurs. Permanently discontinue PADCEV in patients who develop Grade ≥3 peripheral neuropathy.

Ocular disorders were reported in 40% of the 384 patients treated with PADCEV as a single agent in clinical trials in which ophthalmologic exams were scheduled. The majority of these events involved the cornea and included events associated with dry eye such as keratitis, blurred vision, increased lacrimation, conjunctivitis, limbal stem cell deficiency, and keratopathy. Dry eye symptoms occurred in 34% of patients, and blurred vision occurred in 13% of patients, during treatment with PADCEV. The median time to onset to symptomatic ocular disorder was 1.6 months (range: 0 to 19 months). Monitor patients for ocular disorders. Consider artificial tears for prophylaxis of dry eyes and ophthalmologic evaluation if ocular symptoms occur or do not resolve. Consider treatment with ophthalmic topical steroids, if indicated after an ophthalmic exam. Consider dose interruption or dose reduction of PADCEV for symptomatic ocular disorders.

Infusion site extravasation Skin and soft tissue reactions secondary to extravasation have been observed after administration of PADCEV. Of the 753 patients treated with PADCEV as a single agent in clinical trials, 1.5% of patients experienced skin and soft tissue reactions, including 0.3% who experienced Grade 3-4 reactions. Reactions may be delayed. Erythema, swelling, increased temperature, and pain worsened until 2-7 days after extravasation and resolved within 1-4 weeks of peak. Two patients (0.3%) developed extravasation reactions with secondary cellulitis, bullae, or exfoliation. Ensure adequate venous access prior to starting PADCEV and monitor for possible extravasation during administration. If extravasation occurs, stop the infusion and monitor for adverse reactions.

Embryo-fetal toxicity PADCEV can cause fetal harm when administered to a pregnant woman. Advise patients of the potential risk to the fetus. Advise female patients of reproductive potential to use effective contraception during PADCEV treatment and for 2 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with PADCEV and for 4 months after the last dose.

ADVERSE REACTIONS

Most common adverse reactions, including laboratory abnormalities (≥20%) (PADCEV monotherapy)

Rash, aspartate aminotransferase increased, glucose increased, creatinine increased, fatigue, peripheral neuropathy, lymphocytes decreased, alopecia, decreased appetite, hemoglobin decreased, diarrhea, sodium decreased, nausea, pruritus, phosphate decreased, dysgeusia, alanine aminotransferase increased, anemia, albumin decreased, neutrophils decreased, urate increased, lipase increased, platelets decreased, weight decreased and dry skin.

EV-301 Study: 296 patients previously treated with a PD-1/L1 inhibitor and platinum-based chemotherapy.

Serious adverse reactions occurred in 47% of patients treated with PADCEV; the most common (≥2%) were urinary tract infection, acute kidney injury (7% each) and pneumonia (5%). Fatal adverse reactions occurred in 3% of patients, including multiorgan dysfunction (1.0%), hepatic dysfunction, septic shock, hyperglycemia, pneumonitis and pelvic abscess (0.3% each). Adverse reactions leading to discontinuation occurred in 17% of patients; the most common (≥2%) were PN (5%) and rash (4%). Adverse reactions leading to dose interruption occurred in 61% of patients; the most common (≥4%) were PN (23%), rash (11%) and fatigue (9%). Adverse reactions leading to dose reduction occurred in 34% of patients; the most common (≥2%) were PN (10%), rash (8%), decreased appetite and fatigue (3% each). Clinically relevant adverse reactions (<15%) include vomiting (14%), AST increased (12%), hyperglycemia (10%), ALT increased (9%), pneumonitis (3%) and infusion site extravasation (0.7%).

EV-201, Cohort 2 Study: 89 patients previously treated with a PD-1/L1 inhibitor and not eligible for cisplatin-based chemotherapy.

Serious adverse reactions occurred in 39% of patients treated with PADCEV; the most common (≥3%) were pneumonia, sepsis and diarrhea (5% each). Fatal adverse reactions occurred in 8% of patients, including acute kidney injury (2.2%), metabolic acidosis, sepsis, multiorgan dysfunction, pneumonia and pneumonitis (1.1% each). Adverse reactions leading to discontinuation occurred in 20% of patients; the most common (≥2%) was PN (7%). Adverse reactions leading to dose interruption occurred in 60% of patients; the most common (≥3%) were PN (19%), rash (9%), fatigue (8%), diarrhea (5%), AST increased and hyperglycemia (3% each). Adverse reactions leading to dose reduction occurred in 49% of patients; the most common (≥3%) were PN (19%), rash (11%) and fatigue (7%). Clinically relevant adverse reactions (<15%) include vomiting (13%), AST increased (12%), lipase increased (11%), ALT increased (10%), pneumonitis (4%) and infusion site extravasation (1%).

EV-103 Study: 121 patients with previously untreated locally advanced or metastatic urothelial cancer who were not eligible for cisplatin-containing chemotherapy (PADCEV in combination with pembrolizumab)

The **most common adverse reactions** including laboratory abnormalities (≥20%), of PADCEV in combination with pembrolizumab were glucose increased, aspartate aminotransferase increased, rash, hemoglobin decreased, creatinine increased, peripheral neuropathy, lymphocytes decreased, fatigue, alanine aminotransferase increased, sodium decreased, lipase increased, albumin decreased, alopecia, phosphate decreased, decreased weight, diarrhea, pruritus, decreased appetite, nausea, dysgeusia, potassium decreased, neutrophils decreased, urinary tract infection, constipation, potassium increased, calcium increased, peripheral edema, dry eye, dizziness, arthralgia, and dry skin.

Serious adverse reactions occurred in 50% of patients treated with PADCEV in combination with pembrolizumab. The **most common serious adverse reactions** (≥2%) were acute kidney injury (7%), urinary tract infection (7%), urosepsis (5%), sepsis (3.3%), pneumonia (3.3%), hematuria (3.3%), pneumonitis (3.3%), urinary retention (2.5%), diarrhea (2.5%), myasthenia gravis (2.5%), myositis (2.5%), anemia (2.5%), and hypotension (2.5%). **Fatal adverse reactions** occurred in 5% of patients treated with PADCEV in combination with pembrolizumab including sepsis (1.6%), bullous dermatitis (0.8%), myasthenia gravis (0.8%), and pneumonitis/ILD (0.8%). Adverse reactions leading to discontinuation of PADCEV occurred in 36% of patients. The **most common adverse reactions (≥2%) leading to discontinuation** of PADCEV were peripheral neuropathy (20%) and rash (6%). Adverse reactions leading to dose interruption of PADCEV occurred in 69% of patients. The **most common adverse reactions (≥2%) leading to dose interruption** of PADCEV were peripheral neuropathy (18%), rash (12%), lipase increased (6%), pneumonitis (6%), diarrhea (4.1%), acute kidney injury (3.3%), alanine aminotransferase increased (3.3%), fatigue (3.3%), neutropenia (3.3%), urinary tract infection (3.3%), amylase increased (2.5%), anemia (2.5%), COVID-19 (2.5%), hyperglycemia (2.5%), and hypotension (2.5%). Adverse reactions leading to dose reduction of PADCEV occurred in 45% of patients. The **most common adverse reactions (≥2%) leading to dose reduction** of PADCEV were peripheral neuropathy (17%), rash (12%), fatigue (5%), neutropenia (5%), and diarrhea (4.1%).

DRUG INTERACTIONS

Effects of other drugs on PADCEV (*Dual P-gp and Strong CYP3A4 Inhibitors*)

Concomitant use with dual P-gp and strong CYP3A4 inhibitors may increase unconjugated monomethyl auristatin E exposure, which may increase the incidence or severity of PADCEV toxicities. Closely monitor patients for signs of toxicity when PADCEV is given concomitantly with dual P-gp and strong CYP3A4 inhibitors.

SPECIFIC POPULATIONS

Lactation Advise lactating women not to breastfeed during treatment with PADCEV and for at least 3 weeks after the last dose.

Hepatic impairment Avoid the use of PADCEV in patients with moderate or severe hepatic impairment.

Please see full Prescribing Information, including BOXED WARNING.

FDA=US Food and Drug Administration; PD-(L)1=programmed death receptor-1 or programmed death-ligand 1.

References: 1. PADCEV [package insert]. Northbrook, IL: Astellas Pharma US, Inc. **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer V.1.2023. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed February 9, 2023. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

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