PADCEV™

enfortumab vedotin

Powder for Concentrate for Solution for Infusion 20 mg and 30 mg vials

Enfortumab Vedotin in relapsed / refractory bladder cancer

This session is sponsored by Astellas Pharma India Pvt. Ltd

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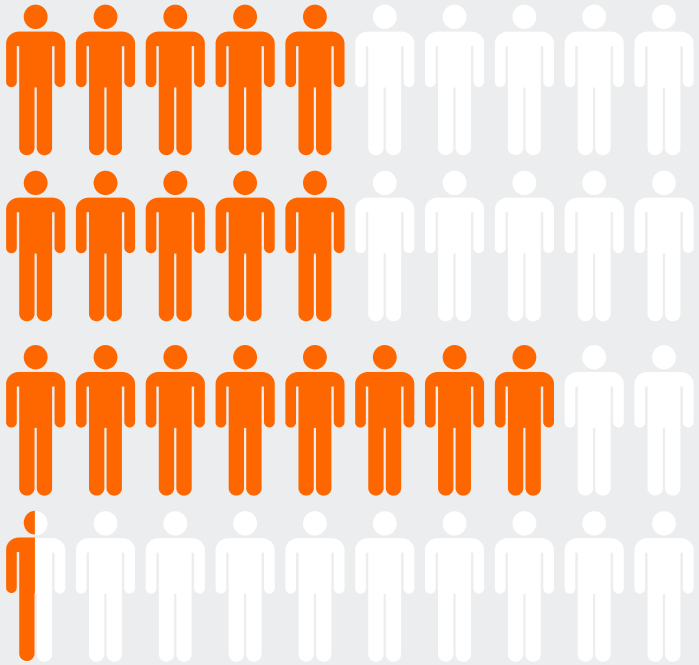
There remains a high unmet treatment need in patients with LA/mUC



Up to 50% of patients with mUC are unfit for first-line cisplatin-based chemotherapy[1]

~50% of patients with LA/mUC may not respond to platinum-based chemotherapy[1]

~70–80% of patients with LA/mUC do not respond to PD-1/L1 inhibitors[2]

~5% of patients with mUC survive for ≥5 years[3]

Furthermore, there are **limited treatment options for patients with LA/mUC** who experience disease progression despite prior treatment with platinum-based chemotherapy and a PD-1/L1 inhibitor[1]

LA/mUC, locally advanced/metastatic urothelial carcinoma; mUC, metastatic urothelial carcinoma; PD-1/L1, programmed cell death protein 1/ligand 1.

1. European Association of Urology. EAU guidelines on muscle-invasive and metastatic bladder cancer. Available at: https://uroweb.org/wp-content/uploads/EAU-Guidelines-on-Muscle-Invasive-and-Metastatic-Bladder-Cancer-2021V2.pdf. Last accessed: November 2021; 2. Kim HS and Seo KH *Investig Clin Urol* 2018;59:285-296; 3. National Cancer Institute. Cancer stat facts: Bladder cancer. Available at: https://seer.cancer.gov/statfacts/html/urinb.html. Last accessed: November 2021.

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EV increases the treatment options for patients with LA/mUC

Enfortumab vedotin is indicated for the treatment of **adult patients with locally advanced (LA) or metastatic urothelial cancer (mUC)** who have received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor and who have received a platinum-containing chemotherapy in the neoadjuvant/adjuvant, locally advanced or metastatic setting[1]

Prior platinum-based chemotherapy in the **neoadjuvant/adjuvant or LA/mUC setting**

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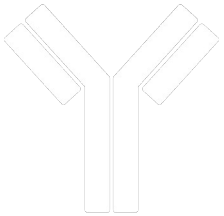


Prior immunotherapy with a PD-1/L1 inhibitor

EV **addresses an unmet need and provides an effective treatment option** for patients previously treated with platinum-based chemotherapy and a PD-1/L1 inhibitor[2]

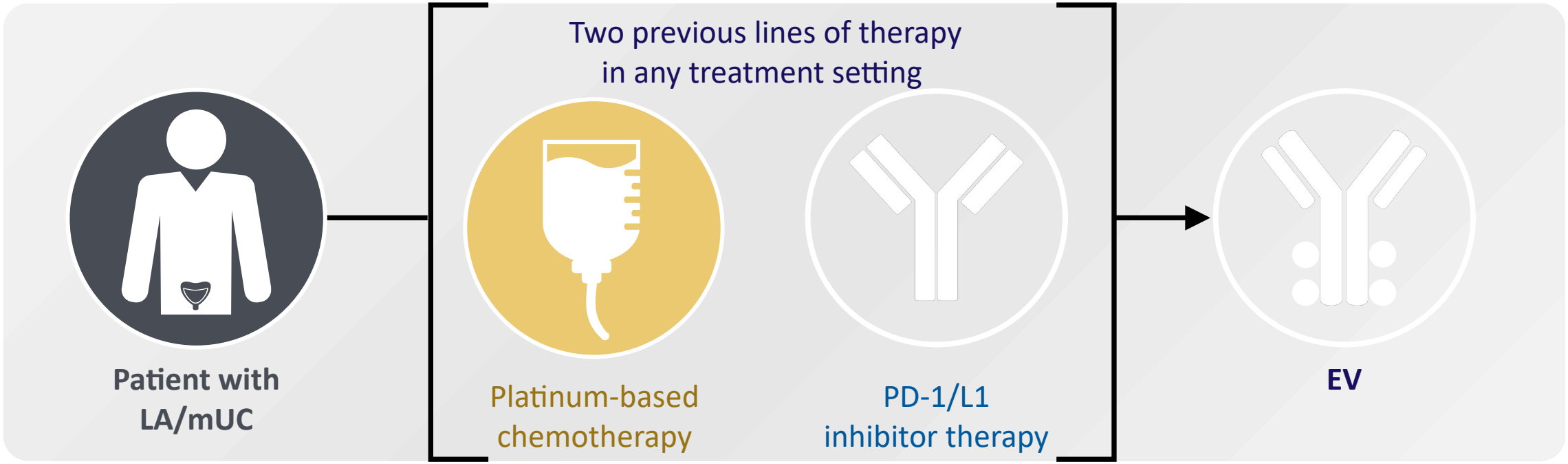
EV, enfortumab vedotin; LA/mUC, locally advanced/metastatic urothelial carcinoma; PD-1/L1, programmed cell death protein 1/ligand 1.

1. PADCEV™ (enfortumab vedotin). Summary of Product Characteristics [draft]; 2. Powles T et al. *N Engl J Med* 2021;384:1125–1135.

EV-301: Enfortumab Vedotin in previously treated advanced urothelial carcinoma

Enfortumab vedotin is a treatment for patients with LA/mUC who have received previous lines of systemic therapy

Enfortumab vedotin is indicated for the treatment of **adult patients with locally advanced (LA) or metastatic urothelial cancer (mUC)** who have received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor and who have received a platinum-containing chemotherapy in the neoadjuvant/adjuvant, locally advanced or metastatic setting



EV was licensed based on the efficacy and safety data from the pivotal Phase III EV-301 study

EV, enfortumab vedotin; LA/mUC, locally advanced/metastatic urothelial carcinoma; PD-1/L1, programmed cell death protein 1/ligand 1.

PADCEV™ (enfortumab vedotin). Summary of Product Characteristics [draft].

EV-301 was designed to confirm a clinical benefit of EV compared with chemotherapy in pre-treated patients with LA/mUC

Platinum-based chemotherapy and **PD-1/L1 inhibitors** are **recommended** treatment options for patients with LA/mUC[1–3]

Patient **survival is poor** and unmet needs remain[4–9]

- Patients may be **unfit for chemotherapy**, while others can become **resistant** to it[8,9]
- Response rates to PD-1/L1 inhibitors, although durable, are **low** (~15–23%)[5,6,9]

There are **limited options** for patients with LA/mUC who experience progressive disease despite treatment with platinum-based chemotherapy and PD-1/L1 inhibitors[1]

EV-301 is a **Phase III trial comparing EV with chemotherapy** in patients with LA/mUC who have received prior platinum-based chemotherapy and experienced progressive disease after treatment with a PD-1/L1 inhibitor[10]

EV, enfortumab vedotin; LA/mUC, locally advanced/metastatic urothelial carcinoma; PD-1/L1, programmed cell death protein 1/ligand 1.

1. European Association of Urology. EAU guidelines on muscle-invasive bladder cancer. Available at: https://uroweb.org/wp-content/uploads/EAU-Guidelines-on-Muscle-Invasive-and-Metastatic-Bladder-Cancer-2021.pdf. Last accessed: November 2021;
2. European Society of Medical Oncology. eUpdate – Bladder cancer treatment recommendations. Available at: www.esmo.org/guidelines/genitourinary-cancers/bladder-cancer/eupdate-bladder-cancer-treatment-recommendations4. Last accessed: November 2021;
3. Flaig TW et al. *J Natl Compr Canc Netw* 2020;18:329–354; 4. Bellmunt J et al. *J Clin Oncol* 2009;27:4454–4461; 5. Bellmunt J et al. *N Engl J Med* 2017;376:1015–1026; 6. Powles T et al. *Lancet* 2018;391:748–757; 7. Simeone JC et al. *Cancer Epidemiol* 2019;60:121–127;
8. Bambury RM, Rosenberg JE. *Front Pharmacol* 2013;4:3; 9. Montazeri K et al. *Expert Rev Anticancer Ther* 2021;21:299–313; 10. Powles T et al. *N Engl J Med* 2021;384:1125–1135.

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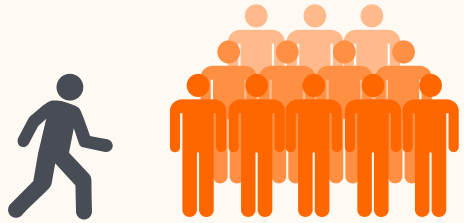
EV-301 compared the efficacy and safety of EV with chemotherapy in patients with previously treated LA/mUC

An international, open-label, randomised Phase III study



Adult patients with unresectable LA/mUC (N=608)

- ECOG PS 0 or 1
- Disease progression during or after PD-1/L1 inhibitor treatment
- Prior platinum-based chemotherapy

R* 1:1

EV (n=301)
1.25 mg/kg 30-minute IV infusion on Days 1, 8, and 15 of a 28-day cycle

Investigator-chosen chemotherapy† (n=307)
Either of the following as an IV infusion on Day 1 of a 21-day cycle:
- Docetaxel 75 mg/m² over 1 hour (n=117)
- Paclitaxel 175 mg/m² over 3 hours (n=112)
- Vinflunine‡ 320 mg/m² over 20 minutes (n=78)

Primary endpoint
- OS

Secondary endpoints
- PFS**
- ORR**
- DCR**
- CRR**
- DOR**
- QoL
- PROs
- Safety and tolerability

A pre-specified interim analysis was performed after 65% of patients had died. The results of the interim analysis were published in 2021 after a median follow-up of 11.1 months and are presented herein. A final analysis was planned after 439 deaths had occurred

*Stratification variables were ECOG PS (0 or 1), geographic region (USA, Western Europe, or rest of the world), and presence of liver metastasis; †Regimen selected by the investigator before randomisation;
‡The use of vinflunine was limited to 35% of patients in the trial and was an option only in regions where it was approved for the treatment of UC; **According to RECIST v1.1.
CRR, complete response rate; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EV, enfortumab vedotin; IV, intravenous; LA/mUC, locally advanced/metastatic urothelial carcinoma;
ORR, overall response rate; OS, overall survival; PD-1/L1, programmed cell death protein 1/ligand 1; PFS, progression-free survival; PRO, patient-reported outcome; QoL, quality of life; R, randomisation; RECIST, Response Evaluation Criteria in Solid Tumours.
Powles T et al. *N Engl J Med* 2021;384:1125–1135.

Patient demographics were balanced between treatment groups

Characteristic	EV (n=301)	Chemotherapy (n=307)
Age (years)		
Median (range)	68.0 (34.0–85.0)	68.0 (30.0–88.0)
≥75 years, n (%)	52 (17.3)	68 (22.1)
Sex, n (%)		
Male	238 (79.1)	232 (75.6)
Female	63 (20.9)	75 (24.4)
Geographic region, n (%)		
Western Europe	126 (41.9)	129 (42.0)
USA	43 (14.3)	44 (14.3)
Rest of the world	132 (43.9)	134 (43.6)
History of tobacco use, n (%)		
Former user	167 (55.5)	164 (53.4)
Current user	29 (9.6)	31 (10.1)
Never used	91 (30.2)	102 (33.2)
Not reported/unknown	14 (4.7)	10 (3.3)
History of diabetes or hyperglycaemia, n (%)	56 (18.6)	58 (18.9)

EV, enfortumab vedotin.

Powles T et al. *N Engl J Med* 2021;384:1125–1135.

Disease characteristics were balanced between treatment groups

Characteristic	EV (n=301)	Chemotherapy (n=307)
ECOG PS score, n (%)		
1	181 (60.1)	183 (59.6)
Bellmunt risk score, n (%)		
0–1	201 (66.8)	208 (67.8)
≥2	90 (29.9)	96 (31.3)
Not reported	10 (3.3)	3 (1.0)
Primary disease site of origin, n (%)		
Upper urinary tract	98 (32.6)	107 (34.9)
Bladder or other site	203 (67.4)	200 (65.1)
Histologic type at initial diagnosis, n/N (%)		
Urothelial or transitional-cell carcinoma	229/301 (76.1)	230/305 (75.4)
Urothelial carcinoma, mixed types	45/301 (15.0)	42/305 (13.8)
Other*	27/301 (9.0)	33/305 (10.8)
Metastatic sites, n/N (%)		
Lymph node only	34/301 (11.3)	28/306 (9.2)
Visceral disease	234/301 (77.7)	250/306 (81.7)
Liver metastasis	93/301 (30.9)	95/307 (30.9)
Prior lines of systemic therapy, n (%)		
1–2	262 (87.0)	270 (87.9)
≥3	39 (13.0)	37 (12.1)
Best response to prior CPI, n (%)		
Responder (CR or PR)	61 (20.3)	50 (16.3)
Non-responder (SD or progressive disease)	207 (68.8)	215 (70.0)
Time since diagnosis of LA/mUC (months), median (range)	14.8 (0.2–114.1)	13.2 (0.3–118.4)

*Other histologic types include adenocarcinoma, squamous-cell carcinoma, and pseudosarcomatic differentiation.

CPI, checkpoint inhibitor; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; EV, enfortumab vedotin; LA/mUC, locally advanced/metastatic urothelial carcinoma; PR, partial response; SD, stable disease.

Powles T et al. *N Engl J Med* 2021;384:1125–1135.

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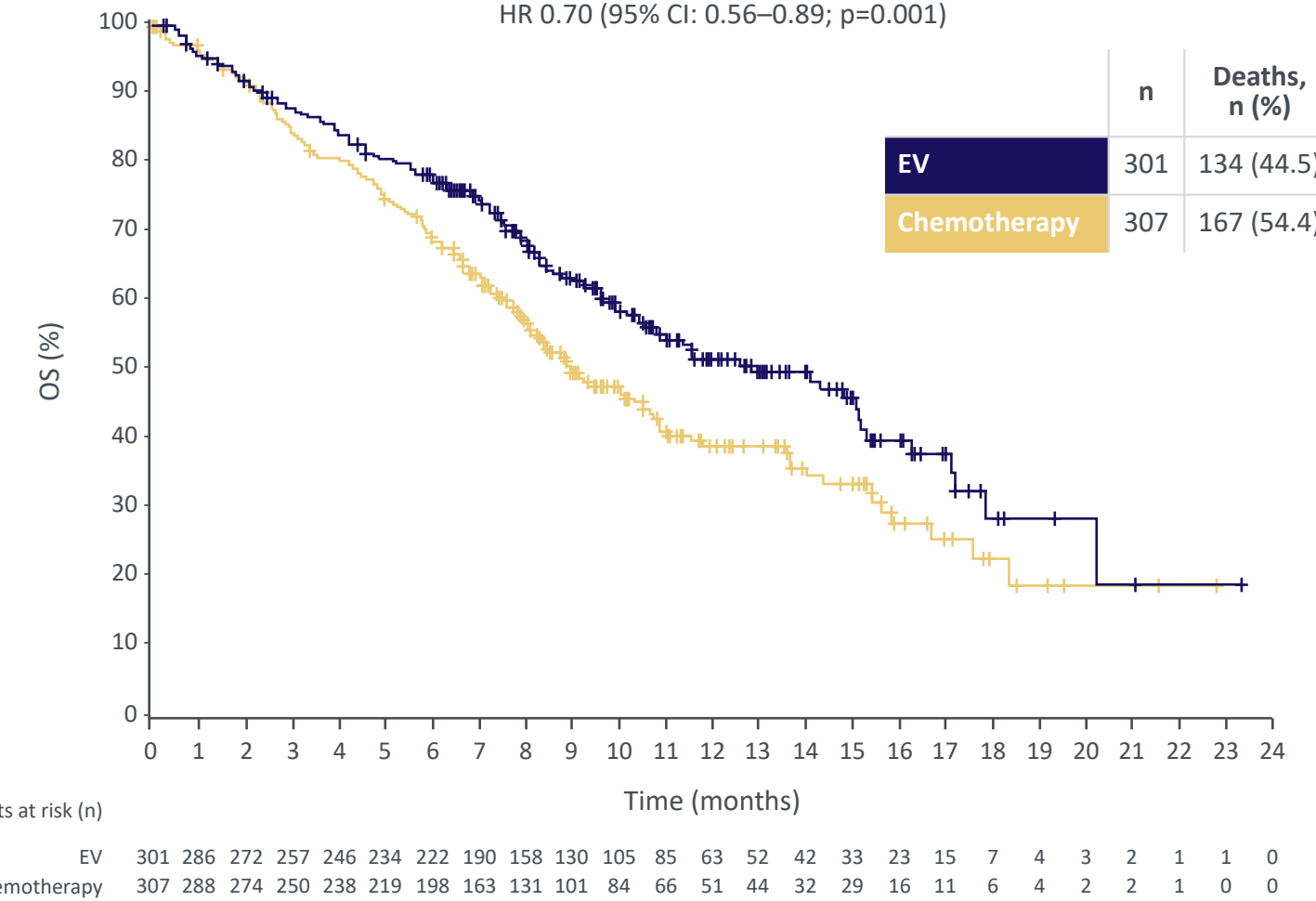
EV significantly reduced the risk of death by 30% compared with chemotherapy

OS (ITT population)

HR 0.70 (95% CI: 0.56–0.89; p=0.001)



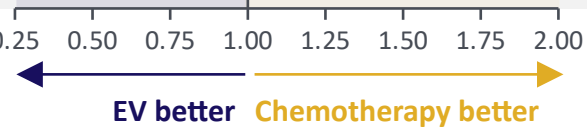
	n	Deaths, n (%)	Median OS, months (95% CI)	Estimated 12-month OS rate, % (95% CI)
EV	301	134 (44.5)	**12.88** (10.58–15.21)	**51.5** (44.6–58.0)
Chemotherapy	307	167 (54.4)	**8.97** (8.05–10.74)	**39.2** (32.6–45.6)

Due to a **significant improvement in OS compared with chemotherapy**, EV-301 was prematurely stopped after the interim analysis of the ITT population

Figure adapted from Powles T et al. 2021.
Median follow-up: 11.1 months.
CI, confidence interval; EV, enfortumab vedotin; HR, hazard ratio; ITT, intention to treat; OS, overall survival.
Powles T et al. *N Engl J Med* 2021;384:1125–1135.

A trend towards an OS benefit of EV compared with chemotherapy was observed in most patient subgroups

Analysis population		Number of deaths/number of patients		HR (95% CI)
		EV	Chemotherapy	
All patients	**All patients**	**134/301**	**167/307**	**0.70 (0.56–0.89)**
Age group: 65 years	<65 years	49/108	66/111	0.68 (0.47–0.99)
	≥65 years	85/193	101/196	0.75 (0.56–1.00)
Age group: 75 years	<75 years	109/249	128/239	0.69 (0.53–0.89)
	≥75 years	25/52	39/68	0.91 (0.55–1.51)
Sex	Male	101/238	132/232	0.61 (0.47–0.79)
	Female	33/63	35/75	1.17 (0.72–1.89)
Geographic region	Western Europe	57/126	72/129	0.76 (0.53–1.07)
	United States	25/43	25/44	0.88 (0.51–1.54)
	Rest of the world	52/132	70/134	0.64 (0.45–0.92)
Primary site of tumour	Upper urinary tract	44/98	52/107	0.85 (0.57–1.27)
	Bladder or other site	90/203	115/200	0.67 (0.51–0.88)
ECOG PS score	0	40/120	46/124	0.81 (0.53–1.24)
	1	94/181	121/183	0.67 (0.51–0.87)
Liver metastasis	Yes	53/93	63/95	0.66 (0.46–0.96)
	No	81/208	104/212	0.73 (0.55–0.98)
Previous systemic therapies	1–2	115/262	147/270	0.69 (0.54–0.88)
	≥3	19/39	20/37	0.88 (0.47–1.64)
Best response among patients who previously received CPI treatment	Response*	18/61	23/50	0.63 (0.34–1.17)
	No response†	100/207	120/215	0.76 (0.58–0.99)
Pre-selected chemotherapy	Paclitaxel	63/141	59/112	0.71 (0.49–1.01)
	Docetaxel	41/87	67/117	0.71 (0.48–1.04)
	Vinflunine	30/73	41/78	0.77 (0.48–1.24)

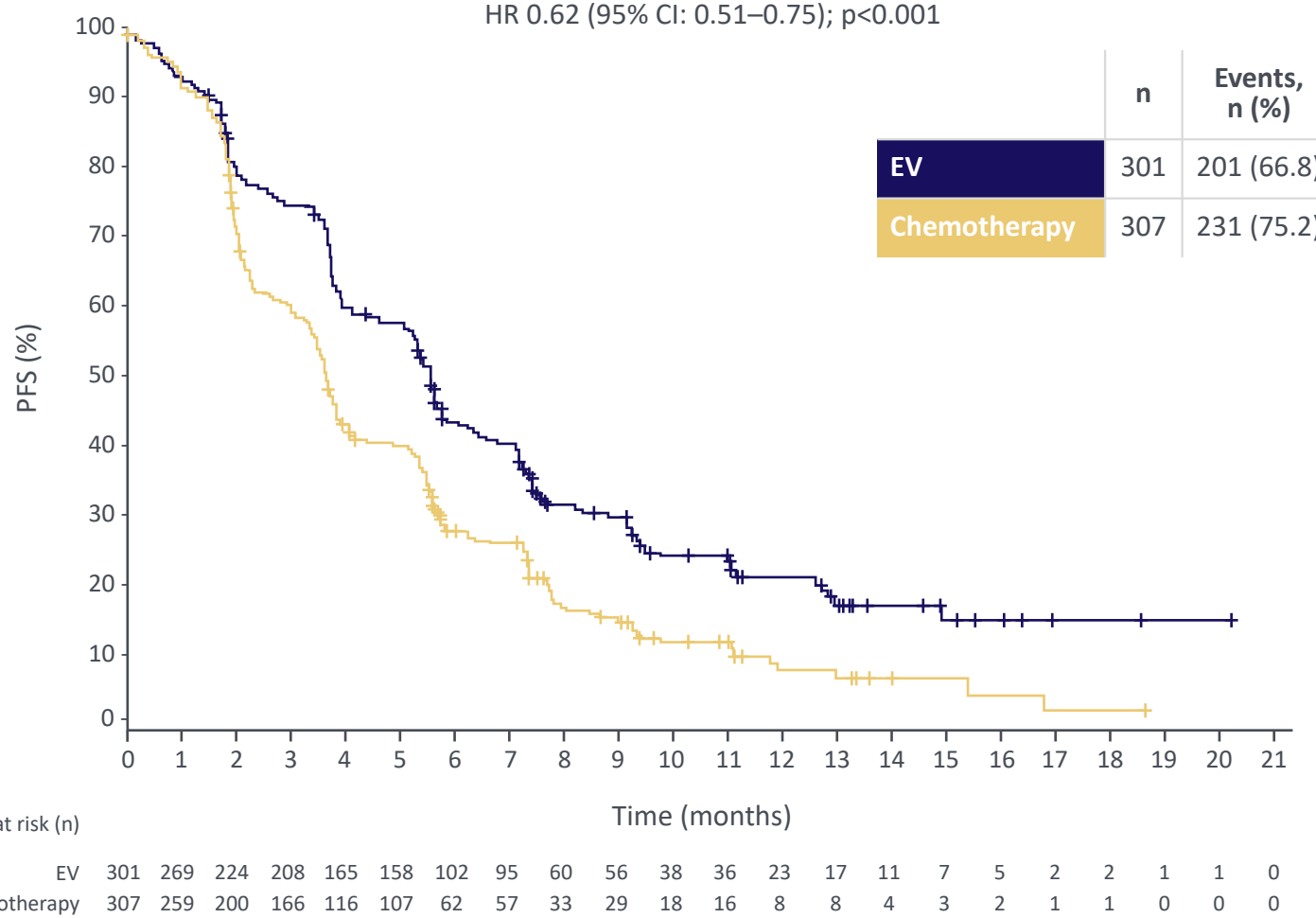


Median follow-up: 11.1 months. Pre-specified subgroup analyses of the intention-to-treat population (all patients who underwent randomization). The trial did not power for statistical comparison of subgroups.
*Confirmed complete response or partial response; †Stable disease or progressive disease.
CI, confidence interval; CPI, checkpoint inhibitor; ECOG PS, Eastern Cooperative Oncology Group performance status; EV, enfortumab vedotin; HR, hazard ratio; OS, overall survival.
Powles T et al. *N Engl J Med* 2021;384:1125–1135.

EV significantly reduced the risk of progression or death by 38% compared with chemotherapy

PFS (ITT population)

HR 0.62 (95% CI: 0.51–0.75); p<0.001

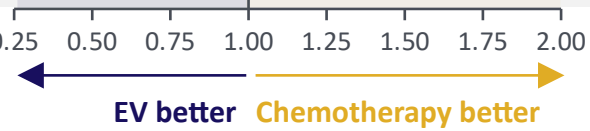


	n	Events, n (%)	Median PFS, months (95% CI)
EV	301	201 (66.8)	**5.55** (5.32–5.82)
Chemotherapy	307	231 (75.2)	**3.71** (3.52–3.94)

Figure adapted from Powles T et al. 2021.
Median follow-up: 11.1 months.
CI, confidence interval; EV, enfortumab vedotin; HR, hazard ratio; ITT, intention to treat; PFS, progression-free survival.
Powles T et al. *N Engl J Med* 2021;384:1125–1135.

There was a trend towards a PFS benefit of EV compared with chemotherapy in most patient subgroups

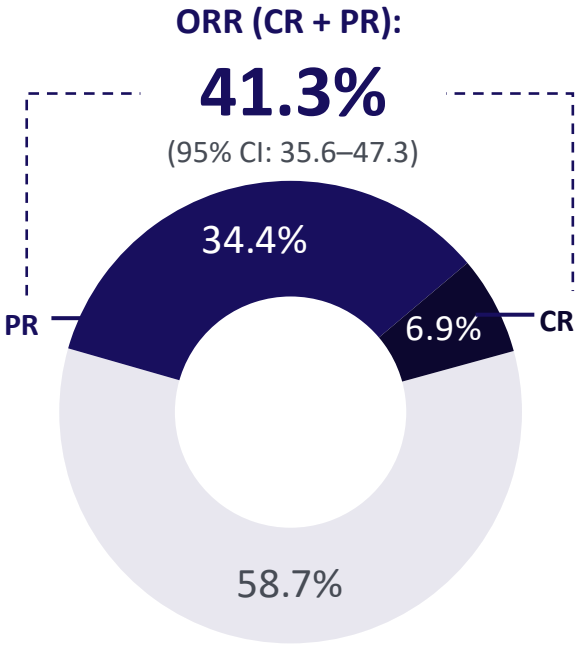
Analysis population[1]		Number of events/number of patients		HR (95% CI)
		EV	Chemotherapy	
All patients	**All patients**	**201/301**	**231/307**	**0.62 (0.51–0.75)**
Age group: 65 years	<65 years	75/108	80/111	0.70 (0.51–0.97)
	≥65 years	126/193	151/196	0.62 (0.49–0.78)
Age group: 75 years	<75 years	166/249	180/239	0.61 (0.49–0.75)
	≥75 years	35/52	51/68	0.89 (0.58–1.37)
Sex	Male	153/238	180/232	0.58 (0.47–0.72)
	Female	48/63	51/75	1.00 (0.67–1.49)
Geographic region	Western Europe	86/126	95/129	0.69 (0.51–0.92)
	United States	30/43	35/44	0.62 (0.38–1.01)
	Rest of the world	85/132	101/134	0.60 (0.45–0.80)
Primary site of tumour	Upper urinary tract	63/98	74/107	0.72 (0.51–1.00)
	Bladder or other site	138/203	157/200	0.61 (0.48–0.76)
ECOG PS score	0	71/120	86/124	0.62 (0.45–0.85)
	1	130/181	145/183	0.66 (0.52–0.84)
Liver metastasis	Yes	71/93	75/95	0.60 (0.43–0.83)
	No	130/208	156/212	0.65 (0.51–0.82)
Previous systemic therapies	1–2	175/262	203/270	0.64 (0.52–0.79)
	≥3	26/39	28/37	0.67 (0.39–1.15)
Best response among patients who previously received CPI treatment	Response*	32/61	36/50	0.51 (0.32–0.83)
	No response†	146/207	160/215	0.70 (0.57–0.87)
Pre-selected chemotherapy	Paclitaxel	96/141	90/112	0.63 (0.47–0.84)
	Docetaxel	56/87	87/117	0.54 (0.38–0.75)
	Vinflunine	49/73	54/78	0.83 (0.57–1.23)

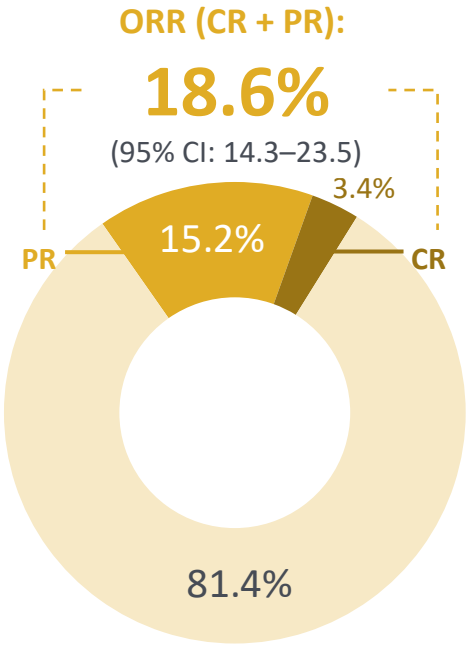


Median follow-up: 11.1 months. Pre-specified subgroup analyses of the intention-to-treat population (all patients who underwent randomization). The trial did not power for statistical comparison of subgroups.[2]
*Confirmed complete response or partial response; †Stable disease or progressive disease.[2]
CI, confidence interval; CPI, checkpoint inhibitor; ECOG PS, Eastern Cooperative Oncology Group performance status; EV, enfortumab vedotin; HR, hazard ratio; PFS, progression-free survival.
1. Powles T et al. *N Engl J Med* 2021;384:1125–1135 (supplementary appendix); 2. Powles T et al. *N Engl J Med* 2021;384:1125–1135.

In EV-301, tumour response rates observed with EV were more than double the rates with chemotherapy

Investigator-assessed clinical response rate*





The confirmed ORR was **~2.2 times higher in the EV group** than the chemotherapy group (41.3% vs 18.6%; p<0.001)

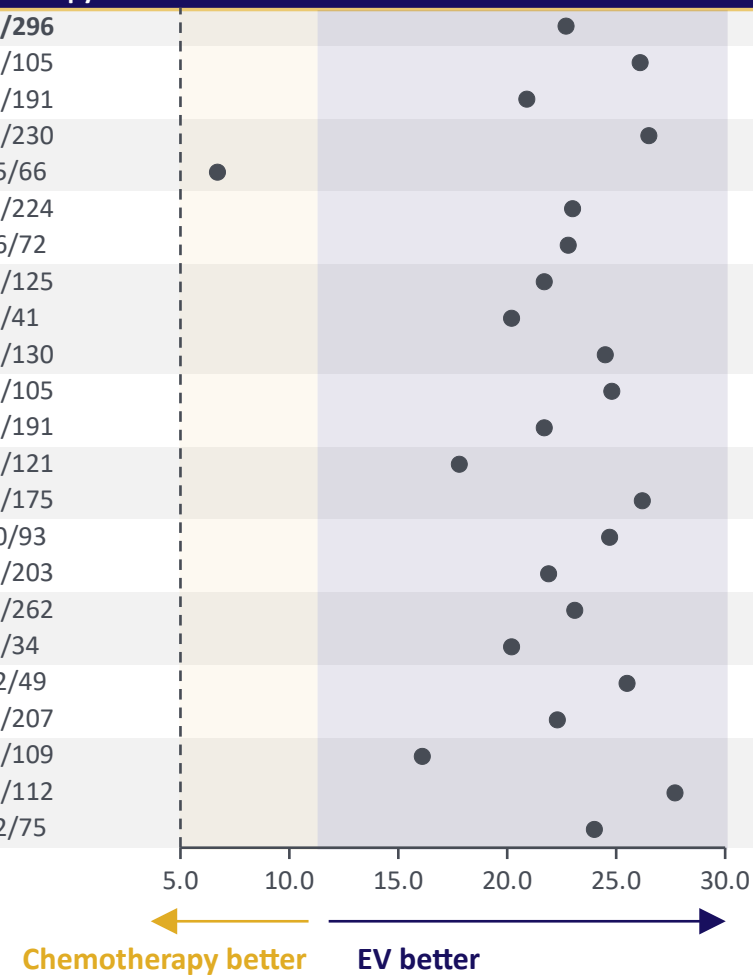
Median follow-up: 23.8 months. Analysis of the intention-to-treat population (all randomized patients).
*Responses according to RECIST v1.1, response evaluable population.

CI, confidence interval; CR, complete response; EV, enfortumab vedotin; ORR, overall response rate; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors.

Rosenberg JE, et al. Ann Oncol 2023;34(11):1047-1054.

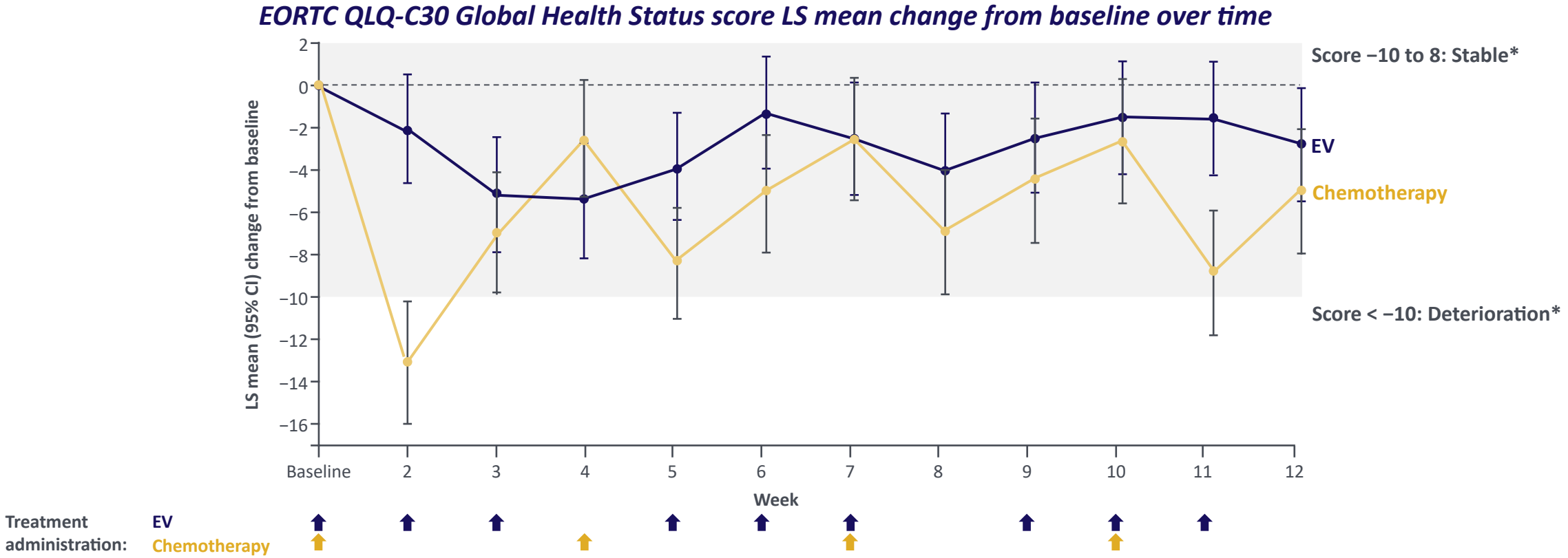
There was a trend towards a higher ORR with EV compared with chemotherapy across patient subgroups

Analysis population[1]		Number of events/number of patients		Absolute difference, % (95% CI)
		EV	Chemotherapy	
All patients	**All patients**	**117/288**	**53/296**	**22.7 (14.7–30.6)**
Age group: 65 years	<65 years	42/104	15/105	26.1 (12.4–38.5)
	≥65 years	75/184	38/191	20.9 (10.8–30.6)
Age group: 75 years	<75 years	102/237	38/230	26.5 (17.6–35.2)
	≥75 years	15/51	15/66	6.7 (−11.6–24.6)
Sex	Male	90/228	37/224	23.0 (13.7–31.8)
	Female	27/60	16/72	22.8 (5.6–39.0)
Geographic region	Western Europe	46/117	22/125	21.7 (9.2–33.8)
	United States	15/43	6/41	20.2 (−1.2–40.3)
	Rest of the world	56/128	25/130	24.5 (12.3–35.9)
Primary site of tumour	Upper urinary tract	43/98	20/105	24.8 (11.1–37.8)
	Bladder or other site	74/190	33/191	21.7 (11.6–31.1)
ECOG PS score	0	49/115	30/121	17.8 (5.0–30.2)
	1	68/173	23/175	26.2 (15.8–36.1)
Liver metastasis	Yes	33/93	10/93	24.7 (10.0–38.7)
	No	84/195	43/203	21.9 (12.1–31.3)
Previous systemic therapies	1–2	103/251	47/262	23.1 (14.5–31.4)
	≥3	14/37	6/34	20.2 (−3.6–41.7)
Best response among patients who previously received CPI treatment	Response*	28/56	12/49	25.5 (6.3–43.4)
	No response†	79/199	36/207	22.3 (12.7–31.7)
Pre-selected chemotherapy	Paclitaxel	56/134	28/109	16.1 (3.5–28.3)
	Docetaxel	33/84	13/112	27.7 (13.6–40.9)
	Vinflunine	28/70	12/75	24.0 (7.6–39.4)



Median follow-up: 11.1 months. Pre-specified subgroup analyses of the intention-to-treat population (all patients who underwent randomization). The trial did not power for statistical comparison of subgroups.[2]
*Confirmed complete response or partial response; †Stable disease or progressive disease.[2]
CI, confidence interval; CPI, checkpoint inhibitor; ECOG PS, Eastern Cooperative Oncology Group performance status; EV, enfortumab vedotin; HR, hazard ratio; ORR, overall response rate.
1. Powles T et al. *N Engl J Med* 2021;384:1125–1135 (supplementary appendix); 2. Powles T et al. *N Engl J Med* 2021;384:1125–1135.

Baseline QOL was maintained with EV in EV-301, with more consistency vs chemotherapy



EV was associated with a **numerically smaller deterioration and less variability in patient-reported QOL scores** compared with chemotherapy

*Prespecified threshold values defining a clinically meaningful change for patients.

CI, confidence interval; EORTC, European Organisation for Research and Treatment of Cancer; EV, enfortumab vedotin; LS, least squares; QLQ-C30, Quality of Life Questionnaire Core 30; QOL, quality of life

Mamtani R, et al. J Clin Oncol 2021;39(Suppl 15):4539-4539.

EV maintained baseline QoL with less variability versus chemotherapy when assessed over the first 12 weeks, and meaningfully improved most QoL domains

Over the first 12 weeks of treatment, overall patient-reported QoL, assessed using EORTC QLQ-C30 Global Health Status, was **maintained** with EV, and was more stable with EV compared with chemotherapy[1]

EV was associated with a **significant reduction in pain** from baseline compared with chemotherapy at Week 12, although loss of appetite was significantly increased[1]

Patients who received EV experienced a confirmed improvement in 10 of 15 QLQ-C30 subscales, including **all functioning domains** and **most symptom domains**, including pain, fatigue, dyspnoea and constipation[1]

These results should be interpreted in the context of the open-label study design,[2] meaning that patients knew which treatment they were receiving; this could have influenced their responses when completing the QoL questionnaire[3]

EORTC, European Organisation for Research and Treatment of Cancer; EV, enfortumab vedotin; QLQ-C30, Quality of Life Questionnaire Core 30; QoL, quality of life.

1. Mamtani R et al. Presented at ASCO 2021. 4539; 2. PADCEV™ (enfortumab vedotin). Summary of Product Characteristics [draft]; 3. US FDA. Guidance for Industry. Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. Available at: https://www.fda.gov/media/77832/download. Last accessed November 2021.

The overall incidence of TRAEs was similar between groups, although the types of TRAEs differed between EV and chemotherapy

Event, n (%)	EV (n=296)		Chemotherapy (n=291)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any TRAE*	**278 (93.9)**	**152 (51.4)**	**267 (91.8)**	**145 (49.8)**
Most common TRAEs†				
Alopecia	134 (45.3)	0	106 (36.4)	0
Peripheral sensory neuropathy‡	100 (33.8)	9 (3.0)	62 (21.3)	6 (2.1)
Pruritus	95 (32.1)	4 (1.4)	13 (4.5)	0
Fatigue	92 (31.1)	19 (6.4)	66 (22.7)	13 (4.5)
Decreased appetite	91 (30.7)	9 (3.0)	68 (23.4)	5 (1.7)
Diarrhoea	72 (24.3)	10 (3.4)	48 (16.5)	5 (1.7)
Dysgeusia	72 (24.3)	0	21 (7.2)	0
Nausea	67 (22.6)	3 (1.0)	63 (21.6)	4 (1.4)
Maculopapular rash	48 (16.2)	22 (7.4)	5 (1.7)	0
Anaemia	34 (11.5)	8 (2.7)	59 (20.3)	22 (7.6)
Decreased neutrophil count	30 (10.1)	18 (6.1)	49 (16.8)	39 (13.4)
Neutropenia	20 (6.8)	14 (4.7)	24 (8.2)	18 (6.2)
Decreased white cell count	16 (5.4)	4 (1.4)	31 (10.7)	20 (6.9)
Febrile neutropenia	2 (0.7)	2 (0.7)	16 (5.5)	16 (5.5)

TRAEs with a ≥10% greater incidence with EV than chemotherapy

Haematological TRAEs more common with chemotherapy than EV

Median follow-up: 11.1 months. Analysis of the safety population (all patients who received any amount of study drug).
*TRAEs are adverse events for which there is a reasonable possibility that the event was caused by study treatment, according to the study investigator; †TRAEs that occurred in ≥20% of patients in either treatment group or Grade ≥3 TRAEs that occurred in ≥5% of patients in either treatment group; ‡A total of 113 patients (55 in the EV group and 58 in the chemotherapy group) had pre-existing peripheral neuropathy.
EV, enfortumab vedotin; TRAE, treatment-related adverse event.
Powles T et al. *N Engl J Med* 2021;384:1125–1135.

The incidence of deaths in the EV group was consistent with trials of other agents in patients with LA/mUC refractory to platinum-based chemotherapy[1–5]

Event, n (%)[1,2]	EV (n=296)	Chemotherapy (n=291)
TEAEs leading to death	**21 (7.1)**	**16 (5.5)**
TEAEs leading to death (excluding progressive disease)	**11 (3.7)**	**11 (3.8)**
TRAEs* leading to death	**7 (2.4)**	**3 (1.0)**
Multi-organ dysfunction syndrome	2 (0.7)	0
Abnormal hepatic function	1 (0.3)	0
Hyperglycaemia	1 (0.3)	0
Pelvic abscess	1 (0.3)	0
Pneumonia	1 (0.3)	0
Septic shock	1 (0.3)	0
Neutropenic sepsis	0	1 (0.3)
Sepsis	0	1 (0.3)
Pancytopenia	0	1 (0.3)

Potential confounders of death in patients of both groups included disease characteristics, pre-existing conditions, and poor prognostic factors[1]

Median follow-up: 11.1 months. Analysis of the safety population (all patients who received any amount of study drug).[1]
*TRAEs are adverse events for which there is a reasonable possibility that the event was caused by study treatment, according to the study investigator.[1]
EV, enfortumab vedotin; LA/mUC, locally advanced/metastatic urothelial carcinoma; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.
1. Powles T et al. *N Engl J Med* 2021;384:1125–1135; 2. Powles T et al. *N Engl J Med* 2021;384:1125–1135 (supplementary appendix); 3. Powles T et al. *Lancet* 2018;391:748–757; 4. Petrylak DP et al. *Lancet* 2017;390:2266–2277; 5. Petrylak DP et al. *Lancet Oncol* 2020;21:105–120.

Most TRAEs were successfully managed with dose reduction or interruption, with a low proportion of patients requiring withdrawal of treatment

Modification of EV dose was most commonly required for neuropathic events, fatigue, low neutrophil count, and skin reactions

Event, n (%)	EV (n=296)	Chemotherapy (n=291)
TRAEs* leading to dose reduction	**96 (32.4)**	**80 (27.5)**
Most common events:†		
Peripheral sensory neuropathy	21 (7.1)	18 (6.2)
Maculopapular rash	13 (4.4)	0
Decreased appetite	10 (3.4)	3 (1.0)
Fatigue	8 (2.7)	11 (3.8)
TRAEs* leading to dose interruption	**151 (51.0)**	**55 (18.9)**
Most common events:†		
Peripheral sensory neuropathy	46 (15.5)	4 (1.4)
Fatigue	16 (5.4)	4 (1.4)
Neutrophil count decreased	15 (5.1)	10 (3.4)
Maculopapular rash	13 (4.4)	0
Rash	10 (3.4)	0
Peripheral neuropathy	9 (3.0)	1 (0.3)
TRAEs* leading to dose withdrawal‡	**40 (13.5)**	**33 (11.3)**

Median follow-up: 11.1 months. Analysis of the safety population (all patients who received any amount of study drug).[2]
*TRAEs are adverse events for which there is a reasonable possibility that the event was caused by study treatment, according to the study investigator;[2] †Events occurring in ≥3% of patients in any treatment group;[1] ‡There were no TRAEs leading to dose withdrawal that occurred in ≥3% of patients in any treatment group.[1]
EV, enfortumab vedotin; TRAE, treatment-related adverse event.
1. Powles T et al. *N Engl J Med* 2021;384:1125–1135 (supplementary appendix); 2. Powles T et al. *N Engl J Med* 2021;384:1125–1135.

The majority of AESI were mild to moderate in severity

Event,* n (%)[1]	EV (n=296)						Chemotherapy (n=291)					
	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Skin reactions	**139 (47.0)**	**41 (13.9)**	**55 (18.6)**	**42 (14.2)**	**1 (0.3)**	**0**	**46 (15.8)**	**30 (10.3)**	**14 (4.8)**	**2 (0.7)**	**0**	**0**
Rash	130 (43.9)	41 (13.9)	46 (15.5)	42 (14.2)	1 (0.3)	0	28 (9.6)	21 (7.2)	6 (2.1)	1 (0.3)	0	0
SCAR†	60 (20.3)	20 (6.8)	25 (8.4)	14 (4.7)	1 (0.3)	0	22 (7.6)	12 (4.1)	8 (2.7)	2 (0.7)	0	0
Peripheral neuropathy	**137 (46.3)**	**44 (14.9)**	**78 (26.4)**	**15 (5.1)**	**0**	**0**	**89 (30.6)**	**45 (15.5)**	**37 (12.7)**	**7 (2.4)**	**0**	**0**
Sensory events‡	130 (43.9)	43 (14.5)	76 (25.7)	11 (3.7)	0	0	86 (29.6)	44 (15.1)	35 (12.0)	7 (2.4)	0	0
Motor events	22 (7.4)	5 (1.7)	12 (4.1)	5 (1.7)	0	0	7 (2.4)	5 (1.7)	2 (0.7)	0	0	0
Ocular disorders	**55 (18.6)**	**40 (13.5)**	**13 (4.4)**	**2 (0.7)**	**0**	**0**	**14 (4.8)**	**11 (3.8)**	**2 (0.7)**	**1 (0.3)**	**0**	**0**
Dry eye	47 (15.9)	34 (11.5)	11 (3.7)	2 (0.7)	0	0	9 (3.1)	6 (2.1)	2 (0.7)	1 (0.3)	0	0
Blurred vision	12 (4.1)	10 (3.4)	2 (0.7)	0	0	0	6 (2.1)	5 (1.7)	0	1 (0.3)	0	0
Corneal disorders	2 (0.7)	2 (0.7)	0	0	0	0	0	0	0	0	0	0
Infusion-related reactions	**26 (8.8)**	**11 (3.7)**	**11 (3.7)**	**4 (1.4)**	**0**	**0**	**13 (4.5)**	**6 (2.1)**	**7 (2.4)**	**0**	**0**	**0**
Systemic events	23 (7.8)	10 (3.4)	9 (3.0)	4 (1.4)	0	0	9 (3.1)	4 (1.4)	5 (1.7)	0	0	0
Local events	3 (1.0)	1 (0.3)	2 (0.7)	0	0	0	6 (2.1)	4 (1.4)	2 (0.7)	0	0	0
Infusion site reactions	2 (0.7)	0	2 (0.7)	0	0	0	4 (1.4)	3 (1.0)	1 (0.3)	0	0	0
Extravasation site reactions	3 (1.0)	1 (0.3)	2 (0.7)	0	0	0	4 (1.4)	2 (0.7)	2 (0.7)	0	0	0
Hyperglycaemia	**19 (6.4)**	**3 (1.0)**	**4 (1.4)**	**11 (3.7)**	**0**	**1 (0.3)**	**1 (0.3)**	**0**	**1 (0.3)**	**0**	**0**	**0**

Median follow-up: 11.1 months. Analysis of the safety population (all patients who received any amount of study drug).[2]
*TRAEs are adverse events for which there is a reasonable possibility that the event was caused by study treatment, according to the study investigator;[2] †Composite MedDRA query high level term including: Stomatitis, drug eruption, conjunctivitis, dermatitis bullous, skin exfoliation, blister, erythema multiforme, exfoliative rash, fixed eruption, mouth ulceration, pemphigus, and toxic skin eruption;[1] ‡Represents any peripheral neuropathy sensory events including: Peripheral sensory neuropathy, peripheral neuropathy, paraesthesia, polyneuropathy, hypoaesthesia, neurotoxicity, dysaesthesia, gait disturbance, burning sensation, neuralgia, and sensory loss.[1]
AESI, adverse event of special interest; EV, enfortumab vedotin; MedDRA, Medical Dictionary for Regulatory Activities; SCAR, severe cutaneous adverse reaction; TRAE, treatment-related adverse event.
1. Powles T et al. *N Engl J Med* 2021;384:1125–1135 (supplementary appendix); 2. Powles T et al. *N Engl J Med* 2021;384:1125–1135.

AESIs generally occurred in the first few months of initiating treatment

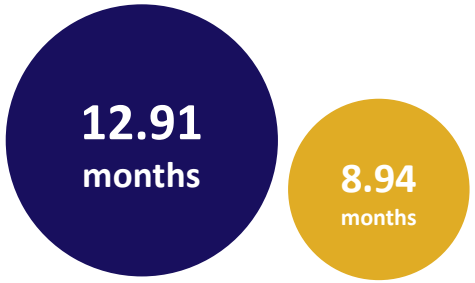
	EV (n=296)		Chemotherapy (n=291)	
Event,* n (%)[1]	**n**	**Months, median (range)**	**n**	**Months, median (range)**
Skin reactions	139	0.43 (0.03–12.68)	46	0.66 (0.07–9.56)
Peripheral neuropathy	137	2.69 (0.03–11.99)	89	0.82 (0.03–9.07)
Corneal disorders	2	4.34 (1.91–6.77)	0	NA
Dry eye	47	1.91 (0.30–9.66)	9	2.46 (0.03–5.09)
Blurred vision	12	2.45 (0.07–5.09)	6	0.87 (0.03–4.14)
Infusion-related reactions	26	0.51 (0.03–9.40)	13	0.03 (0.03–3.19)
Hyperglycaemia	19	0.56 (0.26–5.78)	1	1.41 (1.41–1.41)

Median follow-up: 11.1 months. Analysis of the safety population (all patients who received any amount of study drug).[2]
*TRAEs are adverse events for which there is a reasonable possibility that the event was caused by study treatment, according to the study investigator.[2]
AESI, adverse event of special interest; EV, enfortumab vedotin; NA, not applicable; TRAE, treatment-related adverse event.
1. Powles T et al. *N Engl J Med* 2021;384:1125–1135 (supplementary appendix); 2. Powles T et al. *N Engl J Med* 2021;384:1125–1135.

EV significantly improved outcomes vs chemotherapy in patients previously treated with platinum-based chemotherapy and a PD-1/L1 inhibitor[1,2]

Key outcomes from EV-301

30% lower
risk of **death** with EV vs single-agent chemotherapy[1]

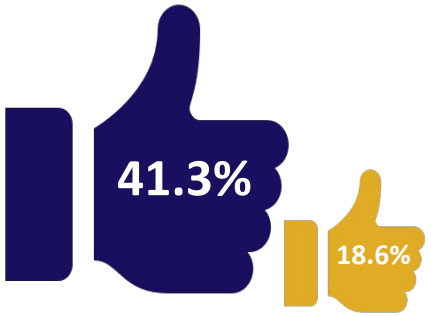


Median OS

37% lower
risk of **progression or death** with EV vs single-agent chemotherapy[1]

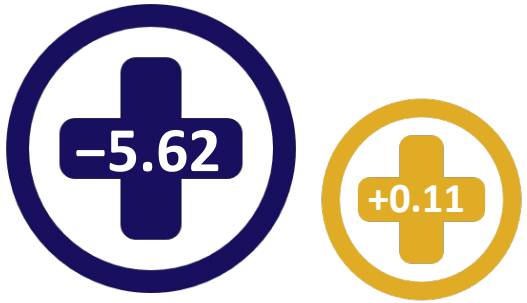
Median PFS

~2.2 times higher
rate of **complete or partial response** with EV vs single-agent chemotherapy[1]



ORR

Significant reduction
in **pain** from baseline with EV vs single-agent chemotherapy[2]



EORTC QLQ-C30 mean pain symptom score*

Median follow-up: 23.8 months.[1]
*Data at Week 12.[2]

EORTC, European Organisation for Research and Treatment of Cancer; EV, enfortumab vedotin; ORR, objective response rate; OS, overall survival; PD-1/L1, programmed cell death protein 1/ligand 1; PFS, progression-free survival; QLQ-C30, Quality of Life Questionnaire Core 30

1. Rosenberg JE, et al. Ann Oncol 2023;34(11):1047-1054. 2. Mamtani R, et al. J Clin Oncol 2021;39(Suppl 15):4539-4539.

MAT-IN-PAD-2024-00006

Summary – EV-301

In EV-301, an international, open-label, **randomized, Phase III study** of patients with la/mUC who were previously treated with platinum-based chemotherapy and a PD-1/L1 inhibitor, **EV significantly improved key outcomes vs chemotherapy**:[1]*

- Median OS: **30% lower risk of death** with EV vs single-agent chemotherapy
- Medium PFS: **37% lower risk of progression or death** with EV vs single-agent chemotherapy
- ORR: **~2.2 times higher rate of complete or partial response** with EV vs single-agent chemotherapy

EV is an **effective treatment** for patients with la/mUC who have previously been treated with chemotherapy and a PD-1/L1 inhibitor, having consistently demonstrated **ORRs of 40–45%** across its clinical programme[1,3,4]

*Median follow-up: 23.8 months.[1]

EORTC, European Organisation for Research and Treatment of Cancer; EV, enfortumab vedotin; la/mUC, locally advanced/metastatic urothelial carcinoma; ORR, objective response rate; OS, overall survival; PD-1/L1, programmed cell death protein 1/ligand 1; PFS, progression-free survival; QLQ-C30, Quality of Life Questionnaire Core 30

1. Rosenberg JE, et al. Ann Oncol 2023;34(11):1047-1054. 2. Mamtani R, et al. J Clin Oncol 2021;39(Suppl 15):4539-4539. 3. Rosenberg JE et al. J Clin Oncol 2020;38:1041–1049. 4. Rosenberg JE et al. J Clin Oncol 2019;37:2592–2600.

Use of real-world evidence to support decision-making on Enfortumab Vedotin

astellas

Real-World Experience With EV

UNITE registry (academic collaboration across 16 US institutions)

260 patients treated with EV monotherapy

- ORR 52%
- PFS 6.8 months
- OS 14.4 months

ORR higher for pure urothelial (58%) versus variant histology (42%)

EV, enfortumab vedotin; ORR, overall response rate; OS, overall survival; PFS, progression-free survival

Koshkin VS, et al. Cancer 2022;128(6):1194-1205.

MAT-IN-PAD-2024-00006

UNITE Registry: Patient Subsets Treated With EV Monotherapy

Subgroups	Total Pt #	ORR (%)	p-value
Urothelial histology	142	58	0.06
Variant histology	66	42	
Bladder primary	151	50	0.21
Upper tract primary	56	61	
Age ≥75 years	69	51	0.85
Age <75 years	139	53	
ECOG 0/1	173	56	0.18
ECOG 2/3	34	41	
Neuropathy at baseline	71	62	0.08
No neuropathy	139	48	
Diabetes at baseline	29	59	0.60
No diabetes	183	51	
eGFR ≥ 30 mL/min	187	54	0.27
eGFR < 30 mL/min	25	40	
FGFR3 altered	28	57	0.93
FGFR3 wild type	102	54	

ECOG, Eastern Cooperative Oncology; eGFR, estimated glomerular filtration rate; EV, enfortumab vedotin; FGFR3, fibroblast growth factor receptor 3; ORR, observed response rate; pt, patient

Koshkin VS, et al. Cancer 2022;128(6):1194-1205.

UNITE Study (1)

Urothelial Cancer Network to Investigate Therapeutic Experiences (UNITE)

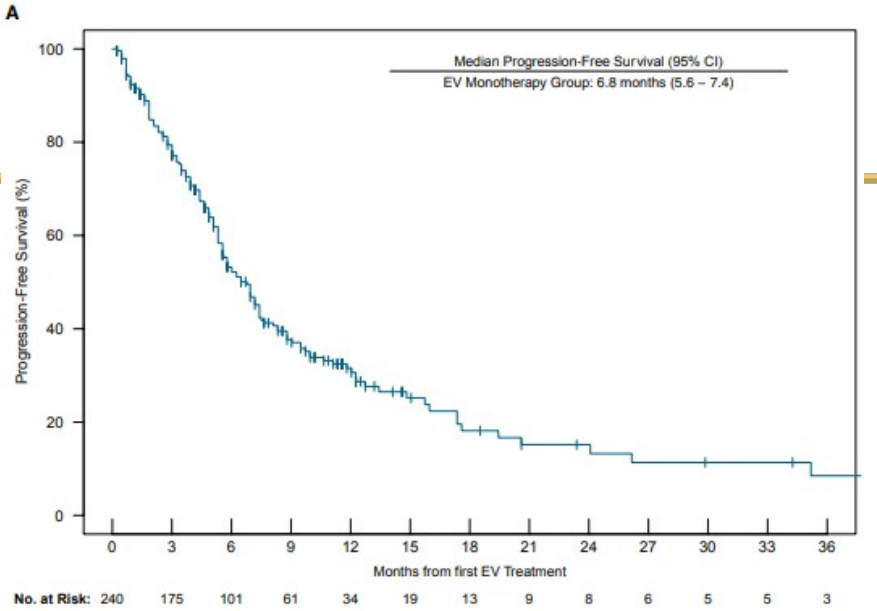
Large, multi-institutional, retrospective cohort of patients with aUC treated with novel agents

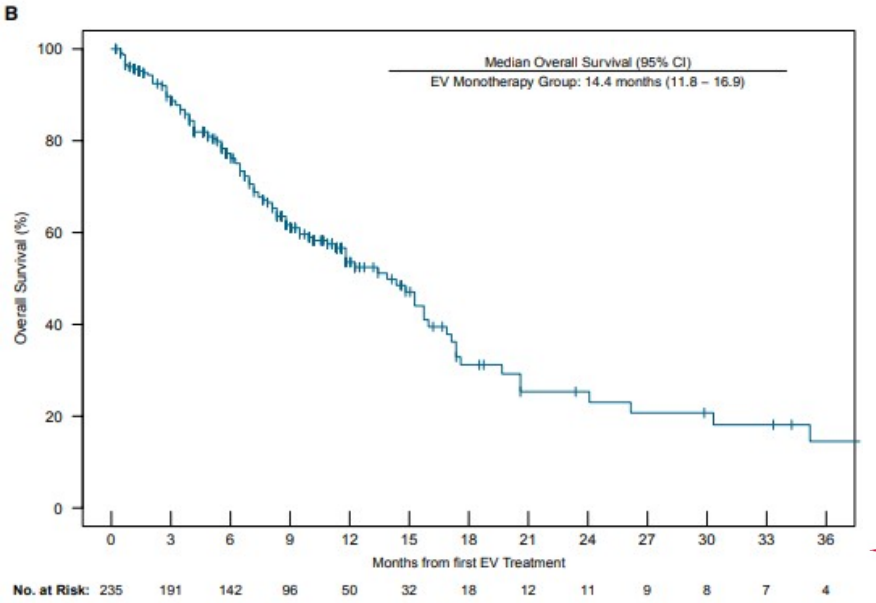
304 patients from 16 academic institutions

- 260 received EV monotherapy
- 67% had 2+ prior lines
- 78% treated in real-world setting

PFS and OS better than 301 study

- PFS: 6.8 vs 5.5 mo
- OS: 14.4 vs 12.9 mo





aUC, advanced urothelial carcinoma; EV, enfortumab vedotin; mo, month; OS, overall survival; PFS, progression-free survival

Koshkin VS, et al. Cancer 2022;128(6):1194-1205.

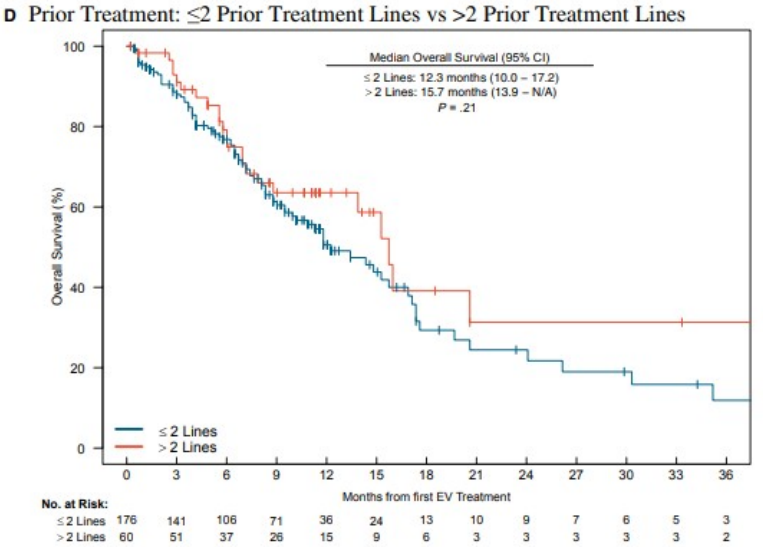
UNITE Study (2)

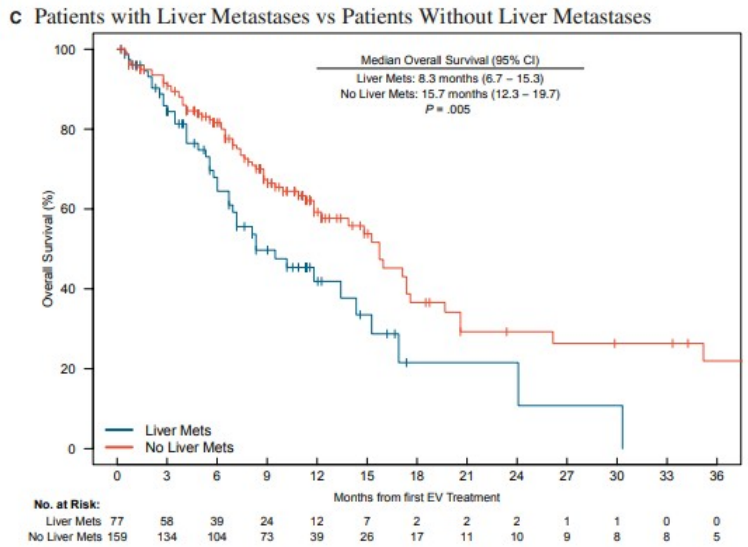
No difference in heavily pre-treated patients

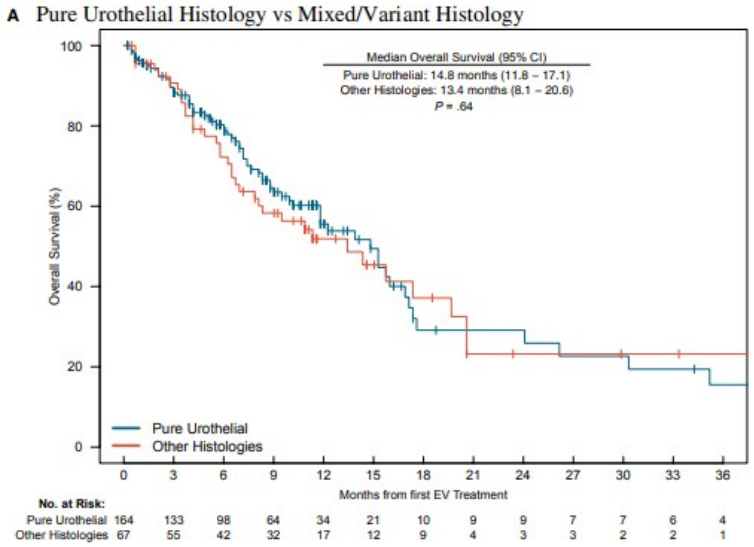
No difference in mixed histologies

No difference in primary site (UTUC vs BL)

No difference in high/low TMB, or PD-L1







BL, bladder; CI, confidence interval; mets, metastases; OS, overall survival; PD-L1, programmed death ligand-1; TMB, tumour mutational burden; UTUC, upper tract urothelial carcinoma

Koshkin VS, et al. Cancer 2022;128(6):1194-1205.

MAT-IN-PAD-2024-00006

UNITE: Certain Histology Variants Associated With Poor Outcomes Demonstrated Responses to EV (ASCO GU 2024)

Variant	ORR	UC predominant (<50% HV)	ORR	HV predominant (50–99% HV)	ORR	pHV (100% HV)	ORR
Squamous (n=94)	**47%** (36/76)	70	**55%** (31/56)	17	**33%** (5/15)	7	**0%** (0/5)
Micropapillary (n=41)	**35%** (12/34)	35	**38%** (11/29)	6	**20%** (1/5)	0	-
Plasmacytoid (n=23)	**53%** (9/17)	18	**64%** (9/14)	2	**Not evaluable**	3	**0%** (0/3)
Sarcomatoid (n=21)	**47%** (8/17)	15	**38%** (5/13)	4	**100%** (3/3)	2	**0%** (0/1)
Adenocarcinoma/glandular (n=9)	**56%** (5/9)	8	**63%** (5/8)	1	**0%** (0/1)	0	-
NE/Small Cell (n=9)	**0%** (0/8)	3	**0%** (0/3)	4	**0%** (0/3)	2	**0%** (0/2)
Nested (n=2)	**50%** (1/2)	1	**0%** (0/1)	1	**100%** (1/1)	0	-
Lipid cell variant (n=1)	**100%** (1/1)	1	**100%** (1/1)	0	-	0	-
Any HV	**44%** (72/164)	151	**50%** (62/125)	35	**36%** (10/28)	14	**0%** (0/11)

EV, enfortumab vedotin; HV, histology variant; NE, neuroendocrine; ORR, observed response rate; pHV, pure histology variant; UC, urothelial carcinoma

Jindal T, et al. J Clin Oncol 2024;42(Suppl 4):652-652.

UNITE Study (3)

Efficacy for EV in 3L is reproduced in North American academic ‘real-world’ patients

What about other populations?

3L, third-line; EV, enfortumab vedotin

MAT-IN-PAD-2024-00006

Real-World Evidence from a European Database

Zschaebitz S, et al. ASCO GU 2024[1]

Retrospective analysis from 25 German and Swiss hospitals

N=188 patients received EV (4L+ in 43%)

AE data similar to 301 study (reported using CTCAE)

32 vs 51%

ORR similar to 301 study (determined using RECIST)

46 vs 41%

PFS and OS similar to 301 study

PFS: 7 vs 5.5 mo

OS: 12 vs 12.9 mo

Table 1. Patient characteristics at start of EV.

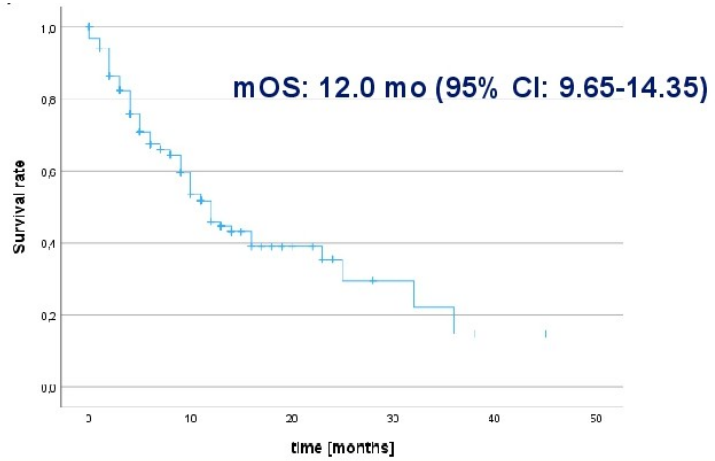
no. (%)	n=188
Median age (range)	66 (31-89)
age >/= 75 yr	42 (22.3)
Sex, male	127 (76.6)
ECOG Score	
0	68 (19.1)
1	73 (38.8)
2	20 (10.6)
≥ 3	6 (3.2)
Missing	21 (11.2)
Prior treatment lines	
0	1 (0.5)
1	8 (4.3)
2	99 (52.7)
3	48 (25.5)
4	26 (13.8)
5	6 (3.2)
Prior treatment	
Platin-based CTX	177 (94.1)
Cisplatin	146 (77.7)
Carboplatin	40 (21.3)
Vinflunine	54 (28.7)
Taxane	33 (17.6)
ICI	165 87.8)
Pembrolizumab	97 (51.6)
Avelumab	47 25.0)
Nivolumab	22 (11.7)
Atezolizumab	10 (5.3)
FGFR inhibitor	7 (3.7)
Sacituzumab govitecan	2 (1.1)

4L+, fourth-line and beyond; CTX, chemotherapy; CTCAE, common terminology criteria for adverse events; ECOG, Eastern Cooperative Oncology Group; EV, enfortumab vedotin; FGFR, fibroblast growth factor receptor; ICI, immune checkpoint inhibitor; mo, month; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; RECIST, response evaluation criteria in solid tumors; yr, year

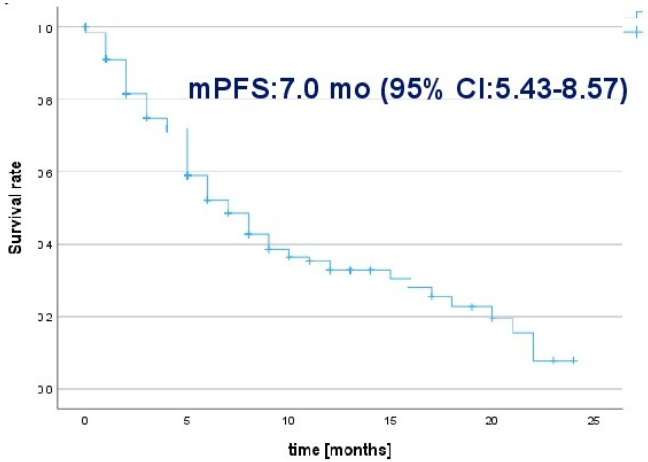
1. Zschaebitz S, et al. J Clin Oncol 2024;42(Suppl 4):553-553.

EV in Germany and Switzerland

Median OS



Median PFS



no. (%)	n=188
Objective response rate	87 (46.28)
Disease control rate	109 (57.98)
Best overall response	
Complete remission	8 (4.3)
Partial remission	79 (42.0)
Stable disease	22 (11.7)
Progressive disease	53 (28.2)
Unknown/could not be evaluated	11 (5.9)
Median PFS – mo. (95% CI)	7.00 (5.43-8.57)
Median OS – mo. (95% CI)	12.00 (9.65-14.35)

no. (%)	All grade	Grade 3-5
Treatment emergent AE– no. (%)	134 (71.3)	61 (32.4)
Neuropathy	63 (33.5)	18 (9.5)
Dermatotoxicity	48 (25.5)	8 (4.3)
Fatigue	43 (22.9)	7 (3.7)
Hematotoxicity	22 (11.6)	11 (5.9)
Diarrhea	21 (11.1)	5 (2.7)
Pruritus	13 (6.9)	2 (1.1)
Ocular toxicity	11 (5.9)	1 (0.5)
Respiratory toxicity	8 (4.3)	4 (2.1)
Hyperglycemia	3 (1.6)	2 (1.1)

AE, adverse event; CI, confidence interval; EV, enfortumab vedotin; mo, month; mOS, median overall survival; mPFS, median progression-free survival; OS, overall survival; PFS, progression-free survival

Zschaebitz S, et al. J Clin Oncol 2024;42(Suppl 4):553-553.

EV in Japan

Hayakawa N, et al. 2023[1]

N=97 patients received EV at 5 centers in Japan

Median age 71 y

Clinical response 43% (similar to 41% ORR)

Adverse events noted in patients included

- Grade 3 rash, 9%
- Grade 3 peripheral neuropathy, 3%
- Grade 3 hyperglycemia, 3%

Table. Characteristics of adverse events (≥10 patients)

Event-no (%)	Any grade	Grade≤3
Any adverse event	88 (90.7%)	26 (26.8%)
Skin disorder	61 (62.9%)	9 (9.3%)
Dysgeusia	36 (37.1%)	0 (0.0%)
Peripheral neuropathy	34 (35.1%)	3 (3.1%)
Gastrointestinal disorder	29 (29.9%)	3 (3.1%)
Hyperglycemia	18 (18.6%)	3 (3.1%)
Alopecia	16 (16.5%)	0 (0.0%)
Fatigue	15 (15.5%)	1 (1.0%)

EV, enfortumab vedotin; ORR, overall response rate; y, year

1. Hayakawa N, et al. Ann Oncol 2023;34:S1561-S1562.

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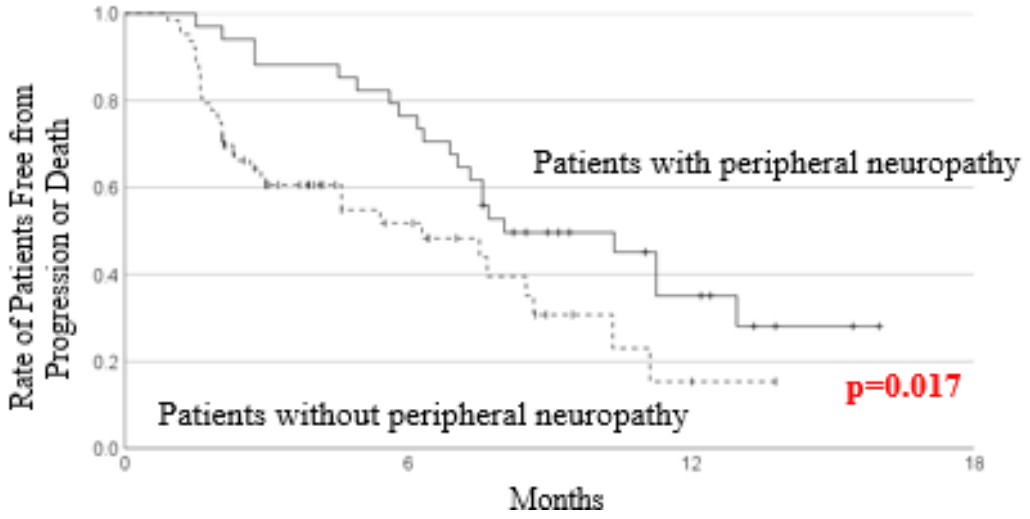
EV in Japan
Hayakawa N, et al. 2023[1]

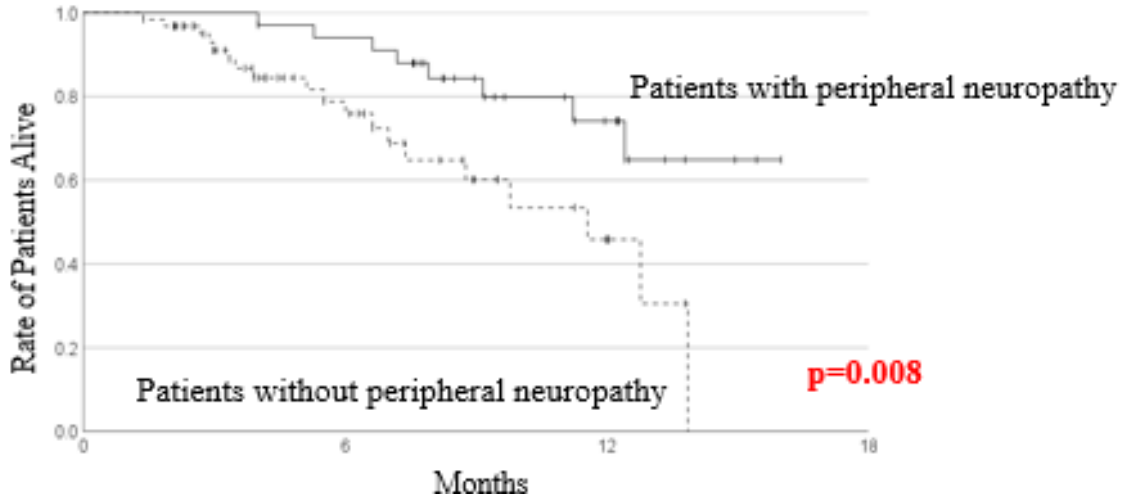
Patients who had any grade peripheral neuropathy had longer PFS and OS

Figure. Association between the clinical outcome and EV-associated peripheral neuropathy in patients treated with EV

Progression-free survival



Overall survival



EV, enfortumab vedotin; OS, overall survival; PFS, progression-free survival

1. Hayakawa N, et al. Ann Oncol 2023;34:S1561-S1562.

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Real-World Evidence: Enfortumab Vedotin

Efficacy, as measured by response rate, PFS and OS, observed in the 301 study is reproduced in real-world patient populations in North America, Europe and Asia.

Toxicity, as measured by AEs, observed in real-world patient populations is similar to the 301 study.

AE, adverse event; OS, overall survival; PFS, progression-free survival

Abridged prescribing information for PADCEV

ABBREVIATED PRESCRIBING INFORMATION OF PADCEV™ **(**enfortumab vedotin) 20 mg and 30 mg powder for concentrate for solution for infusion (Please refer the full prescribing information for further details)

1. Name of the medicinal product: PADCEV™ (enfortumab vedotin) 20 mg and 30 mg powder for concentrate for solution for infusion **2. QUALITATIVE AND QUANTITATIVE COMPOSITION:** Each vial contains either 20 mg or 30 mg enfortumab vedotin. After reconstitution, each mL of solution contains 10 mg of enfortumab vedotin. **3. PHARMACEUTICAL FORM:** single-dose vials containing either 20 mg or 30 mg enfortumab vedotin as sterile, preservative-free, white to off-white lyophilized powder for reconstitution for intravenous infusion. **4. CLINICAL PARTICULARS 4.1 Therapeutic indication:** PADCEV as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer who have previously received a platinum-containing chemotherapy and a programmed death receptor 1 or programmed death ligand 1 inhibitor. **4.2 Posology and method of administration** *Posology:* The recommended dose of enfortumab vedotin is 1.25 mg/kg (up to a maximum of 125 mg for patients ≥100 kg). It must be administered as an intravenous infusion over 30 minutes on Days 1, 8 and 15 of a 28-day cycle until disease progression or unacceptable toxicity. Dose modifications: For information on recommended dose reductions for adverse reactions as well as instructions on dose modifications (interruption, reduction and discontinuation) in patients experiencing adverse reactions refer to section 4.2 of the PI *Elderly*: No dose adjustment is necessary in patients ≥65 years of age. *Renal impairment*: No dose adjustment is necessary in patients with mild [creatinine clearance (CrCL) >60-90 mL/min], moderate (CrCL 30–60 mL/min) or severe (CrCL 15–<30 mL/min) renal impairment. Enfortumab vedotin has not been evaluated in patients with end stage renal disease (CrCL <15 mL/min). *Hepatic impairment*: No dose adjustment is necessary in patients with mild hepatic impairment [total bilirubin of 1 to 1.5 × upper limit of normal (ULN) and aspartate transaminase (AST) any, or total bilirubin ≤ ULN and AST > ULN]. Enfortumab vedotin has only been evaluated in a limited number of patients with moderate hepatic impairment and has not been evaluated in patients with severe hepatic impairment. *Pediatric population:* There is no relevant use of enfortumab vedotin in the pediatric population for the indication of locally advanced or metastatic urothelial cancer. **4.3 Contraindications:** None **4.4 Special warnings and precautions for use:** Skin reactions: Skin reactions are anticipated on-target events, as Nectin-4 is expressed in the skin. Skin reactions, predominantly mild to moderate maculopapular rash, have occurred with enfortumab vedotin. Severe cutaneous adverse reactions, including SJS and TEN, with fatal outcome have also occurred in patients treated with enfortumab vedotin, predominantly during the first cycle of treatment. Starting with the first cycle and throughout treatment, monitor patients for skin reactions. Consider appropriate treatment such as topical corticosteroids and antihistamines for mild to moderate skin reactions. For Grade 2 worsening skin reactions, consider withholding PADCEV until toxicity is Grade ≤1. For severe (Grade 3) skin reactions, suspected SJS or TEN, withhold PADCEV and consider referral for specialized care. Permanently discontinue PADCEV for confirmed SJS or TEN; Grade 4 or recurrent Page **2** of **2**

Grade 3 skin reactions. Hyperglycemia: Hyperglycemia and diabetic ketoacidosis (DKA), including fatal events, occurred in patients with and without pre-existing diabetes mellitus, treated with enfortumab vedotin. Hyperglycemia occurred more frequently in patients with pre-existing hyperglycemia or a high body mass index (≥30 kg/m2). Blood glucose levels should be monitored regularly in patients with or at risk for diabetes mellitus or hyperglycemia. If blood glucose is elevated (>13.9 mmol/L; >250 mg/dL), withhold PADCEV. Peripheral neuropathy: Peripheral neuropathy, predominantly sensory, has occurred with enfortumab vedotin, including Grade ≥3 reactions. Monitor patients for symptoms of new or worsening peripheral neuropathy as these patients may require a delay, dose reduction or discontinuation of PADCEV. Ocular disorders: Ocular disorders, predominantly dry eye, occurred in patients treated with enfortumab vedotin. Severe (Grade 3) ocular disorders only occurred in 3 patients (0.4%). Monitor patients for ocular disorders such as dry eye. Consider artificial tears for prophylaxis of dry eye and refer patient for ophthalmologic evaluation if ocular symptoms do not resolve or worsen. Infusion site extravasation :Skin and soft tissue injury following enfortumab vedotin administration has been observed when extravasation occurred. Ensure good venous access prior to starting PADCEV and monitor for possible infusion site extravasation during administration. If extravasation occurs, stop the infusion and monitor for adverse reactions.**4.7 Effects on ability to drive and use machines**: PADCEV has no or negligible influence on the ability to drive and use machines. **4.8 Undesirable effects:** Summary of the safety profile: The safety of enfortumab vedotin was evaluated as monotherapy in 680 patients who received at least one dose of enfortumab vedotin 1.25 mg/kg in two phase 1 studies (EV-101 and EV-102), one phase 2 study (EV-201) and one phase 3 study (EV-301). Serious adverse events occurred in 45% of patients. The most common serious adverse reactions (≥2%) were diarrhoea (2%) and hyperglycemia (2%). Nineteen percent of patients permanently discontinued enfortumab vedotin for adverse events; the most common adverse reaction (≥2%) leading to dose discontinuation was peripheral sensory neuropathy (4%). Adverse events leading to dose interruption occurred in 62% of patients; the most common adverse reactions (≥2%) leading to dose interruption were peripheral sensory neuropathy (15%), fatigue (7%), rash maculo-papular (4%), aspartate aminotransferase increased (4%), alanine aminotransferase increased (4%), anaemia (3%), diarrhoea (3%) and hyperglycemia (3%). Thirty-five percent of patients required a dose reduction due to an adverse event; the most common adverse reactions (≥2%) leading to a dose reduction were peripheral sensory neuropathy (10%), fatigue (5%), rash maculo-papular (4%) and decreased appetite (2%). **OVERDOSE:** There is no known antidote for overdosage with Enfortumab vedotin. In case of overdosage, the patient should be closely monitored for adverse reactions, and supportive treatment should be administered as appropriate taking into consideration the half-life of 3.6 days (ADC) and 2.6 days (MMAE). **For full prescribing information please write to: MARKETING AUTHORISATION HOLDER: Astellas Pharma India Private Limited,** 301,3rd Floor, C and B Square,127 Andheri Kurla Road, Chakala, Andheri (East), Mumbai – 400 069. (Version: PADCEV/aPI/India/Ver.1.0/Feb 2024)

PADCEV™
enfortumab vedotin
Powder for Concentrate for Solution
for Infusion 20 mg and 30 mg vials

Thank You!

astellas

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