PADCEV®
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Injection for IV infusion 20 mg & 30 mg vials

ADVERSE REACTIONS INFORMATION GUIDE

PADCEV® J-CODE J9177

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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.

Please see Important Safety Information and full Prescribing Information, including BOXED WARNING for Serious Skin Reactions.

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.**

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.

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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.

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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

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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.

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About this Adverse Reactions Information Guide

The select adverse reactions (ARs) information provided within this guide is based on the data available from PADCEV® trials and other clinical sources

This tool contains detailed information about:

- Possible ARs, including risk factors
- Common Terminology Criteria of Adverse Events (CTCAE) grading information
- Dose modifications by severity from the full Prescribing Information
- Strategies for monitoring and treatment of these select ARs if your patients are currently experiencing them, or if you believe they are at an increased risk of experiencing these ARs
- Adverse reaction resolution and improvement data from clinical trials

It is critical that your patients understand the importance of timely symptom reporting to help ensure you can provide assistance and support as soon as possible.[1,2]

Have your patients download a copy of **Understanding Possible Side Effects With PADCEV** to help guide them through AR consultation conversations.

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When your patient experiences an AR:

Consult the full Prescribing Information for dose modifications (Section 2.2) related to adverse events[3]

- Efficacy results from the clinical trials reflect full and modified dosing regimens[3]
- In the EV-302 trial of adults with locally advanced or metastatic urothelial cancer who received at least one dose of PADCEV® and pembrolizumab:
  - 73% had their PADCEV dose interrupted because of ARs[3]
  - 42% had their PADCEV dose reduced because of ARs[3]
  - 35% discontinued their PADCEV treatment because of ARs[3]
- In the EV-301 trial of adults with locally advanced or metastatic urothelial cancer who previously received a platinum-containing chemotherapy and a PD-(L)1 inhibitor:
  - 61% had their PADCEV dose interrupted because of ARs[3]
  - 34% had their PADCEV dose reduced because of ARs[3]
  - 17% discontinued their PADCEV treatment because of ARs[3]
- In the EV-201 (Cohort 2) trial of adults with locally advanced or metastatic urothelial cancer who were ineligible for cisplatin-containing chemotherapy and have previously received a PD-(L)1 inhibitor:
  - 60% had their PADCEV dose interrupted because of ARs[3]
  - 49% had their PADCEV dose reduced because of ARs[3]
  - 20% discontinued their PADCEV treatment because of ARs[3]

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Summary of incidence rates and median times to onset for select warning and precautions
In combination with pembrolizumab

Select warnings and precautions

The combination data below are based on exposure to PADCEV® in combination with pembrolizumab at 1.25 mg/kg in 564 patients in EV-302 and EV-103.

Evaluate patients for ARs at each visit, as they may occur at any time during treatment with PADCEV in combination with pembrolizumab.

Select warnings and precautions[3]	Incidence rates[3]		Median time to onset[3]
	In combination		
	All grades	Grade ≥3	In combination
Skin reactions	70%	Grades 3-4: 17%* Grade 5: 0.2%	**Severe skin reactions** 1.7 months (range: 0.1 to 17.2 months)
Hyperglycemia[4]	19%[4]	9.2%[4]	0.7 months (range: 0 to 16.8 months)[4]
Pneumonitis/ILD	10%	Grades 3-4: 4% Grade 5: 0.4%	4 months (range: 0.3 to 26 months)
Peripheral neuropathy (PN)	67%	Grade 3: 7%	**Grade ≥2 PN** 6 months (range: 0.3 to 25 months)
Ocular disorders[4]	31.9%[4]	—	—
Infusion site extravasation	1.6[4]	0.2%[4]	—

*These reactions included maculo-papular rash, bullous dermatitis, dermatitis, exfoliative dermatitis, pemphigoid, rash, erythematous rash, macular rash, and papular rash.[3]

This is not the full list of ARs that have been reported in clinical trials of PADCEV. Hematologic toxicities and nonhematologic toxicities have been observed after administration of PADCEV. Please see the full Prescribing Information for a complete list.[3]

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Summary of risk factors and select warnings and precautions

The incidence rates and median times to onset data below are based on exposure to PADCEV® as a single agent at 1.25 mg/kg in 720 patients in EV-301, EV-201, EV-203, EV-101, and EV-102. Ocular disorders reflect 384 patients in EV-201, EV-101, and EV-102.

Evaluate patients for ARs at each visit, as they may occur at any time during treatment with PADCEV.

Select warnings and precautions[3]	Incidence rates[3] Monotherapy		Median time to onset[3]	Risk factors		AR resolution and improvement information
	All grades	Grade ≥3	Monotherapy			
Skin reactions	58%	14%*	**Severe skin reactions** 0.6 months (range: 0.1 to 8 months)	• Prior history of dermatologic conditions[1†] • Rash/pruritus[1†]	• Allergies[1†] • Dry skin[1†] • Immunosuppression[1†] • High sun exposure[1†]	Page 16
Hyperglycemia	17%	Grades 3-4: 7% Grade 5: 0.3%	0.5 months (range: 0 to 20 months)	• Per the USPI, higher BMI and baseline HbA1c resulted in higher incidences of Grade 3-4 events[3]	• Diabetes[1†] • Illness/infection[1†] • Use of systemic steroids[1†]	Page 22
Pneumonitis/ILD	3%	0.8%	2.9 months (range: 0.6 to 6 months)	• None identified in the PADCEV Prescribing Information		—
Peripheral neuropathy (PN)	53%	5%	**Grade ≥2 PN** 4.9 months (range: 0.1 to 20 months)	• Previous anticancer therapy[1†] • Comorbid conditions (eg, diabetes)[1†] • Older age[1†]	• Spinal involvement of metastatic urothelial cancer[1†] • Nonmalignant spinal disease[1†]	Page 31
Ocular disorders	40%	—	1.7 months (range: 0 to 30.6 months)	• Older age for dry eyes[1†] • Contact lens use for keratitis[1†]		—
Infusion site extravasation	1%	0.3%	Generally immediately after administration, but possible delayed onset (eg, 24 hours)[‡]	• Poor venous access[2§]		—

*These reactions included 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.[3]
†General risk factors identified in Pace, et al. 2021.
‡Not a median time to onset.
§General risk factor identified in Wengström Y, et. al. 2008.

This is not the full list of ARs that have been reported in clinical trials of PADCEV. Hematologic toxicities and nonhematologic toxicities have been observed after administration of PADCEV. Please see the full Prescribing Information for a complete list.[3]

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Skin reactions
Incidence, time to onset, and resolution in combination with pembrolizumab

Severe cutaneous adverse reactions, including fatal cases of Stevens-Johnson syndrome (SJS) or Toxic Epidermal Necrolysis (TEN), occurred in patients treated with PADCEV®. SJS and TEN occurred predominantly during the first cycle of treatment, but may occur later.[3]

Skin reactions in clinical trials of PADCEV in combination with pembrolizumab[3,4]

PADCEV was evaluated in combination with pembrolizumab. ARs were graded using National Cancer Institute CTCAE v4.03.

	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.[3]

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. 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%).[3]

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.[3]

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Skin reactions in clinical trials of PADCEV® alone[3-5]

PADCEV was evaluated as a single agent. ARs were graded using National Cancer Institute CTCAE v4.03.

	Monotherapy (n=720)	
	All grades	Grades 3-4
Skin reactions (all types)	58%	14%*
Pruritus	34%	—
Maculo-papular rash	23%	—

*These reactions included maculo-papular rash, erythematous rash, rash or drug eruption, SDRIFE, bullous dermatitis, exfoliative dermatitis, and palmar-plantar erythrodysesthesia.[3]

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)[3]:

- 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.[3]

For additional adverse reaction resolution and improvement data for skin reactions from clinical trials of PADCEV as a single agent, see pages 15-16.

CTCAE v5.0 grading scale for select skin reactions[6]

Skin and subcutaneous disorders				
CTCAE term	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
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
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)
TEN	—	—	—	Skin sloughing covering ≥30% BSA with associated symptoms (eg, erythema, purpura, epidermal detachment)

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

Treatment for skin reactions: modifications for PADCEV dosing[3]

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

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

Refer to the pembrolizumab Prescribing Information for the recommended dosing information of pembrolizumab.

Skin reactions
Monitoring and clinical considerations

There are general characteristics that may predispose patients to skin reactions, including prior history of a dermatologic condition, rash/pruritus, allergies, dry skin, immunosuppression, and/or high sun exposure.* In monotherapy clinical trials, of those who experienced a severe skin reaction, more than half of incidents occurred during the first treatment cycle with PADCEV®. In combination therapy trials, of those who experienced a severe skin reaction, more than half of incidents occurred before the second month of treatment with PADCEV with pembrolizumab.[1,3]

Clinical considerations for treating with PADCEV

- Educate patients on the potential for skin reactions, common signs or symptoms, and importance of early reporting[1,3]*
- Starting with the first cycle and throughout treatment, monitor patients for skin reactions[3]
- Consider PADCEV dose modifications or appropriate treatment. As clinically indicated, consider topical corticosteroids (eg, over-the-counter hydrocortisone, triamcinolone, clobetasol) and antihistamines (eg, diphenhydramine, cetirizine), or for severe cases, systemic corticosteroids. Also consider topical antibiotics or antifungals for treatment of secondary infections[1]*
- Dermatologist referral is indicated for[1]*:
  - 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

Other considerations for treating with PADCEV

Treatment strategies for mild-to-moderate rash[1]*:

- Consider fragrance-free moisturizers applied twice daily (ideally within 15 minutes after showering/bathing); unscented creams and emollients twice daily (eg, white petrolatum); 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 anticancer treatment includes[1]*:

- 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

*Adapted from Pace, et al. 2021.

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Please see Important Safety Information and full Prescribing Information, including BOXED WARNING for Serious Skin Reactions.

Skin reactions
Incidence of events in clinical trials of PADCEV® as a single agent

The results on improvement and resolution of skin reactions are observational data from patients with locally advanced or metastatic urothelial cancer treated with PADCEV as a single agent in 2 EV clinical trials.[4]

- In Cohort 1 of EV-201, patients received prior treatment with a PD-1 or PD-L1 inhibitor and a platinum-based chemotherapy
- In Cohort 2 of EV-201, patients received prior treatment with a PD-1 or PD-L1 inhibitor and were ineligible for cisplatin-based chemotherapy

Results on improvement and resolution of skin reactions from EV-301 were not available.

To fully characterize skin reaction events, a combination of an SSQ/CMQ for dermatologic events (5 high-level terms under the high-level group term of Epidermal and Dermal Conditions) and the MedDRA version 23.0 SMQ of Severe Cutaneous Adverse Reaction was used. Events from both categories ("any rashes" SSQ/CMQ and "Severe Cutaneous Adverse Reaction" SMQ) are together referred to as "skin reactions."[4]

These data are not generalizable and cannot be used to predict adverse event outcomes. The EV-201 data are from a single-arm, multi-cohort, multicenter trial with the major efficacy outcome measures of confirmed objective response rate (ORR) and duration of response (DOR) as assessed by blinded independent central review (BICR) using RECIST v1.1. The results presented are provided only as descriptive clinical information.[3]

Treatment-emergent skin reactions[4]*		
	EV-201, Cohort 1	EV-201, Cohort 2
Grade 1, % (n/N)	22% (27/125)	34% (30/89)
Grade 2, % (n/N)	20% (25/125)	16% (14/89)
Grade 3, % (n/N)	12% (15/125)	16% (14/89)
Grade 4, % (n/N)	—	1% (1/89)
All grades, % (n/N)	54% (67/125)	66% (59/89)

Data cutoff date for EV-201 Cohort 1 and EV-201 Cohort 2 safety data was September 8, 2020.
*Patients could have more than one event. For each preferred term, multiple occurrences of events within a patient are counted only once at the highest severity grade.

Skin reactions
Resolution and improvement of events in clinical trials of PADCEV® as a single agent

Summary of resolution or improvement of patients with treatment-emergent events[4]		
	EV-201, Cohort 1	**EV-201, Cohort 2**
Patients with all events resolved,[*†] % (n/n)	81% (54/67)	68% (40/59)
Patients with some events resolved or improved,[*‡] % (n/n)	15% (10/67)	14% (8/59)
Patients with no events resolved or improved,[*] % (n/n)	5% (3/67)	19% (11/59)
Time to resolution or improvement of treatment-emergent events[4‡]		
	EV-201, Cohort 1	**EV-201, Cohort 2**
Median time to resolution,[†] months (min, max)	0.72 (0.03, 14.65)	0.92 (0.07, 19.58)
Median time to improvement,[‡] months (min, max)	0.82 (0.16, 2.20)	0.56 (0.53, 1.64)

Data cutoff date for EV-201 Cohort 1 and EV-201 Cohort 2 safety data was September 8, 2020.
*Patients could have more than one event. For each preferred term, multiple occurrences of events within a patient are counted only once at the highest severity grade.
†Resolution is defined as events outcome of "Recovered/Resolved" or "Recovered/Resolved with Sequelae," or returning to baseline grade as of the last assessment for conditions that are ongoing at baseline.
‡For events that are not resolved, improvement is defined as at least one grade improvement from the worst grade at the last assessment.

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Hyperglycemia in clinical trials of PADCEV® in combination with pembrolizumab[4]

PADCEV was evaluated in combination with pembrolizumab. ARs were graded using National Cancer Institute CTCAE v4.03.

	In combination (n=564)	
	All grades	Grades 3-4
Hyperglycemia	19%	9.2%

In combination		
Median time to onset of hyperglycemia	0.7 months	Range: 0 to 16.8 months

Hyperglycemia
Incidence and time to onset in monotherapy

Hyperglycemia and diabetic ketoacidosis (DKA), including fatal events, occurred in patients with and without pre-existing diabetes mellitus treated with PADCEV®. Fatal events of hyperglycemia and diabetic ketoacidosis occurred in one patient each (0.1%). Patients with baseline HbA1c ≥8% were excluded from clinical trials.[3]

Hyperglycemia in clinical trials of PADCEV alone[3-5]

PADCEV was evaluated as a single agent. ARs were graded using National Cancer Institute CTCAE v4.03.

	Monotherapy (n=720)	
	All grades	Grades 3-4
Hyperglycemia	17%	7%

Monotherapy		
Median time to onset of hyperglycemia	0.5 months	Range: 0 to 20 months

The incidence of Grade 3-4 hyperglycemia increased consistently in patients with higher BMI and in patients with higher baseline HbA1c. 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 by the time of last evaluation. Hyperglycemia led to discontinuation of PADCEV in 0.7% of patients.[3]

Please see Important Safety Information and full Prescribing Information, including BOXED WARNING for Serious Skin Reactions.

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CTCAE grading scale for hyperglycemia[6,7]

Metabolism and nutrition disorders				
CTCAE term	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
Hyperglycemia	FBG >ULN-160 mg/dL* Abnormal glucose above baseline with no medical intervention†	FBG >160 mg/dL-250 mg/dL* Change in daily management from baseline for a diabetic; oral antiglycemic agent initiated; workup for diabetes†	FBG >250 mg/dL-500 mg/dL* Insulin therapy initiated; hospitalization indicated†	FBG >500 mg/dL* Life-threatening consequences; urgent intervention indicated†

*Adapted from CTCAE v4.03.
†Adapted from CTCAE v5.0.

PADCEV dose modifications for hyperglycemia[3]	
	Blood glucose >250 mg/dL
Dose modification for hyperglycemia	Withhold until elevated blood glucose has improved to ≤250 mg/dL, then resume treatment at the same dose level.

Refer to the pembrolizumab Prescribing Information for the recommended dosing information of pembrolizumab.

Risk factors for hyperglycemia

- In clinical trials of PADCEV® as a single agent, Grade 3-4 hyperglycemia increased consistently in patients with higher BMI and higher baseline HbA1c. Closely monitor blood glucose levels in patients with, or at risk for, diabetes mellitus or hyperglycemia[3]
- Potential risk factors for hyperglycemia in a patient on anticancer therapy include diabetes mellitus, illness/infection, and use of systemic steroids[1]*

Clinical and other considerations for treating with PADCEV*

Educate patients on potential for hyperglycemia, common signs or symptoms, and importance of early reporting[1]

Assess baseline HbA1c measurement before starting PADCEV, and routinely monitor nonfasting blood glucose levels prior to each PADCEV dose[1]

Patients with a history of diabetes or hyperglycemia should inform their primary care professional or endocrinologist about their treatment with PADCEV[1]

- Consider optimizing blood glucose control for these patients prior to starting PADCEV as their cancer status allows

*Adapted from Pace, et al. 2021.

Hyperglycemia
Incidence of events in clinical trials of PADCEV® as a single agent

The results on improvement and resolution of hyperglycemia are observational data from patients with locally advanced or metastatic urothelial cancer treated with PADCEV as a single agent in 2 EV clinical trials.[4]

- In Cohort 1 of EV-201, patients received prior treatment with a PD-1 or PD-L1 inhibitor and a platinum-based chemotherapy
- In Cohort 2 of EV-201, patients received prior treatment with a PD-1 or PD-L1 inhibitor and were ineligible for cisplatin-based chemotherapy

Results on improvement and resolution of hyperglycemia from EV-301 were not available.

Hyperglycemia was evaluated using a MedDRA-based SSQ/CMQ analysis that contains 55 preferred terms.[4]

These data are not generalizable and cannot be used to predict adverse event outcomes. The EV-201 data are from a single-arm, multi-cohort, multicenter trial with the major efficacy outcome measures of confirmed ORR and DOR as assessed by BICR using RECIST v1.1. The results presented are provided only as descriptive clinical information.[3]

Treatment-emergent hyperglycemia reactions[4]*		
	EV-201, Cohort 1	EV-201, Cohort 2
Grade 1, % (n/N)	3% (4/125)	3% (3/89)
Grade 2, % (n/N)	5% (6/125)	6% (5/89)
Grade 3, % (n/N)	7% (9/125)	8% (7/89)
Grade 4, % (n/N)	1% (1/125)	1% (1/89)
All grades, % (n/N)	16% (20/125)	18% (16/89)

Data cutoff date for EV-201 Cohort 1 and EV-201 Cohort 2 safety data was September 8, 2020.

*Patients could have more than one event. For each preferred term, multiple occurrences of events within a patient are counted only once at the highest severity grade.

Hyperglycemia
Resolution and improvement of events in clinical trials of PADCEV® as a single agent

Summary of resolution or improvement of patients with treatment-emergent events[4]		
	EV-201, Cohort 1	EV-201, Cohort 2
Patients with all events resolved,*† % (n/n)	70% (14/20)	50% (8/16)
Patients with some events resolved or improved,*‡ % (n/n)	10% (2/20)	31% (5/16)
Patients with no events resolved or improved,* % (n/n)	20% (4/20)	19% (3/16)
Time to resolution or improvement of treatment-emergent events[4‡]		
	EV-201, Cohort 1	EV-201, Cohort 2
Median time to resolution,† months (min, max)	0.85 (0.10, 13.67)	0.95 (0.26, 6.70)
Median time to improvement,‡ months (min, max)	0.59 (0.59, 0.59)	0.39 (0.23, 4.04)

Data cutoff date for EV-201 Cohort 1 and EV-201 Cohort 2 safety data was September 8, 2020.
*Patients could have more than one event. For each preferred term, multiple occurrences of events within a patient are counted only once at the highest severity grade.
†Resolution is defined as events outcome of "Recovered/Resolved" or "Recovered/Resolved with Sequelae," or returning to baseline grade as of the last assessment for conditions that are ongoing at baseline.
‡For events that are not resolved, improvement is defined as at least one grade improvement from the worst grade at the last assessment.

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Pneumonitis/ILD
Incidence and time to onset

Severe, life-threatening, or fatal pneumonitis/ILD occurred in patients treated with PADCEV®.[3]

Pneumonitis/ILD in clinical trials of PADCEV in combination with pembrolizumab[3,4]

PADCEV was evaluated in combination with pembrolizumab. ARs were graded using National Cancer Institute CTCAE v4.03.

	In combination (n=564)	
	All grades	Grades 3-4
Pneumonitis/ILD	10%	4%

In combination		
Median time to onset of pneumonitis/ILD	4 months	Range: 0.3 to 26 months

The incidence of pneumonitis/ILD, including severe events, occurred at a higher rate when PADCEV was given in combination with pembrolizumab. A fatal event of pneumonitis/ILD occurred in 2 patients (0.4%).

Pneumonitis/ILD in clinical trials of PADCEV alone[3-5]

PADCEV was evaluated as a single agent. ARs were graded using National Cancer Institute CTCAE v4.03.

	Monotherapy (n=720)	
	All grades	Grades 3-4
Pneumonitis/ILD	3%	0.8%

Monotherapy		
Median time to onset of pneumonitis/ILD	2.9 months	Range: 0.6 to 6 months

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CTCAE v5.0 grading scale for pneumonitis[6]

Respiratory, thoracic, and mediastinal disorders				
CTCAE term	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
Pneumonitis	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; medical intervention indicated; limiting instrumental ADL	Severe symptoms; limiting self-care ADL; oxygen indicated	Life-threatening respiratory compromise; urgent intervention indicated (eg, tracheotomy or intubation)

PADCEV® dose modifications for pneumonitis/ILD[3]		
	Grade 2	**Grade ≥3**
Dose modification for pneumonitis/ILD*	Withhold until Grade ≤1, then resume treatment at the same dose level or consider dose reduction by one dose level.	Permanently discontinue PADCEV.

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

Refer to the pembrolizumab Prescribing Information for the recommended dosing information of pembrolizumab.

Monitoring for pneumonitis/ILD[3]

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.

Peripheral neuropathy (PN)
Incidence and time to onset in combination with pembrolizumab

Peripheral neuropathy occurred in patients treated with PADCEV® with or without preexisting peripheral neuropathy. Monitor patients for symptoms of new or worsening peripheral neuropathy and consider dose interruption or dose reduction of PADCEV when PN occurs.[3]

PN in clinical trials of PADCEV in combination with pembrolizumab[3,4]

PADCEV was evaluated in combination with pembrolizumab. ARs were graded using National Cancer Institute CTCAE v4.03.

	In combination (n=564)		
	All grades	Grade 2	Grade 3
Incidence of PN	67%	36%	7%

In combination Median time to onset of PN (Grade ≥2)	**6** months	Range: 0.3 to 25 months

The incidence of PN occurred at a higher rate when PADCEV was given in combination with pembrolizumab.[3]

Of the patients who experienced neuropathy and had data regarding resolution (N=373), 13% had complete resolution, and 87% of patients had residual neuropathy at last evaluation. Of the patients with residual neuropathy at last evaluation, 45% (146/326) had Grade ≥2 neuropathy.[3]

For additional adverse reaction resolution and improvement data for PN from clinical trials of PADCEV as a single agent, see pages 30-31.

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PN in clinical trials of PADCEV alone[3-5]

PADCEV was evaluated as a single agent. ARs were graded using National Cancer Institute CTCAE v4.03.

	Monotherapy (n=720)		
	All grades	Grade 2	Grades 3-4
Incidence of PN	53%	30%	5%

Monotherapy		
Median time to onset of PN (Grade ≥2)	4.9 months	Range: 0.1 to 20 months

In monotherapy clinical trials, PN led to treatment discontinuation in 6% of patients.[3]

Of the patients who experienced neuropathy who had data regarding resolution (N=296), 11% had complete resolution, and 89% had residual neuropathy at the time of their last evaluation. Of the patients with residual neuropathy at last evaluation, 50% (132/262) had Grade ≥2 neuropathy.[3]

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CTCAE v5.0 grading scale for PN[6]

Nervous system disorders				
CTCAE term	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
Peripheral motor neuropathy	Asymptomatic; clinical or diagnostic observations only	Moderate symptoms; limiting instrumental ADL	Severe symptoms; limiting self-care ADL	Life-threatening consequences; urgent intervention indicated
Peripheral sensory neuropathy	Asymptomatic	Moderate symptoms; limiting instrumental ADL	Severe symptoms; limiting self-care ADL	Life-threatening consequences; urgent intervention indicated

PADCEV® dose modifications for PN[3]		
Severity*	**Grade 2**	**Grade ≥3**
Dose modification*	Withhold until Grade ≤1, then resume treatment at the same dose level (if first occurrence). For a recurrence, withhold until Grade ≤1, then resume treatment reduced by one dose level.	Permanently discontinue PADCEV.

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

Refer to the pembrolizumab Prescribing Information for the recommended dosing information of pembrolizumab.

General risk factors for PN[1]*

- Certain anticancer therapies
- Comorbidities (eg, diabetes mellitus)
- Older age
- Spinal involvement of metastatic urothelial cancer
- Nonmalignant spinal disease

You may use these questions to help determine if your patient is experiencing symptoms of PN.[1]*

ASK

- Have you developed any numbness, tingling, or discomfort in your hands or feet since starting treatment?
- Have you developed any new or worsened weakness in your arms or legs since starting treatment?

ASK

- Do you have pain or discomfort, such as burning or pins and needles?

ASK

- Do you have numbness or tingling in your fingers or hands or weakness in your arms?
- Do these symptoms interfere with writing, grasping small objects, or fastening clothes?
  - Can you button or zip clothing, thread a needle, and/or sign your name?

ASK

- Do you have numbness or tingling in your toes or feet, or weakness in your legs?
- Do these symptoms interfere with your ability to walk or your balance?

*Adapted from Pace, et al. 2021.

Peripheral neuropathy
Monitoring and clinical considerations

Clinical and other considerations for treating with PADCEV®

- Educate patients and caregivers about signs and symptoms of PN and the importance of prompt reporting and management to reduce the risk of severe and potentially irreversible symptoms[1]*
- For patients at an increased risk of experiencing PN, review the "Additional topics to discuss with your doctor" section in the patient education handout
- Monitor patients for symptoms of new or worsening PN[3]
- At each visit, perform a neurological and musculoskeletal evaluation, and assess the impact of symptoms on daily function compared to baseline[1]*
- Evaluate for alternative contributing etiologies of symptoms (eg, benign spinal disorders, vascular dysfunction, metastatic spinal cord compression)[1]*
- Recommend hard-soled slippers or shoes to reduce risk of foot injury and regular self-examination of feet for injury or impaired skin integrity (for patients with impaired sensation)[1]*
- Consider dose interruption, dose reduction, or discontinuation of PADCEV when PN occurs (refer to the dose modifications on page 27)[3]

*Adapted from Pace, et al. 2021.

The notes sections within the "Understanding Possible Side Effects With PADCEV" patient education handout or a journal can help patients keep a record of how they're feeling during treatment. Writing down when they experience symptoms or changes in how they feel can lead to productive conversations about their care.

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Peripheral neuropathy
Incidence of events in clinical trials of PADCEV® as a single agent

The results on improvement and resolution of PN are observational data from patients with locally advanced or metastatic urothelial cancer treated with PADCEV as a single agent in 2 EV clinical trials.[4]

- In Cohort 1 of EV-201, patients received prior treatment with a PD-1 or PD-L1 inhibitor and a platinum-based chemotherapy
- In Cohort 2 of EV-201, patients received prior treatment with a PD-1 or PD-L1 inhibitor and were ineligible for cisplatin-based chemotherapy

Results on improvement and resolution of PN from EV-301 were not available.

PN was assessed using the PN MedDRA version 23.0 SMQ broad search that contains 82 preferred terms.[4]

These data are not generalizable and cannot be used to predict adverse event outcomes. The EV-201 data are from a single-arm, multi-cohort, multicenter trial with the major efficacy outcome measures of confirmed ORR and DOR as assessed by BICR using RECIST v1.1. The results presented are provided only as descriptive clinical information.[3]

Treatment-emergent PN reactions[4]*		
	EV-201, Cohort 1	EV-201, Cohort 2
Grade 1, % (n/N)	21% (26/125)	16% (14/89)
Grade 2, % (n/N)	31% (39/125)	35% (31/89)
Grade 3, % (n/N)	4% (5/125)	7% (6/89)
Grade 4, % (n/N)	—	1% (1/89)
All grades, % (n/N)	56% (70/125)	58% (52/89)

Data cutoff date for EV-201 Cohort 1 and EV-201 Cohort 2 safety data was September 8, 2020.

*Patients could have more than one event. For each preferred term, multiple occurrences of events within a patient are counted only once at the highest severity grade.

Peripheral neuropathy
Resolution and improvement of events in clinical trials of PADCEV® as a single agent

Summary of resolution and ongoing Grade 1 PN or improvement of patients with treatment-emergent events[4]		
	EV-201, Cohort 1	EV-201, Cohort 2
Patients with all events resolved,*† % (n/n)	21% (15/70)	15% (8/52)
Patients with ongoing Grade 1 at last follow-up, % (n/n)	51% (36/70)	48% (25/52)
Patients with some events resolved or improved,*‡ % (n/n)	34% (24/70)	44% (23/52)
Patients with no events resolved or improved,* % (n/n)	44% (31/70)	40% (21/52)
Time to resolution or improvement of treatment-emergent events[4‡]		
	EV-201, Cohort 1	EV-201, Cohort 2
Median time to resolution,† months (min, max)	1.48 (0.03, 11.93)	1.40 (0.03, 12.45)
Median time to improvement,‡ months (min, max)	2.37 (0.07, 24.64)	1.18 (0.16, 7.66)

Data cutoff date for EV-201 Cohort 1 and EV-201 Cohort 2 safety data was September 8, 2020.
*Patients could have more than one event. For each preferred term, multiple occurrences of events within a patient are counted only once at the highest severity grade.
†Resolution is defined as events outcome of "Recovered/Resolved" or "Recovered/Resolved with Sequelae," or returning to baseline grade as of the last assessment for conditions that are ongoing at baseline.
‡For events that are not resolved, improvement is defined as at least one grade improvement from the worst grade at the last assessment.

Ocular disorders in clinical trials of PADCEV® in combination with pembrolizumab[4]

PADCEV was evaluated in combination with pembrolizumab. ARs were graded using National Cancer Institute CTCAE v4.03.

	In combination (n=564)
	Incidence rate (all grades)
All types	31.9%
Dry eye	27.7%

Ocular disorders
Incidence and time to onset in monotherapy

Ocular disorders have occurred in patients treated with PADCEV® in clinical trials. 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.[3]

Ocular disorders in clinical trials of PADCEV alone[3-5]*

PADCEV was evaluated as a single agent. ARs were graded using National Cancer Institute CTCAE v4.03.

	Monotherapy (n=384)
	Incidence rate (all grades)
All types	40%
Dry eye	30%
Blurred vision	10%

Monotherapy	**1.7 months**	Range: 0 to 30.6 months
Median time to onset of ocular disorders		

*Ophthalmologic exams were scheduled in 384 patients treated with PADCEV as a single agent in clinical trials.[3]

CTCAE v5.0 grading scale for select ocular disorders[6]

Eye disorders				
CTCAE term	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
Blurred vision	Intervention not indicated	Symptomatic; moderate decrease in visual acuity (best corrected visual acuity 20/40 and better, or 3 lines or less decreased vision from known baseline); limiting instrumental ADL	Symptomatic with marked decrease in visual acuity (best corrected visual acuity worse than 20/40, or more than 3 lines of decreased vision from known baseline up to 20/200); limiting self-care ADL	Best corrected visual acuity of 20/200 or worse in the affected eye
Dry eye	Asymptomatic; clinical or diagnostic observations only; symptoms relieved by lubricants	Symptomatic; moderate decrease in visual acuity (best corrected visual acuity 20/40 and better, or 3 lines or less decreased vision from known baseline)	Symptomatic with marked decrease in visual acuity (best corrected visual acuity worse than 20/40, or more than 3 lines of decreased vision from known baseline up to 20/200); limiting self-care ADL	—
Keratitis	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; moderate decrease in visual acuity (best corrected visual acuity 20/40 and better, or 3 lines or less decreased vision from known baseline)	Symptomatic with marked decrease in visual acuity (best corrected visual acuity worse than 20/40, or more than 3 lines of decreased vision from known baseline up to 20/200); corneal ulcer; limiting self-care ADL	Perforation; best corrected visual acuity of 20/200 or worse in the affected eye

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

PADCEV® dose modifications for ocular disorders[3]	
Dose modification	Consider dose interruption or dose reduction of PADCEV for symptomatic ocular disorders.

Refer to the pembrolizumab Prescribing Information for the recommended dosing information of pembrolizumab.

General risk factors for ocular disorders[1]*

- Older age is a risk factor for dry eyes
- Contact lens use increases the risk of developing keratitis. Consider advising patients to use eyeglasses
- Ocular manifestations such as keratitis and corneal ulcerations have been reported with other anticancer therapies, including ADC agents

Clinical and other considerations for treating with PADCEV

Patient education on potential for ocular disorders, common presenting signs or symptoms, and importance of early reporting[1]*

A patient's eye care professional should be informed about their treatment with PADCEV[1]*

Monitor patients for ocular disorders. Consider artificial tears for prophylaxis of dry eyes and ophthalmologic evaluation if ocular symptoms occur or do not resolve[3]

- Consider referral to an ophthalmologist or optometrist for dry, watery eyes; blurred vision; eye pain; or other ocular symptoms that persist or recur[1]*
- Consider treatment with ophthalmic topical steroids, if indicated after an ophthalmic exam[3]

*Adapted from Pace, et al. 2021.

Infusion site extravasation
Incidence and time to onset

Skin and soft tissue reactions secondary to extravasation have been observed after administration of PADCEV®. Reactions may be delayed.[3]

Infusion site extravasation in clinical trials of PADCEV in combination with pembrolizumab[4]

PADCEV was evaluated in combination with pembrolizumab. ARs were graded using National Cancer Institute CTCAE v4.03.

	In combination (n=564)	
	All grades	Grades 3-4
Infusion site extravasation	1.6%	0.2%

Skin and soft tissue reactions secondary to infusion site extravasation in clinical trials of PADCEV alone[3-5]

PADCEV was evaluated as a single agent. ARs were graded using National Cancer Institute CTCAE v4.03.

	Monotherapy (n=720)	
	All grades	Grades 3-4
Skin and soft tissue reactions	1%	0.3%

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.[3]

Please see Important Safety Information and full Prescribing Information, including BOXED WARNING for Serious Skin Reactions.

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CTCAE v5.0 grading scale for infusion site extravasation[6]

General disorders and administration site conditions				
CTCAE term	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
Infusion site extravasation	Painless edema	Erythema with associated symptoms (eg, edema, pain, induration, phlebitis)	Ulceration or necrosis; severe tissue damage; operative intervention indicated	Life-threatening consequences; urgent intervention indicated

Monitoring for infusion site extravasation

Clinical and other considerations for treating with PADCEV®[3]

- Ensure adequate venous access prior to starting PADCEV and monitor for possible extravasation during administration
- Inform patients that infusion site reactions have occurred after administration of PADCEV. These reactions generally occurred immediately after administration, but in some instances had a delayed onset (eg, 24 hours). Instruct patients to contact their healthcare professional immediately if they experience any symptoms of an infusion site reaction
- If extravasation occurs, stop the infusion and monitor for adverse reactions

Nonhematologic toxicity: GI disorders
Grading and treatment with PADCEV® dose modifications

For a list of the most common GI disorders that occurred in patients taking PADCEV in combination with pembrolizumab in the EV-302 clinical trial, see page 42. For a list of the most common GI disorders that occurred in patients taking PADCEV as a single agent in the EV-301 and EV-201 Cohort 2 clinical trials, see pages 44 and 46.

CTCAE v5.0 grading scale for GI disorders[6]

GI disorders				
CTCAE term	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
Constipation	Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema	Persistent symptoms with regular use of laxatives or enemas; limiting instrumental ADL	Obstipation with manual evacuation indicated; limiting self-care ADL	Life-threatening consequences; urgent intervention indicated
Diarrhea	Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline	Increase of 4-6 stools per day over baseline; moderate increase in ostomy output compared to baseline; limiting instrumental ADL	Increase of ≥7 stools per day over baseline; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self-care ADL	Life-threatening consequences; urgent intervention indicated
Nausea	Loss of appetite without alteration in eating habits	Oral intake decreased without significant weight loss, dehydration, or malnutrition	Inadequate oral caloric or fluid intake; tube feeding, total parenteral nutrition, or hospitalization indicated	—

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

PADCEV dose modifications for other nonhematologic toxicity[3]		
Severity*	**Grade 3**	**Grade 4**
Dose modification*	Withhold until Grade ≤1, then resume treatment at the same dose level or consider dose reduction by one dose level.	Permanently discontinue PADCEV.

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

Refer to the pembrolizumab Prescribing Information for the recommended dosing information of pembrolizumab.

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Nonhematologic toxicity: GI disorders
Monitoring and clinical considerations

Clinical considerations for treating with PADCEV®[1]*

- BRAT (bananas, rice, applesauce, toast) diet and avoidance of dairy and heavily spiced foods while experiencing diarrhea
- Adequate oral hydration with reduced appetite, oral intake, and/or diarrhea
- Perform pharmacologic management of nausea and diarrhea (if clinically indicated)
- Consider nutrition consultation, as indicated
- Patient education on potential for gastrointestinal problems
- Be aware of potential gastrointestinal toxicities, including reduced appetite,† taste changes,‡ nausea, and diarrhea§
- Adequate nutrition and hydration may help avoid complications, such as renal dysfunction, functional decline, fluid-electrolyte imbalance, and fatigue
- Supportive care strategies include:
  - Using lemon juice and chewing gum prior to meals
  - Having small, frequent meals
  - Good oral hygiene
  - Drinking water with meals
  - Using plastic instead of metal utensils
  - Using more/less salt and flavoring for food
  - Avoiding food with strong smells

*Adapted from Pace, et al. 2021.
†EV clinical trials classify reduced or decreased appetite based on MedDRA as a metabolism and nutrition disorder.[3]
‡EV clinical trials classify taste changes or dysgeusia based on MedDRA as a nervous system disorder.[3]
§This is not inclusive of all gastrointestinal toxicities.

Hematologic toxicity
Grading and treatment with PADCEV® dose modifications

For a list of the most common hematologic laboratory abnormalities that occurred in patients taking PADCEV in combination with pembrolizumab in the EV-302 clinical trial, see page 43. For a list of the most common hematologic laboratory abnormalities that occurred in patients taking PADCEV as a single agent in the EV-301 and EV-201 Cohort 2 clinical trials, see pages 45 and 47.

CTCAE v5.0 grading scale for hematologic toxicity[6]

Blood and lymphatic system disorders and investigations				
CTCAE term	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
Anemia	Hemoglobin (Hgb) <LLN-10.0 g/dL; <LLN-6.2 mmol/L; <LLN-100 g/L	Hgb <10.0-8.0 g/dL; <6.2-4.9 mmol/L; <100-80 g/L	Hgb <8.0 g/dL; <4.9 mmol/L; <80 g/L; transfusion indicated	Life-threatening consequences; urgent intervention indicated
Lymphocyte count decreased	<LLN-800/mm^3; <LLN-0.8 x 10^9/L	<800-500/mm^3; <0.8-0.5 x 10^9/L	<500-200/mm^3; <0.5-0.2 x 10^9/L	<200/mm^3; <0.2 x 10^9/L
Neutrophil count decreased	<LLN-1500/mm^3; <LLN-1.5 x 10^9/L	<1500-1000/mm^3; <1.5-1.0 x 10^9/L	<1000-500/mm^3; <1.0-0.5 x 10^9/L	<500/mm^3; <0.5 x 10^9/L

PADCEV dose modifications for hematologic toxicity[3]		
Severity*	**Grade 3, or Grade 2 thrombocytopenia**	**Grade 4**
Dose modification*	Withhold until Grade ≤1, then resume treatment at the same dose level or consider dose reduction by one dose level.	Withhold until Grade ≤1, then reduce dose by one dose level or discontinue treatment.

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

Refer to the pembrolizumab Prescribing Information for the recommended dosing information of pembrolizumab.

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Please see Important Safety Information and full Prescribing Information, including BOXED WARNING for Serious Skin Reactions.

Hematologic toxicity
Monitoring and clinical considerations

Clinical and other considerations for treating with PADCEV®[1]*

- The detection of hematologic laboratory abnormalities, such as anemia, neutropenia, and thrombocytopenia requires regular monitoring
- Monitor complete blood count with differential prior to each PADCEV dose
- Advise patients to use a thermometer at home and immediately report a temperature of 100.4 °F or greater
- Communicate the importance of frequent hand hygiene

*Adapted from Pace, et al. 2021.

Adverse reactions in the EV-302 clinical trial (previously untreated patients)[3]

Talk with your patients about adverse reactions that may occur during treatment with PADCEV® and pembrolizumab

ADVERSE REACTIONS ≥15% (ALL GRADES) IN PATIENTS TREATED WITH PADCEV IN COMBINATION WITH PEMBROLIZUMAB[3]

	PADCEV IN COMBINATION WITH PEMBROLIZUMAB (n=440)		CHEMOTHERAPY (n=433)	
ADVERSE REACTION, %	**ALL GRADES**	**GRADES 3-4**	**ALL GRADES**	**GRADES 3-4**
Skin and subcutaneous tissue disorders				
Rash*	68	15	15	0
Pruritus	41	1.1	7	0
Alopecia	35	0.5	8	0.2
Dry skin	17	0.2	1	0
General disorders and administration site conditions				
Fatigue*	51	6	57	7
Pyrexia	18	0.7	16	1.2
Nervous system disorders				
Peripheral neuropathy*	67	8	14	0
Dysgeusia	21	0	9	0
Metabolism and nutrition disorders				
Decreased appetite	33	1.8	26	1.8
Gastrointestinal disorders				
Diarrhea	38	4.5	16	1.4
Nausea	26	1.6	41	2.8
Constipation	26	0	34	0.7
Investigations				
Decreased weight	33	3.6	9	0.2
Eye disorders				
Dry eye*	24	0	2.1	0
Infections and infestations				
Urinary tract infection	21	5	19	8

*Includes: multiple terms.

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Laboratory abnormalities in the EV-302 clinical trial[3]

SELECTED LABORATORY ABNORMALITIES REPORTED IN ≥15% (ALL GRADES) OF PATIENTS TREATED WITH PADCEV® IN COMBINATION WITH PEMBROLIZUMAB[3]

	PADCEV IN COMBINATION WITH PEMBROLIZUMAB		CHEMOTHERAPY	
LABORATORY ABNORMALITY, %	**ALL GRADES***	**GRADES 3-4***	**ALL GRADES***	**GRADES 3-4***
Chemistry				
Increased aspartate aminotransferase	75	5	39	3
Increased creatinine	71	3	68	3
Increased glucose	66	14	54	5
Increased alanine aminotransferase	59	5	49	3
Decreased sodium	46	13	47	13
Decreased phosphate	44	9	36	9
Decreased albumin	39	2	35	0.5
Decreased potassium	26	5	16	3
Increased potassium	24	1	36	4
Increased calcium	21	1	14	0.2
Hematology				
Decreased lymphocytes	58	15	59	17
Decreased hemoglobin	53	7	89	33
Decreased neutrophils	30	9	80	50

- Median duration of exposure to PADCEV was 7 months (range: 0.3 to 31.9 months)[3]
- 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%)[3]
- 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%)[3]

- **Adverse reactions leading to discontinuation** of PADCEV occurred in 35% of patients. The most common adverse reactions (≥2%) leading to discontinuation of PADCEV were peripheral neuropathy (15%), rash (4.1%), and pneumonitis/ILD (2.3%)[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 peripheral neuropathy (22%), rash (16%), COVID-19 (10%), diarrhea (5%), pneumonitis/ILD (4.8%), fatigue (3.9%), hyperglycemia (3.6%), increased alanine aminotransferase (3%), and pruritus (2.5%)[3]
- **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%), peripheral neuropathy (13%), and fatigue (2.7%)[3]

*The denominator used to calculate the rate varied from 407 to 439 based on the number of patients with a baseline value and at least one post-treatment value.

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Adverse reactions in the EV-301 clinical trial (post-platinum, post–PD-(L)1 patients)[3]

ADVERSE REACTIONS (≥15%) IN PATIENTS TREATED WITH PADCEV®[3]

	PADCEV (n=296)		CHEMOTHERAPY (n=291)	
ADVERSE REACTION, %	**ALL GRADES**	**GRADES 3-4**	**ALL GRADES**	**GRADES 3-4**
Skin and subcutaneous tissue disorders				
Rash*	54	14	20	0.3
Alopecia	47	0	38	0
Pruritus	34	2	7	0
Dry skin	17	0	4	0
General disorders and administration site conditions				
Fatigue*	50	9	40	7
Pyrexia*	22	2	14	0
Nervous system disorders				
Peripheral neuropathy*	50	5	34	3
Dysgeusia*	26	0	8	0
Metabolism and nutrition disorders				
Decreased appetite	41	5	27	2
Gastrointestinal disorders				
Diarrhea*	35	4	23	2
Nausea	30	1	25	2
Constipation	28	1	25	2
Abdominal pain*	20	1	14	3
Musculoskeletal and connective tissue disorders				
Musculoskeletal pain*	25	2	35	5
Eye disorders				
Dry eye*	24	0.7	6	0.3
Infections and infestations				
Urinary tract infection*	17	6	13	3
Vascular disorders				
Hemorrhage*	17	3	13	2
Investigations				
Decreased weight	16	0.3	7	0

*Includes: multiple terms.

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Laboratory abnormalities in the EV-301 clinical trial[3]

SELECTED LABORATORY ABNORMALITIES REPORTED IN ≥15% (GRADES 2-4) OR ≥5% (GRADES 3-4) OF PATIENTS TREATED WITH PADCEV®[3]

	PADCEV*		CHEMOTHERAPY*	
LABORATORY ABNORMALITY, %	**GRADES 2-4**	**GRADES 3-4**	**GRADES 2-4**	**GRADES 3-4**
Hematology				
Decreased lymphocytes	41	14	34	18
Decreased hemoglobin	28	4	42	14
Decreased neutrophils	27	12	25	17
Chemistry				
Decreased phosphate	39	8	24	6
Increased glucose (non-fasting)	33	9	27	6
Increased creatinine	18	2	13	0
Decreased potassium	16	2	7	3
Increased lipase	13	8	7	4
Increased sodium	8	8	5	5

- The median duration of exposure to PADCEV was 5 months (range: 0.5 to 19 months)[3]
- Serious adverse reactions occurred in 47% of patients treated with PADCEV. The most common serious adverse reactions (≥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/ILD, and pelvic abscess (0.3% each)[3]
- **Adverse reactions leading to discontinuation** occurred in 17% of patients; the most common adverse reactions (≥2%) leading to discontinuation were peripheral neuropathy (5%), and rash (4%)[3]
- **Adverse reactions leading to dose interruption** occurred in 61% of patients; the most common adverse reactions (≥4%) leading to dose interruption were peripheral neuropathy (23%), rash (11%), and fatigue (9%)[3]
- **Adverse reactions leading to dose reduction** occurred in 34% of patients; the most common adverse reactions (≥2%) leading to dose reduction were peripheral neuropathy (10%), rash (8%), decreased appetite (3%), and fatigue (3%)[3]

*The denominator used to calculate the rate varied from 262 to 287 based on the number of patients with a baseline value and at least one post-treatment value.

Please see Important Safety Information and full Prescribing Information, including BOXED WARNING for Serious Skin Reactions.

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Adverse reactions in the EV-201 Cohort 2 trial (cisplatin-ineligible, post–PD-(L)1 patients)[3]

ADVERSE REACTIONS ≥15% (ALL GRADES) OR ≥5% (GRADES 3-4) OF PATIENTS TREATED WITH PADCEV®[3]

	PADCEV (n=89)	
ADVERSE REACTION, %	**ALL GRADES**	**GRADES 3-4**
Skin and subcutaneous tissue disorders		
Rash*	66	17
Alopecia	53	0
Pruritus	35	3
Dry skin	19	1
Nervous system disorders		
Peripheral neuropathy*	58	8
Dysgeusia*	29	0
General disorders and administration site conditions		
Fatigue*	48	11
Metabolism and nutrition disorders		
Decreased appetite	40	6
Hyperglycemia	16	9
Gastrointestinal disorders		
Diarrhea*	36	8
Nausea	30	1
Investigations		
Decreased weight	35	1
Eye disorders		
Dry eye*	30	0

*Includes: multiple terms.

Please see Important Safety Information and full Prescribing Information, including BOXED WARNING for Serious Skin Reactions.

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Laboratory abnormalities in the EV-201 Cohort 2 clinical trial[3]

SELECTED LABORATORY ABNORMALITIES REPORTED IN ≥15% (GRADES 2-4) OR ≥5% (GRADES 3-4) OF PATIENTS TREATED WITH PADCEV®[3]

	PADCEV (n=88)*	
LABORATORY ABNORMALITY, %	**GRADES 2-4***	**GRADES 3-4***
Hematology		
Decreased lymphocytes	43	15
Decreased hemoglobin	34	5
Decreased neutrophils	20	9
Chemistry		
Increased glucose (non-fasting)	36	13
Decreased phosphate	25	7
Increased creatinine	23	3
Increased lipase	18	11
Increased urate	9	9
Increased potassium	8	6
Decreased sodium	7	7

- Median duration of exposure was 5.98 months (range: 0.3-24.6 months)[3]
- Serious adverse reactions occurred in 39% of patients treated with PADCEV. The most common serious adverse reactions (≥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)[3]
- **Adverse reactions leading to discontinuation** occurred in 20% of patients; the most common adverse reaction (≥2%) leading to discontinuation was peripheral neuropathy (7%)[3]
- **Adverse reactions leading to dose interruption** occurred in 60% of patients; the most common adverse reactions (≥3%) leading to dose interruption were peripheral neuropathy (19%), rash (9%), fatigue (8%), diarrhea (5%), increased aspartate aminotransferase (3%), and hyperglycemia (3%)[3]
- **Adverse reactions leading to dose reduction** occurred in 49% of patients; the most common adverse reactions (≥3%) leading to dose reduction were peripheral neuropathy (19%), rash (11%), and fatigue (7%)[3]

*Based on the number of patients with a baseline value and at least one post-treatment value.

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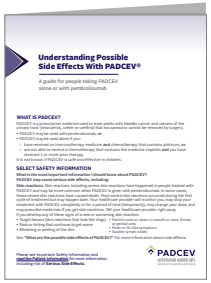
Additional patient AR resources



Download a digital copy of the **Understanding Possible Side Effects With PADCEV®** resource to share with your patients. Use this tool to review adverse reactions with your patients and to discuss possible treatment for these side effects.

Download a digital copy of the **PADCEV Patient Brochure** to share with your patients. This tool includes information about treatment with PADCEV.

Contact your Seagen/Astellas representative for a copy of this resource and others, and visit PADCEV.com/hcp/resources for more helpful tools.

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

References: 1. 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):E1-9. **2.** Wengström Y, Margulies A. European Oncology Nursing Society Task Force: European Oncology Nursing Society extravasation guidelines. Eur J Oncol Nurs. 2008;12(4):357-361. **3.** PADCEV [package insert]. Northbrook, IL: Astellas Pharma US, Inc. **4.** Seagen Inc. and Astellas. PADCEV. Data on File. **5.** Protocol for: Powles T, Rosenberg JE, Sonpavde GP, et al. Enfortumab vedotin in previously treated advanced urothelial carcinoma. N Engl J Med 2021;384:1125-35. **6.** National Cancer Institute. Common terminology criteria for adverse events (CTCAE) v5.0 (11-27-2017). https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf. Accessed 09-22-2022. **7.** National Cancer Institute. Common terminology criteria for adverse events (CTCAE) v4.03. (06-14-2010). https://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03/CTCAE_4.03_2010-06-14_QuickReference_8.5x11.pdf. Accessed 09-22-2022.

ADC=antibody-drug conjugate; ADL=activities of daily living; BMI=body mass index; BSA=body surface area; FBG=fasting blood glucose; GI=gastrointestinal; HbA1c=hemoglobin A1c; ICU=intensive care unit; ILD=interstitial lung disease; LLN=lower limit of normal; MedDRA=Medical Dictionary for Regulatory Activities; PD-(L)1=programmed death receptor-1 or programmed death-ligand 1; RECIST=Response Evaluation Criteria in Solid Tumors; SMQ=Standardized MedDRA Queries; SPF=sun protection factor; SSQ/CMQ=sponsor-specified query/custom MedDRA query; ULN=upper limit of normal; USPI=United States prescribing information.

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