Informational Resource for Skin Reactions During Treatment With PADCEV®

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

A resource to assist with identifying and addressing skin reactions during treatment

PADCEV, as a single agent or in combination with pembrolizumab, can cause severe and fatal cutaneous adverse reactions, including Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). Withhold PADCEV and consider referral for specialized care for suspected SJS, TEN, or for Grade 3 skin reactions. During each visit, closely monitor patients for signs and symptoms of new or worsening skin reactions, and consider dose interruption, dose reduction, or discontinuation of PADCEV when skin reactions occur. Dose modifications were common in the clinical trials of PADCEV and were an important way to treat adverse reactions.[1]

ENCOURAGE PATIENTS TO IMMEDIATELY INFORM THEIR HEALTHCARE PROVIDER ABOUT ANY NEW OR WORSENING SIGNS OF SKIN REACTIONS[1]:

- Target lesions (skin reactions that look like rings)
- Rash or itching that continues to get worse
- Blistering or peeling of skin
- Painful sores or ulcers in mouth or nose, throat, or genital area
- Fever or flu-like symptoms
- Swollen lymph nodes

Consider asking screening questions to monitor patients for these signs and symptoms.

Early identification and treatment of skin reactions is important

POTENTIAL SCREENING QUESTIONS TO ASSIST IN IDENTIFICATION OF SKIN REACTIONS[1]:

- Are you experiencing any new or worsening rashes, blistering or peeling of skin?
- Have you had a fever or other flu-like symptoms?
- Have you noticed any sores or ulcers in your mouth or nose, throat, or genital area?

Please refer to the Prescribing Information for a full list of potential adverse reactions.

Starting with the first cycle and throughout treatment, closely monitor patients for skin reactions[1]

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.**

INDICATION

PADCEV, in combination with pembrolizumab, is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer (mUC).

PADCEV, as a single agent, is indicated for the treatment of adult patients with locally advanced or 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.

DOSE MODIFICATIONS FOR SKIN REACTIONS[1]

SEVERITY*	PADCEV DOSE MODIFICATION*
For persistent or recurrent Grade 2 skin reactions	■ **Consider withholding** until Grade ≤1 ▫ Then **resume** treatment at the same dose level or dose reduce by one dose level
Grade 3 skin reactions	■ **Withhold** until Grade ≤1 ▫ Then **resume** treatment at the same dose level or dose reduce by one dose level
Suspected SJS or TEN	■ **Immediately withhold**, consult a specialist to confirm the diagnosis. If not SJS/TEN, see Grade 2-4 skin reactions
Confirmed SJS **or** TEN; Grade 4 **or** recurrent Grade 3 skin reactions	■ **Permanently discontinue**

■ WITHHOLD ■ RESUME ■ DISCONTINUE

*Grade 1 is mild; Grade 2 is moderate; Grade 3 is severe; Grade 4 is life-threatening.

PADCEV RECOMMENDED DOSE REDUCTION SCHEDULE[1]

The recommended dose of PADCEV (as a single agent or in combination with pembrolizumab) is 1.25 mg/kg (up to a maximum of 125 mg for patients ≥100 kg).

Starting dose	1st dose **reduction**	2nd dose **reduction**	3rd dose **reduction**
DOSE LEVEL: **1.25 mg/kg up to 125 mg**	DOSE LEVEL: **1.0 mg/kg up to 100 mg**	DOSE LEVEL: **0.75 mg/kg up to 75 mg**	DOSE LEVEL: **0.5 mg/kg up to 50 mg**

Refer to the PADCEV Prescribing Information for the recommended dosing schedule of PADCEV as a single agent or in combination with pembrolizumab. Refer to the pembrolizumab Prescribing Information for the recommended dosing information of pembrolizumab.

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

Skin reactions incidence and time to onset in PADCEV® clinical trials

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.[1]

SKIN REACTIONS IN CLINICAL TRIALS OF PADCEV IN COMBINATION WITH PEMBROLIZUMAB[1,2]

The combination data below are based on exposure to PADCEV in combination with pembrolizumab in EV-302 and EV-103. Adverse reactions (ARs) were graded using National Cancer Institute CTCAE v4.03.[1,3,4]

	In combination (n=564)	
	All grades	Grades 3-4
Skin reactions (all types)	70%	17%*
Pruritus	41.1%	1.6%
Rash maculo-papular	36%	9.6%

*These reactions included maculo-papular rash, bullous dermatitis, dermatitis, exfoliative dermatitis, pemphigoid, rash, erythematous rash, macular rash, and papular rash.[1]

In combination
Median time to onset of severe skin reactions
1.7 months
Range: 0.1 to 17.2 months

The incidence of skin reactions, including severe events, occurred at a higher rate when PADCEV was given in combination with pembrolizumab. The majority of the skin reactions that occurred with combination therapy included maculo-papular rash, macular rash, and papular rash. A fatal reaction of bullous dermatitis occurred in one patient (0.2%).[1]

Skin reactions led to discontinuation of PADCEV in 6% of patients. Of the patients who experienced a skin reaction and had data regarding resolution (N=391), 59% had complete resolution and 41% had residual skin reactions at their last evaluation. Of the patients with residual skin reactions at last evaluation, 27% (43/159) had Grade ≥2 skin reactions.[1]

SKIN REACTIONS IN CLINICAL TRIALS OF PADCEV ALONE[1,2]

The data below are based on exposure to PADCEV as a single agent in EV-301, EV-201, EV-203, EV-101, and EV-102. ARs were graded using National Cancer Institute CTCAE v4.03.[1,2,5]

	Monotherapy (n=720)	
	All grades	Grades 3-4
Skin reactions (all types)	58%	14%†
Pruritus	34%	1.8%
Rash maculo-papular	23%	5.8%

†These reactions included maculo-papular rash, erythematous rash, rash or drug eruption, SDRIFE, bullous dermatitis, exfoliative dermatitis, and palmar-plantar erythrodysesthesia.[1]

Monotherapy
Median time to onset of severe skin reactions
0.6 months
Range: 0.1 to 8 months

In clinical trials of PADCEV as a single agent, 3.1% of patients discontinued PADCEV due to skin reactions. Among patients experiencing a skin reaction leading to dose interruption who then restarted PADCEV (n=75)[1]:

- 24% of patients restarting at the same dose experienced recurrent severe skin reactions
- 24% of patients restarting at a reduced dose experienced recurrent severe skin reactions

Of the patients who experienced a skin reaction and had data regarding resolution (N=328), 58% had complete resolution and 42% had residual skin reactions at their last evaluation. Of the patients with residual skin reactions at last evaluation, 39% (53/137) had Grade ≥2 skin reactions.[1]

Clinical considerations for skin reactions while treating with PADCEV

- Inform patients that severe skin reactions, including SJS and TEN with fatal outcomes have occurred after administration of PADCEV, predominantly during the first cycle of treatment but may occur later. Educate patients on the potential for skin reactions, common signs or symptoms, and importance of immediately reporting[1]
- Starting with the first cycle and throughout treatment, monitor patients for skin reactions[1]
- Consider PADCEV dose modifications or appropriate treatment. As clinically indicated, consider topical corticosteroids and antihistamines[1]

Other considerations for treating skin reactions while on anticancer treatments[6‡]

Treatment strategies for rash:

- Consider fragrance-free moisturizers applied twice daily (ideally within 15 minutes after showering/bathing); unscented creams and emollients at least twice daily (eg, white petrolatum for prophylactic use and after rash appears); and creams containing anti-itch ingredients (eg, pramoxine, camphor, menthol, oatmeal) may be helpful for itchy rash. Please consult PADCEV full Prescribing Information for specific PADCEV information

General advice for skin care during and after cancer treatment may include:

- Using mild detergents and skin cleansers
- Using alcohol-free, fragrance-free hypoallergenic moisturizers
- Using hypoallergenic makeup
- Avoiding over-the-counter acne medications
- Sunscreen (SPF 30 or greater and free of para-aminobenzoic acid)
- Lukewarm rather than hot water for bathing
- Proper hydration

Consider referral to a dermatologist for:

- Reactions that exceed 30% of BSA (Grade ≥3)
- Reactions that involve the mucosa, bullous lesions, or exfoliation
- Reactions that do not respond to a combination of steroids, antihistamines, and dose modifications
- Early referral to dermatology for lower-grade skin reactions is also a reasonable approach for proactive evaluation and management

‡Adapted from Pace, et al. 2021; based on the anecdotal experiences of the authors, which included nurses and advanced practice providers, in clinical practice caring for patients who received PADCEV as a single agent.

BSA=body surface area; CTCAE=Common Terminology Criteria for Adverse Events; SDRIFE=symmetrical drug-related intertriginous and flexural exanthema; SPF=sun protection factor

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Skin reactions grading

CTCAE V5.0 GRADING SCALE FOR SELECT SKIN REACTIONS[7]

CTCAE term	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Dry skin	Covering <10% BSA and no associated erythema or pruritus	Covering 10%-30% BSA and associated with erythema or pruritus; limiting instrumental ADL	Covering >30% BSA and associated with pruritus; limiting self-care ADL	—	—
Erythema multiforme	Target lesions covering <10% BSA and not associated with skin tenderness	Target lesions covering 10%-30% BSA and associated with skin tenderness	Target lesions covering >30% BSA and associated with oral or genital erosions	Target lesions covering >30% BSA; associated with fluid or electrolyte abnormalities; ICU care or burn unit indicated	Death
Pruritus	Mild or localized; topical intervention indicated	Widespread and intermittent; skin changes from scratching (eg, edema, papulation, excoriations, lichenification, oozing/crusts); oral intervention indicated; limiting instrumental ADL	Widespread and constant; limiting self-care ADL or sleep; systemic corticosteroid or immunosuppressive therapy indicated	—	—
Rash maculo-papular	Macules/papules covering <10% BSA with or without symptoms (eg, pruritus, burning, tightness)	Macules/papules covering 10%-30% BSA with or without symptoms (eg, pruritus, burning, tightness); limiting instrumental ADL; rash covering >30% BSA with or without mild symptoms	Macules/papules covering >30% BSA with moderate or severe symptoms; limiting self-care ADL	—	—
SJS	—	—	Skin sloughing covering <10% BSA with associated signs (eg, erythema, purpura, epidermal detachment, mucous membrane detachment)	Skin sloughing covering 10%-30% BSA with associated signs (eg, erythema, purpura, epidermal detachment, mucous membrane detachment)	Death
TEN	—	—	—	Skin sloughing covering ≥30% BSA with associated symptoms (eg, erythema, purpura, epidermal detachment)	Death

Note: '—' indicates a grade is not available.

ADL=activities of daily living; ICU=intensive care unit.

Contact your Pfizer/Astellas representative for a copy of this resource and others, and visit **PADCEVhcp.com/resources** for more helpful tools.

For more information, call 1-888-4PADCEV (1-888-472-3238) or visit PADCEVhcp.com

Additional patient AR resource

Download a digital copy of the **Adverse Reactions Information Guide** to share with your patients. This tool includes information about adverse reactions your patients may experience while taking PADCEV.

Download Adverse Reactions Information Guide

References: 1. PADCEV. Package insert. Northbrook, IL: Astellas Pharma US, Inc; 2024. **2.** Pfizer Inc. and Astellas. PADCEV. Data on File. **3.** Protocol for: O'Donnell PH, Milowsky MI, Petrylak DP, et al. Enfortumab vedotin with or without pembrolizumab in cisplatin-ineligible patients with previously untreated locally advanced or metastatic urothelial cancer. *J Clin Oncol*. 2023;41(25):4107-4117. **4.** Protocol for: Powles T, Valderrama BP, Gupta S, et al; for the EV-302 Trial Investigators. Enfortumab vedotin and pembrolizumab in untreated advanced urothelial cancer. *N Engl J Med*. 2024;390(10):875-888. **5.** Protocol for: Powles T, Rosenberg JE, Sonpavde GP, et al. Enfortumab vedotin in previously treated advanced urothelial carcinoma. *N Engl J Med*. 2021;384(12):1125-1135. **6.** Pace A, Brower B, Conway D, Leis D. Enfortumab vedotin: nursing perspectives on the management of adverse events in patients with locally advanced or metastatic urothelial carcinoma. *Clin J Oncol Nurs*. 2021;25(2):E1-E9. **7.** U.S. Department of Health and Human Services. Common terminology criteria for adverse events (CTCAE) v5.0. Published November 27, 2017. Accessed February 2, 2024. https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf.

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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 70% (all grades) of the 564 patients treated with PADCEV in combination with pembrolizumab in clinical trials. When PADCEV was given in combination with pembrolizumab, the incidence of skin reactions, including severe events, occurred at a higher rate compared to PADCEV as a single agent. 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 17% of patients (Grade 3: 16%, Grade 4: 1%), 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 (0.2%). The median time to onset of severe skin reactions was 1.7 months (range: 0.1 to 17.2 months). Skin reactions led to discontinuation of PADCEV in 6% of patients.

Skin reactions occurred in 58% (all grades) of the 720 patients treated with PADCEV as a single agent in clinical trials. Twenty-three percent (23%) of patients had maculo-papular rash and 34% had pruritus. Grade 3-4 skin reactions occurred in 14% 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 0.6 months (range: 0.1 to 8 months). Among patients experiencing a skin reaction leading to dose interruption who then restarted PADCEV (n=75), 24% of patients restarting at the same dose and 24% of patients restarting at a reduced dose experienced recurrent severe skin reactions. Skin reactions led to discontinuation of PADCEV in 3.1% 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), 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, 17% of the 720 patients treated with PADCEV developed hyperglycemia of any grade; 7% of patients developed Grade 3-4 hyperglycemia (Grade 3: 6.5%, Grade 4: 0.6%). Fatal events of hyperglycemia and DKA 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. The median time to onset of hyperglycemia was 0.5 months (range: 0 to 20 months). Hyperglycemia led to discontinuation of PADCEV in 0.7% of patients. Five percent (5%) of patients required initiation of insulin therapy for treatment of hyperglycemia. Of the patients who initiated insulin therapy for treatment of hyperglycemia, 66% (23/35) discontinued insulin at the time of last evaluation. 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. When PADCEV was given in combination with pembrolizumab, 10% of the 564 patients treated with combination therapy had pneumonitis/ILD of any grade and 4% had Grade 3-4. A fatal event of pneumonitis/ILD occurred in two patients (0.4%). The incidence of pneumonitis/ILD, including severe events, occurred at a higher rate when PADCEV was given in combination with pembrolizumab compared to PADCEV as a single agent. The median time to onset of any grade pneumonitis/ILD was 4 months (range: 0.3 to 26 months).

In clinical trials of PADCEV as a single agent, 3% of the 720 patients treated with PADCEV had pneumonitis/ILD of any grade and 0.8% had Grade 3-4. The median time to onset of any grade pneumonitis/ILD was 2.9 months (range: 0.6 to 6 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) When PADCEV was given in combination with pembrolizumab, 67% of the 564 patients treated with combination therapy had PN of any grade, 36% had Grade 2 neuropathy, and 7% had Grade 3 neuropathy. The incidence of PN occurred at a higher rate when PADCEV was given in combination with pembrolizumab compared to PADCEV as a single agent. The median time to onset of Grade ≥2 PN was 6 months (range: 0.3 to 25 months).

PN occurred in 53% of the 720 patients treated with PADCEV as a single agent in clinical trials including 38% with sensory neuropathy, 8% with muscular weakness and 7% with motor neuropathy. Thirty percent of patients experienced Grade 2 reactions and 5% experienced Grade 3-4 reactions. PN occurred in patients treated with PADCEV with or without preexisting PN. The median time to onset of Grade ≥2 PN was 4.9 months (range: 0.1 to 20 months). Neuropathy led to treatment discontinuation in 6% of patients.

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

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 30% of patients, and blurred vision occurred in 10% of patients, during treatment with PADCEV. The median time to onset to symptomatic ocular disorder was 1.7 months (range: 0 to 30.6 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 720 patients treated with PADCEV as a single agent in clinical trials, 1% 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 in combination with pembrolizumab)

Increased aspartate aminotransferase (AST), increased creatinine, rash, increased glucose, PN, increased lipase, decreased lymphocytes, increased alanine aminotransferase (ALT), decreased hemoglobin, fatigue, decreased sodium, decreased phosphate, decreased albumin, pruritus, diarrhea, alopecia, decreased weight, decreased appetite, increased urate, decreased neutrophils, decreased potassium, dry eye, nausea, constipation, increased potassium, dysgeusia, urinary tract infection and decreased platelets.

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

Increased glucose, increased AST, decreased lymphocytes, increased creatinine, rash, fatigue, PN, decreased albumin, decreased hemoglobin, alopecia, decreased appetite, decreased neutrophils, decreased sodium, increased ALT, decreased phosphate, diarrhea, nausea, pruritus, increased urate, dry eye, dysgeusia, constipation, increased lipase, decreased weight, decreased platelets, abdominal pain, dry skin.

EV-302 Study: 440 patients with previously untreated la/mUC (PADCEV in combination with pembrolizumab)

Serious adverse reactions occurred in 50% of patients treated with PADCEV in combination with pembrolizumab. The most common serious adverse reactions (≥2%) were rash (6%), acute kidney injury (5%), pneumonitis/ILD (4.5%), urinary tract infection (3.6%), diarrhea (3.2%), pneumonia (2.3%), pyrexia (2%), and hyperglycemia (2%). **Fatal adverse reactions** occurred in 3.9% of patients treated with PADCEV in combination with pembrolizumab including acute respiratory failure (0.7%), pneumonia (0.5%), and pneumonitis/ILD (0.2%).

Adverse reactions leading to discontinuation of PADCEV occurred in 35% of patients. The **most common adverse reactions (≥2%) leading to discontinuation** of PADCEV were PN (15%), rash (4.1%) and pneumonitis/ILD (2.3%). Adverse reactions leading to dose interruption of PADCEV occurred in 73% of patients. The **most common adverse reactions (≥2%) leading to dose interruption** of PADCEV were PN (22%), rash (16%), COVID-19 (10%), diarrhea (5%), pneumonitis/ILD (4.8%), fatigue (3.9%), hyperglycemia (3.6%), increased ALT (3%) and pruritus (2.5%). Adverse reactions leading to dose reduction of PADCEV occurred in 42% of patients. The **most common adverse reactions (≥2%) leading to dose reduction** of PADCEV were rash (16%), PN (13%) and fatigue (2.7%).

EV-103 Study: 121 patients with previously untreated la/mUC who were not eligible for cisplatin-containing chemotherapy (PADCEV in combination with pembrolizumab)

Serious adverse reactions occurred in 50% of patients treated with PADCEV in combination with pembrolizumab; the most common (≥2%) were acute kidney injury (7%), urinary tract infection (7%), urosepsis (5%), sepsis (3.3%), pneumonia (3.3%), hematuria (3.3%), pneumonitis/ILD (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 (≥2%) were PN (20%) and rash (6%). **Adverse reactions leading to dose interruption** of PADCEV occurred in 69% of patients; the most common (≥2%) were PN (18%), rash (12%), increased lipase (6%), pneumonitis/ILD (6%), diarrhea (4.1%), acute kidney injury (3.3%), increased ALT (3.3%), fatigue (3.3%), neutropenia (3.3%), urinary tract infection (3.3%), increased amylase (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 (≥2%) were PN (17%), rash (12%), fatigue (5%), neutropenia (5%), and diarrhea (4.1%).

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

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%), hepatic dysfunction, septic shock, hyperglycemia, pneumonitis/ILD, 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).

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

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/ILD (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%), increased AST, 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%).

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 3 weeks after the last dose.

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

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

astellas

Pfizer Oncology

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