Genitourinary Masterclass

Deeper insights: What the latest data tells us about today's SOC for advanced UC

Professor Tom Powles
Barts Cancer Centre at St Bartholomew's Hospital, London, UK

Dr Shilpa Gupta
Cleveland Clinic Taussig Cancer Institute, Cleveland, Ohio, US

Prescribing Information is available at the end of this presentation.
This promotional meeting is fully sponsored and supported by Astellas, including speaker-related honoraria and production of materials. It is intended for healthcare professionals only.
EV, in combination with P, is indicated for the 1L treatment of adult patients with unresectable/mUC who are eligible for platinum-containing chemotherapy.[1]
Please note: This indication has received EMA approval; reimbursement in some EU countries is still pending.
EV as monotherapy is indicated for the treatment of adult patients with LA/mUC who have previously received a platinum-containing chemotherapy and a PD-1/L1 inhibitor.[1]

1L, first line; AE, adverse event; EMA, European Medicines Agency; EV, enfortumab vedotin; LA, locally advanced; mUC, metastatic urothelial carcinoma; P, pembrolizumab; PD-1/L1, programmed death-1/ligand-1; SOC, standard of care; UC, urothelial carcinoma.

1. PADCEV™ (enfortumab vedotin). Summary of Product Characteristics.

Date of preparation: June 2025 | Job code: MAT-NL-PAD-2025-00051

▼ This medicinal product is subject to additional monitoring.

NL: Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system. Nederland: Nederlands Bijwerkingen Centrum Lareb;
Website: www.lareb.nl

UK: Adverse events should be reported.
Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for 'MHRA yellow card' in the Google Play Store or Apple App Store. Adverse events should also be reported to Astellas Pharma Ltd on 0800 783 5018

PADCEV™ ▼
enfortumab vedotin
Injection for IV infusion 20 mg & 30 mg vials

astellas

Disclosures of Professor Powles

Advisory roles:

- Astellas Pharma, AstraZeneca, BMS, Eisai, Exelixis, Ipsen, Incyte, Johnson & Johnson, Mashup Ltd, Merck, Merck Serono, MSD, Novartis, Pfizer, Roche and Seagen Inc.

Travel, accommodation and expenses:

- AstraZeneca, Ipsen, MSD, Pfizer and Roche

Honoraria:

- Astellas Pharma, AstraZeneca, BMS, Eisai, Exelixis, Gilead Sciences, GmbH & Co. KG, Ipsen, Incyte, Johnson & Johnson/Janssen, Mashup Ltd, Merck, Merck Serono, Merck Sharp & Dohme LLC, Novartis, Pfizer, Roche Laboratories Inc and Seagen Inc.

Research funding:

- Astellas Pharma, AstraZeneca, BMS, Eisai, Exelixis, Ipsen, Johnson & Johnson, Merck Serono, MSD, Novartis, Pfizer, Roche and Seagen Inc.

Disclosures of Dr Gupta

Advisory roles:

- Astellas Pharma, AstraZeneca, BMS, Ipsen, Bicycle Therapeutics, Johnson & Johnson, Merck, Novartis, Pfizer, Gilead and Seagen Inc.

Travel, accommodation, and expenses:

- Astellas Pharma and Merck

Honoraria:

- Astellas Pharma, AstraZeneca, BMS, Ipsen, Bicycle Therapeutics, Johnson & Johnson, Merck, Novartis, Pfizer, and Gilead

Research funding (to institution)

- Merck, BMS, Flare Therapeutics, Tyra Biosciences, Roche, Novartis, Pfizer, and Seagen Inc.

Disclaimer

This presentation includes data from trials of compounds and combinations not currently licenced for the treatment of UC

Always refer to your local prescribing information

UC, urothelial cancer.

Genitourinary Masterclass

Deeper insights: What the latest data tells us about today's SOC for advanced UC

Part 1

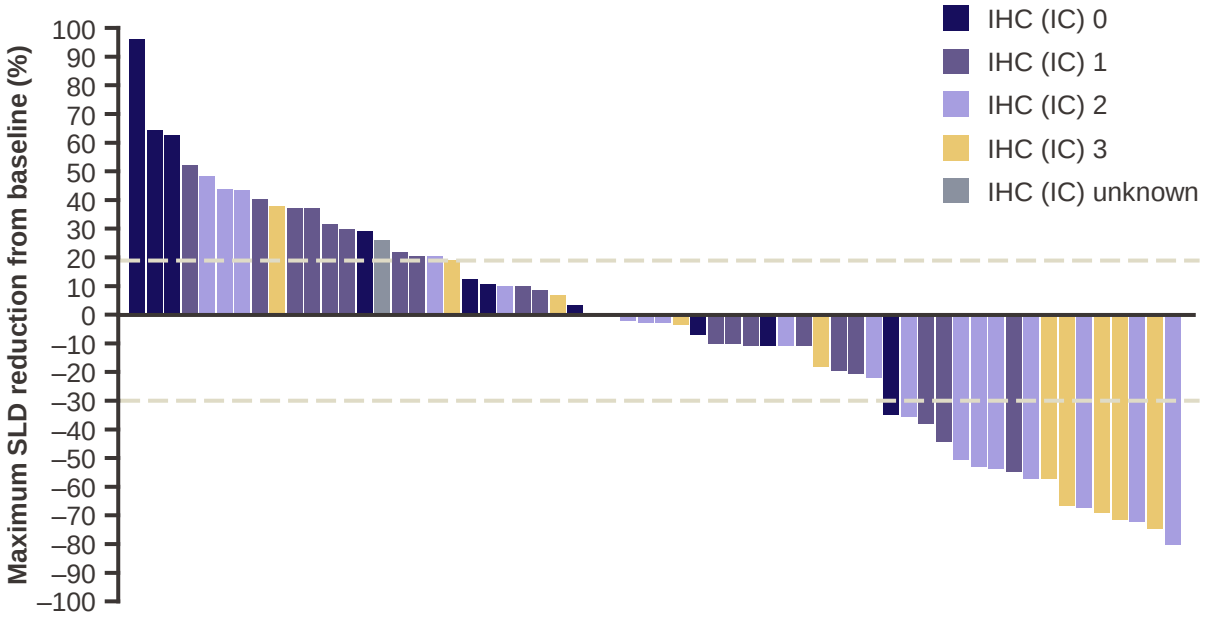
Professor Tom Powles

Barts Cancer Centre at St Bartholomew's Hospital, London, UK

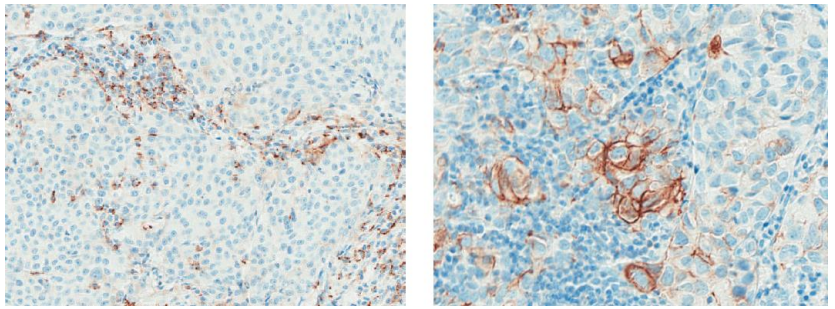
astellas

A breakthrough for UBC in 2014: Phase I trial investigating atezolizumab, an anti–PD-L1 agent, for treatment of UBC*

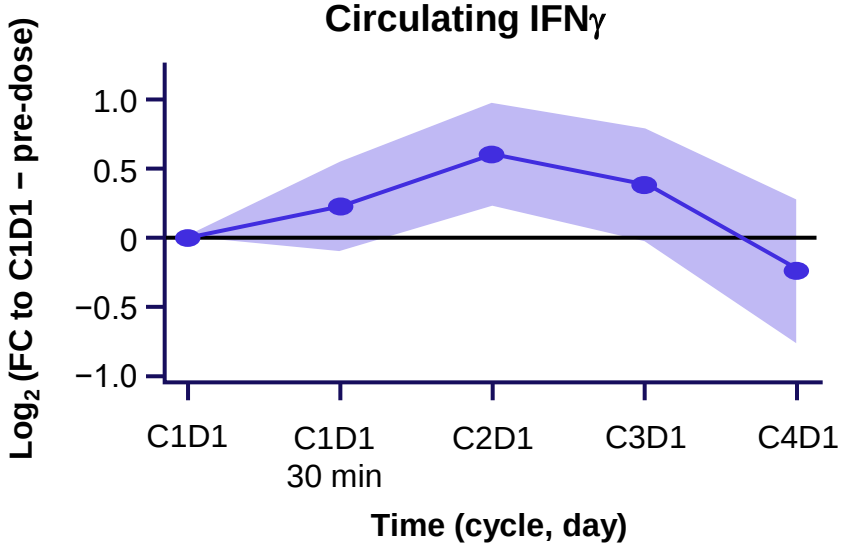
Maximum reduction (%) from baseline in the SLD for target lesions; +20% and −30% are marked by dashed lines



PD-L1 expression on tumour-infiltrating immune cells and tumour cells



Circulating IFNγ



***This trial investigated patients with UBC selecting by PD-L1 status to test the hypothesis that patients who are PD-L1-positive might specifically respond to MPDL3280A. The cohort was later expanded to include patients regardless of PD-L1 status to determine whether PD-L1 negative patients could also respond. 57% of patients reported a treatment-related adverse event. Most of these were Grade 1 or 2, and many were transient in nature.**

C#D#, Cycle # Day #; IC, immune cell; IFN, interferon; IHC, immunohistochemistry; PD-L1, programmed cell death ligand 1; SLD, sum of the longest diameter; UBC, urothelial bladder cancer.

Powles T et al. *Nature* 2014;515:558–562.

Monotherapy PD-1/L1 trials in bladder cancer in chronological order

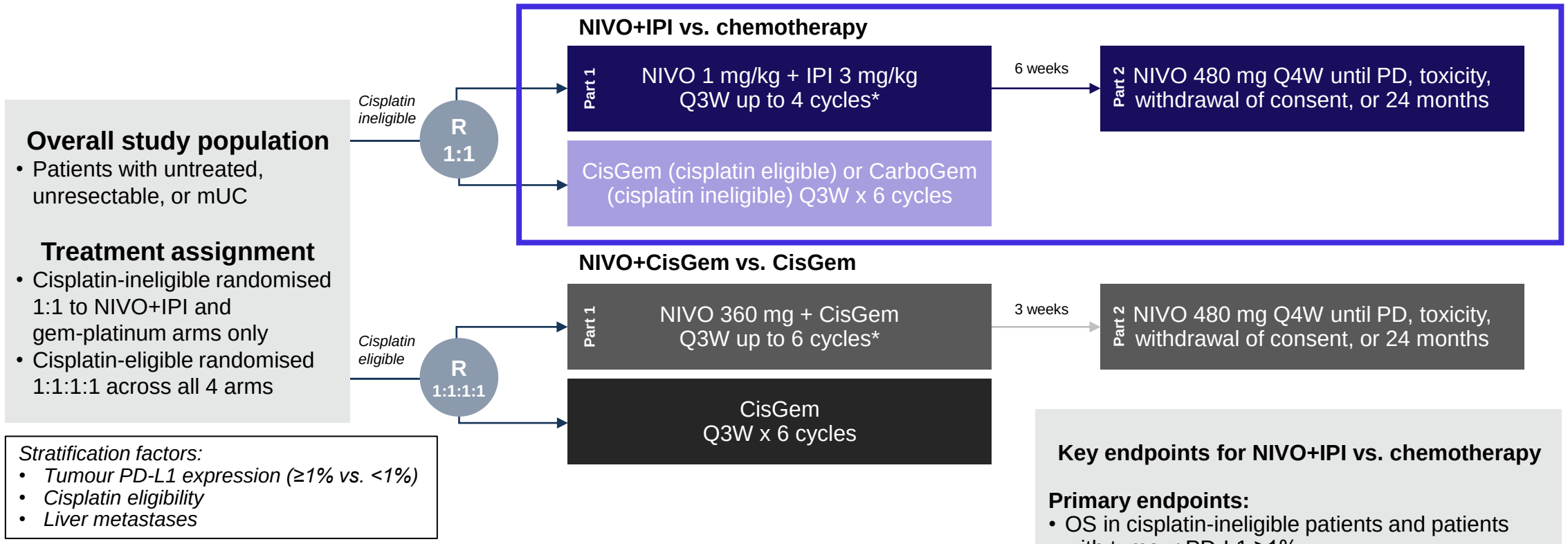
Setting	Study name	Study drug	PD-L1 biomarker endpoint	MOA	Achieved primary endpoint	OS +ve
Advanced disease[1]	KN45	Pembrolizumab	ITT	PD1	Yes	Yes
Advanced disease[2]	IM211	Atezolizumab	PD-L1 +ve	PD-L1	No	No
Advanced disease[3]	DANUBE	Durvalumab	PD-L1 +ve	PD-L1	No	No
Advanced disease[3]	DANUBE	Durva/Treme	ITT	PD-L1/CTLA4	No	No
Advanced disease[4]	KN361	Pembrolizumab	PD-L1 +ve	PD-1	No	No
Advanced disease[5]	IM130	Atezolizumab	PD-L1 +ve	PD-L1	No	No
Advanced disease[6]	Javelin	Avelumab	ITT	PD-L1	Yes	Yes
Advanced disease[7]	CM901	Ipilimumab/nivolumab	PD-L1/ITT	PD-1/CTLA4	No	No
Adjuvant[8]	**CM274**	**Nivolumab**	**ITT**	**PD-1**	**Yes**	**No**
Adjuvant[9]	IM010	Atezolizumab	ITT	PD-L1	No	No
Adjuvant[10]	Ambassador	Pembrolizumab	ITT	PD-1	Yes	No
Perioperative[11]	Niagara	Durvalumab	ITT	PD-L1	Yes	Yes
NMIBC[12]	CREST	Sasanlimab	ITT	PD-1	Yes	No
NMIBC[13]	Potomac	Durvalumab	ITT (press release)	PD-L1	Yes	No

CTLA4, cytotoxic T-lymphocyte associated protein 4; ITT, intention to treat; MOA, mode of action; NMIBC, non-muscle invasive bladder cancer; OS, overall survival; PD-1, programmed cell death 1; PD-L1, programmed cell death ligand 1.

1. Fradet Y et al. *Ann Oncol* 2019;30(6):970–976; 2. Powles T et al. *Lancet* 2018;391(10122):748–757; 3. Powles T et al. *Lancet Oncol* 2020;21:1574–1588; 4. Powles T et al. *Lancet Oncol* 2021;22:931–945; 5. Galsky MD et al. *Lancet* 2020;395:1547–1557; 6. Powles T et al. *NEJM* 2020;383(13):1218–1230; 7. UroToday. ASCO 2025: Nivolumab + Ipilimumab versus Gemcitabine + Carboplatin Chemotherapy for Previously Untreated Unresectable or Metastatic Urothelial Carcinoma: Final Results for Cisplatin-Ineligible Patients from the CheckMate 901 Trial. Available at: https://www.urotoday.com/conference-highlights/asco-2025/asco-2025-bladder-cancer/160801-asco-2025-nivolumab-ipilimumab-versus-gemcitabine-carboplatin-chemotherapy-for-previously-untreated-unresectable-or-metastatic-urothelial-carcinoma-final-results-for-cisplatin-ineligible-patients-from-the-checkmate-901-trial.html. Last accessed: June 2025; 8. Bajorin DF et al. *NEJM* 2021;384(22):2102–2114; 9. Bellmunt J et al. *Lancet Oncol* 2021;22(4):525–537; 10. Apolo AB et al. *NEJM* 2025;391(1):45–55; 11. Powles T et al. *NEJM* 2024;391(19):1773–1786; 12. Shore ND et al. Nat Med 2025. doi:10.1038/s41591-025-03738-z. Online ahead of print;
13. AstraZeneca. Imfinzi regimen demonstrated statistically significant and clinically meaningful improvement in disease-free survival for high-risk non-muscle-invasive bladder cancer in POTOMAC Phase III trial. Available at: https://www.astrazeneca.com/media-centre/press-releases/2025/imfinzi-improved-dfs-in-early-bladder-cancer.html. Last accessed: June 2025.

CheckMate 901: Overall study design[1,2]

Phase III, open-label, randomised trial in patients with untreated unresectable or metastatic UC



The combination of nivolumab and ipilimumab is not licenced for the treatment of unresectable or metastatic UC.

*In part 1, a minimum of one cycle of combination therapy is required before proceeding to nivolumab monotherapy dosing (part 2).

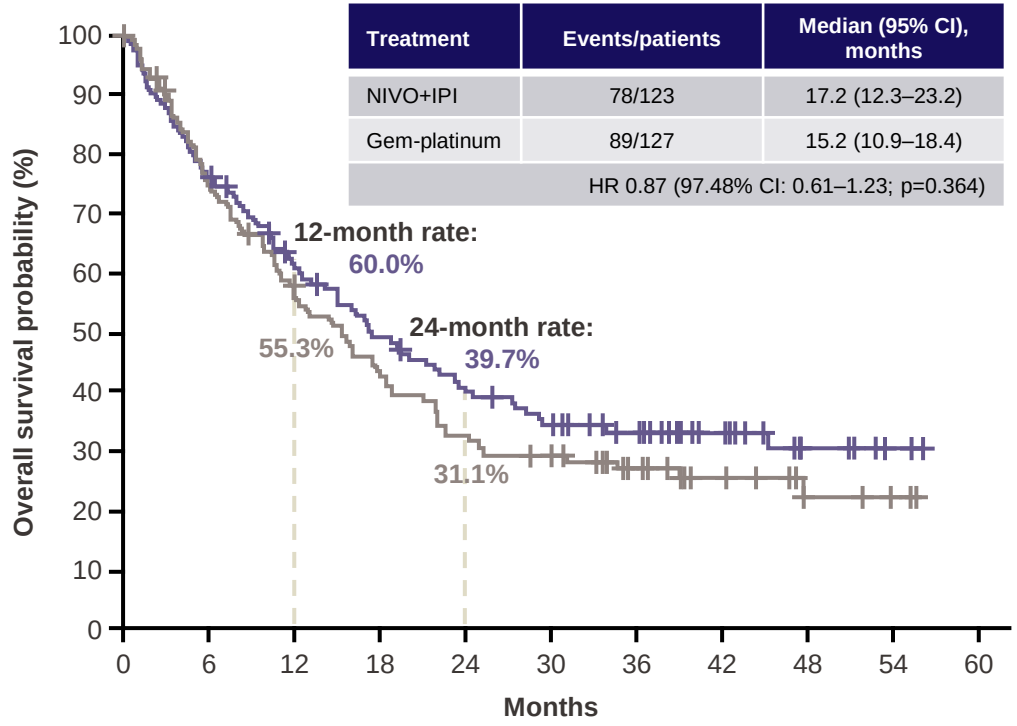
ASCO, American Society for Clinical Oncology; BICR, blinded independent central review; Carbo, carboplatin; Cis, cisplatin; Gem, gemcitabine; IPI, ipilimumab; m, metastatic; NIVO, nivolumab; OS, overall survival; PD, progression of disease; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; Q3W, every 3 weeks; R, randomised; UC, urothelial carcinoma.

1. van der Heijden M et al. *N Engl J Med* 2023;389:1778–1789; 2. UroToday. Nivolumab + Ipilimumab versus Gemcitabine + Carboplatin Chemotherapy for Previously Untreated Unresectable or Metastatic Urothelial Carcinoma: Final Results for Cisplatin-Ineligible Patients from the CheckMate 901 Trial. Available at: https://www.urotoday.com/conference-highlights/asco-2025/asco-2025-bladder-cancer/160801-asco-2025-nivolumab-ipilimumab-versus-gemcitabine-carboplatin-chemotherapy-for-previously-untreated-unresectable-or-metastatic-urothelial-carcinoma-final-results-for-cisplatin-ineligible-patients-from-the-checkmate-901-trial.html?tmpl=component&print=1. Last accessed: July 2025.

OS in PD-L1 ≥1% and all randomised patients (cisplatin-eligible and -ineligible)

OS in PD-L1 ≥1% (primary endpoint)*†

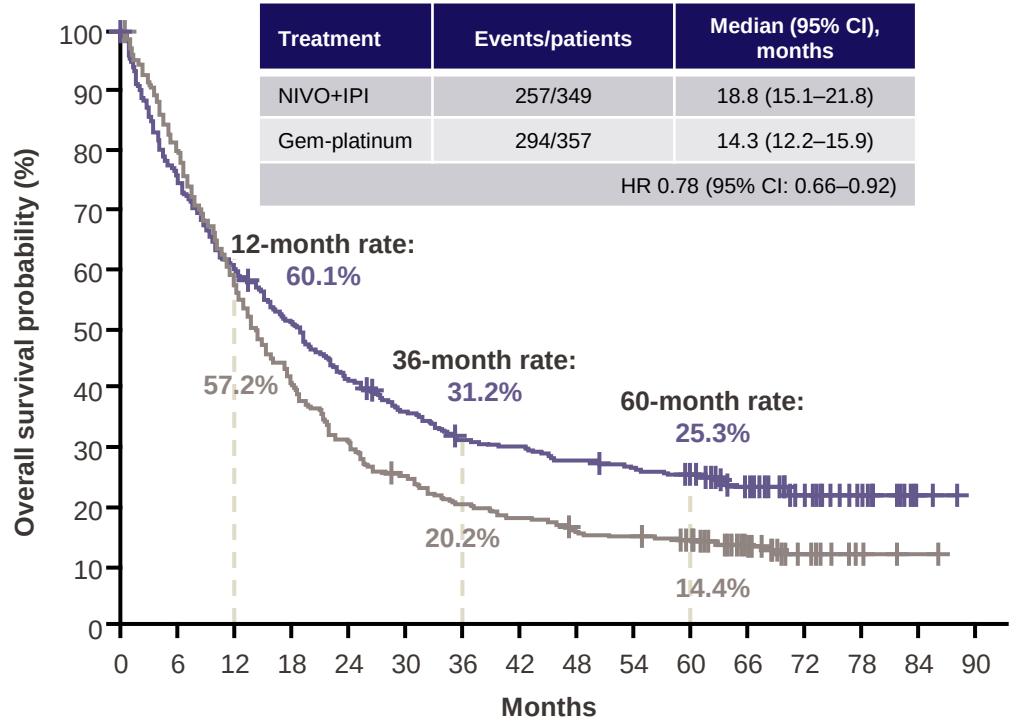
Treatment	Events/patients	Median (95% CI), months
NIVO+IPI	78/123	17.2 (12.3–23.2)
Gem-platinum	89/127	15.2 (10.9–18.4)
		HR 0.87 (97.48% CI: 0.61–1.23; p=0.364)



NIVO + IPI	123	89	67	52	42	34	26	16	6	2	0
Gem-platinum	127	87	64	48	36	31	21	12	5	3	0

OS in all randomised (secondary endpoint)‡

Treatment	Events/patients	Median (95% CI), months
NIVO+IPI	257/349	18.8 (15.1–21.8)
Gem-platinum	294/357	14.3 (12.2–15.9)
		HR 0.78 (95% CI: 0.66–0.92)



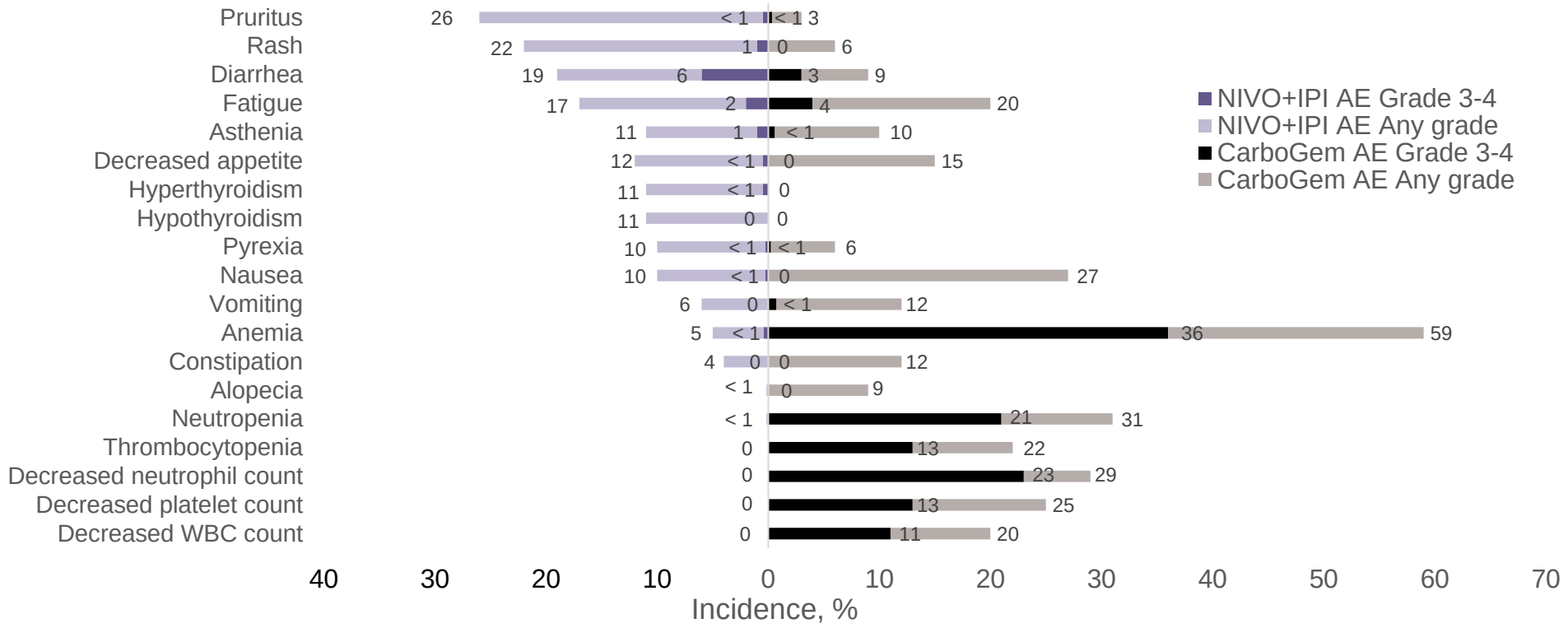
NIVO + IPI	349	255	201	168	136	116	100	96	89	83	76	51	28	12	3	0
Gem-platinum	357	270	193	138	103	83	67	61	51	49	43	25	14	5	3	0

*Survival rates above 24 months were not shown due to minimum follow-up time not reached; †Database lock in patients with PD-L1 ≥1% was 20 April 2022; ‡Database lock in all randomised patients was 30 September 2024.
CI, confidence interval; Gem, gemcitabine; HR, hazard ratio; IPI, ipilimumab; NIVO, nivolumab; OS, overall survival; PD-L1, programmed cell death ligand 1.
The combination of nivolumab and ipilimumab is not licenced for the treatment of unresectable or metastatic UC.

UroToday. Nivolumab + Ipilimumab versus Gemcitabine + Carboplatin Chemotherapy for Previously Untreated Unresectable or Metastatic Urothelial Carcinoma: Final Results for Cisplatin-Ineligible Patients from the CheckMate 901 Trial. Available at: https://www.urotoday.com/conference-highlights/asco-2025/asco-2025-bladder-cancer/160801-asco-2025-nivolumab-ipilimumab-versus-gemcitabine-carboplatin-chemotherapy-for-previously-untreated-unresectable-or-metastatic-urothelial-carcinoma-final-results-for-cisplatin-ineligible-patients-from-the-checkmate-901-trial.html?tmpl=component&print=1. Last accessed: June 2025.

Treatment-related AEs in cisplatin-ineligible patients

	NIVO+IPI (n=218)		CarboGem (n=211)	
Treatment-related AE, %	**Any grade**	**Grade 3–4**	**Any grade**	**Grade 3–4**
Any	89	47	93	76
Leading to discontinuation	31	23	14	12



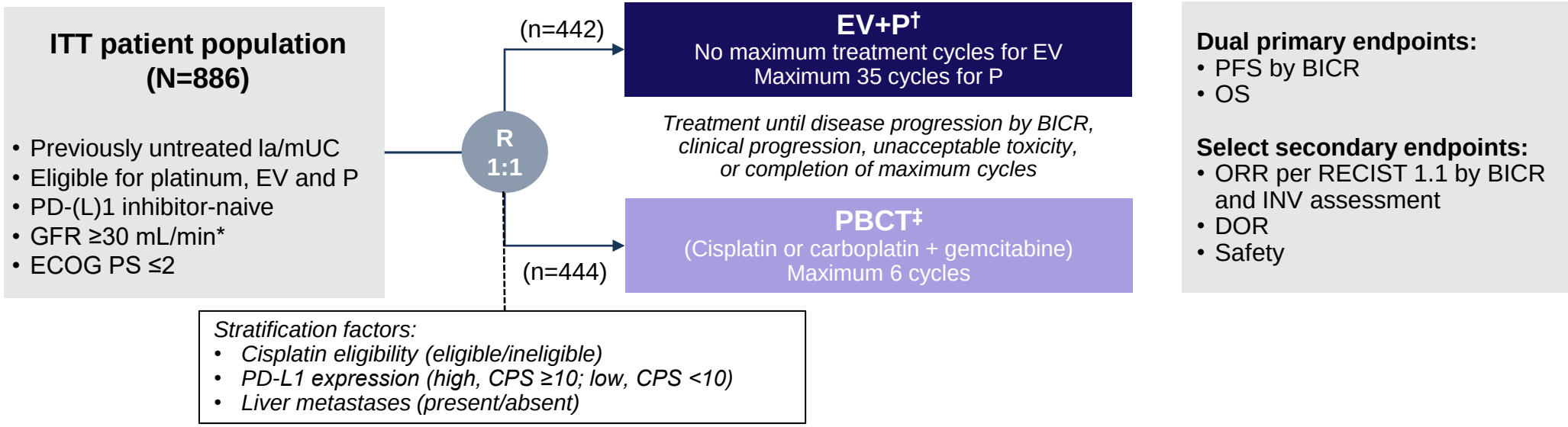
Out of 8 total treatment-related deaths, 7 were in the NIVO+IPI arm and 1 was in the CarboGem arm

The combination of nivolumab and ipilimumab is not licenced for the treatment of unresectable or metastatic UC.

AE, adverse event; carbo, carboplatin; Gem, gemcitabine; IPI, ipilimumab; NIVO, nivolumab; WBC, white blood cell.

UroToday. Nivolumab + Ipilimumab versus Gemcitabine + Carboplatin Chemotherapy for Previously Untreated Unresectable or Metastatic Urothelial Carcinoma: Final Results for Cisplatin-Ineligible Patients from the CheckMate 901 Trial. Available at: https://www.urotoday.com/conference-highlights/asco-2025/asco-2025-bladder-cancer/160801-asco-2025-nivolumab-ipilimumab-versus-gemcitabine-carboplatin-chemotherapy-for-previously-untreated-unresectable-or-metastatic-urothelial-carcinoma-final-results-for-cisplatin-ineligible-patients-from-the-checkmate-901-trial.html?tmpl=component&print=1. Last accessed: June 2025.

EV-302 study design[1,2]



Primary analysis: Median duration of follow-up for survival was 17.2 months:[1]

- At 12 months and 18 months, 67.3% and 59.6% of patients were still in remission in the EV+P group; 35.2% and 19.3% were in remission in the PBCT group

Long-term analysis: 29.1 months (95% CI: 28.5–29.9) of median follow-up:[2,3]

- 54 (12%) patients remained on EV+P treatment and no patients remained on PBCT
- 218 (49%) patients in the EV+P arm and 131 (30%) patients in the PBCT arm remained on study

Data cutoff: 8 August 2024.

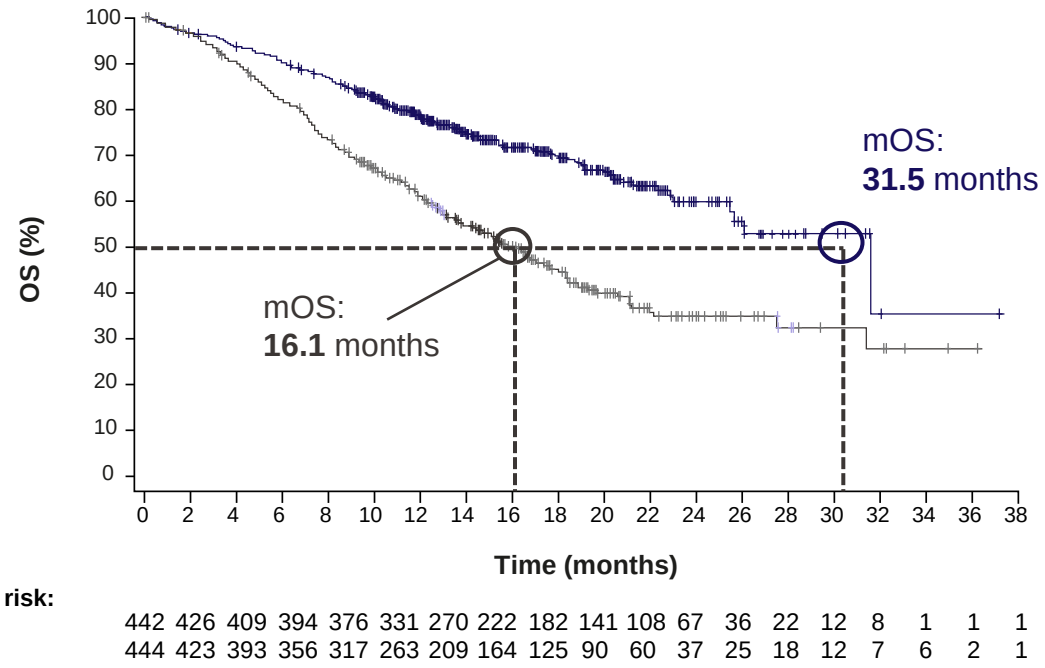
*Patients with ECOG PS of 2 were required to also meet the additional criteria: haemoglobin ≥10 g/dL and GFR ≥50 mL/min but may not have NYHA class III heart failure; †Patients received 3-week cycles of EV (1.25 mg/kg; IV) on Days 1 and 8 and P (200 mg; IV) on Day 1; ‡Cisplatin eligibility and assignment/dosing of cisplatin vs. carboplatin were protocol defined.

BICR, blinded independent central review; CPS, combined positive score; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EV, enfortumab vedotin; GFR, glomerular filtration rate; INV, investigator; ITT, intent to treat; la/mUC, locally advanced or metastatic urothelial cancer; NYHA, New York Heart Association; ORR, objective response rate; OS, overall survival; P, pembrolizumab; PBCT, platinum-based chemotherapy; PD-(L)1, programmed death (ligand) 1; PFS, progress-free survival; RECIST, Response Evaluation Criteria in Solid Tumours.

1. Powles T et al. *N Engl J Med* 2024;390:875–888; 2. Powles T, presented at ASCO GU 2025, Abstract 664; 3. Powles T et al. *Ann Oncol* 2025; https://doi.org/10.1016/j.annonc.2025.05.536.

EV-302 primary analysis: OS and PFS were nearly doubled with EV+P vs. PBCT

OS in the overall population (primary analysis)[1]



	EV+P	PBCT	HR (95% CI) p-value
mOS,[1] months	31.5	16.1	0.47 (0.38–0.58) <0.001
mPFS,[1] months	12.5	6.3	0.45 (0.38–0.54) <0.001
ORR,[1] %	67.7	44.4	–
CR,[1] %	29.1	12.5	–
TRAE[1] Any grade, % Grade ≥3, %	97.0 55.9	95.6 69.5	–
TRAE leading to discontinuation,[1] %	EV or P: 35.0; EV 29.5; P 21.4	18.5	–
QOL,[2] (EORTC QLQ-C30)	Least squares mean change from baseline up to week 26 favoured EV+P		
mTTCD,[2] months (95% CI)	5.9 (4.50–10.02)	3.2 (1.84–NE)	-

Median follow-up: 17.2 months.

AE, adverse event; CI, confidence interval; Cis, cisplatin; CR, complete response; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Core Quality of Life questionnaire; EV, enfortumab vedotin; Gem, gemcitabine; HR, hazard ratio; (m)OS, (median) overall survival; (m)PFS, (median) progression-free survival; Nivo, nivolumab; ORR, objective response rate; P, pembrolizumab; PBCT, platinum-based chemotherapy; QOL, quality of life; TRAE, treatment-related adverse event; mTTCD, median time to confirmed deterioration; wk, week.

1. Powles T et al. *N Engl J Med* 2024;390:875–888; 2. Gupta S, et al. *Lancet Oncol*. 2025;26:795-805.

EV-302 primary analysis: EV+P had an overall lower rate of Grade ≥3 AEs vs. PBCT

TRAE occurrence, %	EV+P		PBCT	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Overall	97.0	55.9	95.6	69.5

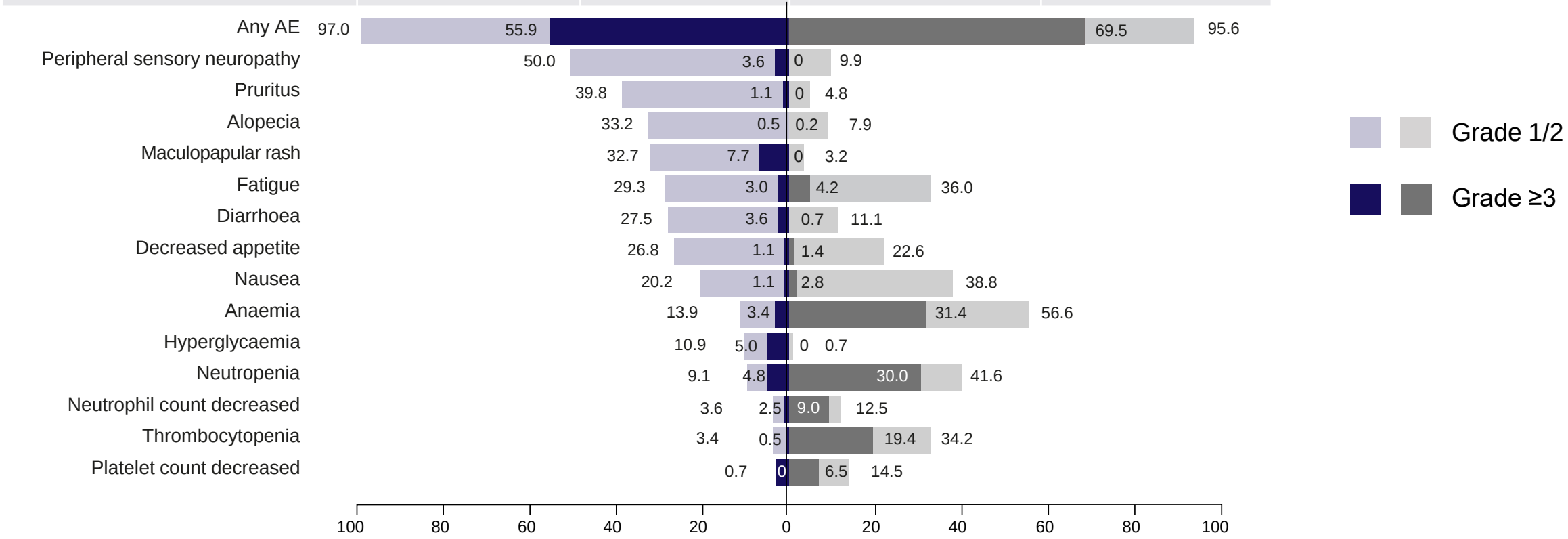


Figure adapted from Powles T et al. *N Engl J Med* 2024;390:875–888.

TRAEs shown in the figure are any grade by preferred term in ≥20% of patients for any grade in either arm; Grade ≥3 TRAEs shown occurred in ≥5% of the patients in either treatment group.

AE, adverse event; EV, enfortumab vedotin; P, pembrolizumab; PBCT, platinum-based chemotherapy; TRAE, treatment-related adverse event.

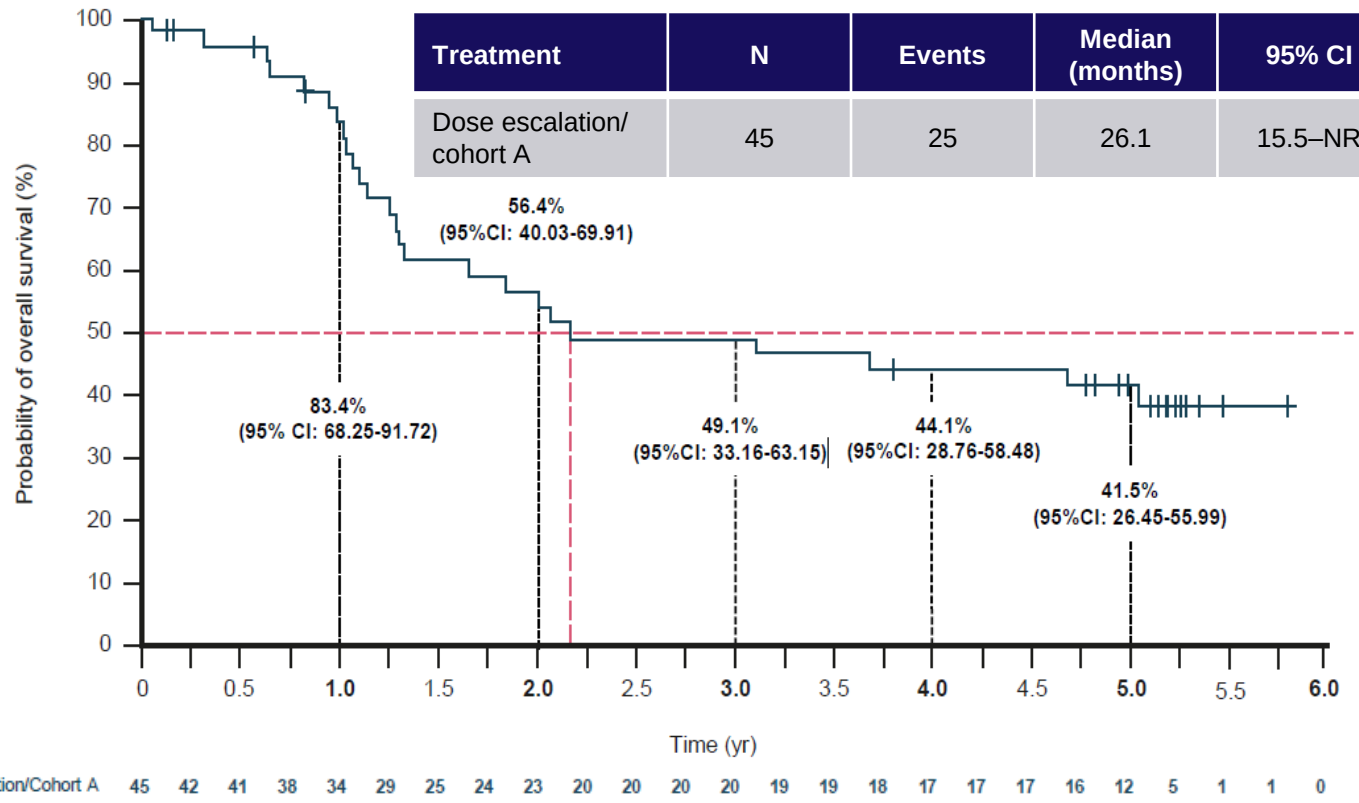
Powles T et al. *N Engl J Med* 2024;390:875–888

EV-103 Cohort A: A 5-year follow-up in Cis-ineligible patients treated with EV+P

- A Phase Ib/II, multicohort study
- Patients with previously untreated LA/mUC receiving EV+P
- The **safety profile** of EV+P **was consistent** with data from previous trials, with no new signals observed

OS update (follow-up at 5 years)

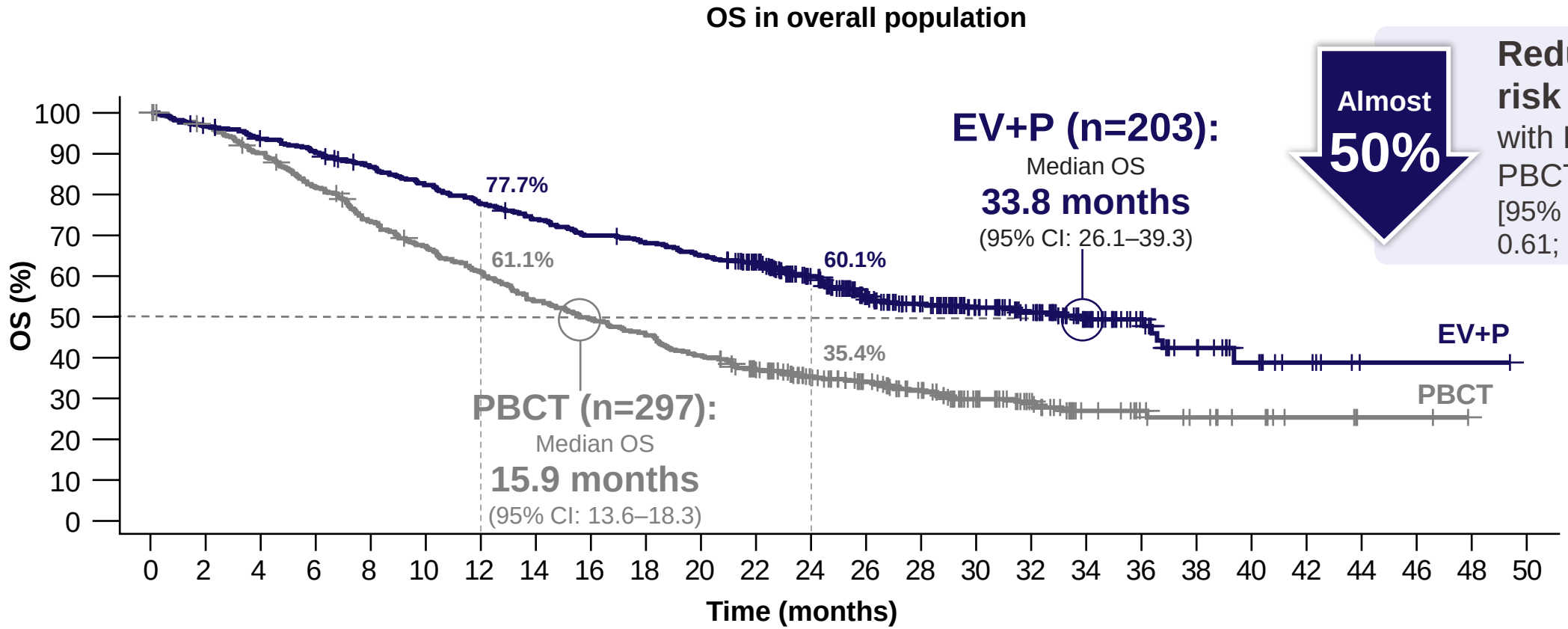
Treatment	N	Events	Median (months)	95% CI
Dose escalation/ cohort A	45	25	26.1	15.5–NR



The survival rate at 5 years was estimated to be **41.5% for patients treated with EV+P,** which exceeds historical data from the Phase II/III EORTC 30986 study

*Results by investigator assessment have been previously published.
AE, adverse event; BICR, blinded independent central review; CI, confidence interval; cis, cisplatin; DCR, disease control rate; DOR, duration of response; EORTC, European Organisation for Research and Treatment of Cancer; EV, enfortumab vedotin; LA/mUC, locally advanced/metastatic urothelial carcinoma; NR, not reached; ORR, overall response rate; OS, overall survival; P, pembrolizumab; PFS, progression-free survival; PK, pharmacokinetics; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumours.
Rosenberg JE et al. Presented at ESMO 2024. Abstract 1968P.

After an additional 1-year follow-up, EV+P more than doubled OS vs. PBCT, exceeding the previous data cut-off[1,2]



Almost 50%

Reduction in risk of death with EV+P* vs. PBCT*(HR 0.51 [95% CI: 0.43–0.61; p<0.00001])†

No. at risk

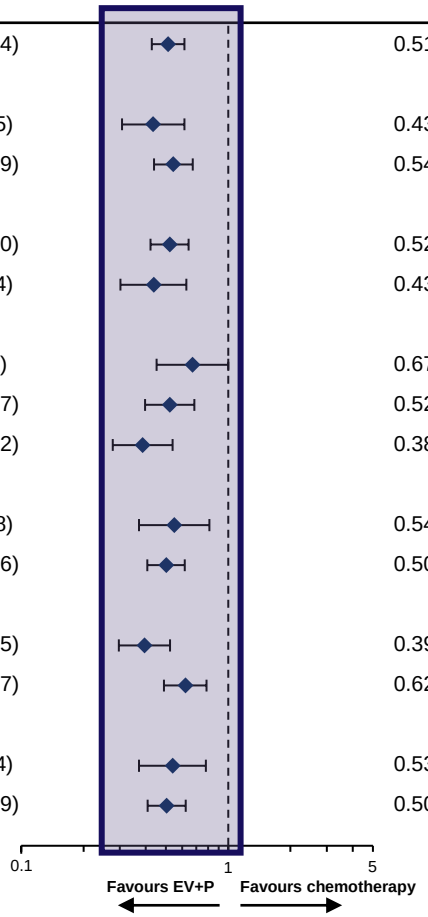
EV+P	442	426	409	394	375	356	336	319	302	293	280	252	206	161	133	102	79	52	32	19	11	6	1	1	1
PBCT	444	423	393	356	317	290	263	233	214	197	176	148	121	102	81	59	43	24	18	13	9	5	2	2	

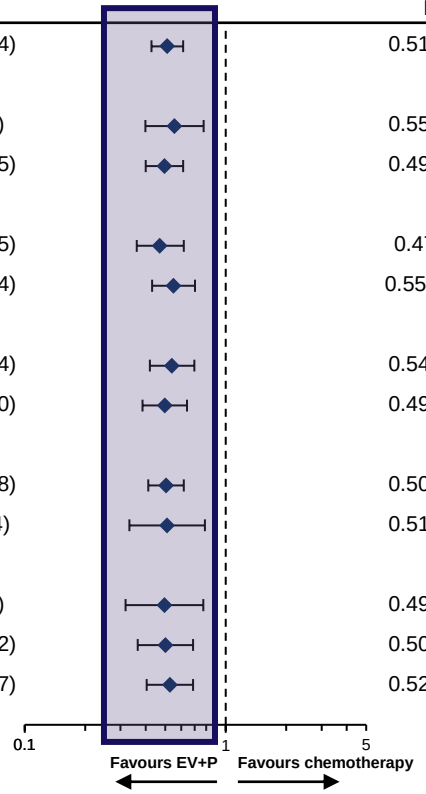
Median follow-up: 21.9 months. Data cut-off: 8 August 2024.
*Events/N were 203/442 for EV+P and 297/444 for PBCT; †P-value is nominal and descriptive.
CI, confidence interval; EV, enfortumab vedotin; HR, hazard ratio; OS, overall survival; P, pembrolizumab; PBCT, platinum-based chemotherapy.
1. Powles T, presented at ASCO GU 2025, Abstract 664; 2. Powles T et al. *Ann Oncol* 2025; https://doi.org/10.1016/j.annonc.2025.05.536.

The OS benefit of EV+P was consistent with that of the overall population regardless of patient subgroup[1,2]

OS in prespecified subgroups

	Median OS, months (event/N)		
	EV+P	PBCT	HR (95% CI)
Overall	33.8 (203/442)	15.9 (297/444)	0.513 (0.428–0.614)
Age			
<65 years	39.3 (59/144)	18.7 (87/135)	0.434 (0.307–0.614)
≥65 years	27.1 (144/298)	14.6 (210/309)	0.544 (0.439–0.674)
Race			
White	26.1 (158/308)	15.1 (207/290)	0.521 (0.422–0.644)
Other	36.3 (45/134)	19.1 (90/154)	0.436 (0.302–0.629)
Region			
North America	25.7 (57/103)	21.0 (54/85)	0.672 (0.451–1.000)
Europe	25.6 (90/172)	14.6 (140/197)	0.522 (0.397–0.687)
Rest of world	NR (56/167)	15.5 (103/162)	0.386 (0.277–0.539)
Sex			
Female	25.4 (46/98)	14.6 (70/108)	0.549 (0.371–0.811)
Male	33.8 (157/344)	16.4 (227/336)	0.501 (0.407–0.617)
ECOG PS			
0	36.5 (77/223)	18.7 (136/215)	0.394 (0.296–0.524)
1-2	22.8 (126/219)	13.3 (160/227)	0.621 (0.490–0.787)
Primary disease site of origin			
Upper tract	36.5 (60/135)	18.3 (63/104)	0.538 (0.371–0.781)
Lower tract	32.9 (142/305)	15.6 (233/339)	0.504 (0.408–0.623)
Liver metastases			
Present	19.1 (68/100)	10.1 (82/99)	0.556 (0.399–0.776)
Absent	39.3 (135/342)	18.3 (215/345)	0.496 (0.400–0.615)
PD-L1 expression			
Low (CPS <10)	31.2 (91/184)	15.1 (136/185)	0.472 (0.36–0.618)
High (CPS ≥10)	36.5 (111/254)	17.1 (158/254)	0.550 (0.431– 0.703)
Cisplatin eligibility			
Eligible	36.7 (101/244)	18.7 (143/234)	0.541 (0.419–0.699)
Ineligible	25.6 (102/198)	12.7 (154/210)	0.498 (0.386–0.642)
Metastatic disease site			
Visceral metastases	25.7 (163/318)	13.5 (235/318)	0.505 (0.412–0.619)
Lymph node only	NR (34/103)	24.4 (54/104)	0.512 (0.332–0.789)
Renal function			
Normal	39.3 (33/84)	18.6 (61/95)	0.496 (0.318–0.773)
Mild	36.5 (69/165)	18.4 (101/162)	0.502 (0.365–0.689)
Moderate/severe	25.6 (101/193)	13.3 (135/187)	0.528 (0.405–0.689)

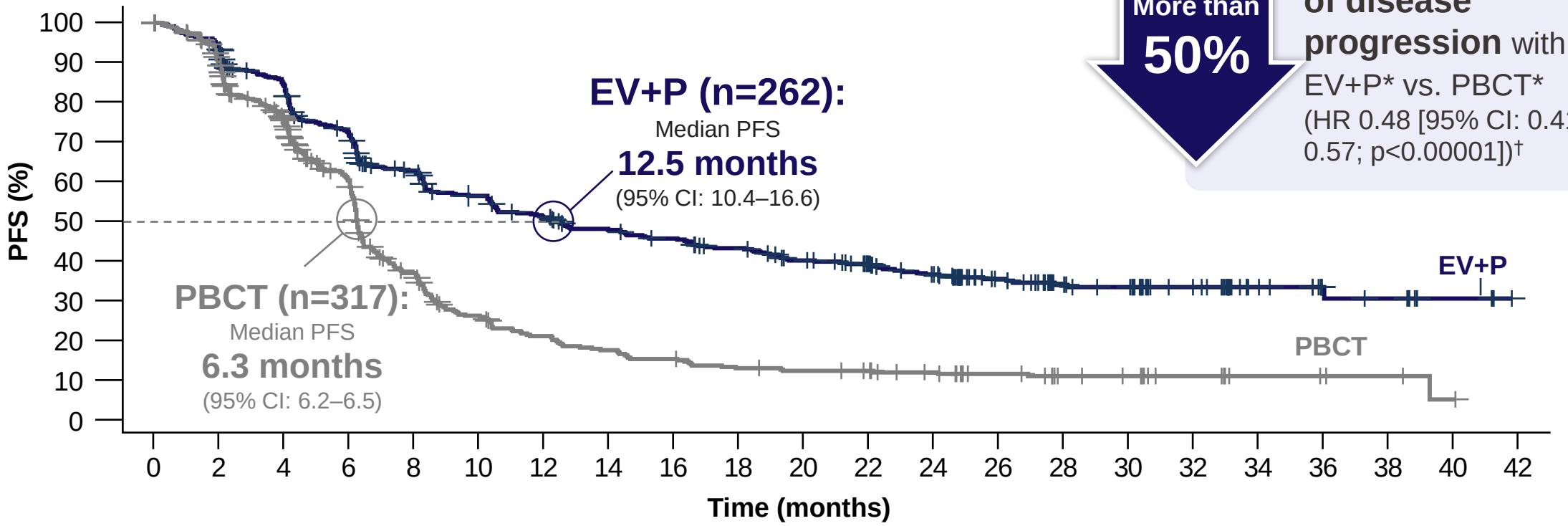




Median follow-up: 29.1 months. Data cut-off: 8 August 2024.
CI, confidence interval; CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EV, enfortumab vedotin; HR, hazard ratio; NE, not estimable; OS, overall survival; P, pembrolizumab; PBCT, platinum-based chemotherapy; PD-L1, programmed death-ligand 1.
1. Powles T, presented at ASCO GU 2025, Abstract 664; 2. Powles T et al. *Ann Oncol* 2025; https://doi.org/10.1016/j.annonc.2025.05.536.

After an additional 1-year follow-up, EV+P almost doubled PFS vs. PBCT[1,2]

PFS in overall population



More than **50%**

Reduction in risk of disease progression with EV+P* vs. PBCT* (HR 0.48 [95% CI: 0.41–0.57; p<0.00001])†

No. at risk

EV+P	442	409	361	304	254	223	200	182	172	159	143	128	109	82	62	57	42	22	14	10	4
PBCT	444	379	296	213	125	86	68	57	50	42	39	37	31	23	16	14	9	5	4	3	1

Data cutoff: 8 August 2024.

*Events/N were 262/442 for EV+P and 317/444 for PBCT; †P-value is nominal and descriptive.

EV, enfortumab vedotin; P, pembrolizumab; PBCT, platinum-based chemotherapy; PFS, progression-free survival.

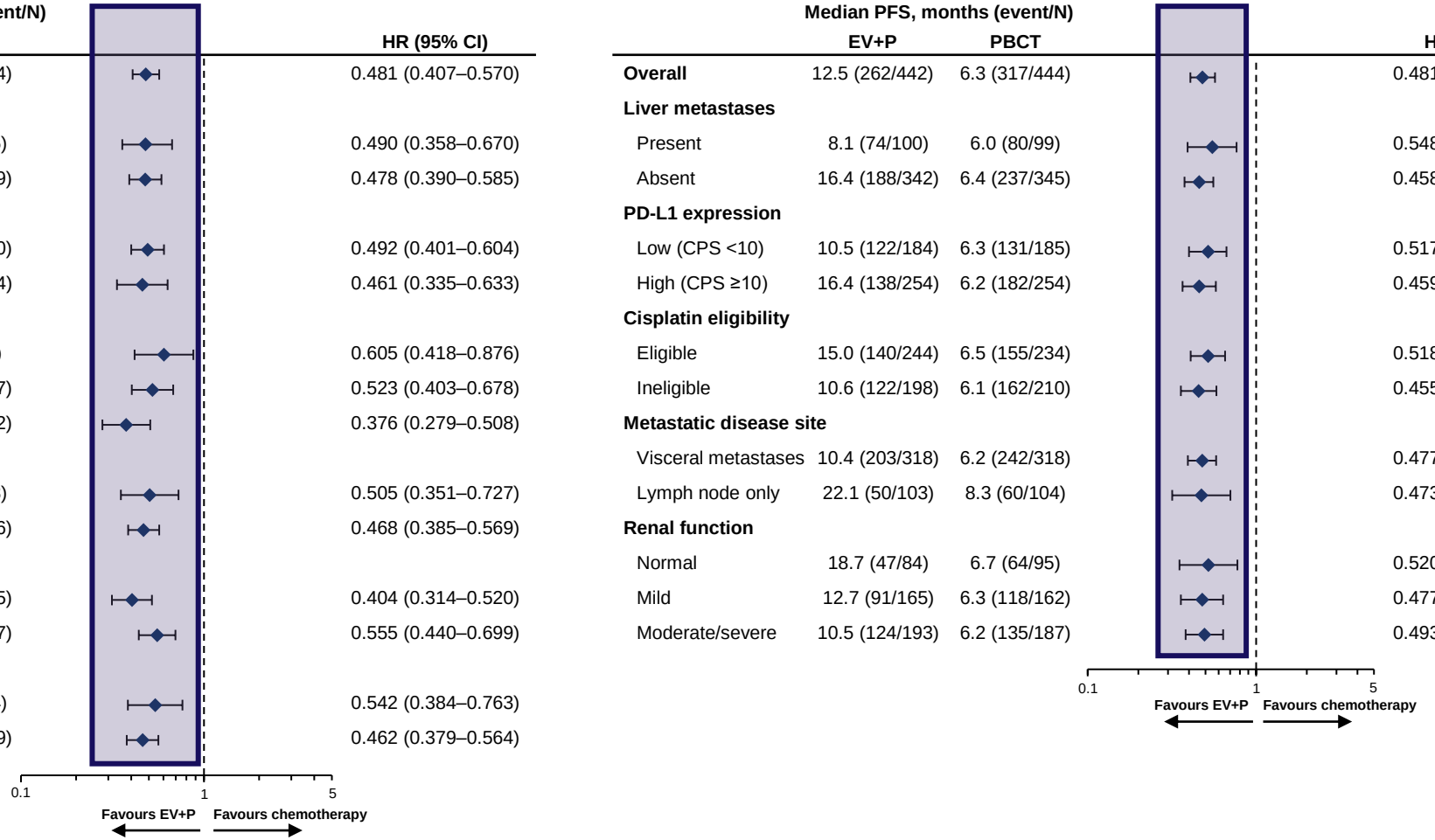
1. Powles T, presented at ASCO GU 2025, Abstract 664; 2. Powles T et al. *Ann Oncol* 2025; https://doi.org/10.1016/j.annonc.2025.05.536.

The PFS benefit of EV+P was consistent with that of the overall population regardless of patient subgroup[1,2]

PFS by BICR in prespecified subgroups

	Median PFS, months (event/N) EV+P	PBCT	HR (95% CI)
Overall	12.5 (262/442)	6.3 (317/444)	0.481 (0.407–0.570)
Age			
<65 years	14.6 (87/144)	6.4 (90/135)	0.490 (0.358–0.670)
≥65 years	12.3 (175/298)	6.2 (227/309)	0.478 (0.390–0.585)
Race			
White	10.5 (191/308)	6.2 (214/290)	0.492 (0.401–0.604)
Other	19.2 (71/134)	6.5 (103/154)	0.461 (0.335–0.633)
Region			
North America	10.3 (72/103)	6.3 (57/85)	0.605 (0.418–0.876)
Europe	10.4 (102/172)	6.3 (149/197)	0.523 (0.403–0.678)
Rest of world	19.3 (88/167)	6.2 (111/162)	0.376 (0.279–0.508)
Sex			
Female	10.4 (59/98)	6.1 (75/108)	0.505 (0.351–0.727)
Male	14.0 (203/344)	6.3 (242/336)	0.468 (0.385–0.569)
ECOG PS			
0	17.3 (121/223)	6.7 (151/215)	0.404 (0.314–0.520)
1-2	9.3 (141/219)	6.1 (166/227)	0.555 (0.440–0.699)
Primary disease site of origin			
Upper tract	12.3 (81/135)	6.2 (70/104)	0.542 (0.384–0.763)
Lower tract	12.8 (179/305)	6.3 (246/339)	0.462 (0.379–0.564)

	Median PFS, months (event/N) EV+P	PBCT	HR (95% CI)
Overall	12.5 (262/442)	6.3 (317/444)	0.481 (0.407–0.570)
Liver metastases			
Present	8.1 (74/100)	6.0 (80/99)	0.548 (0.392–0.766)
Absent	16.4 (188/342)	6.4 (237/345)	0.458 (0.376–0.557)
PD-L1 expression			
Low (CPS <10)	10.5 (122/184)	6.3 (131/185)	0.517 (0.400–0.667)
High (CPS ≥10)	16.4 (138/254)	6.2 (182/254)	0.459 (0.365–0.576)
Cisplatin eligibility			
Eligible	15.0 (140/244)	6.5 (155/234)	0.518 (0.409–0.655)
Ineligible	10.6 (122/198)	6.1 (162/210)	0.455 (0.357–0.580)
Metastatic disease site			
Visceral metastases	10.4 (203/318)	6.2 (242/318)	0.477 (0.393–0.579)
Lymph node only	22.1 (50/103)	8.3 (60/104)	0.473 (0.317–0.704)
Renal function			
Normal	18.7 (47/84)	6.7 (64/95)	0.520 (0.350–0.774)
Mild	12.7 (91/165)	6.3 (118/162)	0.477 (0.358–0.636)
Moderate/severe	10.5 (124/193)	6.2 (135/187)	0.493 (0.381–0.637)



Data cutoff: 8 August 2024.

BICR, blinded independent central review; CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; EV, enfortumab vedotin; HR, hazard ratio; P, pembrolizumab; PD-L1, programmed death ligand 1; PFS, progression-free survival

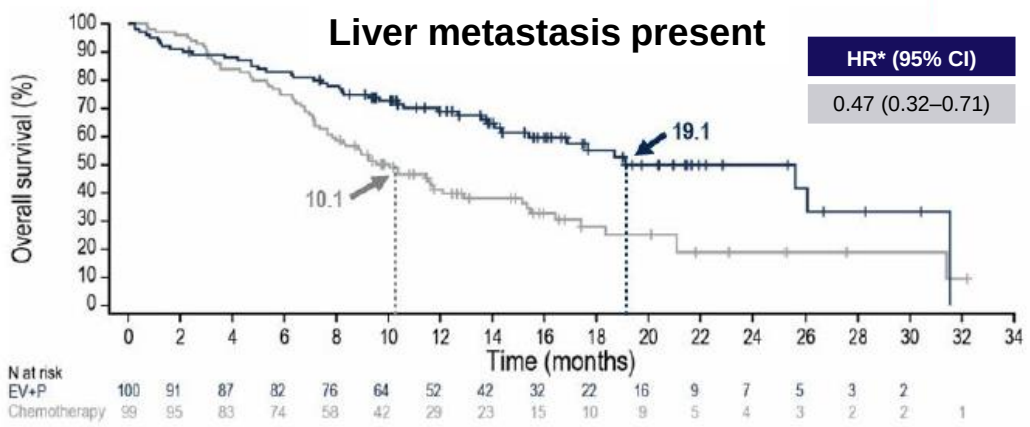
1. Powles T, presented at ASCO GU 2025, Abstract 664; 2. Powles T et al. *Ann Oncol* 2025; https://doi.org/10.1016/j.annonc.2025.05.536.

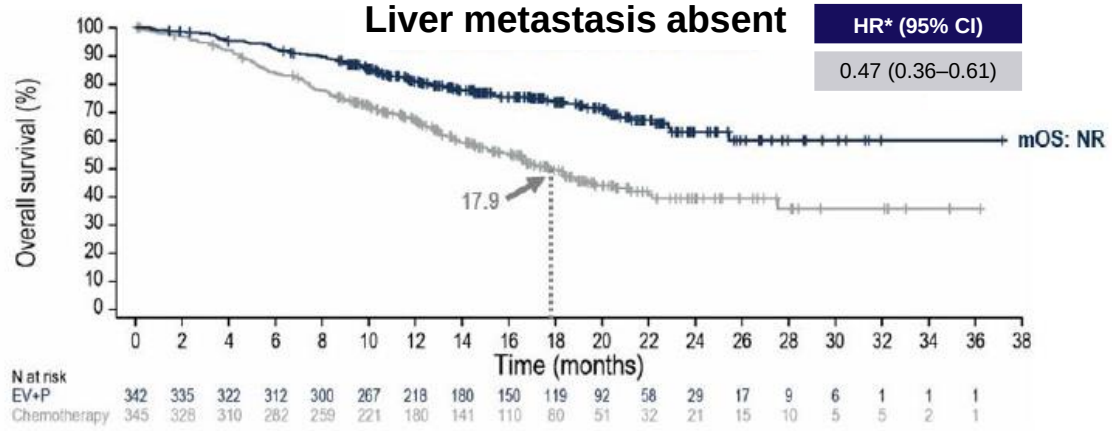
Genitourinary Masterclass

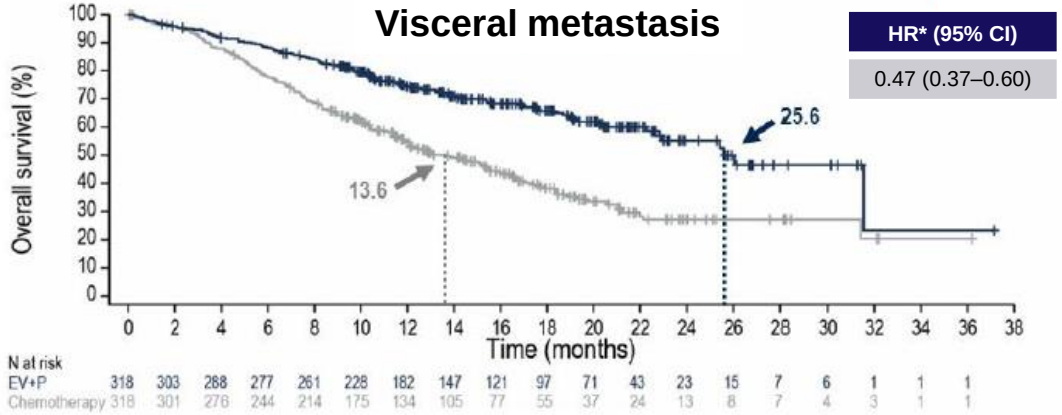
Key subgroup analyses

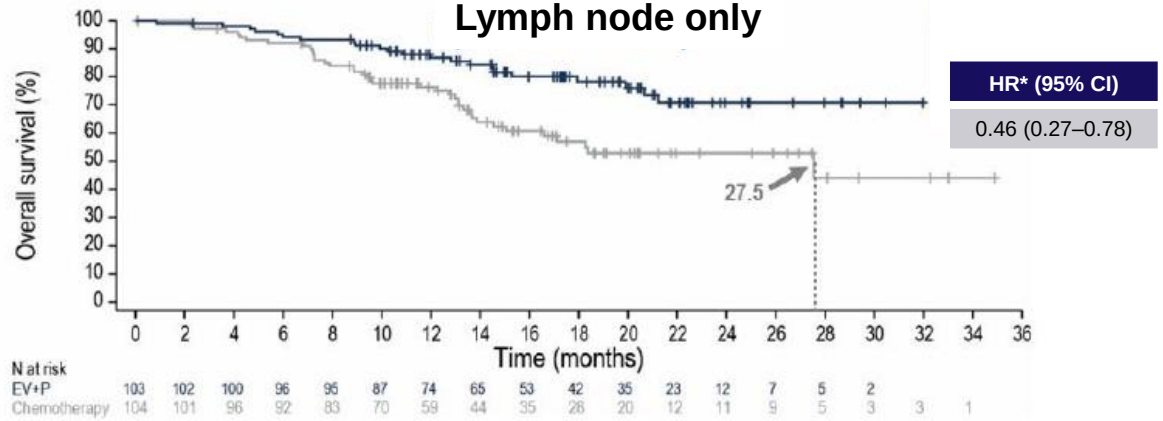
OS benefit was consistent with the overall population regardless of the presence or absence of liver or visceral metastases

Subgroup analysis of EV-302 primary readout





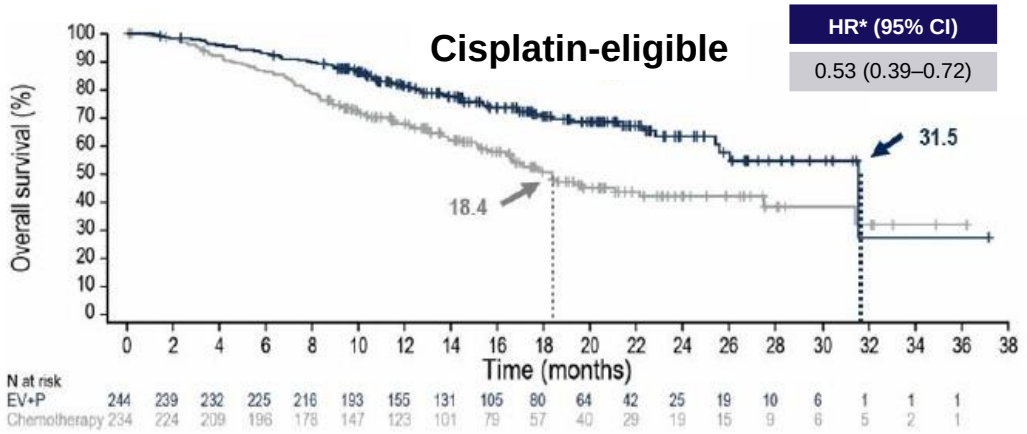


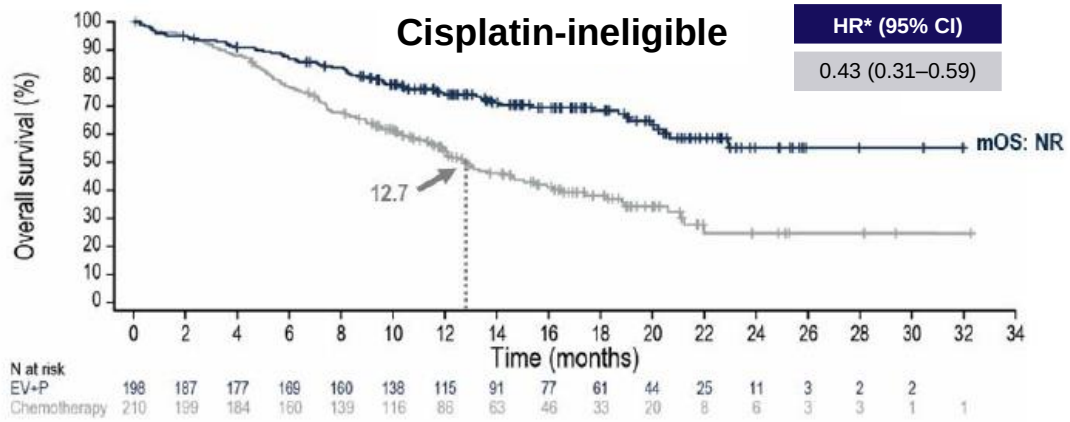


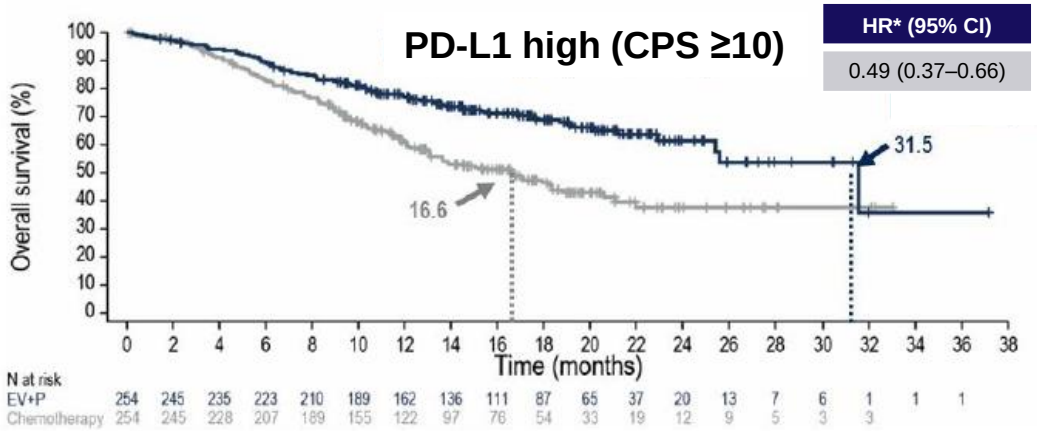
Data cutoff: 8 August 2023.
*Calculated using stratified Cox proportional hazards model. A hazard ratio <1 favours the EV+P arm.
CI, confidence interval; EV, enfortumab vedotin; HR, hazard ratio; mOS, median OS; NR, not reached; OS, overall survival; P, pembrolizumab.
Van der Heijden MS et al. presented at ASCO GU 2024. LBA530.

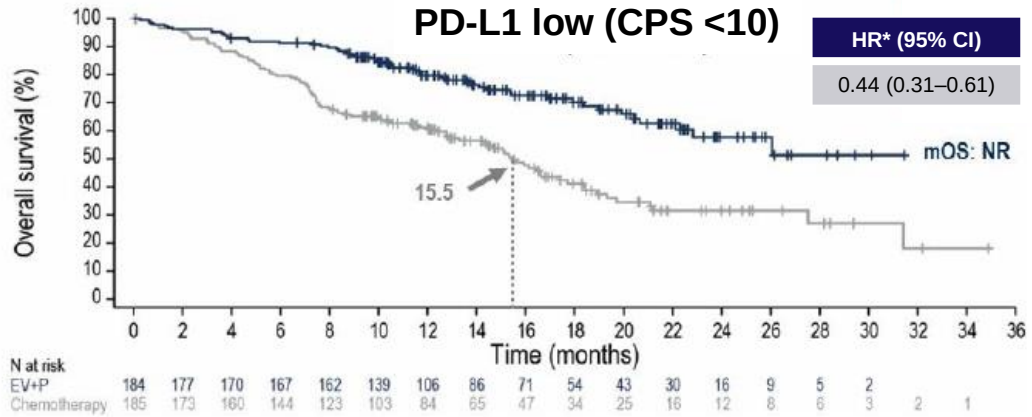
OS benefit was consistent with the overall population regardless of the cisplatin eligibility or PD-L1 expression status

Subgroup analysis of EV-302 primary readout







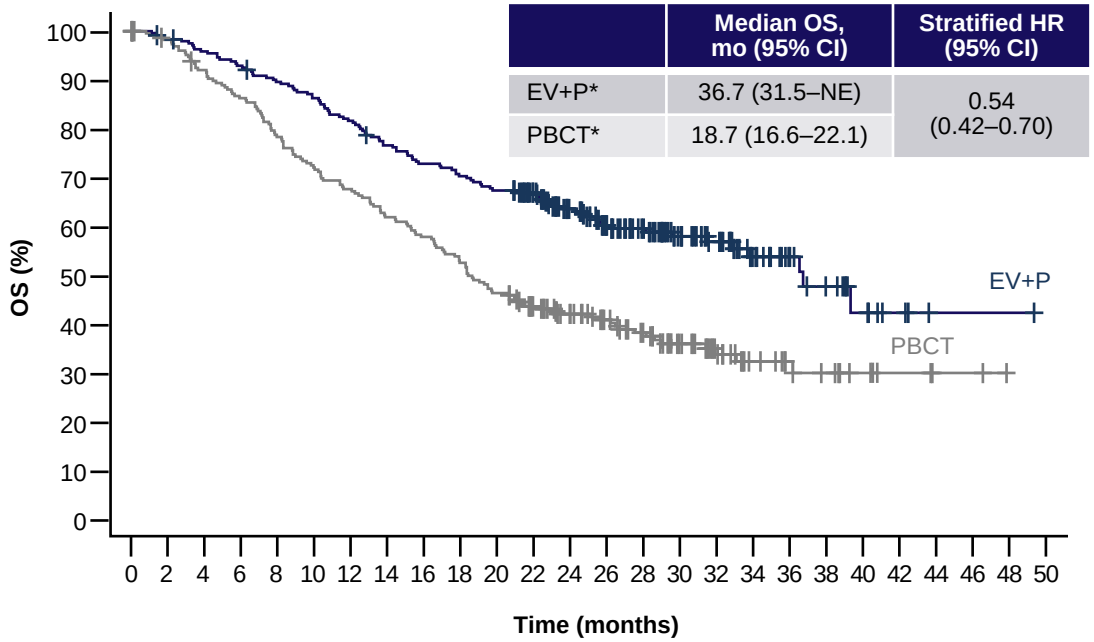


Data cutoff: 8 August 2023.
*Calculated using stratified Cox proportional hazards model. A hazard ratio <1 favours the EV+P arm.
CI, confidence interval; CPS, combined positive score; EV, enfortumab vedotin; HR, hazard ratio; mOS, median overall survival; NR, not reached; OS, overall survival; P, pembrolizumab; PD-L1, programmed cell death ligand 1.
Van der Heijden MS et al. presented at ASCO GU 2024. LBA530.

With longer treatment, OS benefit of EV+P remained consistent with the overall population regardless of cisplatin eligibility

Subgroup analysis of EV-302 updated analysis

Cisplatin-eligible

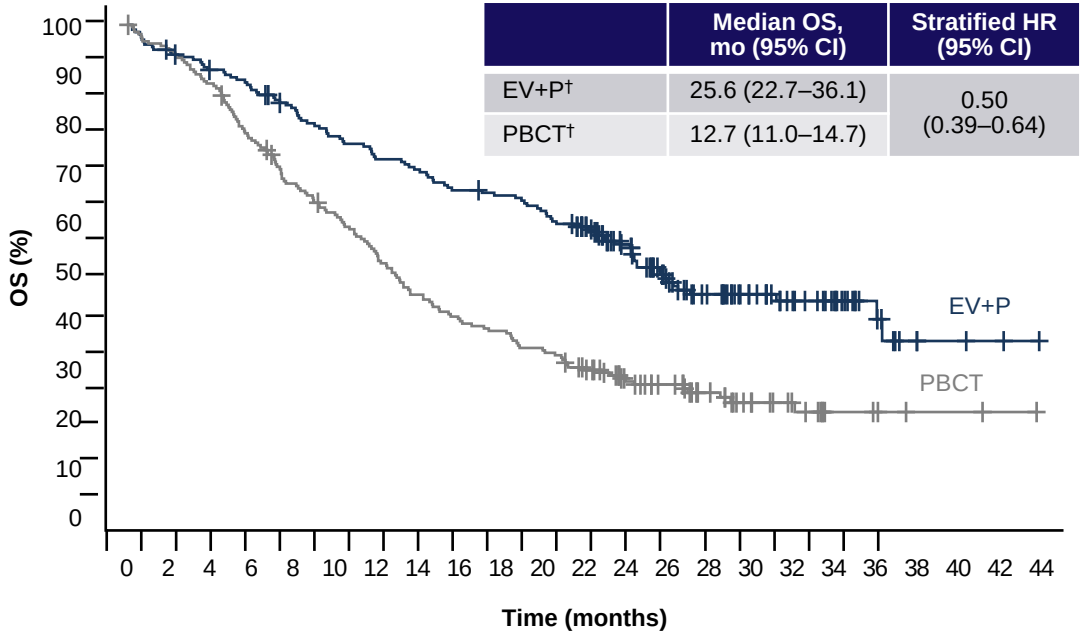


	Median OS, mo (95% CI)	Stratified HR (95% CI)
EV+P*	36.7 (31.5–NE)	0.54 (0.42–0.70)
PBCT*	18.7 (16.6–22.1)	

No. at risk

EV+P	244	239	232	225	216	208	197	184	175	169	162	147	121	98	83	64	50	30	20	14	8	4	1	1	1
PBCT	234	224	209	196	178	164	154	141	132	120	106	90	77	65	54	41	30	19	14	11	7	4	2	2	

Cisplatin-ineligible



	Median OS, mo (95% CI)	Stratified HR (95% CI)
EV+P†	25.6 (22.7–36.1)	0.50 (0.39–0.64)
PBCT†	12.7 (11.0–14.7)	

No. at risk

EV+P	198	187	177	169	159	148	139	135	127	124	118	105	85	63	50	38	29	22	12	5	3	2	
PBCT	210	199	184	160	139	126	109	92	82	77	70	58	44	37	27	18	13	5	4	2	2	1	

Data cutoff: 8 August 2024.

*Events/N in the cisplatin-eligible population were 101/244 for EV+P and 143/234 for PBCT; †Events/N in the cisplatin-ineligible population were 102/198 for EV+P and 154/210 for PBCT.

CI, confidence interval; EV, enfortumab vedotin; HR, hazard ratio; mo, month; NE, not estimable; OS, overall survival; P, pembrolizumab; PBCT, platinum-based chemotherapy.

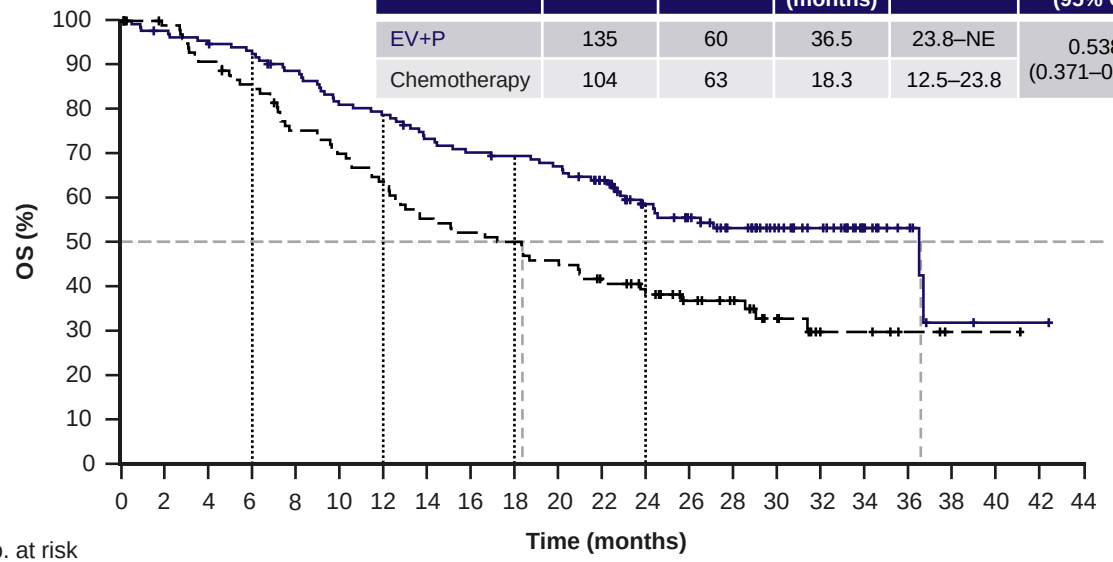
1. Powles T et al. presented at ASCO GU 2025. Abstract 664; 2. Powles T et al. *Ann Oncol* 2025; https://doi.org/10.1016/j.annonc.2025.05.536.

OS continued to demonstrate sustained benefit of EV+P vs. PBCT across prespecified subgroups with longer treatment

Subgroup analysis of EV-302 updated analysis

Primary disease site of origin in the upper tract

	N	Events	Median (months)	95% CI	Hazard ratio (95% CI)
EV+P	135	60	36.5	23.8–NE	0.538 (0.371–0.781)
Chemotherapy	104	63	18.3	12.5–23.8	

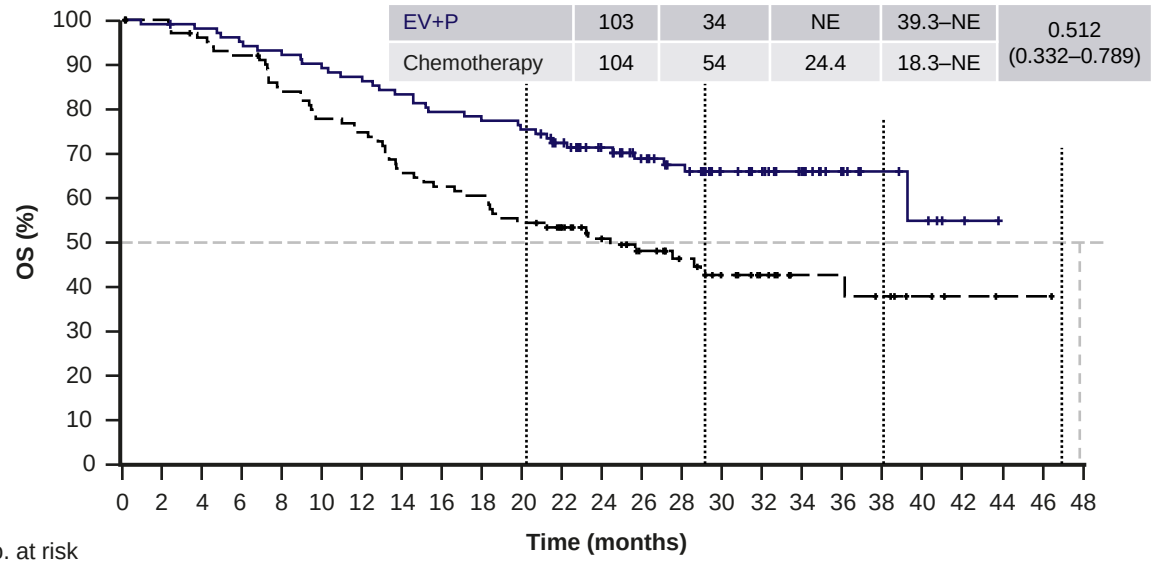


No. at risk

EV+P	135	131	126	123	116	106	103	95	91	89	86	77	57	50	41	32	25	13	7	2	1	1	0
Chemotherapy	104	97	89	83	72	67	61	53	50	48	44	37	32	25	21	13	7	6	3	1	1	0	0

LN-only metastases

	N	Events	Median (months)	95% CI	Hazard ratio (95% CI)
EV+P	103	34	NE	39.3–NE	0.512 (0.332–0.789)
Chemotherapy	104	54	24.4	18.3–NE	



No. at risk

EV+P	103	102	100	96	94	91	88	85	81	79	77	70	61	52	46	34	30	21	13	7	5	2	0	0	0
Chemotherapy	104	101	96	92	83	77	74	65	62	60	54	47	39	32	26	20	15	9	9	7	4	2	1	1	0

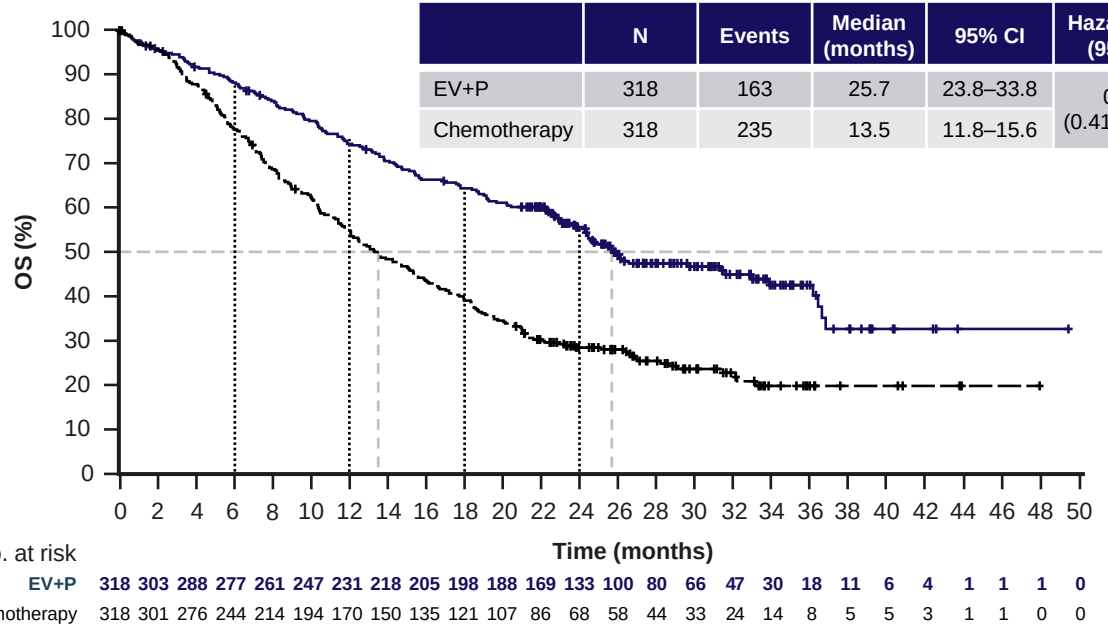
Data cutoff: 8 August 2024.
CI, confidence interval; EV, enfortumab vedotin; HR, hazard ratio; LN, lymph node; NE, not estimable; OS, overall survival; P, pembrolizumab; PBCT, platinum-based chemotherapy.
Bedke J et al. Presented at ASCO 2025. #4571.

OS continued to demonstrate sustained benefit of EV+P vs. PBCT across prespecified subgroups with longer treatment

Subgroup analysis of EV-302 updated analysis

Presence of visceral metastases

	N	Events	Median (months)	95% CI	Hazard ratio (95% CI)
EV+P	318	163	25.7	23.8–33.8	0.505 (0.412–0.619)
Chemotherapy	318	235	13.5	11.8–15.6	

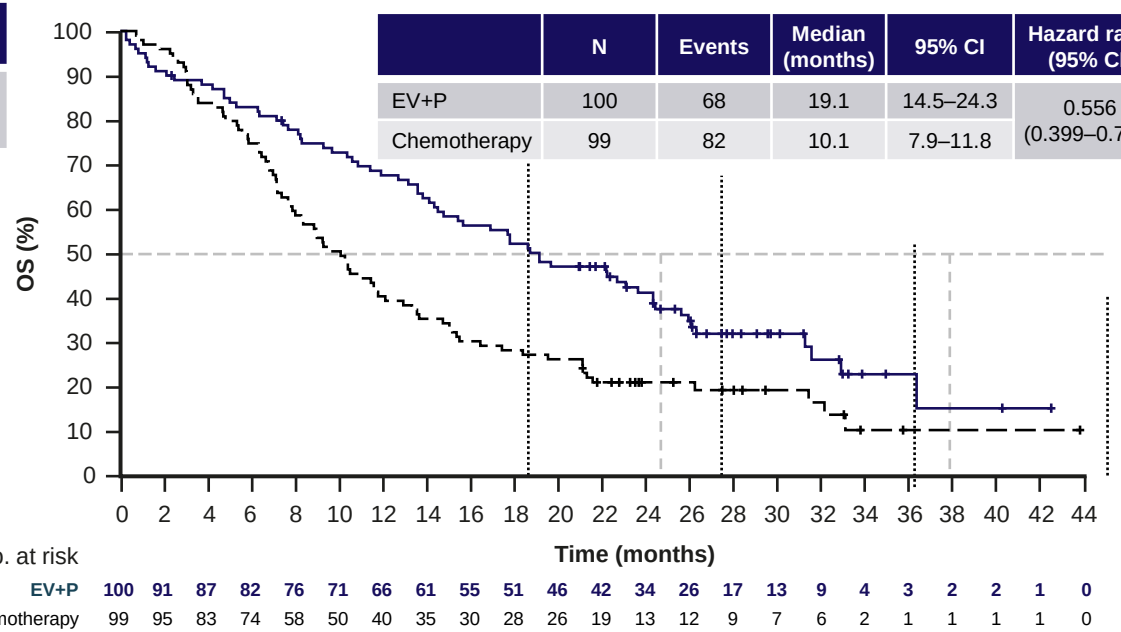


No. at risk

EV+P	318	303	288	277	261	247	231	218	205	198	188	169	133	100	80	66	47	30	18	11	6	4	1	1	1	0
Chemotherapy	318	301	276	244	214	194	170	150	135	121	107	86	68	58	44	33	24	14	8	5	5	3	1	1	0	0

Presence of liver metastases

	N	Events	Median (months)	95% CI	Hazard ratio (95% CI)
EV+P	100	68	19.1	14.5–24.3	0.556 (0.399–0.776)
Chemotherapy	99	82	10.1	7.9–11.8	



No. at risk

EV+P	100	91	87	82	76	71	66	61	55	51	46	42	34	26	17	13	9	4	3	2	2	1	0
Chemotherapy	99	95	83	74	58	50	40	35	30	28	26	19	13	12	9	7	6	2	1	1	1	1	0

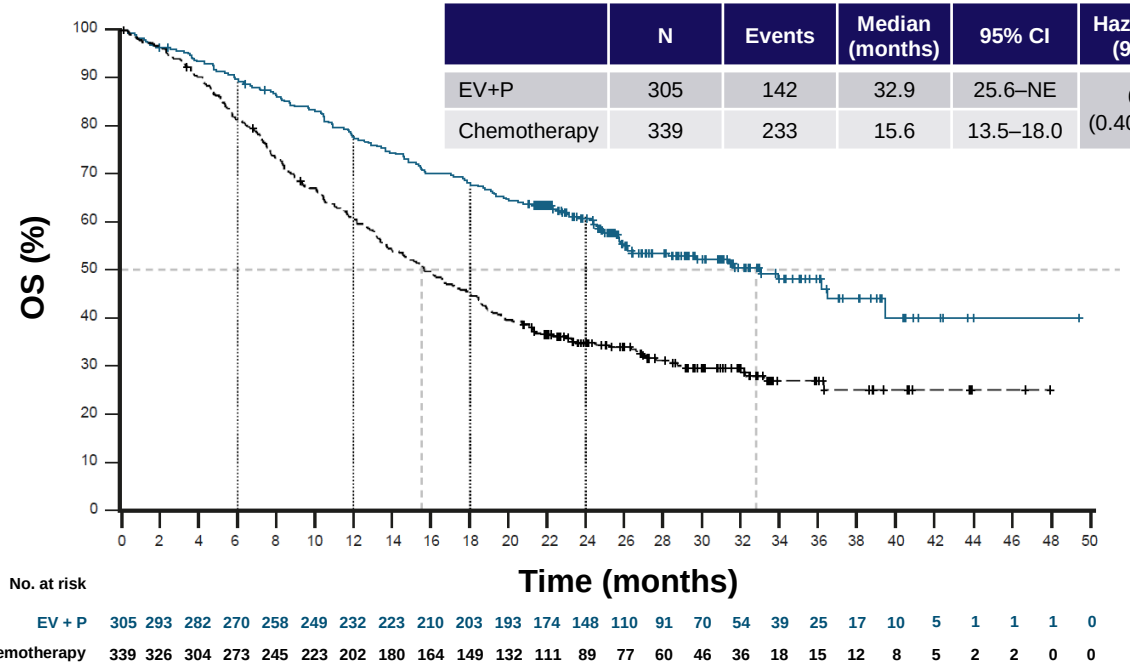
Data cutoff: 8 August 2024.
CI, confidence interval; EV, enfortumab vedotin; OS, overall survival; P, pembrolizumab; PBCT, platinum-based chemotherapy.
Bedke J et al. Presented at ASCO 2025. #4571.

OS continued to demonstrate sustained benefit of EV+P vs. PBCT across prespecified subgroups with longer treatment

Subgroup analysis of EV-302 updated analysis

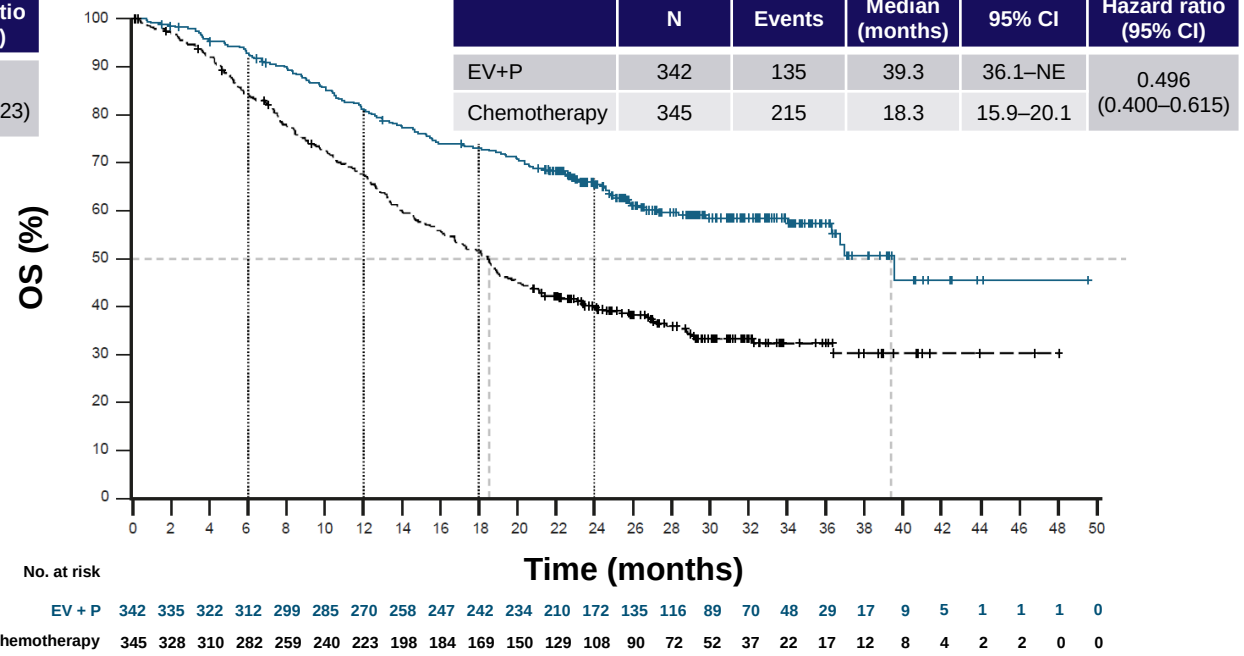
Primary disease site of origin in the lower tract*

	N	Events	Median (months)	95% CI	Hazard ratio (95% CI)
EV+P	305	142	32.9	25.6–NE	0.504 (0.408–0.623)
Chemotherapy	339	233	15.6	13.5–18.0	



Absence of liver metastases*

	N	Events	Median (months)	95% CI	Hazard ratio (95% CI)
EV+P	342	135	39.3	36.1–NE	0.496 (0.400–0.615)
Chemotherapy	345	215	18.3	15.9–20.1	



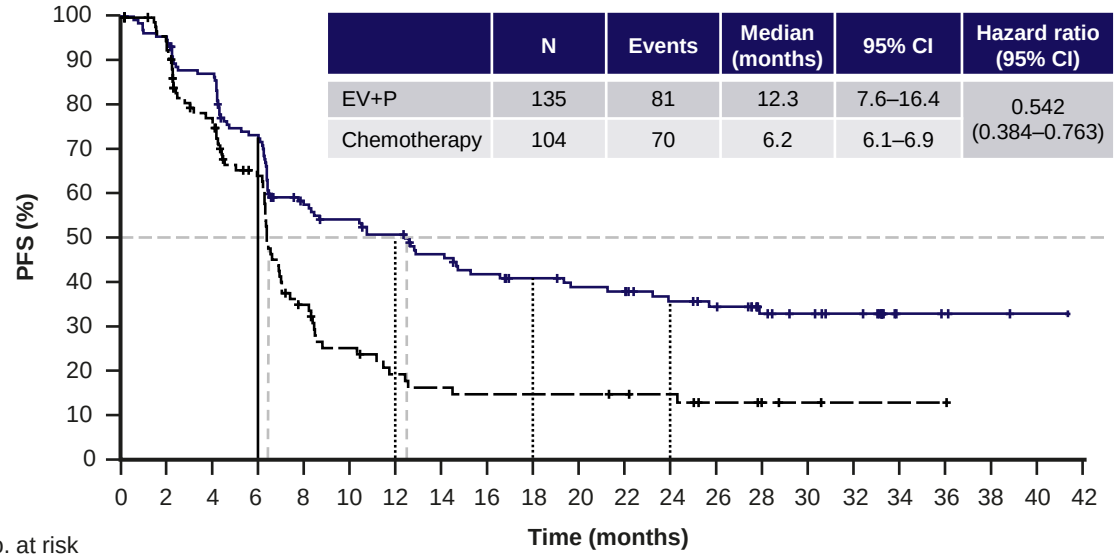
Data cutoff: 8 August 2024.
*Censored observations are indicated by a “+” symbol.
CI, confidence interval; EV, enfortumab vedotin; OS, overall survival; P, pembrolizumab; PBCT, platinum-based chemotherapy.
Bedke J et al. Presented at ASCO 2025. #4571.

PFS continued to demonstrate sustained benefit of EV+P vs. PBCT across prespecified subgroups with longer treatment

Subgroup analysis of EV-302 updated analysis

Primary disease site of origin in the upper tract

	N	Events	Median (months)	95% CI	Hazard ratio (95% CI)
EV+P	135	81	12.3	7.6–16.4	0.542 (0.384–0.763)
Chemotherapy	104	70	6.2	6.1–6.9	

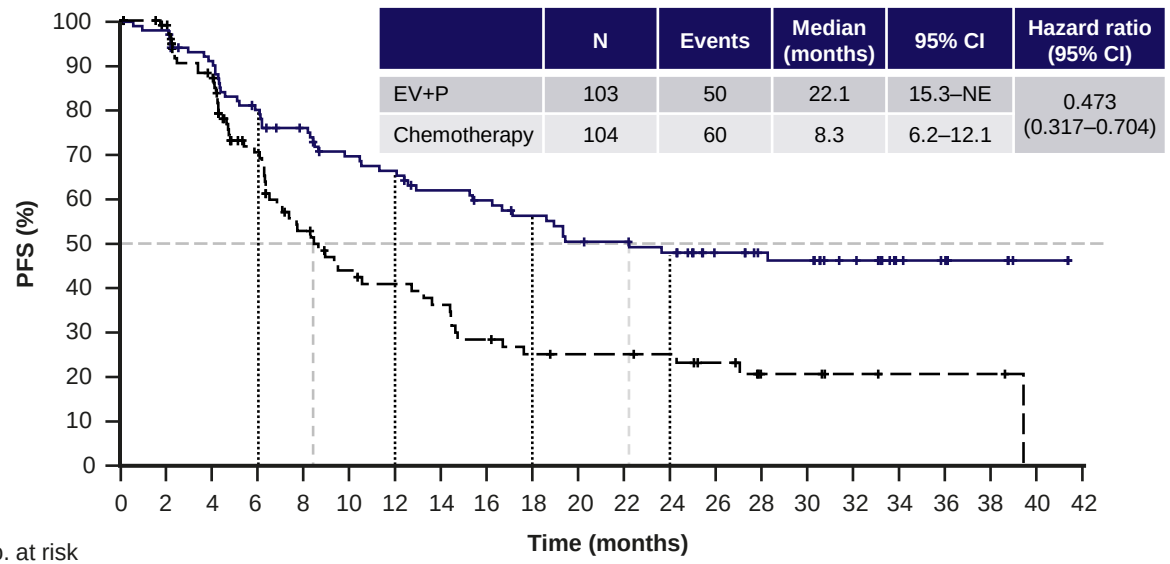


No. at risk

EV+P	135	124	112	92	69	64	59	51	46	42	39	36	32	28	21	18	15	4	3	2	1	0
Chemotherapy	104	86	65	51	26	18	13	11	10	10	10	9	8	5	3	2	1	1	0	0	0	0

LN-only metastases

	N	Events	Median (months)	95% CI	Hazard ratio (95% CI)
EV+P	103	50	22.1	15.3–NE	0.473 (0.317–0.704)
Chemotherapy	104	60	8.3	6.2–12.1	



No. at risk

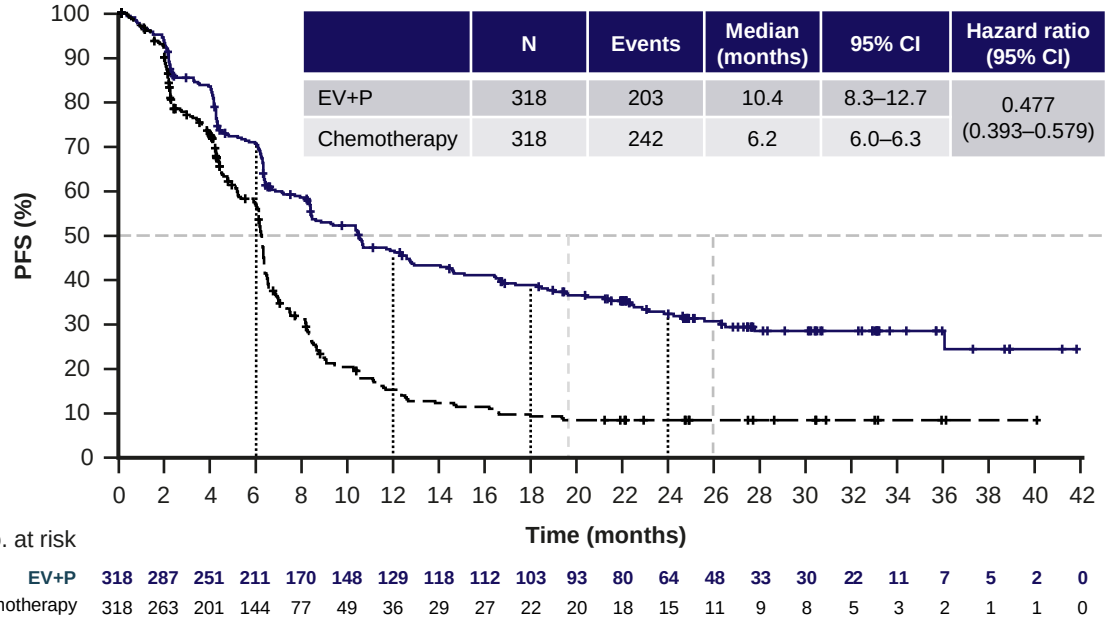
EV+P	103	101	90	78	72	64	60	55	52	48	43	42	39	31	27	26	20	11	7	5	2	0
Chemotherapy	104	95	76	52	37	29	26	23	18	15	14	14	13	10	5	5	3	2	2	2	0	0

Data cutoff: 8 August 2024.
CI, confidence interval; EV, enfortumab vedotin; LN, lymph node; NE, not estimable; P, pembrolizumab; PBCT, platinum-based chemotherapy; PFS, progression-free survival.
Bedke J et al. Presented at ASCO 2025. #4571.

PFS continued to demonstrate sustained benefit of EV+P vs. PBCT across prespecified subgroups with longer treatment

Subgroup analysis of EV-302 updated analysis

Presence of visceral metastases

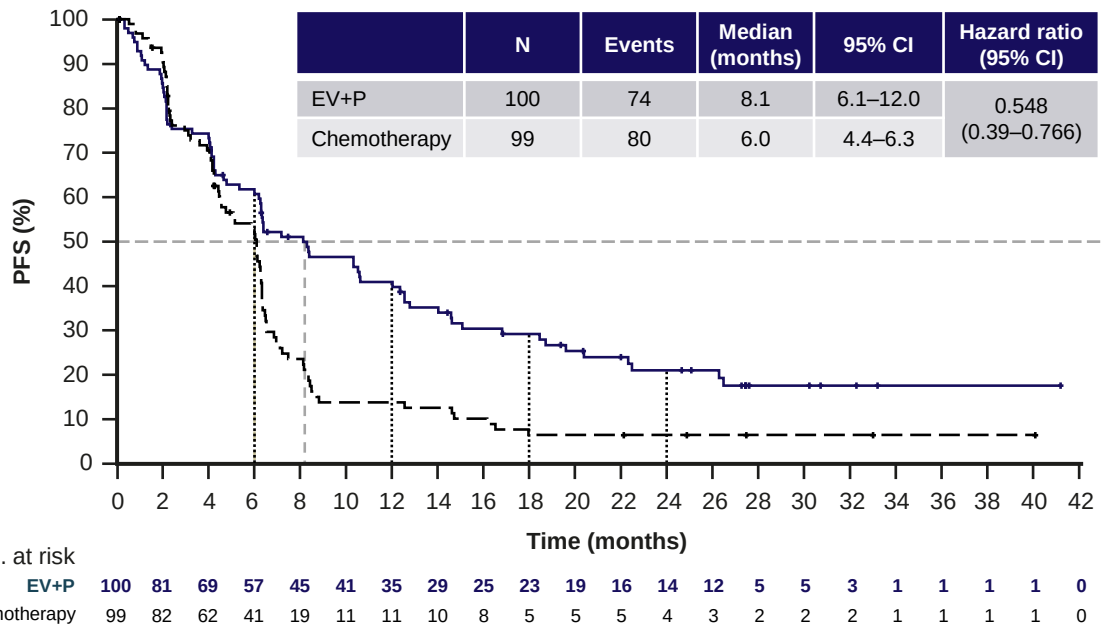


	N	Events	Median (months)	95% CI	Hazard ratio (95% CI)
EV+P	318	203	10.4	8.3–12.7	0.477 (0.393–0.579)
Chemotherapy	318	242	6.2	6.0–6.3	

No. at risk

EV+P	318	287	251	211	170	148	129	118	112	103	93	80	64	48	33	30	22	11	7	5	2	0
Chemotherapy	318	263	201	144	77	49	36	29	27	22	20	18	15	11	9	8	5	3	2	1	1	0

Presence of liver metastases



	N	Events	Median (months)	95% CI	Hazard ratio (95% CI)
EV+P	100	74	8.1	6.1–12.0	0.548 (0.39–0.766)
Chemotherapy	99	80	6.0	4.4–6.3	

No. at risk

EV+P	100	81	69	57	45	41	35	29	25	23	19	16	14	12	5	5	3	1	1	1	1	0
Chemotherapy	99	82	62	41	19	11	11	10	8	5	5	5	4	3	2	2	2	1	1	1	1	0

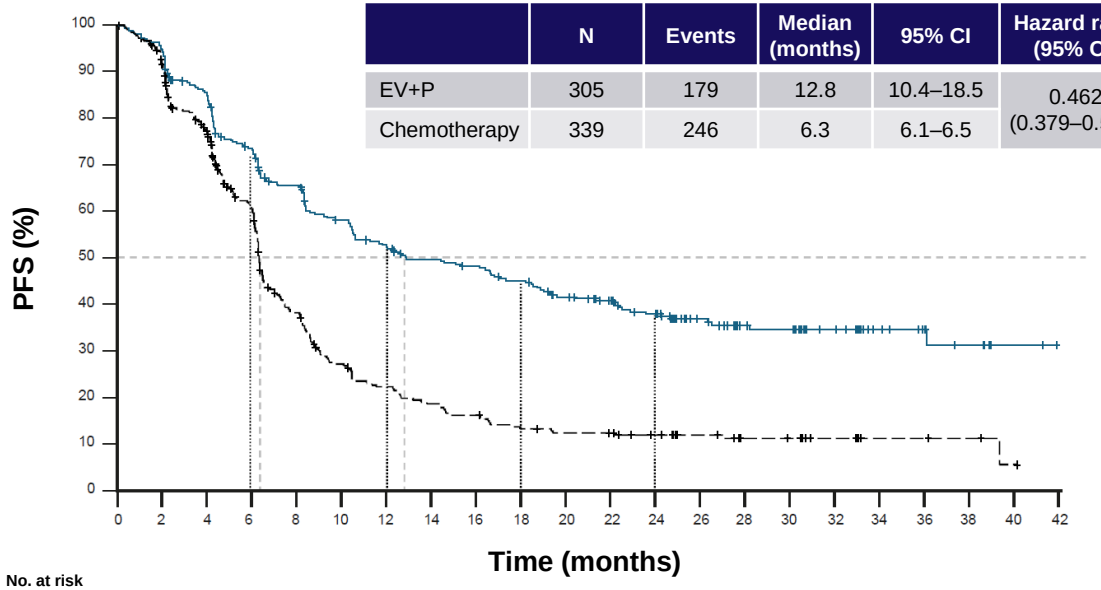
Data cutoff: 8 August 2024.
CI, confidence interval; EV, enfortumab vedotin; P, pembrolizumab; PBCT, platinum-based chemotherapy; PFS, progression-free survival.
Bedke J et al. Presented at ASCO 2025. #4571.

PFS continued to demonstrate sustained benefit of EV+P vs. PBCT across prespecified subgroups with longer treatment

Subgroup analysis of EV-302 updated analysis

Primary disease site of origin in the lower tract

	N	Events	Median (months)	95% CI	Hazard ratio (95% CI)
EV+P	305	179	12.8	10.4–18.5	0.462 (0.379–0.564)
Chemotherapy	339	246	6.3	6.1–6.5	

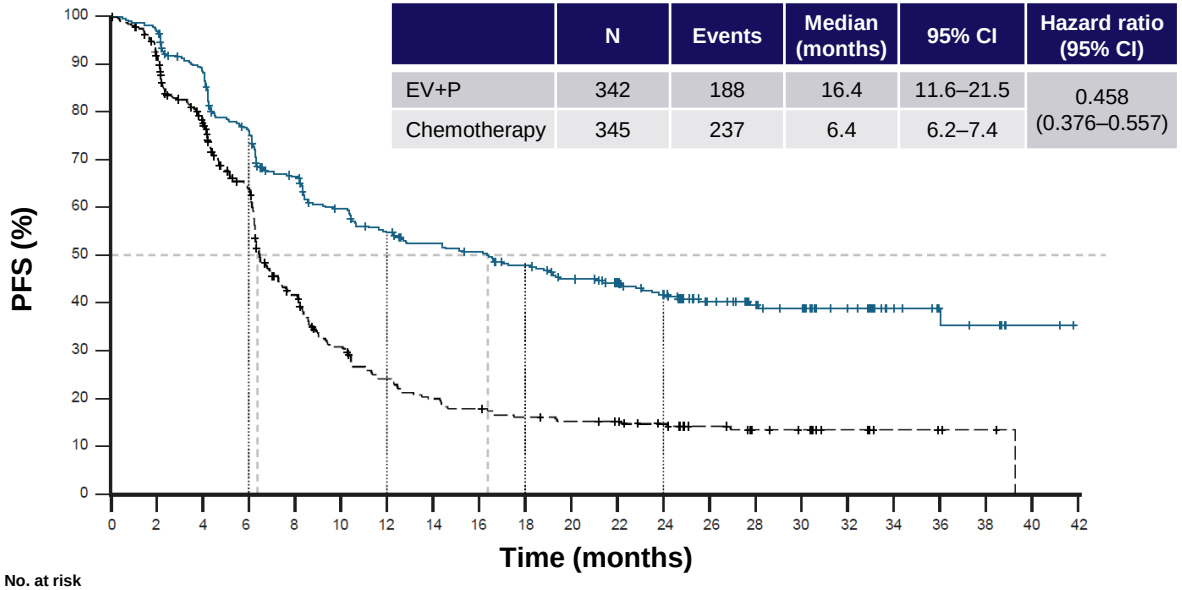


No. at risk

EV + P	305	283	248	211	184	159	141	131	126	117	104	92	77	54	41	39	27	18	11	8	3	0
Chemotherapy	339	293	231	162	99	68	55	46	40	32	29	28	23	18	13	12	8	4	4	3	1	0

Absence of liver metastases

	N	Events	Median (months)	95% CI	Hazard ratio (95% CI)
EV+P	342	188	16.4	11.6–21.5	0.458 (0.376–0.557)
Chemotherapy	345	237	6.4	6.2–7.4	



No. at risk

EV + P	342	328	292	247	209	182	165	153	147	136	124	112	95	70	57	52	39	21	13	9	3	0
Chemotherapy	345	297	234	172	106	75	57	47	42	37	34	32	27	20	14	12	7	4	3	2	0	0

Data cutoff: 8 August 2024.
CI, confidence interval; EV, enfortumab vedotin; P, pembrolizumab; PBCT, platinum-based chemotherapy; PFS, progression-free survival.
Bedke J et al. Presented at ASCO 2025. #4571.

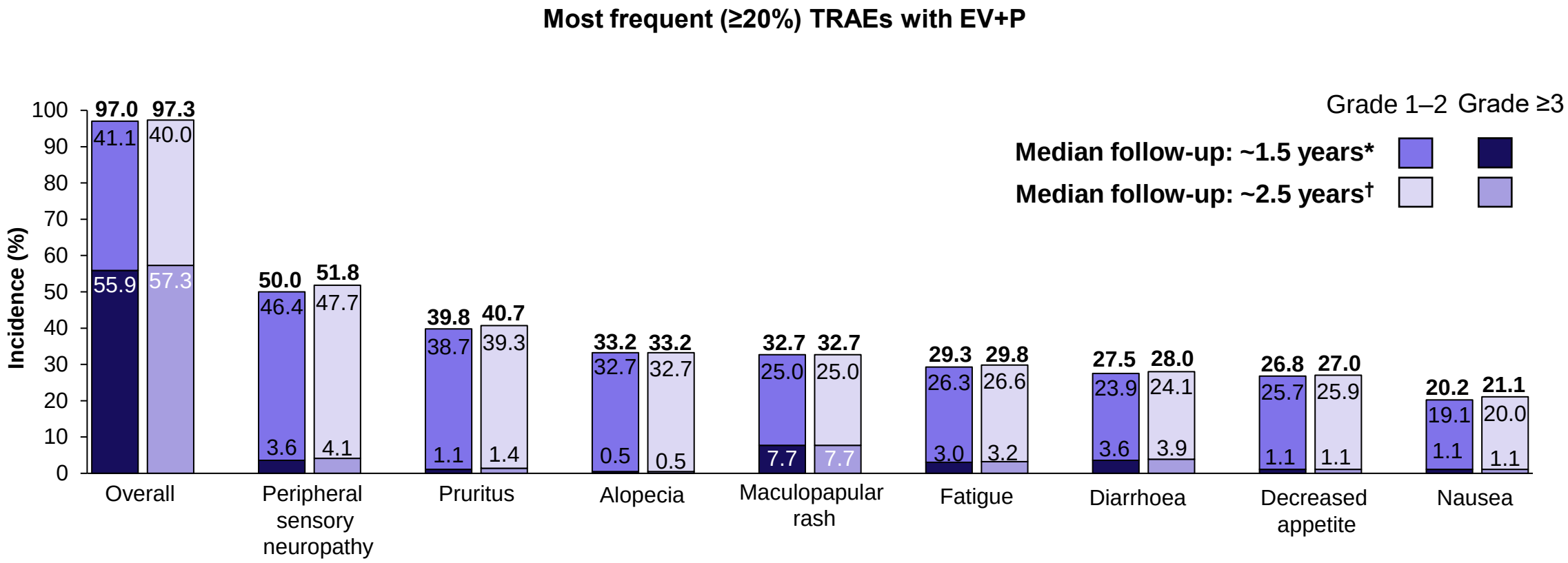
In the EV+P arm, treatment-related AESIs for EV were primarily Grade <3

Subgroup analysis of EV-302 updated analysis

Event	Upper tract (n=135)		Lower tract (n=303)		LN-only mets (n=103)		Visceral mets present (n=316)		Liver mets present (n=99)		Liver mets absent (n=341)	
	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
Peripheral neuropathy, n (%)*	89 (65.9)	10 (7.4)	193 (63.7)	23 (7.6)	72 (69.9)	9 (8.7)	196 (62.0)	22 (7.0)	53 (53.5)	6 (6.1)	230 (67.4)	27 (7.9)
Sensory events, n (%)	88 (65.2)	8 (5.9)	178 (58.7)	13 (4.3)	67 (65.0)	7 (6.8)	185 (58.5)	13 (4.1)	49 (49.5)	4 (4.0)	218 (63.9)	17 (5.0)
Motor events, n (%)	8 (5.9)	2 (1.5)	37 (12.2)	12 (4.0)	16 (15.5)	2 (1.9)	28 (8.9)	11 (3.5)	9 (9.1)	3 (3.0)	36 (10.6)	11 (3.2)
Skin reactions, n (%)	96 (71.1)	28 (20.7)	199 (65.7)	42 (13.9)	78 (75.7)	14 (13.6)	203 (64.2)	54 (17.1)	64 (64.6)	12 (12.1)	232 (68.0)	58 (17.0)
Rash, n (%)	92 (68.1)	27 (20.0)	182 (60.1)	40 (13.2)	68 (66.0)	14 (13.6)	193 (61.1)	51 (16.1)	59 (59.6)	11 (11.1)	216 (63.3)	56 (16.4)
Hyperglycaemia, n (%)	13 (9.6)	80 (5.9)	47 (15.5)	20 (6.6)	17 (16.5)	7 (6.8)	39 (12.3)	19 (6.0)	9 (9.1)	6 (6.1)	51 (15.0)	22 (6.5)
Ocular disorders, n (%)	29 (21.5)	0	65 (21.5)	0	24 (23.3)	0	65 (20.6)	0	20 (20.2)	0	75 (22.0)	0
Dry eye, n (%)	24 (17.8)	0	59 (19.5)	0	21 (20.4)	0	57 (18.0)	0	16 (16.2)	0	68 (19.9)	0
Corneal disorder, n (%)	3 (2.2)	0	8 (2.6)	0	4 (3.9)	0	7 (2.2)	0	3 (3.0)	0	8 (2.3)	0
Blurred vision, n (%)	8 (5.9)	0	13 (4.3)	0	2 (1.9)	0	19 (6.0)	0	6 (6.1)	0	15 (4.4)	0
Infusion-related reactions, n (%)	2 (1.5)	0	13 (4.3)	0	2 (1.9)	0	19 (6.0)	0	6 (6.1)	0	15 (4.4)	0

Data cutoff: 8 August 2024.
*Peripheral neuropathy standardised MedDRA queries (broad scope).
AESI, adverse event of special interest; EV, enfortumab vedotin; LN, lymph node; medDRA, Medical Dictionary for Regulatory Activities; met, metastasis; P, pembrolizumab.
Bedke J et al. Presented at ASCO 2025. #4571.

With an additional 1 year of follow-up in EV-302, no new safety signals were identified with EV+P[1,2]



In the EV-302 long-term follow up, the frequency and grade of EV+P related TRAEs remained consistent with those of the primary analysis

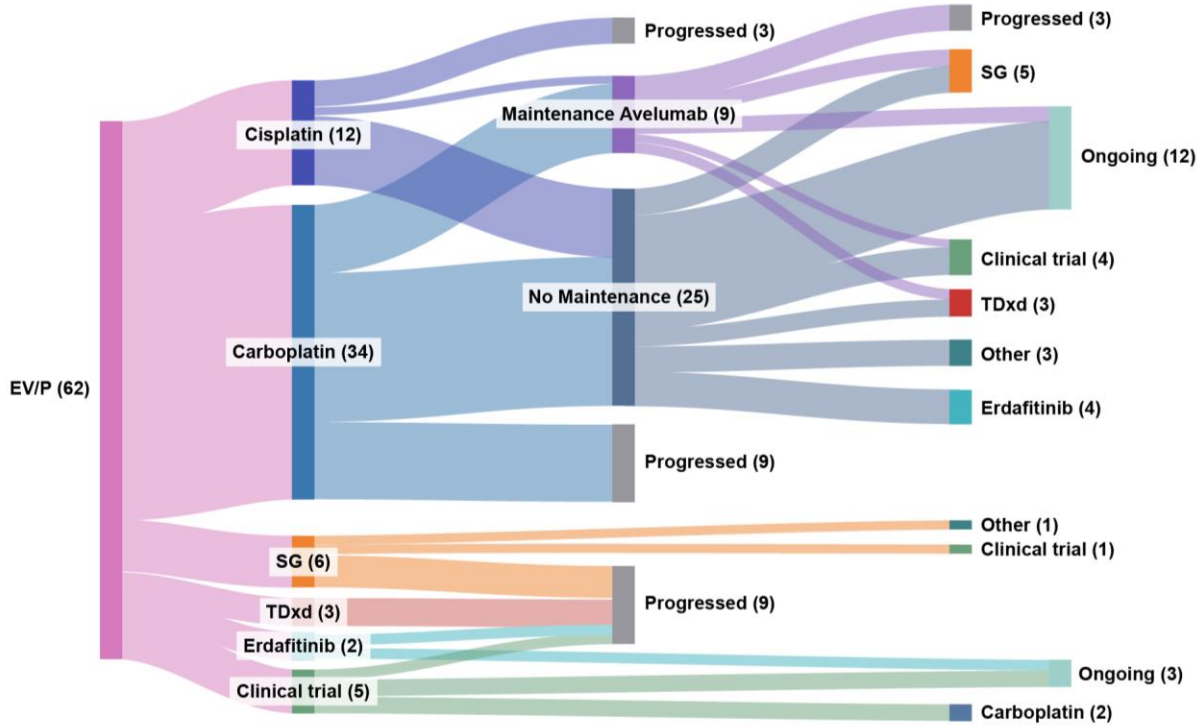
Data cut-off: *8 August 2023; †8 August 2024.
EV, enfortumab vedotin; P, pembrolizumab; TRAE, treatment-related adverse event.
1. Powles T, presented at ASCO GU 2025, Abstract 664; 2. Powles T et al. *Ann Oncol* 2025; https://doi.org/10.1016/j.annonc.2025.05.536.

Treatment after EV+P for 1L unresectable or mUC

A retrospective cohort study of patients with mUC treated with EV+P at Memorial Sloan Kettering Cancer Center

- Clinical data were collected through manual chart review. Treatment response to both EV+P and subsequent PBCT was assessed by physician evaluation according to RECIST v1.1
- Of 236 patients treated with EV+P between October 2018 and December 2024, 62 patients received subsequent systemic treatment

Treatment patterns after EV+P



Disclaimer: small sample size.

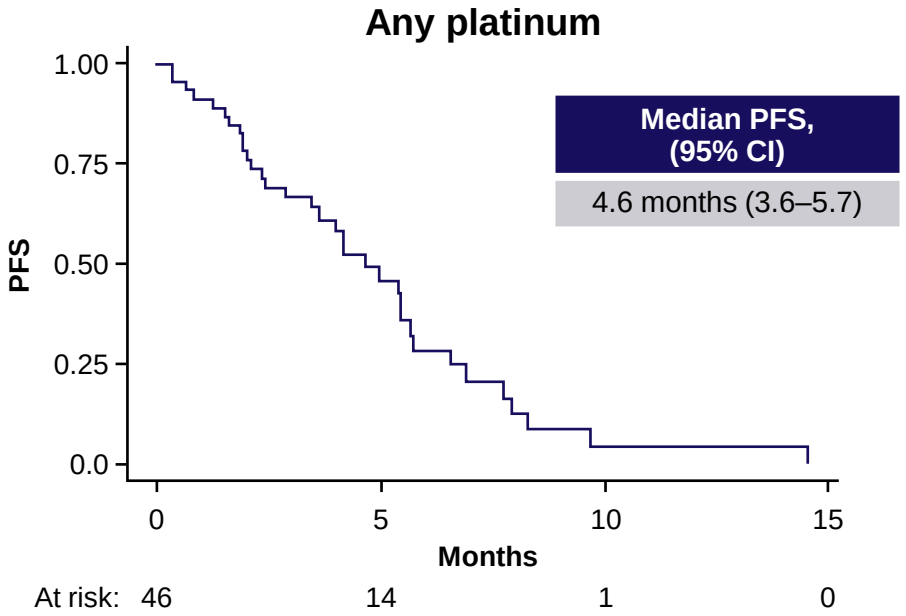
Subsequent treatments included trials and treatments are not licensed in the EU/UK for UC.

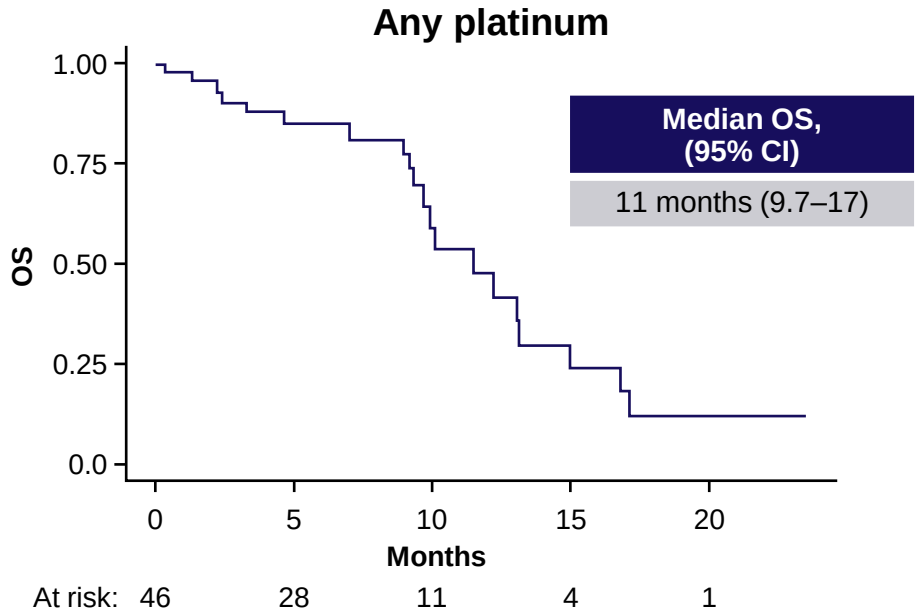
1L, first line; EV, enfortumab vedotin; (m)UC, (metastatic) urothelial carcinoma; P, pembrolizumab; PBCT, platinum-based chemotherapy; RECIST, Response Evaluation Criteria in Solid Tumours; SG, sacituzumab govitecan; TDxd, trastuzumab deruxtecan.

UroToday. ASCO 2025: Treatment Patterns and Clinical Outcomes with Platinum-Based Chemotherapy After Enfortumab Vedotin and Pembrolizumab in Patients with Metastatic Urothelial Carcinoma. Available at: https://www.urotoday.com/conference-highlights/asco-2025/asco-2025-bladder-cancer/161056-asco-2025-treatment-patterns-and-clinical-outcomes-with-platinum-based-chemotherapy-after-enfortumab-vedotin-and-pembrolizumab-in-patients-with-metastatic-urothelial-carcinoma.html. Last accessed: June 2025.

Treatment after EV+P for 1L unresectable or mUC

A retrospective cohort study of patients with mUC treated with EV+P at Memorial Sloan Kettering Cancer Center





- Median PFS was 4.6 months (95% CI: 3.6–5.7), and median OS was 11 months (95% CI: 9.7–17.0)
- No significant differences between cisplatin and carboplatin-based regimens were detected for ORR (p=0.7), PFS (p=0.7), or OS (p=0.8)

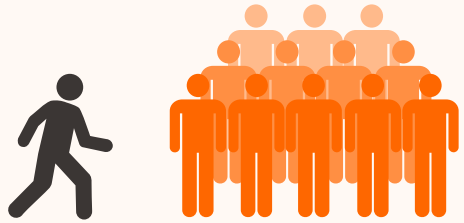
Disclaimer: small sample size.

1L, first line; CI, confidence interval; EV, enfortumab vedotin; OS, overall survival; P, pembrolizumab; ORR, overall response rate; PFS, progression-free survival; UC, urothelial carcinoma.

UroToday. ASCO 2025: Treatment Patterns and Clinical Outcomes with Platinum-Based Chemotherapy After Enfortumab Vedotin and Pembrolizumab in Patients with Metastatic Urothelial Carcinoma. Available at: https://www.urotoday.com/conference-highlights/asco-2025/asco-2025-bladder-cancer/161056-asco-2025-treatment-patterns-and-clinical-outcomes-with-platinum-based-chemotherapy-after-enfortumab-vedotin-and-pembrolizumab-in-patients-with-metastatic-urothelial-carcinoma.html. Last accessed: June 2025.

EV-301 compared the efficacy and safety of EV monotherapy 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)**
Any of the following as an IV infusion on Day 1 of a 21-day cycle:
- Docetaxel 75 mg/m^2 over 1 hour (n=117)
- Paclitaxel 175 mg/m^2 over 3 hours (n=112)
- Vinflunine‡ 320 mg/m^2 over 20 minutes (n=78)

Until radiological disease progression or other treatment discontinuation criteria are met

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. Trial met superiority threshold at the time of interim analysis

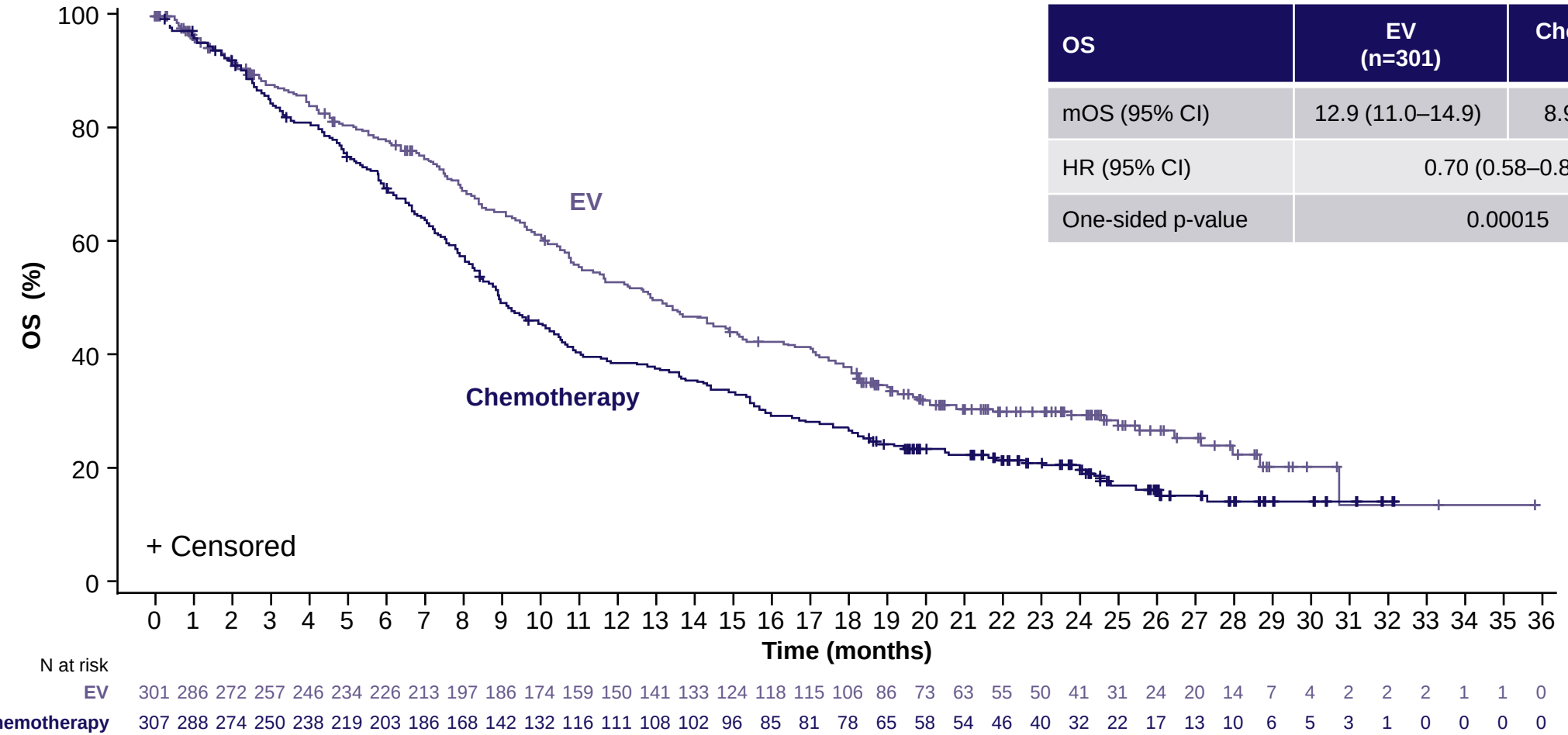
*In EV-301 for patients who had received platinum chemotherapy as neoadjuvant or adjuvant therapy, progression must have occurred within 12 months after completion of treatment; †Stratification variables were ECOG PS (0 or 1), geographic region (USA, Western Europe, or rest of the world), and presence 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.

At a median follow-up of 24 months, the risk of death was reduced by 30% with EV vs. chemotherapy

24-month OS analysis*



OS	EV (n=301)	Chemotherapy (n=307)
mOS (95% CI)	12.9 (11.0–14.9)	8.9 (8.3–10.3)
HR (95% CI)	0.70 (0.58–0.85)	
One-sided p-value	0.00015	

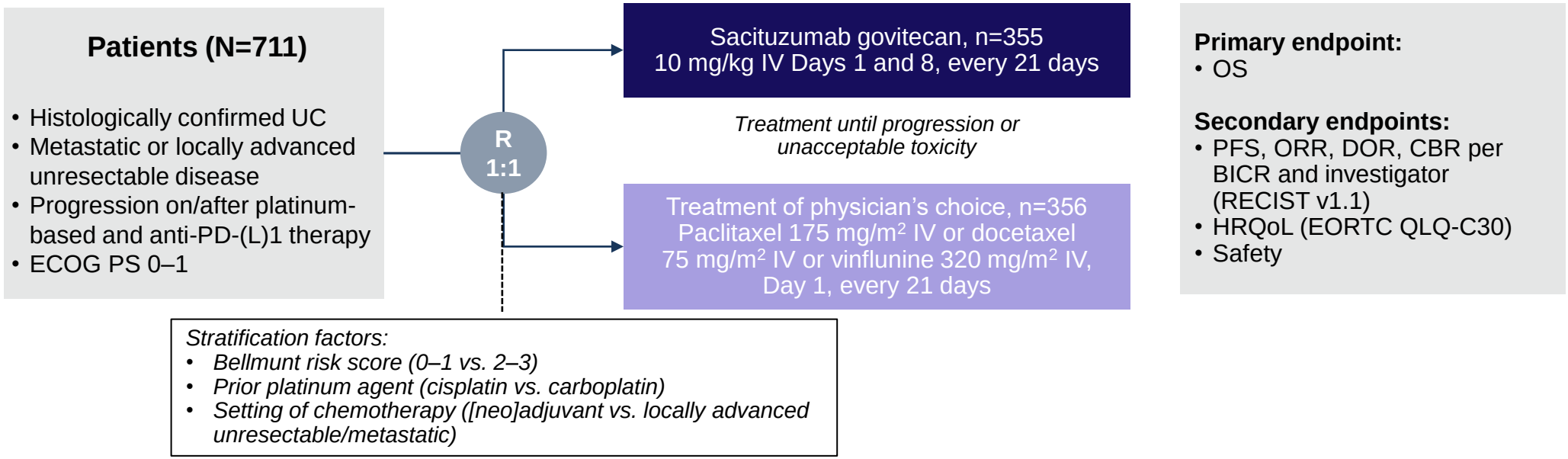
*This was an exploratory analysis. The study met threshold for superiority at time of interim analysis.
CI, confidence interval; EV, enfortumab vedotin; HR, hazard ratio; mOS, median overall survival; OS, overall survival.
Rosenberg JE et al. *Ann Oncol* 2023;13:1047–1054.

TRAE rates at 24 months in the EV and chemotherapy groups were consistent with the interim analysis

TRAEs, n (%)*	EV group (n=296)†		Chemotherapy group (n=291)†	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Any AE	278 (93.9)	155 (52.4)	267 (91.8)	147 (50.5)
Alopecia	135 (45.6)	NR	108 (37.1)	NR
Peripheral sensory neuropathy	103 (34.8)	15 (5.1)	63 (21.6)	6 (2.1)
Pruritus	96 (32.4)	4 (1.4)	14 (4.8)	1 (0.3)
Fatigue	93 (31.4)	20 (6.8)	66 (22.7)	13 (4.5)
Decreased appetite	92 (31.1)	9 (3.0)	69 (23.7)	5 (1.7)
Diarrhoea	74 (25.0)	10 (3.4)	49 (16.8)	5 (1.7)
Dysgeusia	73 (24.7)	NR	22 (7.6)	NR
Nausea	71 (24.0)	3 (1.0)	64 (22.0)	4 (1.4)
Maculopapular rash	50 (16.9)	22 (7.4)	5 (1.7)	0
Anaemia	34 (11.5)	8 (2.7)	63 (21.6)	23 (7.9)
Decreased neutrophil count	31 (10.5)	18 (6.1)	51 (17.5)	41 (14.1)
Neutropenia	20 (6.8)	14 (4.7)	25 (8.6)	18 (6.2)
Decreased white-cell count	15 (5.1)	4 (1.4)	32 (11.0)	21 (7.2)
Febrile neutropenia	2 (0.7)	2 (0.7)	16 (5.5)	16 (5.5)

*Occurring in ≥20% of patients in either treatment group or Grade ≥3 TRAEs occurring in ≥5% of patients in either treatment group; †Safety population.
AE, adverse event; EV, enfortumab vedotin; NR not reported; SJS, Stevens-Johnson syndrome; TEN, toxic epidermal necrolysis; TRAE, treatment-related adverse event.
Rosenberg JE et al. *Ann Oncol* 2023;13:1047–1054.

TROPiCS-04 study design

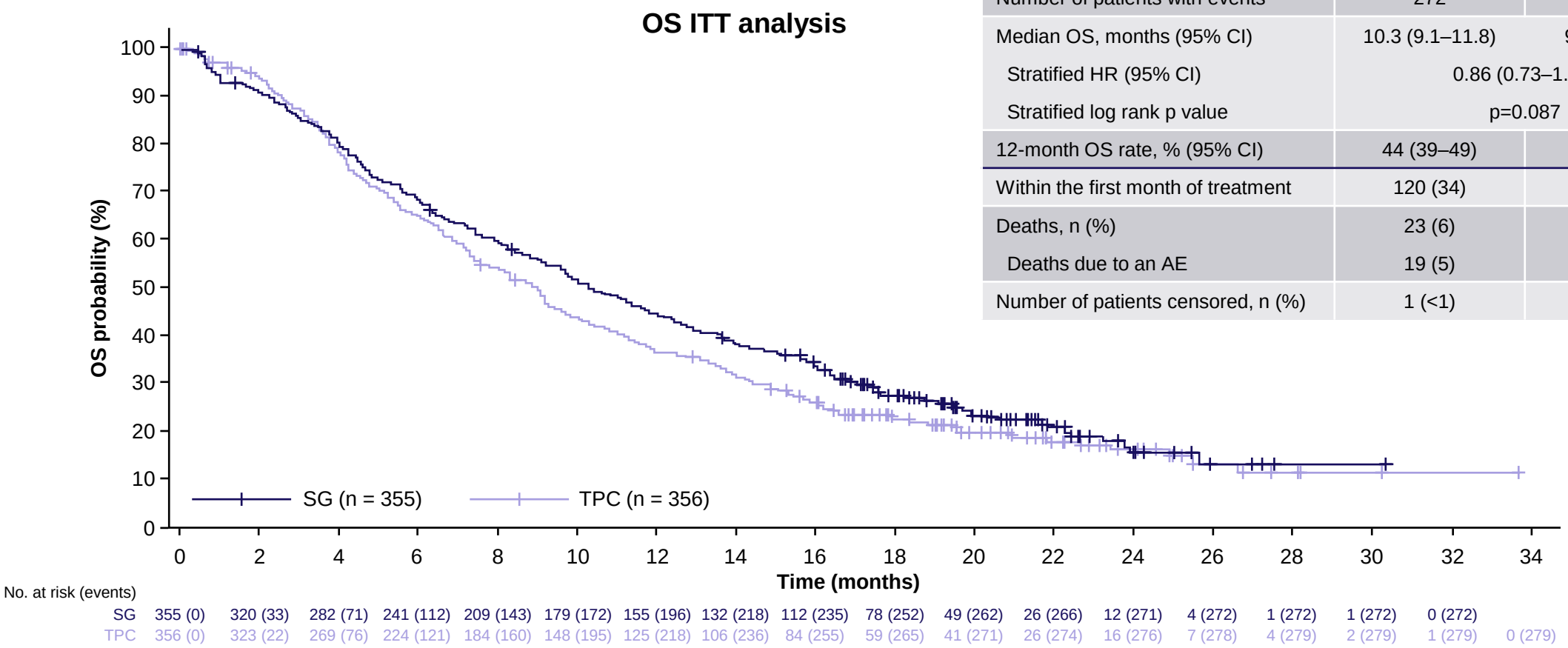


- G-CSF primary prophylactic use for neutropenia was not required per study protocol, but investigators were encouraged to consider prophylaxis in patients with risk factors for febrile neutropenia, per ASCO guidelines for growth factors
  - Following IDMC recommendation, a memorandum sent to the participating sites in September 2022 strongly recommended primary prophylaxis with G-CSF starting in Cycle 1 in patients at risk for developing febrile neutropenia

At data cutoff (8 March 2024), median follow-up was 9.2 months (range 0–33.7).
Sacituzumab govitecan is not licenced for UC in the UK/EU.
ASCO, American Society of Clinical Oncology; BICR, blinded independent central review; CBR, clinical benefit rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EORTC QLQ, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire; G-CSF, granulocyte colony stimulating factor; HRQoL, health-related quality of life; IDMC, Independent Data Monitoring Committee; IV, intravenous; ORR, objective response rate; OS, overall survival; PD-(L)1, programmed death (ligand) 1; PFS, progress-free survival; R, randomisation; RECIST, Response Evaluation Criteria in Solid Tumours; UC, urothelial carcinoma.
Powles T et al. *Ann Oncol* 2025;36:561–571.

The primary endpoint of improved OS with SG vs. TPC was not met

Safety-evaluable patients	SG n=355	TPC n=356
Number of patients with events	272	279
Median OS, months (95% CI)	10.3 (9.1–11.8)	9.0 (7.5–9.7)
Stratified HR (95% CI)	0.86 (0.73–1.02)	
Stratified log rank p value	p=0.087	
12-month OS rate, % (95% CI)	44 (39–49)	37 (32–42)
Within the first month of treatment	120 (34)	60 (18)
Deaths, n (%)	23 (6)	11 (3)
Deaths due to an AE	19 (5)	3 (1)
Number of patients censored, n (%)	1 (<1)	7 (2)



No. at risk (events)

SG	355 (0)	320 (33)	282 (71)	241 (112)	209 (143)	179 (172)	155 (196)	132 (218)	112 (235)	78 (252)	49 (262)	26 (266)	12 (271)	4 (272)	1 (272)	1 (272)	0 (272)	
TPC	356 (0)	323 (22)	269 (76)	224 (121)	184 (160)	148 (195)	125 (218)	106 (236)	84 (255)	59 (265)	41 (271)	26 (274)	16 (276)	7 (278)	4 (279)	2 (279)	1 (279)	0 (279)

At data cutoff (8 March 2024), median follow-up was 9.2 months (range 0–33.7).
Sacituzumab govitecan is not licenced for UC in the UK/EU.
AE, adverse event; CI, confidence interval; HR, hazard ratio; OS, overall survival; SG, sacituzumab govitecan; TPC, treatment of physician's choice.
Powles T et al. *Ann Oncol* 2025;36:561–571.

TROPiCS-04: Safety summary

Safety-evaluable patients	SG (n=349)	TPC (n=337)
Any TRAEs	339 (97)	296 (88)
Grade ≥3 TRAEs	233 (67)	119 (35)
Serious TEAEs	120 (34)	60 (18)
TRAEs leading to discontinuation	39 (11)	42 (12)
TRAEs leading to death	15 (4)	5 (1)

- Grade 5 TEAEs were observed in 7% of patients in the SG group and 2% of patients in the TPC group
  - 16 (5%) events with SG were infections in the setting of neutropenia, of which 14 occurred within the first month of treatment
  - Patients who experienced fatal infections with neutropenia had a higher burden of risk factors for medical complications compared with the overall SG group
    - Age ≥65 years: 81%, prior cystectomy: 56%, prior major urinary tract procedure: 81%, prior radiotherapy: 50%, ≥3 prior anticancer regimens: 50%

At data cutoff (8 March 2024), median follow-up was 9.2 months (range 0–33.7).
Sacituzumab govitecan is not licenced for UC in the UK/EU.
SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event; TPC, treatment of physician's choice; TRAE, treatment-related adverse event;
Powles T et al. *Ann Oncol* 2025;36:561–571.

Job code: MAT-NL-PAD-2025-00051

Genitourinary Masterclass

Deeper insights: What the latest data tells us about today's SOC for advanced UC

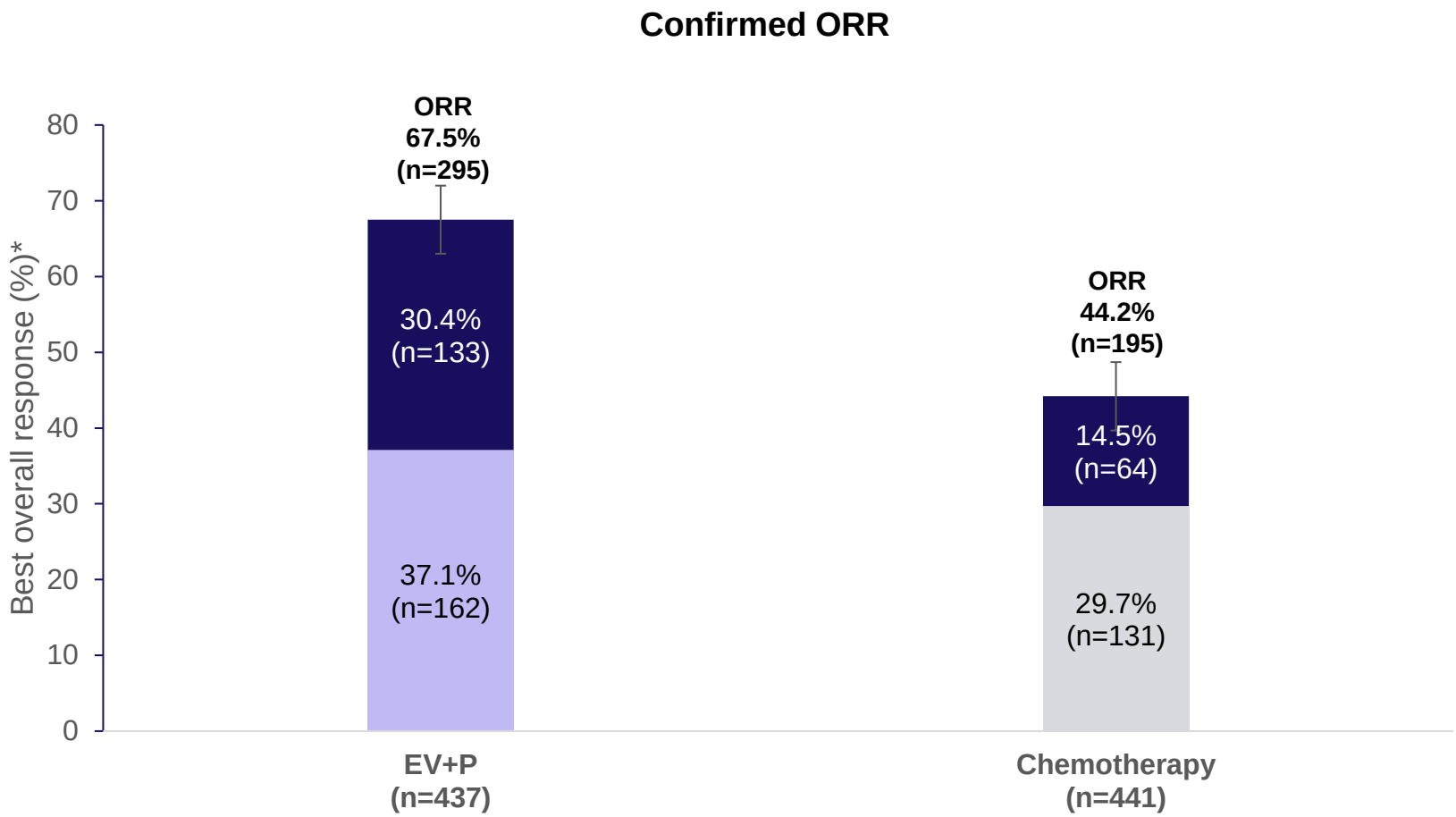
Part 2

Dr Shilpa Gupta

Cleveland Clinic Taussig Cancer Institute,
Cleveland, Ohio, US

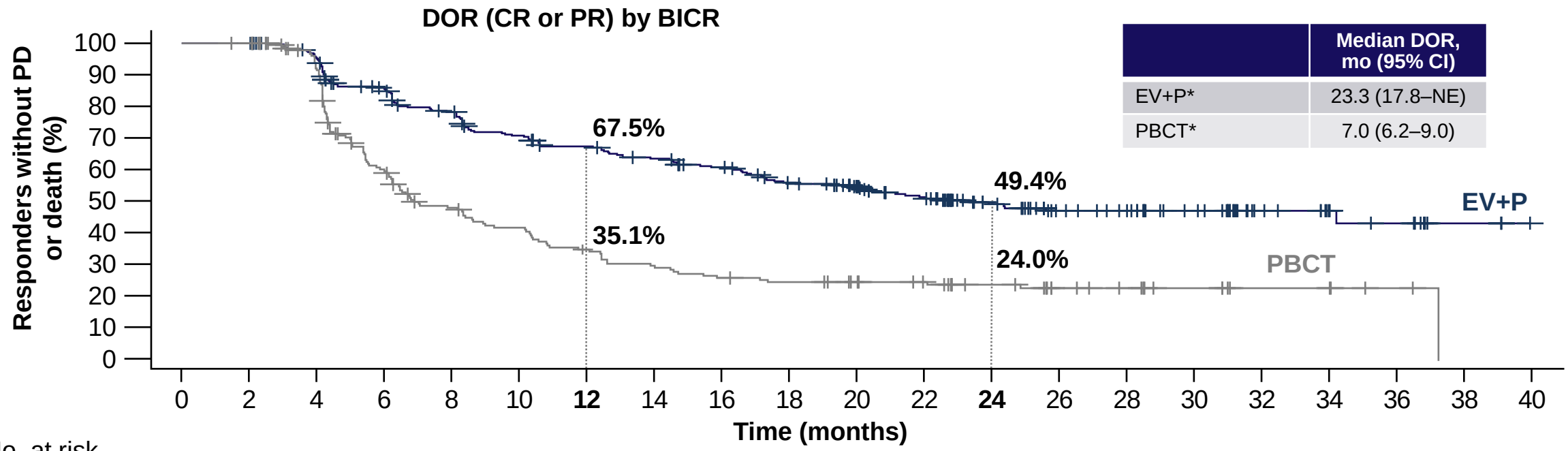
astellas

In EV-302, CR rate for patients treated with EV+P was doubled vs. patients treated with PBCT



Data cutoff: 8 August 2024. Median follow-up time: 29.1 months (95% CI: 28.5–29.9).
*Best overall response according to RECIST v1.1. CR or PR was confirmed with repeat scans ≥28 days after initial response.
BICR, blinded independent central review; CI, confidence interval; CR, complete response; EV, enfortumab vedotin; mo, month; ORR, objective response rate; P, pembrolizumab; PBCT, platinum-based chemotherapy; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumours.
Gupta S et al. Presented at ASCO 2025. #4502.

Among responders, the probability of maintained response at 24 months was ~50% with EV+P vs. 24% for PBCT



	Median DOR, mo (95% CI)
EV+P*	23.3 (17.8–NE)
PBCT*	7.0 (6.2–9.0)

No. at risk

EV+P	295	295	274	238	213	190	177	165	154	137	125	107	78	58	53	40	20	14	10	4
PBCT	195	194	162	102	78	67	55	47	41	38	34	30	23	16	13	9	5	5	2	

	EV+P (n=437)	PBCT (n=441)	Nominal two-sided P-value
Confirmed ORR (CR or PR), n (%) [95% CI]	295 (67.5) [62.9–71.9]	195 (44.2) [39.5–49.0]	<0.00001†
Best overall response, n (%)			
CR	133 (30.4)	64 (14.5)	
PR	162 (37.1)	131 (29.7)	
SD	83 (19.0)	149 (33.8)	

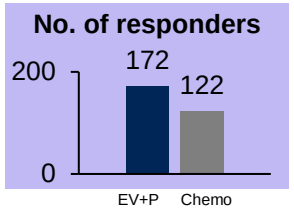
Data cutoff: 8 August 2024.

*Events/N were 137/295 for EV+P and 129/195 for chemotherapy; †P-value is nominal and descriptive.

BICR, blinded independent central review; CR, complete response; DOR, duration of response; EV, enfortumab vedotin; NE, not estimable; P, pembrolizumab; PBCT, platinum-based chemotherapy; PD, progressive disease; PR, partial response; ORR, objective response rate; SD, stable disease.

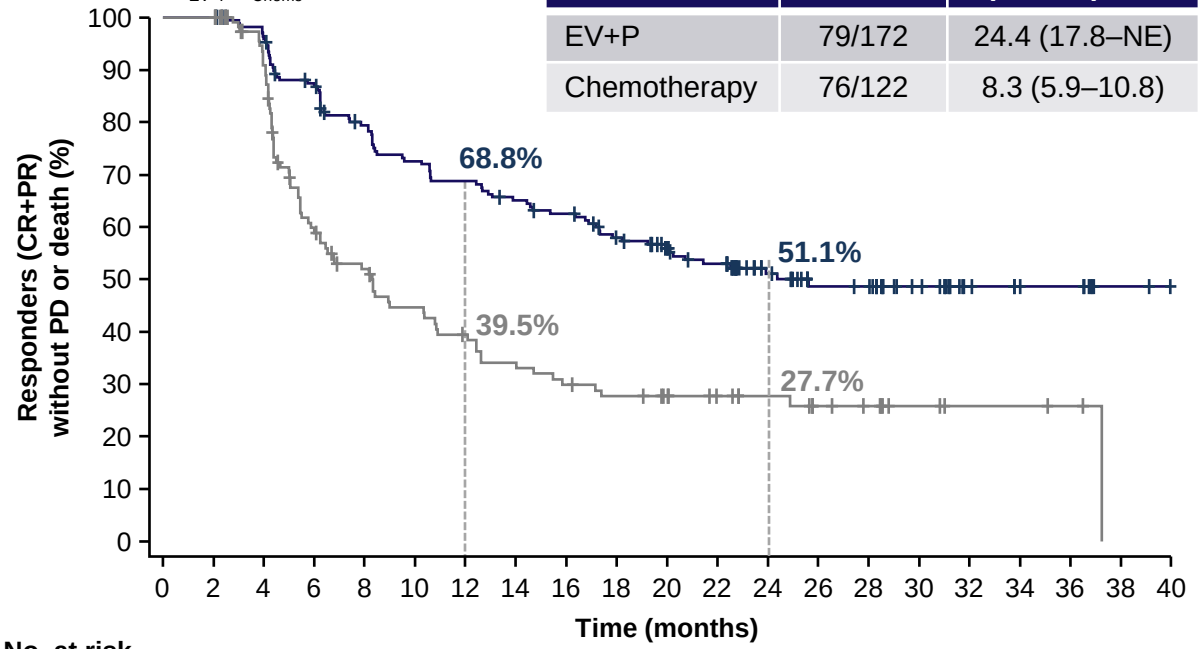
Powles T et al. presented at ASCO GU 2025. Abstract 664.

DOR by BICR (CR+PR) favours EV+P vs. PBCT irrespective of cisplatin eligibility



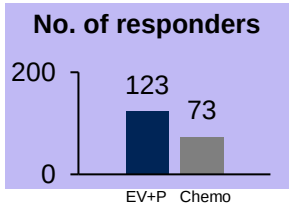
Cisplatin-eligible patients

	Events/N	Median DOR (95% CI), mo
EV+P	79/172	24.4 (17.8–NE)
Chemotherapy	76/122	8.3 (5.9–10.8)



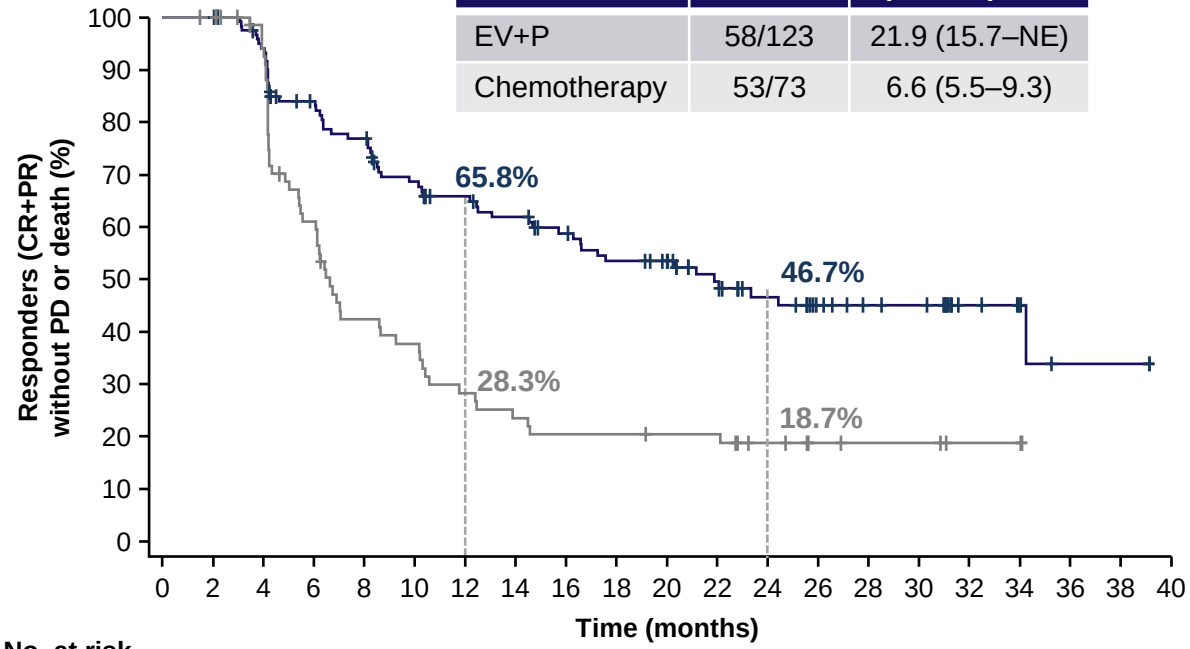
No. at risk

EV+P	172	172	162	144	127	116	110	103	98	87	78	70	48	36	35	23	12	9	8	2
Chemotherapy	122	122	99	62	51	43	37	32	28	25	22	18	15	11	9	5	3	3	2	



Cisplatin-ineligible patients

	Events/N	Median DOR (95% CI), mo
EV+P	58/123	21.9 (15.7–NE)
Chemotherapy	53/73	6.6 (5.5–9.3)

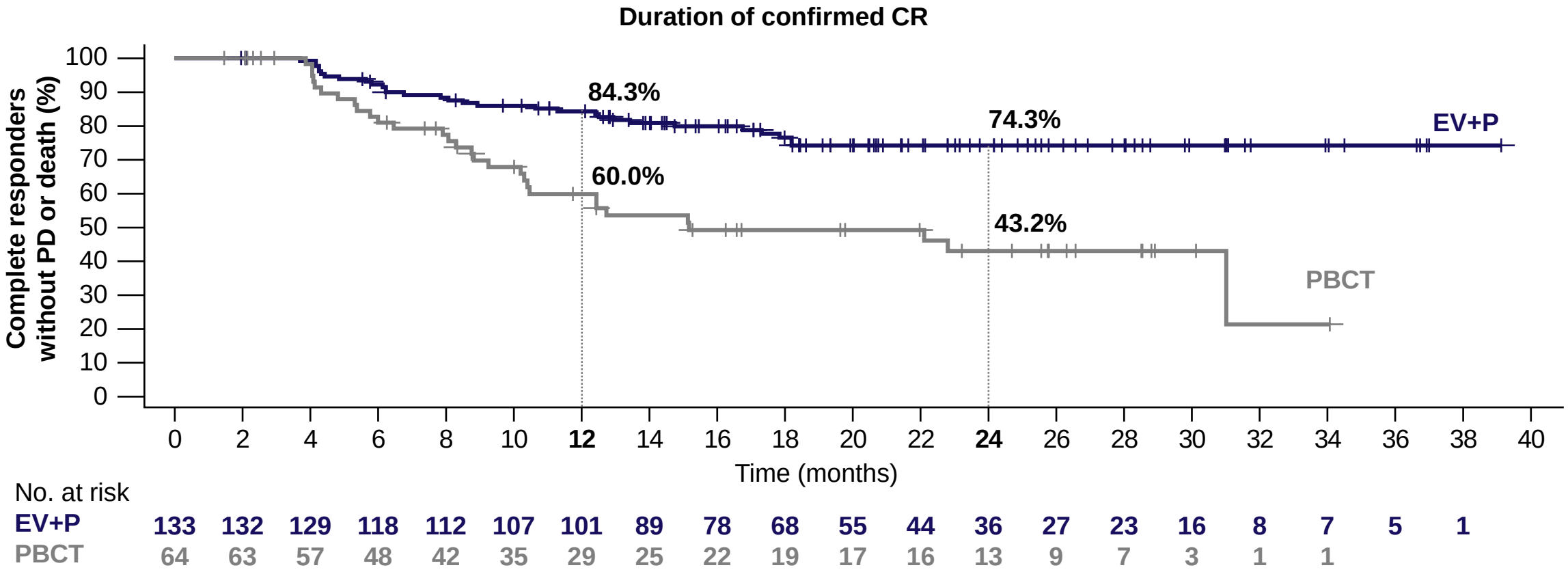


No. at risk

EV+P	123	123	112	94	86	74	67	62	56	50	47	37	30	22	18	17	8	5	2	2
Chemotherapy	73	72	63	40	27	24	18	15	13	13	12	12	8	5	4	4	2	2		

Data cutoff: 8 August 2024. NCT04223856.
BICR, blinded independent committee review; CI, confidence interval; CR, complete response; DOR, duration of response; EV, enfortumab vedotin; mo, month; NE, not evaluable; P, pembrolizumab; PD, progressive disease; PBCT, platinum-based chemotherapy; PD, progression of disease; PR, partial response; OS, overall survival.
Gupta S et al. Presented at ASCO 2025. #4502.

Probability of maintaining CR at 24 months was 74.3% with EV+P vs. 43.2% with PBCT

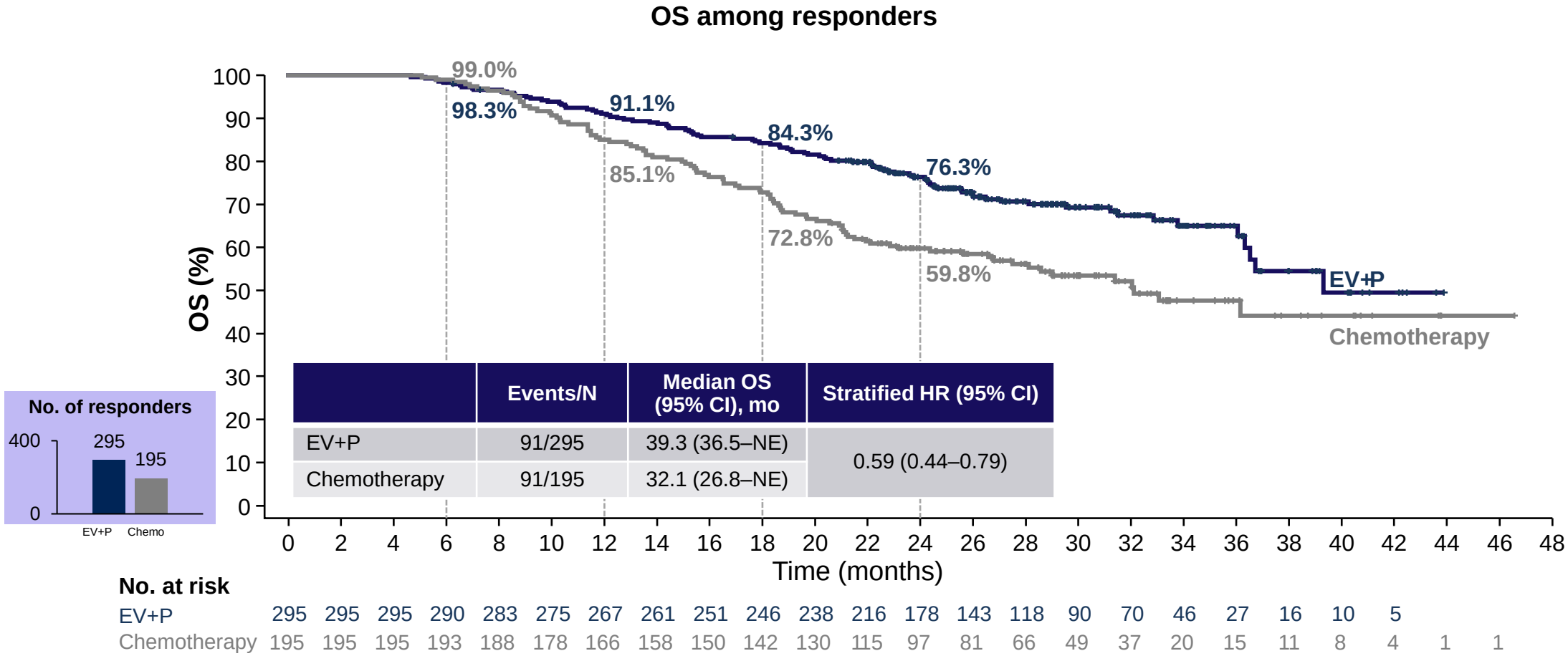


No. at risk

EV+P	133	132	129	118	112	107	101	89	78	68	55	44	36	27	23	16	8	7	5	1
PBCT	64	63	57	48	42	35	29	25	22	19	17	16	13	9	7	3	1	1		

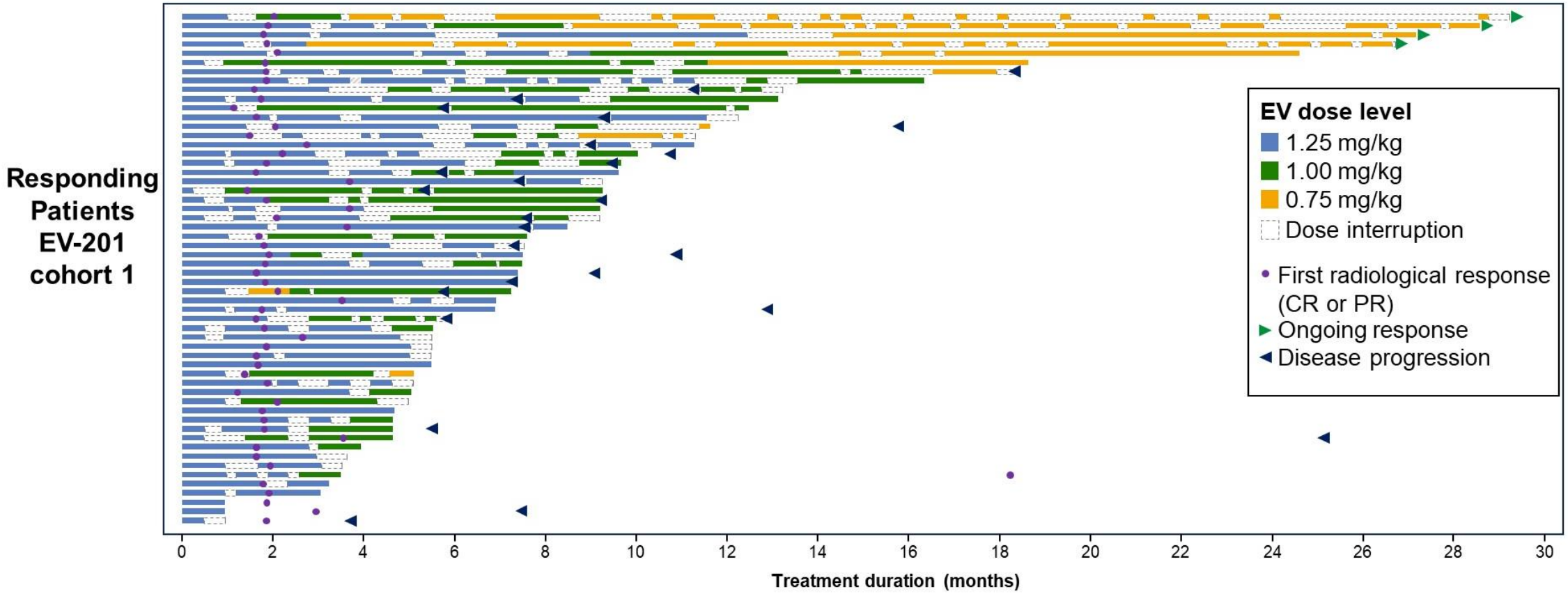
CR, complete response; EV, enfortumab vedotin; P, pembrolizumab; PBCT, platinum-based chemotherapy; PD, progressive disease.
Powles T, presented at ASCO GU 2025, Abstract 664.

Survival rates of responders at 2 years was estimated to be 76.3% for patients treated with EV+P



Data cutoff: 8 August 2024. NCT04223856.
CI, confidence interval; CR, complete response; EV, enfortumab vedotin; HR, hazard ratio; mo, month; NE, not evaluable; P, pembrolizumab; PR, partial response; OS, overall survival.
Gupta S et al. Presented at ASCO 2025. #4502.

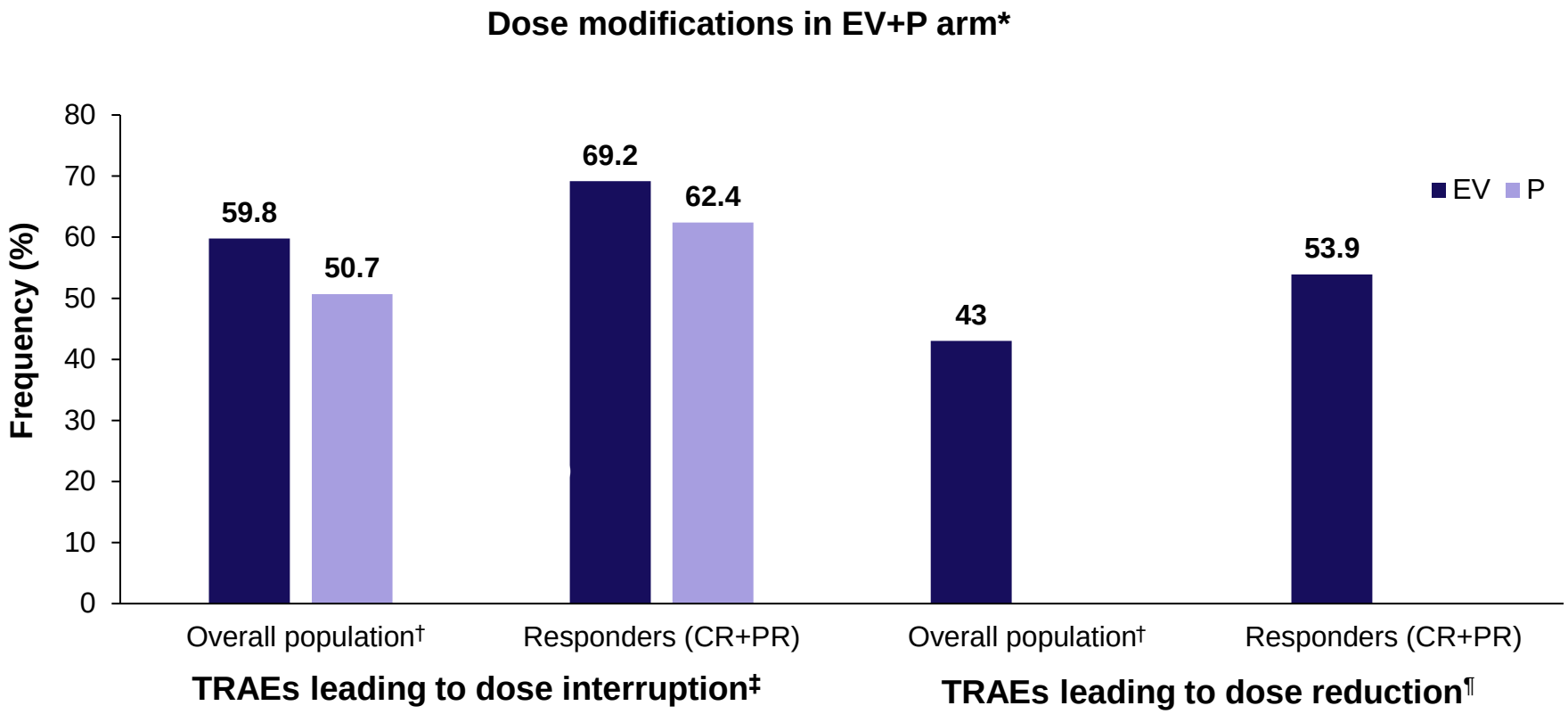
The impact of exposure on outcomes with EV monotherapy in patients with LA/mUC has been investigated in clinical trials



Patients responding to EV monotherapy continue to benefit following dose interruptions and reductions

Slide adapted from Petrylak D et al. Presented at ASCO 2024. Abstract 4503.
All data presented are from a *post hoc*, exploratory analysis.
CR, complete response; EV, enfortumab vedotin; LA/mUC, locally advanced/metastatic urothelial carcinoma; PR, partial response.
Petrylak D et al. Presented at ASCO 2024. Abstract 4503.

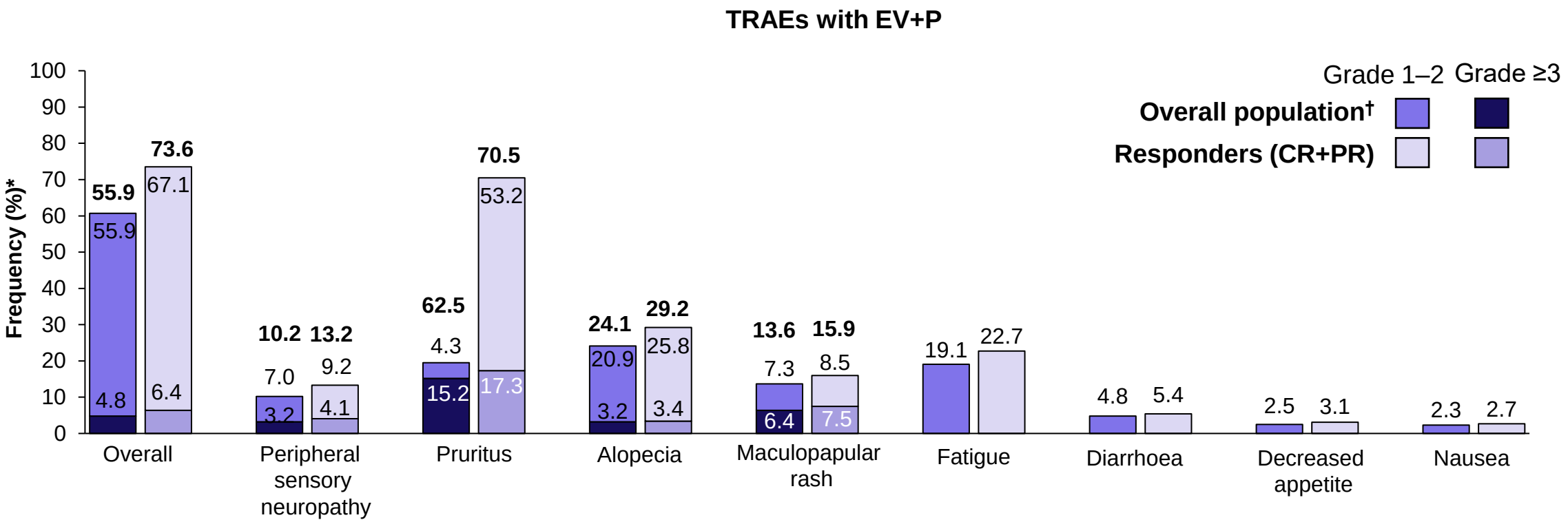
In EV-302 long-term follow-up of 24 months, responders to EV+P maintained response despite dose modifications



Dose modifications due to TRAEs were common among responders (CR+PR) with longer treatment duration

Data cutoff: 8 August 2024.
*TRAEs leading to discontinuation of EV occurred in 36.4% overall and 46.8% of responders. TRAEs leading to discontinuation of P occurred in 24.8% overall and 27.8% of responders; †Overall population refers to evaluable patients in the safety analysis set; ‡Dose interruption includes dose elimination (scheduled dose being skipped) and dose delay (dose not occurring on the scheduled dosing day) as collected on the case report form; ¶No dose reduction was permitted for P.
CR, complete response; EV, enfortumab vedotin; P, pembrolizumab; PR, partial response; TRAE, treatment-related adverse event.
Gupta S et al. Presented at ASCO 2025. #4502.

TRAEs of special interest for EV

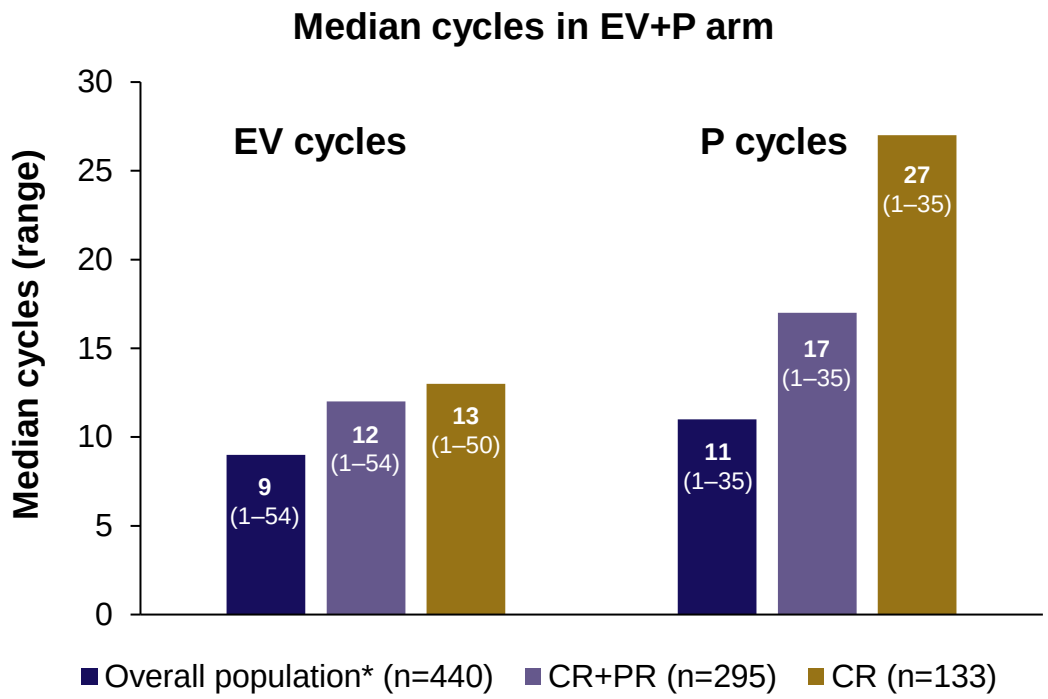


- In the overall population,† median **EV treatment duration** was 7.1 months (median number of cycles was 9)
- For responders, median **EV treatment duration** was 9.7 months (median number of cycles was 12)

The safety profile of EV for responders (CR+PR) was generally consistent with that of the overall population

Data cutoff: 8 August 2024.
Percentages are rounded and may not equal total.
*AEs of special interest for EV in the EV+P arm are shown by medical concept; †Overall population refers to evaluable patients in the safety analysis set.
AE, adverse event; CR, complete response; EV, enfortumab vedotin; P, pembrolizumab; PR, partial response; TRAE, treatment-related adverse event.
Gupta S et al. Presented at ASCO 2025. #4502.

Safety summary of responders vs overall population



Safety summary

Patients with TRAE, n (%)	Overall population (safety analysis set)		Responders (CR+PR)		Patients with CR	
	EV+P (n=440)	Chemo (n=433)	EV+P (n=295)	Chemo (n=195)	EV+P (n=133)	Chemo (n=64)
All grades	428 (97.3)	414 (95.6)	293 (99.3)	189 (96.9)	133 (100.0)	62 (96.9)
Grade ≥3	252 (57.3)	301 (69.5)	181 (61.4)	129 (61.4)	82 (61.7)	46 (71.9)

- In the overall population,* EV+P treatment was given for a median of 12 cycles (range 1–54)
- For responders (CR+PR), EV+P treatment duration was longer (median number of cycles was 19 [range 1–54], and among patients with CR, EV+P was given for a median of 30 cycles (range 1–50)

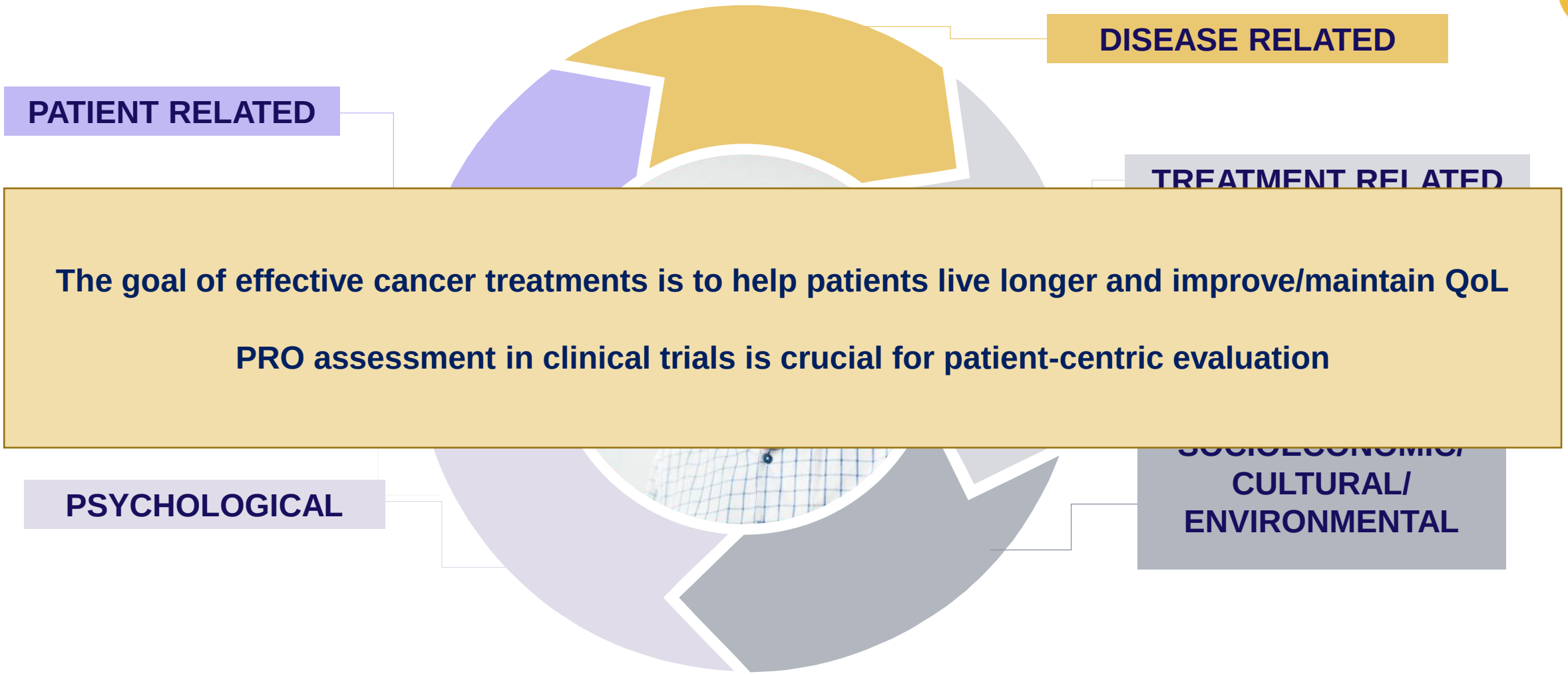
Data cutoff: 8 August 2024. NCT04223856.
*Overall population refers to evaluable patients in the safety analysis set.
AE, adverse event; CR, complete response; EV, enfortumab vedotin; P, pembrolizumab; PBCT, platinum-based chemotherapy; PR, partial response; TRAE, treatment-related AE.
Gupta S et al. Presented at ASCO 2025. #4502.

Genitourinary Masterclass

EV-302 PRO data

What role does QoL play in the broader picture of patient outcomes?

Factors affecting the QoL of a patient with cancer



The goal of effective cancer treatments is to help patients live longer and improve/maintain QoL

PRO assessment in clinical trials is crucial for patient-centric evaluation

PRO, patient-reported outcome; QoL, quality of life.
Speaker's own opinion.

EV-302 PRO collection[1,2]

Baseline
(Day 1, pre-dose and post-randomisation)

Weekly for 12 weeks
(~4 cycles)

Every 3 weeks beyond end of treatment and progression through survival follow-up

EORTC QLQ-C30
(score range 0–100; higher score represents greater symptom burden, higher functioning and better QoL)

Cancer-related symptoms

Appetite loss, constipation, diarrhoea, dyspnoea, fatigue, insomnia, nausea and vomiting, pain

Function

Physical, cognitive, emotional, role, social

QoL/GHS

BPI-SF
(score range 0–10; higher score represents more pain)

Includes

Worst pain, average pain, least pain, pain right now, pain interference, location of pain

- TTPP and mean change from baseline in worst pain (BPI-SF Question 3) at week 26 were pre-specified endpoints included in the hierarchical statistical testing plan
- Pre-specified descriptive analyses included change from baseline and TTCD
- Patients with moderate/severe pain at baseline were a pre-specified subgroup of interest

BPI-SF, Brief Pain Inventory-Short Form; EORTC QLQ, European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire; GHS, global health status; PRO, patient-reported outcome; QoL, quality of life; TTCD, time to confirmed deterioration; TTPP, time to pain progression.

1. Gupta S, et al. *Lancet Oncol* 2025;26:795–805; 2. Gupta S et al. Presented at ASCO 2024. Abstract 4502.

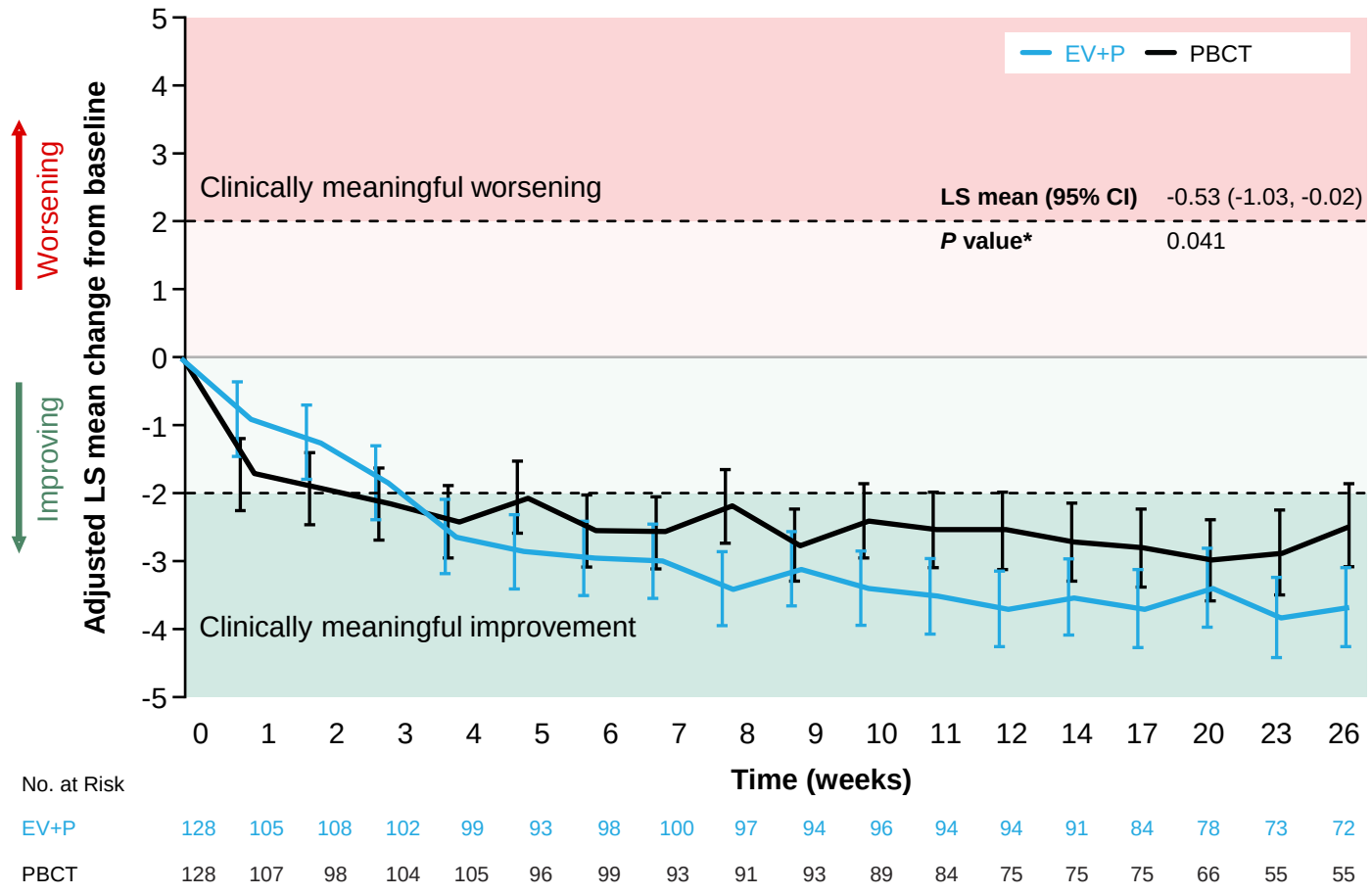
Patients with moderate to severe baseline pain had clinically meaningful improvement in worst pain with EV+P[1,2]

‘Please rate your pain from 0 (no pain) to 10 (pain as bad as you can imagine) that best describes your pain at its worst in the last 24 hours.’

- Approximately one-third of patients had moderate to severe pain at baseline
- Patients in both EV+P and PBCT treatment arms had clinically meaningful improvements in worst pain
  - A 2-point change was considered clinically meaningful
- Greater improvements in pain were observed in the EV+P arm

Please note that these results were not statistically significant

Change in worst pain (BPI-SF) in the EV-302 trial



No. at Risk																		
EV+P	128	105	108	102	99	93	98	100	97	94	96	94	94	91	84	78	73	72
PBCT	128	107	98	104	105	96	99	93	91	93	89	84	75	75	75	66	55	55

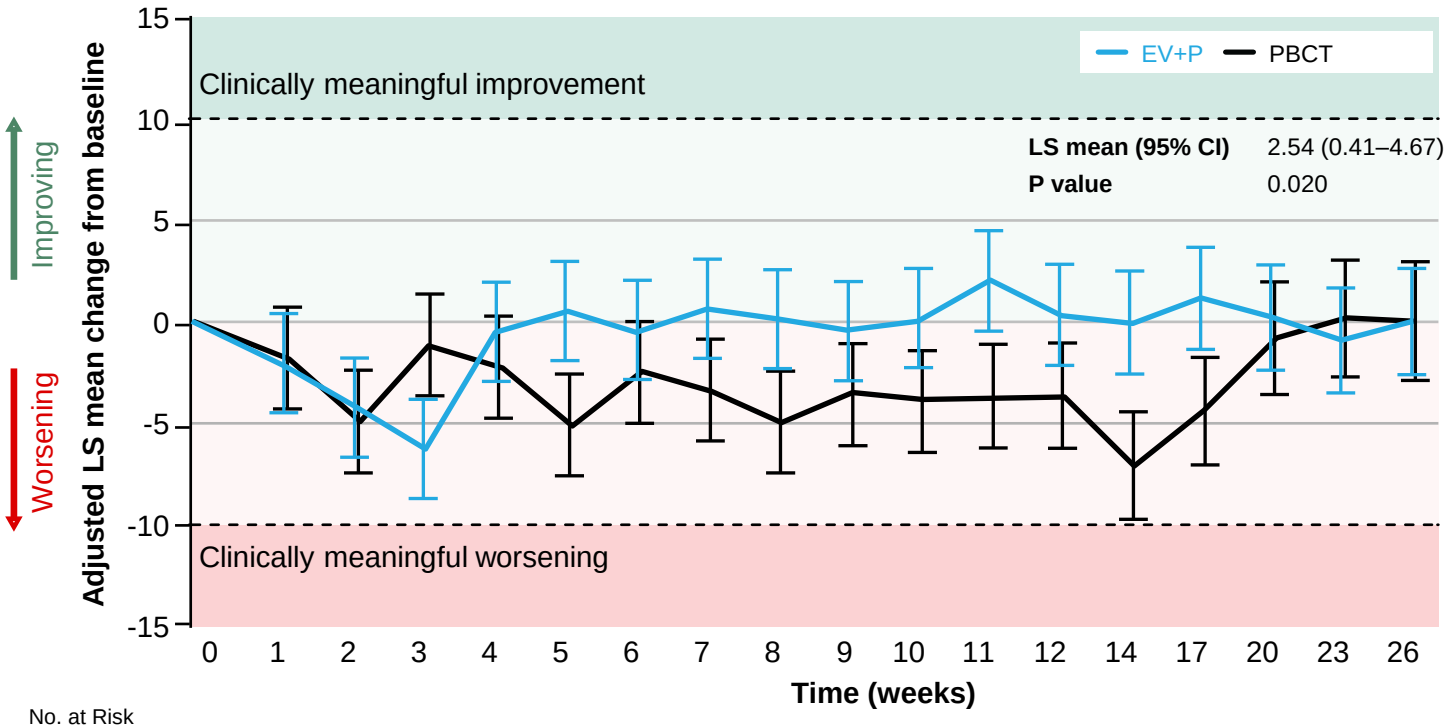
*Nominal *P* value.
BPI-SF, Brief Pain Inventory–Short Form; CI, confidence interval; EV, enfortumab vedotin; LS, least squares; P, pembrolizumab; PBCT, platinum-based chemotherapy.
1. Gupta S, et al. *Lancet Oncol* 2025;26:795–805; 2. Gupta S et al. Presented at ASCO 2024. Abstract 4502.

Patients in the EV+P arm demonstrated improved functioning across all EORTC QLQ-C30 functioning domains[1,2]

‘How would you rate your overall health during the past week?’
‘How would you rate your overall quality of life during the past week?’

- Patients in the EV+P arm had a transient worsening in GHS/QoL score at week 3, followed by a return to baseline at Week 4
- Patients in the PBCT arm had a worsening from Week 1 through Week 14; scores returned to baseline from Week 20
- Median time to confirmed deterioration (mTTCD) was 5.9 months with EV+P and 3.2 months with CT

Change in QLQ-C30 GHS/QoL Score in the EV-302 trial



No. at Risk																		
EV+P	365	321	330	311	314	300	300	306	301	307	299	296	296	289	278	261	252	241
PBCT	350	300	288	300	294	296	282	294	279	278	271	260	256	239	240	204	179	172

Please note that these results were not statistically significant

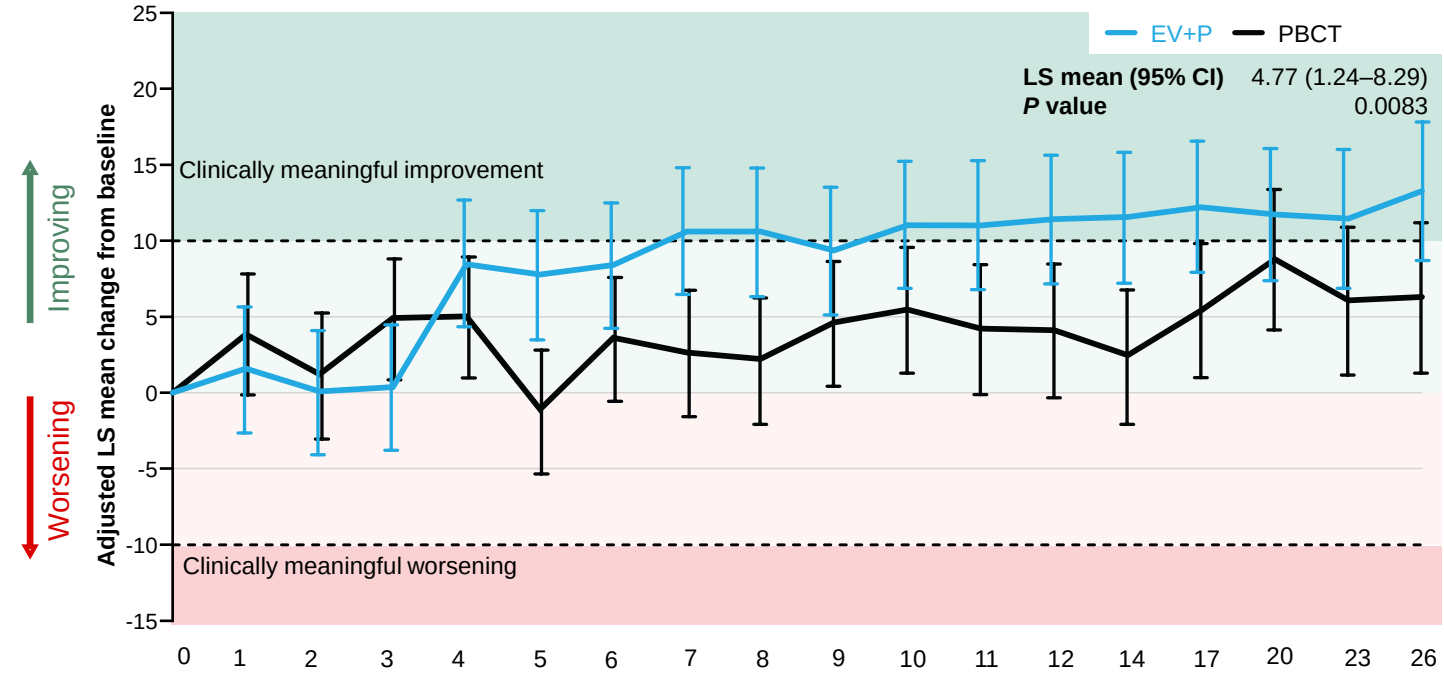
TTCD was defined as a clinically meaningful decrease (a 10-point decrease in EORTC QLQ-C30 from baseline for two consecutive visits).
CI, confidence interval; EV, enfortumab vedotin; GHS, global health status; HR, hazard ratio; LS, least squares; P, pembrolizumab; PBCT, platinum-based chemotherapy; TTCD, time to confirmed deterioration; QoL, quality of life.
1. Gupta S, et al. *Lancet Oncol* 2025;26:795–805; 2. Gupta S et al. Presented at ASCO 2024. Abstract 4502.

Change in EORTC QLQ-C30 GHS/QoL score in patients with moderate/severe pain at baseline favoured EV+P[1,2]

‘How would you rate your overall health during the past week?’
‘How would you rate your overall quality of life during the past week?’

- Patients in the EV+P arm with moderate to severe pain at baseline showed a clinically meaningful improvement in EORTC QLQ-C30 GHS/QoL
  - A 10-point change was considered clinically meaningful

Change in QLQ-C30 GHS/QoL Score in patients with moderate/severe pain at baseline in the EV-302 trial



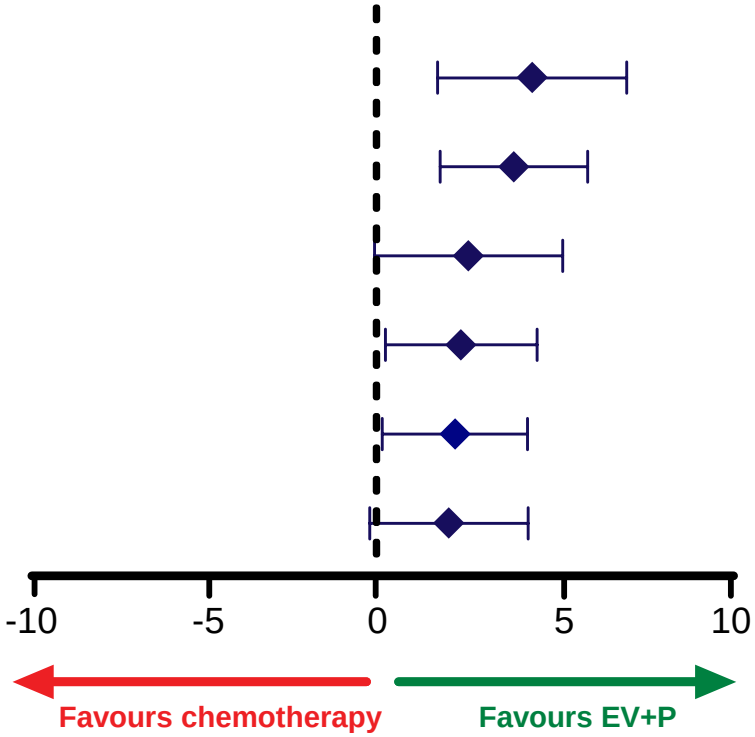
No. at Risk																		
EV+P	122	105	107	102	98	91	97	99	96	94	96	94	94	91	84	78	73	71
PBCT	126	103	96	104	105	96	99	92	91	93	89	84	75	75	75	66	55	55

Please note that these results were not statistically significant

CI, confidence interval; EV, enfortumab vedotin; GHS, global health status; LS, least squares; P, pembrolizumab; PBCT, platinum-based chemotherapy; QoL, quality of life.
1. Gupta S, et al. *Lancet Oncol* 2025;26:795–805; 2. Gupta S et al. Presented at ASCO 2024. Abstract 4502.

Change in EORTC QLQ-C30 Functioning Domains favoured EV+P

Functioning domain	EV+P LS mean (SE)	Chemotherapy LS mean (SE)	EV+P – Chemotherapy LS mean (95% CI)	P value
Role functioning	-5.36 (1.23)	-9.49 (1.26)	4.13 (1.47, 6.79)	0.0024
Physical functioning	-2.63 (0.96)	-6.25 (0.99)	3.62 (1.54, 5.70)	0.0007
Social functioning	-2.94 (1.22)	-5.52 (1.25)	2.57 (−0.07, 5.22)	0.056
GHS/QoL	-0.59 (0.99)	-3.12 (1.01)	2.54 (0.41, 4.67)	0.020
Cognitive functioning	-0.54 (0.95)	-2.69 (0.97)	2.15 (0.10, 4.20)	0.040
Emotional functioning	3.85 (0.97)	1.96 (0.98)	1.89 (−0.19, 3.97)	0.075



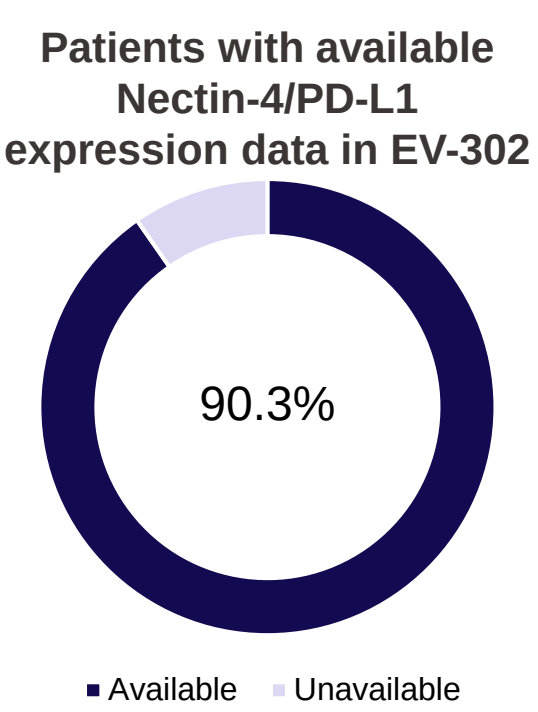
Please note that these results were not statistically significant

CI, confidence interval; EV, enfortumab vedotin; GHS, global health status; HR, hazard ratio; LS, least squares; P, pembrolizumab; PBCT, platinum-based chemotherapy; TTCD, time to confirmed deterioration; QoL, quality of life.
Gupta S, et al. *Lancet Oncol* 2025;26:795–805.

Genitourinary Masterclass

EV-302 Nectin-4 biomarker analysis

EV-302 exploratory analysis of Nectin-4 expression and response to 1L EV+P in LA/mUC



Retrospective assessment of Nectin-4 expression by a CAP-/CLIA-validated Nectin-4 IHC assay in primary or metastatic tumour tissue

↓

H-score of Nectin-4 subgroups: **Low** (<275) or **high** (≥275)

↓

Clinical efficacy (PFS, OS, and ORR) was assessed in **Nectin-4 low and high expression subgroups**

A retrospective, *post hoc* analysis of Nectin-4 expression using a CAP-/CLIA-validated Nectin-4 IHC assay on primary or metastatic tumour tissue. Nectin-4 expression and PD-L1 expression data were available for 800 of the 886 randomised patients (EV+P: n=394; chemotherapy: n=406). PD-L1 expression status was categorised as high (CPS ≥10) or low (CPS <10) using a validated PD-L1 IHC assay. Oncological outcomes and clinical efficacy (PFS, OS, and ORR) were assessed across Nectin-4 expression subgroups.

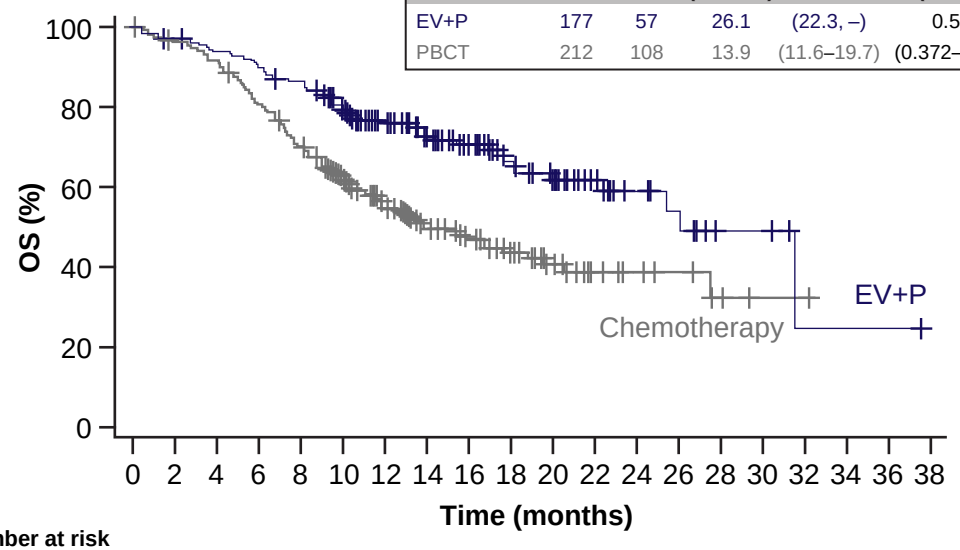
1L, first line; CAP, College of American Pathologists; CLIA, Clinical Laboratory Improvement Amendments; CPS, combined positive score; EV, enfortumab vedotin; IHC, immunohistochemistry; LA/mUC, locally advanced/metastatic urothelial carcinoma; ORR, overall response rate; OS, overall survival; P, pembrolizumab; PD-L1, programmed cell death ligand 1; PFS, progression-free survival.

Powles T, et al. Presented at ESMO 2024. 1966MO.

Regardless of Nectin-4 expression levels, OS was superior with EV+P vs. PBCT in EV-302

OS benefit with EV+P in patients with a Nectin-4 H-score of <275

	N	Events	Median, (months)	95% CI	Stratified HR (95% CI)
EV+P	177	57	26.1	(22.3, –)	0.518
PBCT	212	108	13.9	(11.6–19.7)	(0.372–0.721)

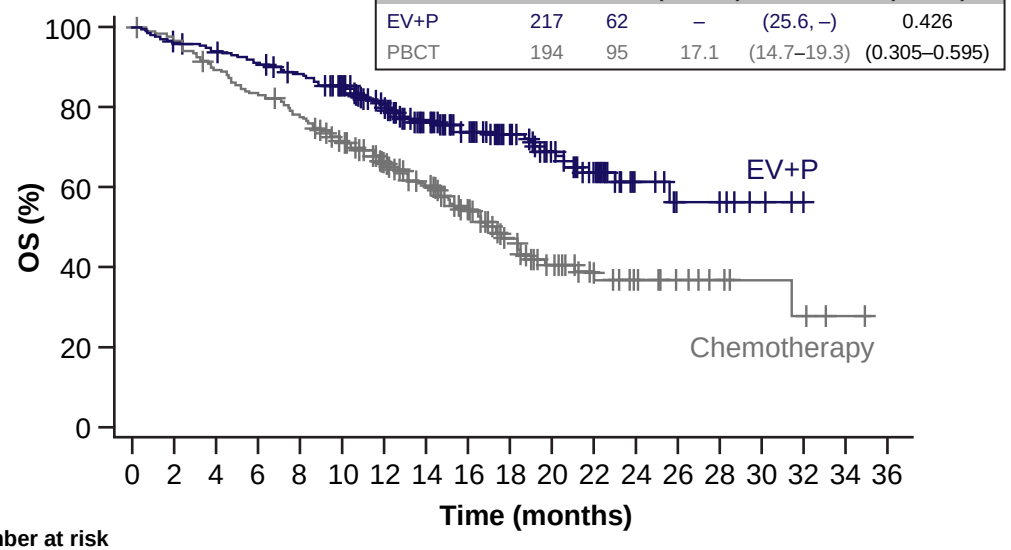


Number at risk

EV+P	177	171	164	157	150	128	102	81	64	46	36	24	15	11	4	4	1	1	1	0
Chemotherapy	212	202	192	169	145	114	87	66	50	36	24	15	10	7	4	1	1	0	0	0

OS benefit with EV+P in patients with a Nectin-4 H-score of ≥275

	N	Events	Median, (months)	95% CI	Stratified HR (95% CI)
EV+P	217	62	–	(25.6, –)	0.426
PBCT	194	95	17.1	(14.7–19.3)	(0.305–0.595)



Number at risk

EV+P	217	208	201	195	186	169	144	121	103	81	59	35	17	8	7	3	0	0	0
Chemotherapy	194	184	168	156	145	126	103	86	65	46	30	19	13	9	6	4	3	1	0

A retrospective, *post hoc* analysis of Nectin-4 expression using a CAP-/CLIA-validated Nectin-4 IHC assay on primary or metastatic tumour tissue. Oncological outcomes and clinical efficacy (PFS, OS, and ORR) were assessed across Nectin-4 expression subgroups.

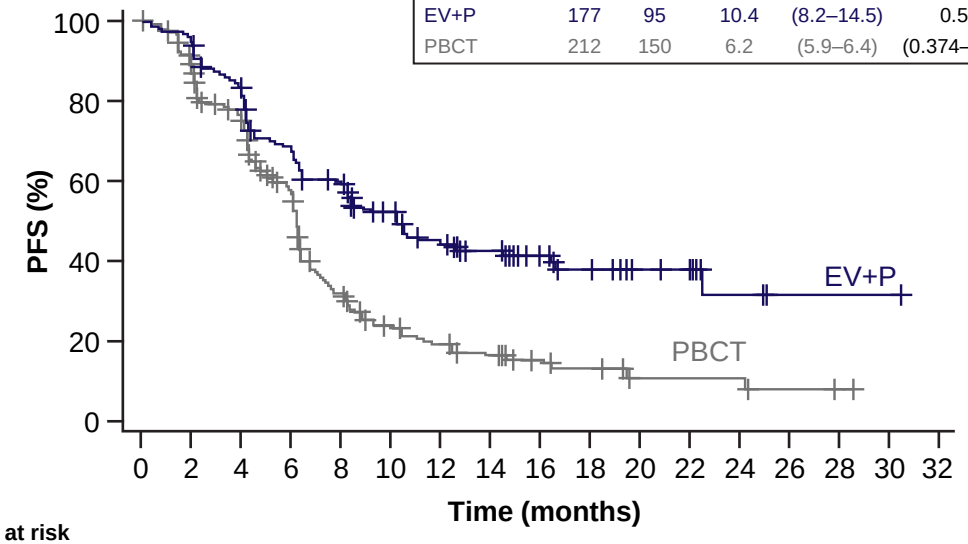
CAP, College of American Pathologists; CI, confidence interval; CLIA, Clinical Laboratory Improvement Amendments; EV, enfortumab vedotin; HR, hazard ratio; IHC, immunohistochemistry; OS, overall survival; ORR, overall response rate; P, pembrolizumab; PBCT, platinum-based chemotherapy; PFS, progression-free survival.

Powles T, et al. Presented at ESMO 2024. 1966MO.

The PFS benefit of EV+P was consistent across Nectin-4 H-score subgroups

PFS benefit with EV+P in patients with a Nectin-4 H-score of <275*

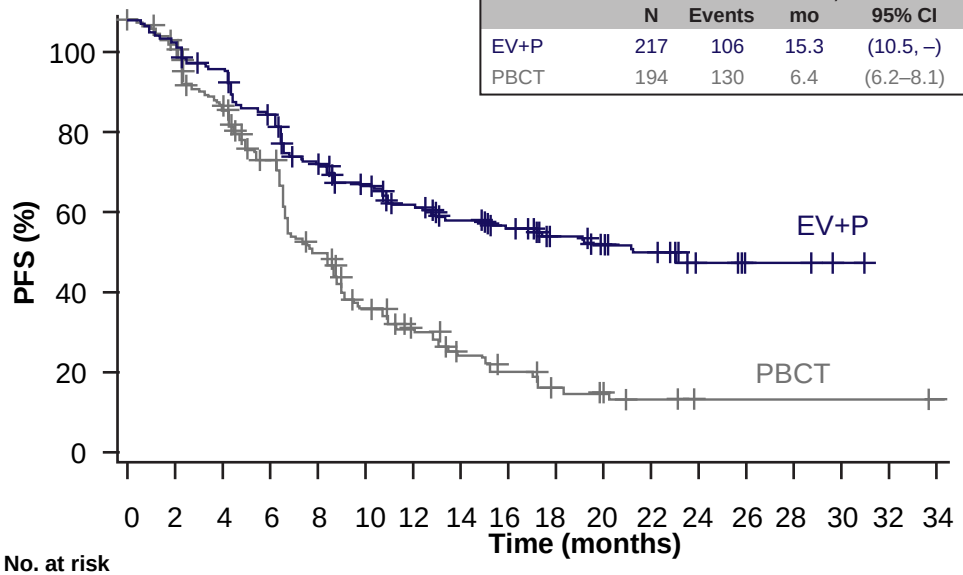
	N	Events	Median, mo	95% CI	Stratified HR (95% CI)
EV+P	177	95	10.4	(8.2–14.5)	0.503
PBCT	212	150	6.2	(5.9–6.4)	(0.374–0.657)



No. at risk																	
EV+P	177	165	138	111	94	72	54	40	28	19	11	9	5	1	1	1	0
PBCT	212	178	142	97	51	33	24	19	14	10	4	4	4	2	1	0	0

PFS benefit with EV+P in patients with a Nectin-4 H-score of ≥275*

	N	Events	Median, mo	95% CI	Stratified HR (95% CI)
EV+P	217	106	15.3	(10.5, –)	0.410
PBCT	194	130	6.4	(6.2–8.1)	(0.313– 0.537)

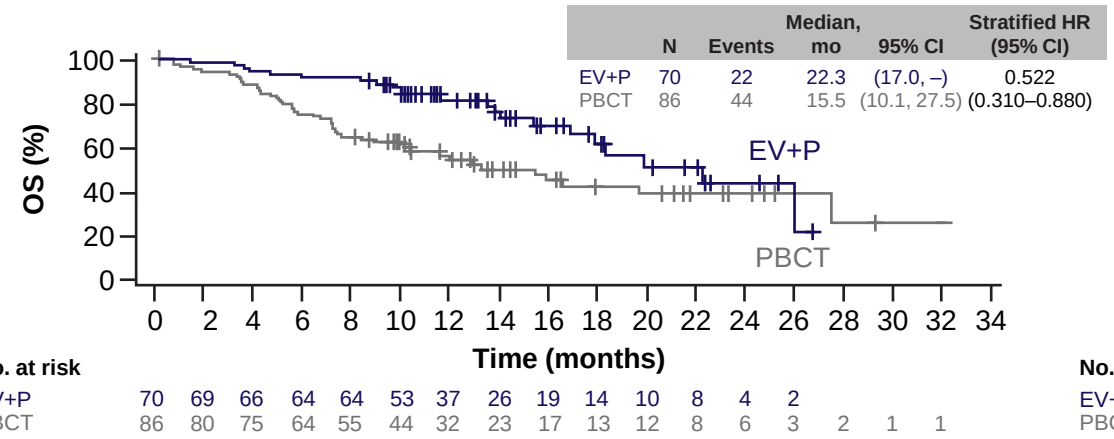


No. at risk																		
EV+P	217	202	186	159	132	111	97	80	66	47	29	21	10	4	2	0	0	0
PBCT	194	166	129	96	63	40	29	20	15	8	4	2	1	1	1	1	1	0

A retrospective, *post hoc* analysis of Nectin-4 expression using a CAP-/CLIA-validated Nectin-4 IHC assay on primary or metastatic tumour tissue. Oncological outcomes and clinical efficacy (PFS, OS, and ORR) were assessed across Nectin-4 expression subgroups.
Data cutoff: 8 August 2023.
*Median nectin-4 H-score was 275 across patients in both arms.
CAP, College of American Pathologists; CI, confidence interval; CLIA, Clinical Laboratory Improvement Amendments; EV, enfortumab vedotin; HR, hazard ratio; IHC, immunohistochemistry; ORR, overall response rate; OS, overall survival; P, pembrolizumab; PBCT, platinum-based chemotherapy; PFS, progression-free survival.
Powles T, et al. Presented at ESMO 2024. 1966MO.

Consistent OS benefits were seen with EV+P across Nectin-4 and PD-L1 subgroups

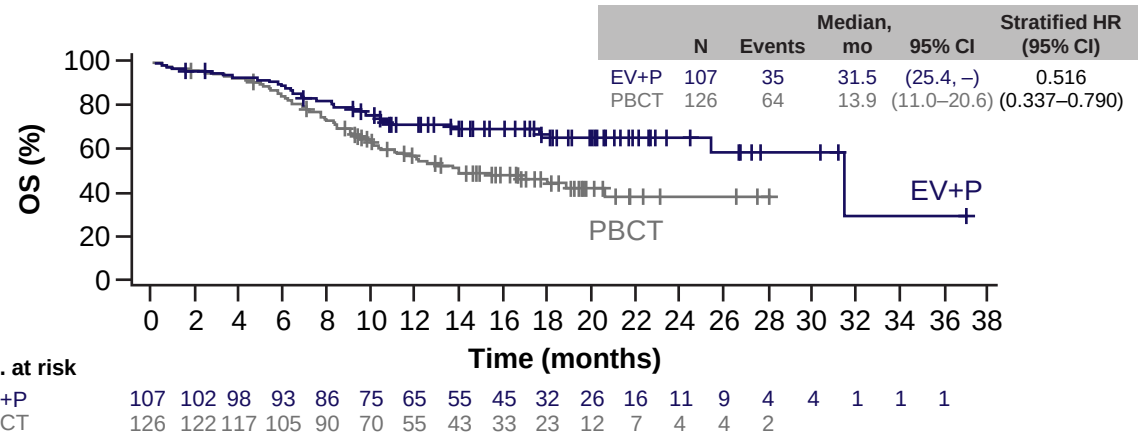
Nectin-4 H-score of <275* / PD-L1 low†



	N	Events	Median, mo	95% CI	Stratified HR (95% CI)
EV+P	70	22	22.3	(17.0, –)	0.522
PBCT	86	44	15.5	(10.1, 27.5)	(0.310–0.880)

No. at risk																	
EV+P	70	69	66	64	64	53	37	26	19	14	10	8	4	2			
PBCT	86	80	75	64	55	44	32	23	17	13	12	8	6	3	2	1	1

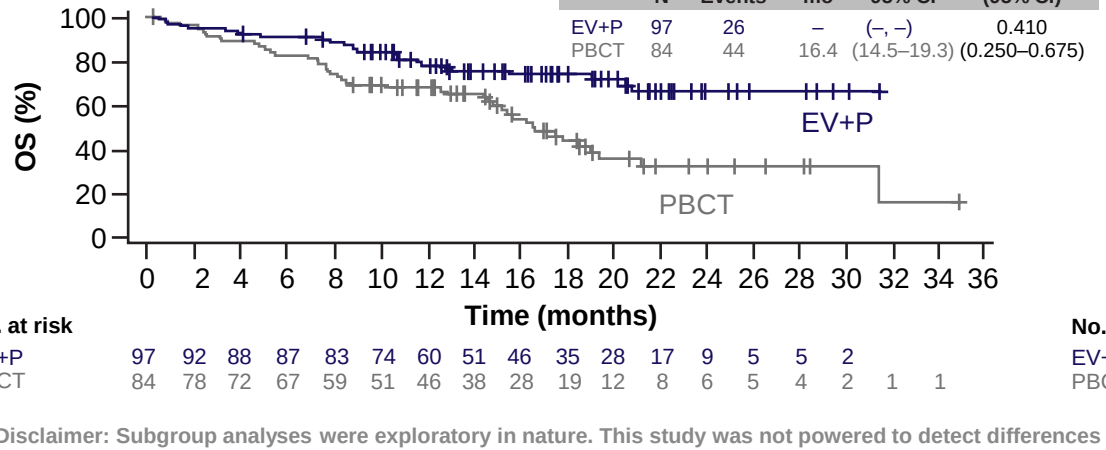
Nectin-4 H-score of <275* / PD-L1 high‡



	N	Events	Median, mo	95% CI	Stratified HR (95% CI)
EV+P	107	35	31.5	(25.4, –)	0.516
PBCT	126	64	13.9	(11.0–20.6)	(0.337–0.790)

No. at risk																	
EV+P	107	102	98	93	86	75	65	55	45	32	26	16	11	9	4	4	1	1	1
PBCT	126	122	117	105	90	70	55	43	33	23	12	7	4	4	2				

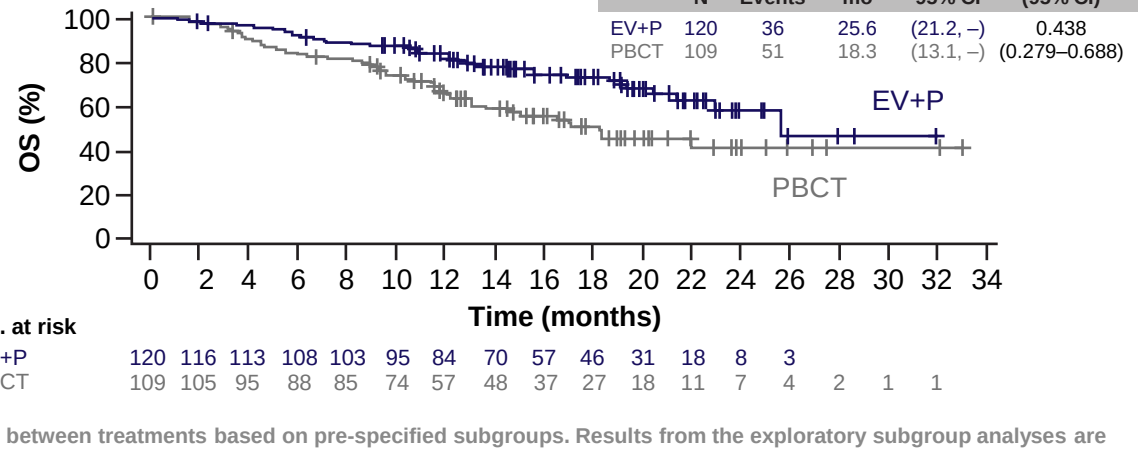
Nectin-4 H-score of ≥275* / PD-L1 low†



	N	Events	Median, mo	95% CI	Stratified HR (95% CI)
EV+P	97	26	–	(–, –)	0.410
PBCT	84	44	16.4	(14.5–19.3)	(0.250–0.675)

No. at risk																	
EV+P	97	92	88	87	83	74	60	51	46	35	28	17	9	5	5	2	
PBCT	84	78	72	67	59	51	46	38	28	19	12	8	6	5	4	2	1	1

Nectin-4 H-score of ≥275* / PD-L1 high‡



	N	Events	Median, mo	95% CI	Stratified HR (95% CI)
EV+P	120	36	25.6	(21.2, –)	0.438
PBCT	109	51	18.3	(13.1, –)	(0.279–0.688)

No. at risk																	
EV+P	120	116	113	108	103	95	84	70	57	46	31	18	8	3			
PBCT	109	105	95	88	85	74	57	48	37	27	18	11	7	4	2	1	1

Disclaimer: Subgroup analyses were exploratory in nature. This study was not powered to detect differences between treatments based on pre-specified subgroups. Results from the exploratory subgroup analyses are descriptive but not conclusive, were not controlled for type I errors, and should be interpreted with caution.

Median follow-up: 17.2 months. Data cut-off date: 8 August 2023.

*The median Nectin-4 H-score was 275 across both arms; †CPS <10; ‡CPS ≥10.

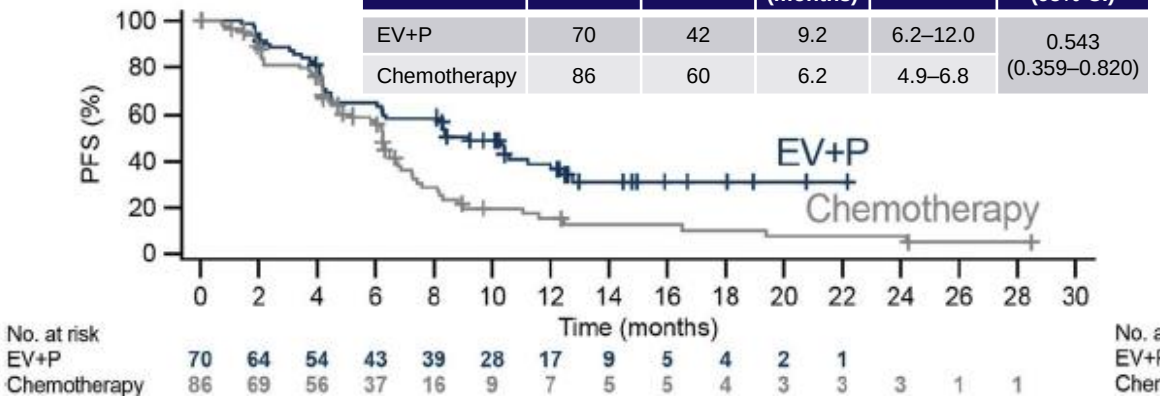
CI, confidence interval; CPS, combined positive score; EV, enfortumab vedotin; HR, hazard ratio; mo, months; OS, overall survival; P, pembrolizumab; PD-L1, programmed cell death ligand 1.

Powles T et al. Presented at ESMO 2024. 1966MO.

Consistent PFS benefits were seen with EV+P across Nectin-4 and PD-L1 subgroups

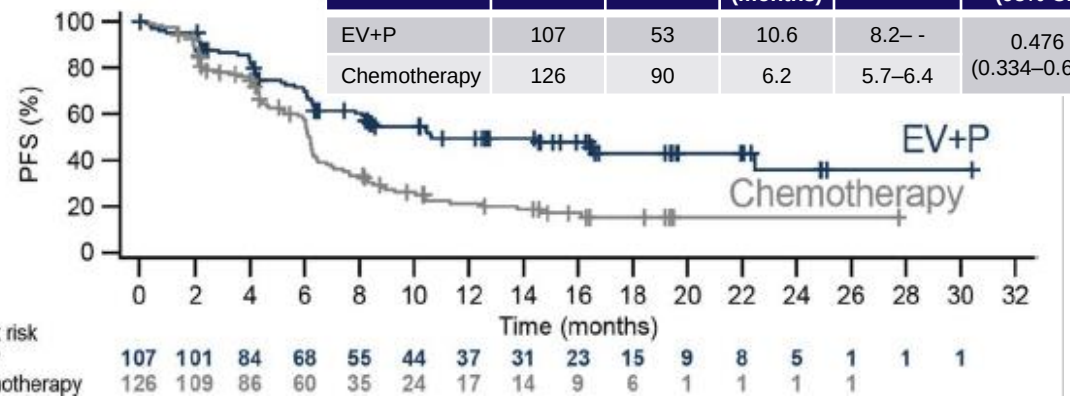
Nectin-4 H-score <275*/PD-L1 low†

	N	Events	Median (months)	95% CI	Stratified HR (95% CI)
EV+P	70	42	9.2	6.2–12.0	0.543 (0.359–0.820)
Chemotherapy	86	60	6.2	4.9–6.8	



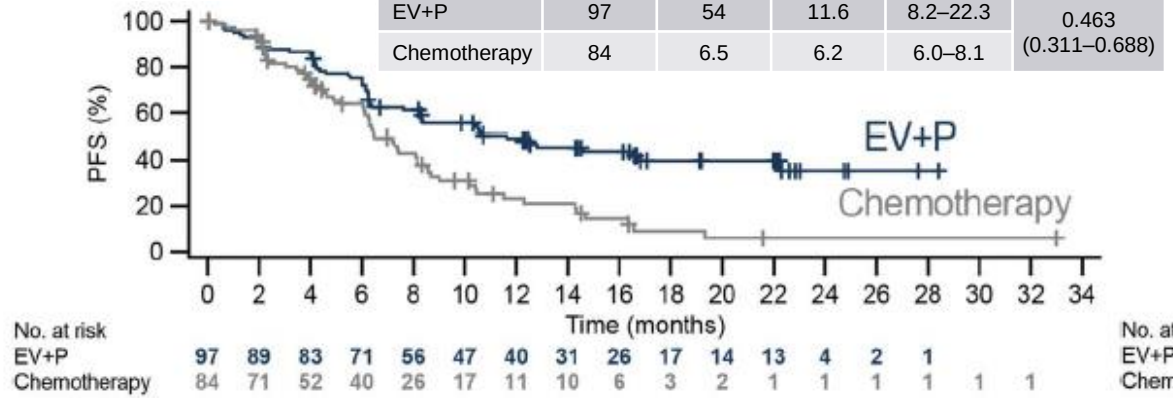
Nectin-4 H-score <275*/PD-L1 high‡

	N	Events	Median (months)	95% CI	Stratified HR (95% CI)
EV+P	107	53	10.6	8.2– -	0.476 (0.334–0.677)
Chemotherapy	126	90	6.2	5.7–6.4	



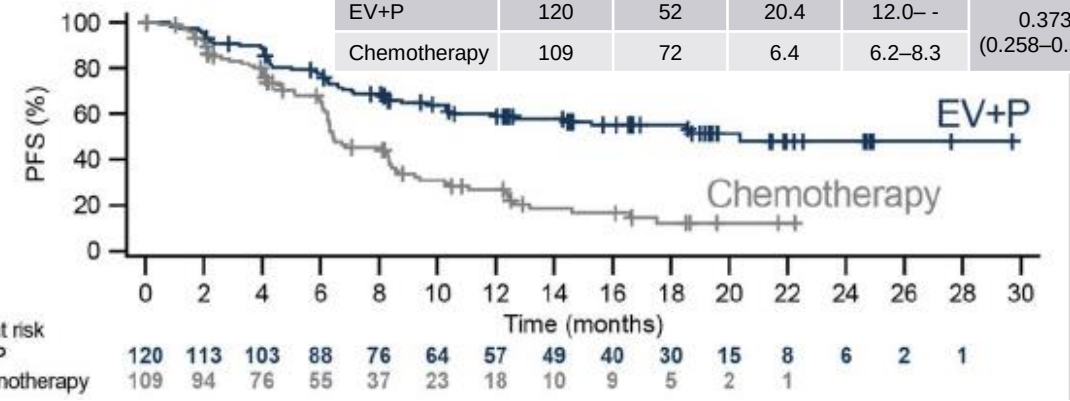
Nectin-4 H-score ≥275*/PD-L1 low†

	N	Events	Median (months)	95% CI	Stratified HR (95% CI)
EV+P	97	54	11.6	8.2–22.3	0.463 (0.311–0.688)
Chemotherapy	84	6.5	6.2	6.0–8.1	



Nectin-4 H-score ≥275*/PD-L1 high‡

	N	Events	Median (months)	95% CI	Stratified HR (95% CI)
EV+P	120	52	20.4	12.0– -	0.373 (0.258–0.539)
Chemotherapy	109	72	6.4	6.2–8.3	



Data cutoff: 8 August 2023.
*The median Nectin-4 H-score was 275 across patients in both arms; †CPS <10; ‡CPS ≥10.
CPS, combined positive score; EV, enfortumab vedotin; P, pembrolizumab; PD-L1, programmed cell death ligand 1; PFS, progression-free survival.

Summary

- After a median follow-up of 2.5 years, EV+P continued to **demonstrate superior efficacy** vs. PBCT in the overall patient population and pre-specified subgroups, more than doubling OS vs. PBCT[1,2]
- EV+P provides a **durable response** for patients with unresectable/mUC[3]
- In the EV+P arm, the proportion of patients achieving CR (~60% cisplatin eligible) was **twice that in the PBCT arm[3]**
- **No new safety signals were identified with EV+P** after an additional 1-year follow-up[1,2]
- Appropriate dose **modifications/interruptions allowed for responders to continue treatment**, with a safety profile similar to that in the overall population despite receiving more cycles of treatment[3]
- EV+P significantly improved survival outcomes vs. PBCT **without detriment to GHS/QoL, pain or functioning**[4]

CR, complete response; EV, enfortumab vedotin; GHS, global health status; mUC, metastatic urothelial carcinoma; OS, overall survival; P, pembrolizumab; platinum-based chemotherapy; QoL, quality of life

1. Powles T, presented at ASCO GU 2025, Abstract 664; 2. Powles T et al. *Ann Oncol* 2025; https://doi.org/10.1016/j.annonc.2025.05.536; 3. Gupta S et al. Presented at ASCO 2025. #4502; 4. Gupta S, et al. *Lancet Oncol* 2025;26:795–805.

Genitourinary Masterclass

astellas

Please refer to the EMA SmPC for PADCEV™ (enfortumab vedotin) via the following link: https://www.ema.europa.eu/en/documents/product-information/padcev-epar-product-information_en.pdf

Please scan the QR code to access the UK aPI for PADCEV

Please scan the QR code to access the NL SmPC for PADCEV

PADCEV is subject to medicinal prescription.
Astellas Pharma B.V., Sylviusweg 62, 2333 BE Leiden, The Netherlands

EMA, European Medicines Agency; aPI, abbreviated Prescribing Information; SmPC, Summary of Product Characteristics.

ABBREVIATED SUMMARY OF PRODUCT CHARACTERISTICS

For full prescribing information refer to the Summary of Product Characteristics (SPC).

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. **NAME OF THE MEDICINAL PRODUCT:** Padcev 20 mg powder for concentrate for solution for infusion **&** Padcev 30 mg powder for concentrate for solution for infusion

QUALITATIVE AND QUANTITATIVE COMPOSITION: Padcev 20 mg powder for concentrate for solution for infusion: One vial of powder for concentrate for solution for infusion contains 20 mg enfortumab vedotin. Padcev 30 mg powder for concentrate for solution for infusion: One vial of powder for concentrate for solution for infusion contains 30 mg enfortumab vedotin. After reconstitution, each mL of solution contains 10 mg of enfortumab vedotin. Enfortumab vedotin is comprised of a fully human IgG1 kappa antibody, conjugated to the microtubule-disrupting agent monomethyl auristatin E (MMAE) via a protease-cleavable maleimidocaproyl valine-citrulline linker. For the full list of excipients, see section 6.1 of the SPC.

PHARMACEUTICAL FORM: Powder for concentrate for solution for infusion. White to off-white lyophilized powder.

CLINICAL PARTICULARS: Therapeutic indications: Padcev, in combination with pembrolizumab, is indicated for the first-line treatment of adult patients with unresectable or metastatic urothelial cancer who are eligible for platinum-containing chemotherapy. 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 (see section 5.1 of the SPC). **Posology and method of administration**: Treatment with Padcev should be initiated and supervised by a physician experienced in the use of anti-cancer therapies. Ensure good venous access prior to starting treatment (see section 4.4 of the SPC). Posology: As monotherapy, the recommended dose of enfortumab vedotin is 1.25 mg/kg (up to a maximum of 125 mg for patients ≥100 kg) administered as an intravenous infusion over 30 minutes on Days 1, 8 and 15 of a 28-day cycle until disease progression or unacceptable toxicity. When given in combination with pembrolizumab, the recommended dose of enfortumab vedotin is 1.25 mg/kg (up to a maximum of 125 mg for patients ≥100 kg) administered as an intravenous infusion over 30 minutes on Days 1 and 8 of every 3-week (21-day) cycle until disease progression or unacceptable toxicity. The recommended dose of pembrolizumab is either 200 mg every 3 weeks or 400 mg every 6 weeks administered as an intravenous infusion over 30 minutes. Patients should be administered pembrolizumab after enfortumab vedotin when given on the same day. Refer to the pembrolizumab SPC for additional dosing information of pembrolizumab.

Table 1. Recommended dose reductions of enfortumab vedotin for adverse reactions

	Dose level
Starting dose	1.25 mg/kg up to 125 mg
First dose reduction	1.0 mg/kg up to 100 mg
Second dose reduction	0.75 mg/kg up to 75 mg
Third dose reduction	0.5 mg/kg up to 50 mg

Dose modifications

Table 2. Dose interruption, reduction and discontinuation of enfortumab vedotin in patients with locally advanced or metastatic urothelial cancer

Adverse reaction	Severity*	Dose modification*
Skin reactions	Suspected Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN) or bullous lesions	Immediately withhold and refer to specialised care.
	Confirmed SJS or TEN; Grade 4 or recurrent Grade 3	Permanently discontinue.
	Grade 2 worsening Grade 2 with fever Grade 3	• Withhold until Grade ≤1. • Referral to specialised care should be considered. • Resume at the same dose level or consider dose reduction by one dose level (see Table 1).
Hyperglycaemia	Blood glucose >13.9 mmol/L (>250 mg/dL)	• Withhold until elevated blood glucose has improved to ≤13.9 mmol/L (≤250 mg/dL). • Resume treatment at the same dose level.
Pneumonitis/ interstitial lung disease (ILD)	Grade 2	• Withhold until Grade ≤1, then resume at the same dose or consider dose reduction by one dose level (see Table 1).
	Grade ≥3	Permanently discontinue.
Peripheral neuropathy	Grade 2	• Withhold until Grade ≤1. • For first occurrence, resume treatment at the same dose level. • For a recurrence, withhold until Grade ≤1, then resume treatment reduced by one dose level (see Table 1).
	Grade ≥3	Permanently discontinue.

*Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events Version 5.0 (NCI-CTCAE v5.0) where Grade 1 is mild, Grade 2 is moderate, Grade 3 is severe and Grade 4 is life threatening.

Special populations: *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) (see section 5.2 of the SPC). *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 AST any, or total bilirubin ≤ ULN and AST > ULN]. Enfortumab vedotin has only been evaluated in a limited number of patients with moderate and severe hepatic impairment. Hepatic impairment is expected to increase the systemic exposure to MMAE (the cytotoxic drug); therefore, patients should be closely monitored for potential adverse events. Due to the sparsity of the data in patients with moderate and severe hepatic impairment, no specific dose recommendation can be given. *Paediatric population:* There is no relevant use of enfortumab vedotin in the paediatric population for the indication of locally advanced or metastatic urothelial cancer.

Method of administration

Padcev is for intravenous use. The recommended dose must be administered by intravenous infusion over 30 minutes. Enfortumab vedotin must not be administered as an intravenous push or bolus injection. For instructions on reconstitution and dilution of the medicinal product before administration, see section 6.6 of the SPC. **Contraindications**: Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 of the SPC. **Special warnings and precautions for use**: Traceability: In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. Skin reactions: Skin reactions are associated with enfortumab vedotin as a result of enfortumab vedotin binding to Nectin-4 expressed in the skin. Fever or flu-like symptoms may be the first sign of a severe skin reaction, and patients should be observed, if this occurs. Mild to moderate skin reactions, predominantly rash maculo-papular, have been reported with enfortumab vedotin. The incidence of skin reactions occurred at a higher rate when enfortumab vedotin was given in combination with pembrolizumab compared to enfortumab vedotin as monotherapy (see section 4.8 of the SPC). 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. Patients should be monitored starting with the first cycle and throughout treatment for skin reactions. Appropriate treatment such as topical corticosteroids and antihistamines can be considered for mild to moderate skin reactions. For suspected SJS or TEN, or in case of bullous lesions onset, withhold treatment immediately and refer to specialised care; histologic confirmation, including consideration of multiple biopsies, is critical to early recognition, as diagnosis and intervention can improve prognosis. Permanently discontinue Padcev for confirmed SJS or TEN, Grade 4 or recurrent Grade 3 skin reactions. For Grade 2 worsening, Grade 2 with fever or Grade 3 skin reactions, treatment should be withheld until Grade ≤1 and referral for specialised care should be considered. Treatment should be resumed at the same dose level or consider dose reduction by one dose level (see section 4.2 of the SPC). Pneumonitis/ILD: Severe, life-threatening or fatal pneumonitis/ILD have occurred in patients treated with enfortumab vedotin. The incidence of pneumonitis/ILD, including severe events occurred at a higher rate when enfortumab vedotin was given in combination with pembrolizumab compared to enfortumab vedotin as monotherapy (see section 4.8 of the SPC). Monitor patients for signs and symptoms indicative of pneumonitis/ILD such as hypoxia, cough, dyspnoea or interstitial infiltrates on radiologic exams. Corticosteroids should be administered for Grade ≥ 2 events (e.g., initial dose of 1-2 mg/kg/day prednisone or equivalent followed by a taper). Withhold Padcev for Grade 2 pneumonitis/ILD and consider dose reduction. Permanently discontinue Padcev for Grade ≥3 pneumonitis/ILD (see section 4.2 of the SPC). Hyperglycaemia: Hyperglycaemia and diabetic ketoacidosis (DKA), including fatal events, occurred in patients with and without pre-existing diabetes mellitus, treated with enfortumab vedotin (see section 4.8 of the SPC). Hyperglycaemia occurred more frequently in patients with pre-existing hyperglycaemia or a high body mass index (≥30 kg/m²). Patients with baseline HbA1c ≥8% were excluded from clinical studies. Blood glucose levels should be monitored prior to dosing and periodically throughout the course of treatment as clinically indicated in patients with or at risk for diabetes mellitus or hyperglycaemia. If blood glucose is elevated >13.9 mmol/L (>250 mg/dL), Padcev should be withheld until blood glucose is ≤13.9 mmol/L (≤250 mg/dL) and treat as appropriate (see section 4.2 of the SPC). Serious infections: Serious infections such as sepsis (including fatal outcomes) have been reported in patients treated with Padcev. Patients should be carefully monitored during treatment for the emergence of possible serious infections. Peripheral neuropathy: Peripheral neuropathy, predominantly peripheral sensory neuropathy, has occurred with enfortumab vedotin, including Grade ≥3 reactions (see section 4.8 of the SPC). Patients with preexisting peripheral neuropathy Grade ≥2 were excluded from clinical studies. Patients should be monitored for symptoms of new or worsening peripheral neuropathy as these patients may require a delay, dose reduction or discontinuation of enfortumab vedotin (see Table 1). Padcev should be permanently discontinued for Grade ≥3 peripheral neuropathy (see section 4.2 of the SPC). Ocular disorders: Ocular disorders, predominantly dry eye, have occurred in patients treated with enfortumab vedotin (see section 4.8 of the SPC). Patients should be monitored for ocular disorders. Consider artificial tears for prophylaxis of dry eye and referral 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 (see section 4.8 of the SPC). 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. Embryo-foetal toxicity and contraception: Pregnant women should be informed of the potential risk to a foetus (see sections 4.6 and 5.3 of the SPC). Females of reproductive potential should be advised to have a pregnancy test within 7 days prior to starting treatment with enfortumab vedotin, to use effective contraception during treatment and for at least 6 months after stopping treatment. Men being treated with enfortumab vedotin are advised not to father a child during treatment and for at least 4 months following the last dose of Padcev. Patient information pack: The prescriber must discuss the risks of Padcev therapy, including combination therapy with pembrolizumab, with the patient. The patient should be provided with the patient information leaflet and patient card with each prescription. **Interactions:** Formal drug–drug interaction studies with enfortumab vedotin have not been conducted. Caution is advised in case of concomitant treatment with CYP3A4 inhibitors. Patients receiving concomitant strong CYP3A4 inhibitors should be monitored more closely for signs of toxicities. Strong CYP3A4 inducers may decrease the exposure of unconjugated MMAE with moderate effect (see section 5.2 of the SPC). **Undesirable effects**: Summary of the safety profile: *Enfortumab vedotin as monotherapy*: The safety of enfortumab vedotin was evaluated as monotherapy in 793 patients who received at least one dose of enfortumab vedotin 1.25 mg/kg in two phase 1 studies (EV-101 and EV-102), three phase 2 studies (EV-103, EV-201 and EV-203) and one phase 3 study (EV-301) (see Table 3). Patients were exposed to enfortumab vedotin for a median duration of 4.7 months (range: 0.3 to 55.7 months). The most common adverse reactions with enfortumab vedotin were alopecia (47.7%), decreased appetite (47.2%), fatigue (46.8%), diarrhoea (39.1%), peripheral sensory neuropathy (38.5%), nausea (37.8%), pruritus (33.4%), dysgeusia (30.4%), anaemia (29.1%), weight decreased (25.2%), rash maculo-papular (23.6%), dry skin (21.8%), vomiting (18.7%), aspartate aminotransferase increased (17%), hyperglycaemia (14.9%), dry eye (12.7%), alanine aminotransferase increased (12.7%) and rash (11.6%). The most common serious adverse reactions (≥2%) were diarrhoea (2.1%) and hyperglycaemia (2.1%). Twenty-one percent of patients permanently discontinued enfortumab vedotin for adverse reactions; the most common adverse reaction (≥2%) leading to dose discontinuation was peripheral sensory neuropathy (4.8%). Adverse reactions leading to dose interruption occurred in 62% of patients; the most common adverse reactions (≥2%) leading to dose interruption were peripheral sensory neuropathy (14.8%), fatigue (7.4%), rash maculo-papular (4%), aspartate aminotransferase increased (3.4%), alanine aminotransferase increased (3.2%), anaemia (3.2%), hyperglycaemia (3.2%), neutrophil count decreased (3%), diarrhoea (2.8%), rash (2.4%) and peripheral motor neuropathy (2.1%). Thirty-eight percent of patients required a dose reduction due to an adverse reaction; the most common adverse reactions (≥2%) leading to a dose reduction were peripheral sensory neuropathy (10.3%), fatigue (5.3%), rash maculo-papular (4.2%) and decreased appetite (2.1%). *Enfortumab vedotin in combination with pembrolizumab*: When enfortumab vedotin is administered in combination with pembrolizumab, refer to the SmPC for pembrolizumab prior to initiation of treatment. The safety of enfortumab vedotin was evaluated in combination with pembrolizumab in 564 patients who received at least one dose of enfortumab vedotin 1.25 mg/kg in combination with pembrolizumab in one phase 2 study (EV-103) and one phase 3 study (EV-302) (see Table 3). Patients were exposed to enfortumab vedotin in combination with pembrolizumab for a median duration of 9.4 months (range: 0.3 to 34.4 months). The most common adverse reactions with enfortumab vedotin in combination with pembrolizumab were peripheral sensory neuropathy (53.4%), pruritus (41.1%), fatigue (40.4%), diarrhoea (39.2%), alopecia (38.5%), rash maculo-papular (36%), weight decreased (36%), decreased appetite (33.9%), nausea (28.4%), anaemia (25.7%), dysgeusia (24.3%), dry skin (18.1%), alanine aminotransferase increased (16.8%), hyperglycaemia (16.7%), aspartate aminotransferase increased (15.4%), dry eye (14.4%), vomiting (13.3%), rash macular (11.3%), hypothyroidism (10.5%) and neutropenia (10.1%). The most common serious adverse reactions (≥2%) were diarrhoea (3%) and pneumonitis (2.3%). Thirty-six percent of patients permanently discontinued enfortumab vedotin for adverse reactions; the most common adverse reactions (≥2%) leading to discontinuation were peripheral sensory neuropathy (12.2%) and rash maculo-papular (2%). Adverse reactions leading to dose interruption of enfortumab vedotin occurred in 72% of patients. The most common adverse reactions (≥2%) leading to dose interruption were peripheral sensory neuropathy (17%), rash maculo-papular (6.9%), diarrhoea (4.8%), fatigue (3.7%), pneumonitis (3.7%), hyperglycaemia (3.4%), neutropenia (3.2%), alanine aminotransferase increased (3%), pruritus (2.3%) and anaemia (2%). Adverse reactions leading to dose reduction of enfortumab vedotin occurred in 42.4% of patients. The most common adverse reactions (≥2%) leading to dose reduction were peripheral sensory neuropathy (9.9%), rash maculo-papular (6.4%), fatigue (3.2%), diarrhoea (2.3%) and neutropenia (2.1%). Tabulated summary of adverse reactions: Adverse reactions observed during clinical studies of enfortumab vedotin as monotherapy or in combination with pembrolizumab, or reported from post-marketing use of enfortumab vedotin are listed in this section by frequency category. Frequency categories are defined as follows: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 3. Adverse reactions in patients treated with enfortumab vedotin

	Monotherapy	In combination with pembrolizumab
Infections and infestations		
Common	Sepsis	Sepsis
Blood and lymphatic system disorders		
Very common	Anaemia	Anaemia
Not known[1]	Neutropenia, febrile neutropenia, neutrophil count decreased	Neutropenia, febrile neutropenia, neutrophil count decreased
Endocrine disorders		
Very common		Hypothyroidism
Metabolism and nutrition disorders		
Very common	Hyperglycaemia, decreased appetite	Hyperglycaemia, decreased appetite
Not known[1]	Diabetic ketoacidosis	Diabetic ketoacidosis
Nervous system disorders		
Very common	Peripheral sensory neuropathy, dysgeusia	Peripheral sensory neuropathy, dysgeusia
Common	Neuropathy peripheral, peripheral motor neuropathy, peripheral sensorimotor neuropathy, paraesthesia, hypoaesthesia, gait disturbance, muscular weakness	Peripheral motor neuropathy, peripheral sensorimotor neuropathy, paraesthesia, hypoaesthesia, gait disturbance, muscular weakness
Uncommon	Demyelinating polyneuropathy, polyneuropathy, neurotoxicity, motor dysfunction, dysaesthesia, muscle atrophy, neuralgia, peroneal nerve palsy, sensory loss, skin burning sensation, burning sensation	Neurotoxicity, dysaesthesia, myasthenia gravis, neuralgia, peroneal nerve palsy, skin burning sensation
Eye disorders		
Very common	Dry eye	Dry eye
Respiratory, thoracic, and mediastinal disorders		
Very common		Pneumonitis/ILD[2]
Common	Pneumonitis/ILD[2]	
Gastrointestinal disorders		
Very common	Diarrhoea, vomiting, nausea	Diarrhoea, vomiting, nausea
Skin and subcutaneous tissue disorders		
Very common	Alopecia, pruritus, rash, rash maculo-papular, dry skin	Alopecia, pruritus, rash maculo-papular, dry skin, rash macular
Common	Drug eruption, skin exfoliation, conjunctivitis, dermatitis bullous, blister, stomatitis, palmar-plantar erythrodysesthesia syndrome, eczema, erythaema, rash erythaematous, rash macular, rash papular, rash pruritic, rash vesicular	Rash, skin exfoliation, conjunctivitis, dermatitis bullous, blister, stomatitis, palmar-plantar erythrodysesthesia syndrome, eczema, erythaema, rash erythaematous, rash papular, rash pruritic, rash vesicular, erythaema multiforme, dermatitis
Uncommon	Dermatitis exfoliative generalised, erythaema multiforme, exfoliative rash, pemphigoid, rash maculovesicular, dermatitis, dermatitis allergic, dermatitis contact, intertrigo, skin irritation, stasis dermatitis, blood blister	Drug eruption, dermatitis exfoliative generalised, exfoliative rash, pemphigoid, dermatitis contact, intertrigo, skin irritation, stasis dermatitis
Not known[1]	Toxic epidermal necrolysis, skin hyperpigmentation, skin discoloration, pigmentation disorder, Stevens Johnson syndrome, epidermal necrosis, symmetrical drug-related intertriginous and flexural exanthaema	Toxic epidermal necrolysis, skin hyperpigmentation, skin discoloration, pigmentation disorder, Stevens Johnson syndrome, epidermal necrosis, symmetrical drug-related intertriginous and flexural exanthaema
Musculoskeletal and connective tissue disorders		
Common		Myositis
General disorders and administration site conditions		
Very common	Fatigue	Fatigue
Common	Infusion site extravasation	Infusion site extravasation
Investigations		
Very common	Alanine aminotransferase increased, aspartate aminotransferase increased, weight decreased	Alanine aminotransferase increased, aspartate aminotransferase increased, weight decreased
Common		Lipase increased
Injury, poisoning and procedural complications		
Common	Infusion related reaction	Infusion related reaction

[1]Based on global post-marketing experience.

[2]Includes: acute respiratory distress syndrome, autoimmune lung disease, immune-mediated lung disease, interstitial lung disease, lung opacity, organising pneumonia, pneumonitis, pulmonary fibrosis, pulmonary toxicity and sarcoidosis.

Description of selected adverse reactions: *Immunogenicity:* A total of 697 patients were tested for immunogenicity to enfortumab vedotin 1.25 mg/kg as monotherapy; 16 patients were confirmed to be positive at baseline for anti-drug antibody (ADA), and in patients that were negative at baseline (N=681), a total of 24 (3.5%) were positive post baseline. A total of 490 patients were tested for immunogenicity against enfortumab vedotin following enfortumab vedotin in combination with pembrolizumab; 24 patients were confirmed to be positive at baseline for ADA, and in patients that were negative at baseline (N=466), a total of 14 (3%) were positive post baseline. The incidence of treatment-emergent anti-enfortumab vedotin antibody formation was consistent when assessed following enfortumab vedotin administration as monotherapy and in combination with pembrolizumab. Due to the limited number of patients with antibodies against Padcev, no conclusions can be drawn concerning a potential effect of immunogenicity on efficacy, safety or pharmacokinetics. *Skin reactions*: In clinical studies of enfortumab vedotin as monotherapy, skin reactions occurred in 57% (452) of the 793 patients treated with enfortumab vedotin 1.25 mg/kg. Severe (Grade 3 or 4) skin reactions occurred in 14% (108) of patients and a majority of these reactions included rash maculo-papular, stomatitis, rash erythematous, rash or drug eruption. The median time to onset of severe skin reactions was 0.7 months (range: 0.1 to 8.2 months). Serious skin reactions occurred in 4.3% (34) of patients. Of the patients who experienced skin reactions and had data regarding resolution (N=366), 61% had complete resolution, 24% had partial improvement, and 15% had no improvement at the time of their last evaluation. Of the 39% of patients with residual skin reactions at last evaluation, 38% had Grade ≥2 events. In clinical studies of enfortumab vedotin in combination with pembrolizumab, skin reactions occurred in 70% (392) of the 564 patients and a majority of these skin reactions included rash maculo-papular, rash macular and rash papular. Severe (Grade 3 or 4) skin reactions occurred in 17% (97) of patients (Grade 3: 16%, Grade 4: 1%). The median time to onset of severe skin reactions was 1.7 months (range: 0.1 to 17.2 months). Of the patients who experienced skin reactions and had data regarding resolution (N=391), 59% had complete resolution, 30% had partial improvement, and 10% had no improvement at the time of their last evaluation. Of the 41% of patients with residual skin reactions at last evaluation, 27% had Grade ≥2 events. *Pneumonitis/ILD*: In clinical studies of enfortumab vedotin as monotherapy, pneumonitis/ILD occurred in 26 (3.3%) of the 793 patients treated with enfortumab vedotin 1.25 mg/kg. Less than 1% of patients experienced severe (Grade 3 or 4) pneumonitis/ILD (Grade 3: 0.5%, Grade 4: 0.3%). Pneumonitis/ILD led to discontinuation of enfortumab vedotin in 0.5% of patients. There were no deaths from pneumonitis/ILD. The median time to onset of any grade pneumonitis/ILD was 2.7 months (range: 0.6 to 6.0 months) and the median duration for pneumonitis/ILD was 1.6 months (range: 0.1 to 43.0 months). Of the 26 patients who experienced pneumonitis/ILD, 8 (30.8%) had resolution of symptoms. In clinical studies of enfortumab vedotin in combination with pembrolizumab, pneumonitis/ILD occurred in 58 (10.3%) of the 564 patients. Severe (Grade 3 or 4) pneumonitis/ILD occurred in 20 patients (Grade 3: 3.0%, Grade 4: 0.5%). Pneumonitis/ILD led to discontinuation of enfortumab vedotin in 2.1% of patients. Two patients experienced a fatal event of pneumonitis/ILD. The median time to onset of any grade pneumonitis/ILD was 4 months (range: 0.3 to 26.2 months). *Hyperglycaemia*: In clinical studies of enfortumab vedotin as monotherapy, hyperglycaemia (blood glucose >13.9 mmol/L) occurred in 17% (133) of the 793 patients treated with enfortumab vedotin 1.25 mg/kg. Serious events of hyperglycaemia occurred in 2.5% of patients, 7% of patients developed severe (Grade 3 or 4) hyperglycaemia and 0.3% of patients experienced fatal events, one event each of hyperglycaemia and diabetic ketoacidosis. The incidence of Grade 3-4 hyperglycaemia increased consistently in patients with higher body mass index and in patients with higher baseline haemoglobin A1C (HbA1c). The median time to onset of hyperglycaemia was 0.5 months (range: 0 to 20.3). Of the patients who experienced hyperglycaemia and had data regarding resolution (N=106), 66% had complete resolution, 19% had partial improvement, and 15% had no improvement at the time of their last evaluation. Of the 34% of patients with residual hyperglycaemia at last evaluation, 64% had Grade ≥2 events. *Peripheral neuropathy*: In clinical studies of enfortumab vedotin as monotherapy, peripheral neuropathy occurred in 53% (422) of the 793 patients treated with enfortumab vedotin 1.25 mg/kg. Five percent of patients experienced severe (Grade 3 or 4) peripheral neuropathy including sensory and motor events. The median time to onset of Grade ≥2 peripheral neuropathy was 5 months (range: 0.1 to 20.2). Of the patients who experienced neuropathy and had data regarding resolution (N=340), 14% had complete resolution, 46% had partial improvement, and 41% had no improvement at the time of their last evaluation. Of the 86% of patients with residual neuropathy at last evaluation, 51% had Grade ≥2 events. *Ocular disorders*: In clinical studies of enfortumab vedotin as monotherapy, 30% of patients experienced dry eye during treatment with enfortumab vedotin 1.25 mg/kg. Treatment was interrupted in 1.5% of patients and 0.1% of patients permanently discontinued treatment due to dry eye. Severe (Grade 3) dry eye only occurred in 3 patients (0.4%). The median time to onset of dry eye was 1.7 months (range: 0 to 30.6 months). Special populations: *Elderly*: Enfortumab vedotin in combination with pembrolizumab has been studied in 173 patients <65 years and 391 patients ≥65 years. Generally, adverse event frequencies were higher in patients ≥65 years of age compared to <65 years of age, particularly for serious adverse events (56.3%, and 35.3%, respectively) and Grade ≥3 events (80.3% and 64.2%, respectively), similar to observations with the chemotherapy comparator. **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).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

België/Belgique: Federaal Agentschap voor Geneesmiddelen en Gezondheidsproducten / Agence fédérale des médicaments et des produits de santé; www.fagg.be / www.afmps.be; Afdeling Vigilantie / Division Vigilance: Website/Site internet: www.eenbijwerkingmelden.be / www.notifierunneffetindesirable.be; e-mail: adr@fagg-afmps.be

Ireland: HPRA Pharmacovigilance, Website: www.hpra.ie or Astellas Pharma Co. Ltd. Tel: +353 1 467 1555, E-mail: irishdrugsafety@astellas.com.

Nederland: Nederlands Bijwerkingen Centrum Lareb; Website: www.lareb.nl

Luxembourg/Luxemburg : Centre Régional de Pharmacovigilance de Nancy ou Division de la pharmacie et des médicaments de la Direction de la santé ; Site internet : www.guichet.lu/pharmacovigilance

MARKETING AUTHORISATION HOLDER:
Astellas Pharma Europe B.V. Sylviusweg 62, 2333 BE Leiden, The Netherlands

MARKETING AUTHORISATION NUMBERS: EU/1/21/1615/001 & EU/1/21/1615/002

DATE OF REVISION OF THE TEXT: December 2024
Job Bag Number: MAT-BX-PAD-2025-00004

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.
Ireland: Astellas Pharma Co. Ltd., Tel.: +353 1 467 1555. SPC may be found at www.medicines.ie.
Delivery Status: subject to medical prescription.
Astellas Pharma B.V.,
NL: Sylviusweg 62, 2333BE Leiden, Netherlands
BE/LU: Medialaan 50, 1800 Vilvoorde, Belgium
IE: Legal classification: S1A.

Prescribing Information: PADCEV™▼ (enfortumab vedotin) 20 mg and 30 mg powder for concentrate for solution for infusion

For full prescribing information refer to the Summary of Product Characteristics (SPC).

Presentation: One vial of PADCEV powder for concentrate for solution for infusion contains either 20 mg or 30 mg enfortumab vedotin. After reconstitution, each ml of solution contains 10 mg of enfortumab vedotin. Enfortumab vedotin is comprised of a fully human IgG1 kappa antibody, conjugated to the microtubule-disrupting agent monomethyl auristatin E (MMAE) via a protease-cleavable maleimidocaproyl valine-citrulline linker.

Indications: PADCEV, in combination with pembrolizumab, is indicated for the first-line treatment of adult patients with unresectable or metastatic urothelial cancer who are eligible for platinum-containing chemotherapy. 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 (see section 5.1 of the SPC).

Posology and method of administration: Treatment with PADCEV should be initiated and supervised by a physician experienced in the use of anti-cancer therapies. PADCEV is for intravenous use. It must not be administered as an intravenous push or bolus injection. Good venous access prior to starting treatment should be ensured (see section 4.4 of the SPC). As monotherapy, 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. When given in combination with pembrolizumab, the recommended dose of enfortumab vedotin is 1.25 mg/kg (up to a maximum of 125 mg for patients ≥100 kg) administered as an intravenous infusion over 30 minutes on Days 1 and 8 of every 3-week (21-day) cycle until disease progression or unacceptable toxicity. The recommended dose of pembrolizumab is either 200 mg every 3 weeks or 400 mg every 6 weeks administered as an intravenous infusion over 30 minutes. Patients should be administered pembrolizumab after enfortumab vedotin when given on the same day. Refer to the pembrolizumab SmPC for additional dosing information of pembrolizumab. For information on recommended dose reductions of enfortumab vedotin 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 SPC. Special Populations: *Elderly:* No dose adjustment is necessary in patients ≥65 years of age (see section 5.2 of the SPC). *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) (see section 5.2 of the SPC). *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 and severe hepatic impairment. Hepatic impairment is expected to increase the systemic exposure to MMAE (the cytotoxic drug); therefore, patients should be closely monitored for potential adverse events. Due to the sparsity of the data in patients with moderate and severe hepatic impairment, no specific dose recommendation can be given (see section 5.2 of the SPC). *Paediatric population:* There is no relevant use of enfortumab vedotin in the paediatric population for the indication of locally advanced or metastatic urothelial cancer.

Contraindications: Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 of the SPC.

Special warnings and precautions for use: Traceability: In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. Skin reactions: Skin reactions are associated with enfortumab vedotin as a result of enfortumab vedotin binding to Nectin-4 expressed in the skin. Fever or flu-like symptoms may be the first sign of a severe skin reaction, and patients should be observed, if this occurs. Mild to moderate skin reactions, predominantly rash maculo-papular, have been reported with enfortumab vedotin. The incidence of skin reactions occurred at a higher rate when enfortumab vedotin was given in combination with pembrolizumab compared to enfortumab vedotin as monotherapy (see section 4.8 of the SPC). Severe cutaneous adverse reactions, including Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), with fatal outcome have also occurred in patients treated with enfortumab vedotin, predominantly during the first cycle of treatment. Patients should be monitored starting with the first cycle and throughout treatment for skin reactions. Appropriate treatment such as topical corticosteroids and antihistamines can be considered for mild to moderate skin reactions. For suspected SJS or TEN, or in case of bullous lesions onset, withhold treatment immediately and refer to specialised care; histologic confirmation, including consideration of multiple biopsies, is critical to early recognition, as diagnosis and intervention can improve prognosis. Permanently discontinue PADCEV for confirmed SJS or TEN, Grade 4 or recurrent Grade 3 skin reactions. For Grade 2 worsening, Grade 2 with fever or Grade 3 skin reactions, treatment should be withheld until Grade ≤1 and referral for specialised care should be considered. Treatment should be resumed at the same dose level or consider dose reduction by one dose level (see section 4.2 of the SPC). Pneumonitis/Interstitial Lung Disease (ILD): Severe, life-threatening or fatal pneumonitis/ILD have occurred in patients treated with enfortumab vedotin. The incidence of pneumonitis/ILD, including severe events occurred at a higher rate when enfortumab vedotin was given in combination with pembrolizumab compared to enfortumab vedotin as monotherapy (see section 4.8 of the SPC). Monitor patients for signs and symptoms indicative of pneumonitis/ILD such as hypoxia, cough, dyspnoea or interstitial infiltrates on radiologic exams. Corticosteroids should be administered for Grade ≥ 2 events (e.g., initial dose of 1-2 mg/kg/day prednisone or equivalent followed by a taper). Withhold PADCEV for Grade 2 pneumonitis/ILD and consider dose reduction. Permanently discontinue PADCEV for Grade ≥3 pneumonitis/ILD (see section 4.2 of the SPC). Hyperglycaemia: Hyperglycaemia and diabetic ketoacidosis (DKA), including fatal events, occurred in patients with and without pre- existing diabetes mellitus, treated with enfortumab vedotin (see section 4.8 of the SPC). Hyperglycaemia occurred more frequently in patients with pre-existing hyperglycaemia or a high body mass index (≥30 kg/m^2). Patients with baseline HbA1c ≥8% were excluded from clinical studies. Blood glucose levels should be monitored prior to dosing and periodically throughout the course of treatment as clinically indicated in patients with or at risk for diabetes mellitus or hyperglycaemia. If blood glucose is elevated >13.9 mmol/L (>250 mg/dL), PADCEV should be withheld until blood glucose is ≤13.9 mmol/L (≤250 mg/dL) and treat as appropriate (see section 4.2 of the SPC). Serious infections: Serious infections such as sepsis (including fatal outcomes) have been reported in patients treated with PADCEV. Patients should be carefully monitored during treatment for the emergence of possible serious infections. Peripheral neuropathy: Peripheral neuropathy, predominantly peripheral sensory neuropathy, has occurred with enfortumab vedotin, including Grade ≥3 reactions (see section 4.8 of the SPC). Patients with pre-existing peripheral neuropathy Grade ≥2 were excluded from clinical studies. Patients should be monitored for symptoms of new or worsening peripheral neuropathy as these patients may require a delay, dose reduction or discontinuation of enfortumab vedotin. PADCEV should be permanently discontinued for Grade ≥3 peripheral neuropathy (see section 4.2 of the SPC). Ocular disorders: Ocular disorders, predominantly dry eye, have occurred in patients treated with enfortumab vedotin (see section 4.8 of the SPC). Patients should be monitored for ocular disorders. Consider artificial tears for prophylaxis of dry eye and referral 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 (see section 4.8 of the SPC). 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. Embryo-foetal toxicity and contraception: Pregnant women should be informed of the potential risk to a foetus (see sections 4.6 and 5.3 of the SPC). Females of reproductive potential should be advised to have a pregnancy test within 7 days prior to starting treatment with enfortumab vedotin, to use effective contraception during treatment and for at least 6 months after stopping treatment. Men being treated with enfortumab vedotin are advised not to father a child during treatment and for at least 4 months following the last dose of PADCEV. Patient information pack: The prescriber must discuss the risks of PADCEV therapy, including combination therapy with pembrolizumab, with the patient. The patient should be provided with the patient information leaflet and patient card with each prescription.

Effects on ability to drive and use machines: PADCEV has no or negligible influence on the ability to drive and use machines.

Interactions: Formal drug–drug interaction studies with enfortumab vedotin have not been conducted. Caution is advised in case of concomitant treatment with CYP3A4 inhibitors. Patients receiving concomitant strong CYP3A4 inhibitors (e.g. boceprevir, clarithromycin, cobicistat, indinavir, itraconazole, nefazodone, nelfinavir, posaconazole, ritonavir, saquinavir, telaprevir, telithromycin, voriconazole) should be monitored more closely for signs of toxicities. Strong CYP3A4 inducers (e.g. rifampicin, carbamazepine, phenobarbital, phenytoin, St John's wort [*Hypericum perforatum*]) may decrease the exposure of unconjugated MMAE with moderate effect (see section 5.2 of the SPC).

Fertility, pregnancy and lactation: Women of childbearing potential/ Contraception in males and females: Refer to 'Special warnings and precautions for use' section above. Pregnancy: PADCEV can cause foetal harm when administered to pregnant women based upon findings from animal studies. PADCEV is not recommended during pregnancy and in women of childbearing potential not using effective contraception. Breast-feeding: Breast-feeding should be discontinued during PADCEV treatment and for at least 6 months after the last dose. Fertility: Men being treated with this medicinal product are advised to have sperm samples frozen and stored before treatment. There are no data on the effect of PADCEV on human fertility.

Undesirable effects: Summary of the safety profile: *Enfortumab vedotin as monotherapy*: The safety of enfortumab vedotin was evaluated as monotherapy in 793 patients who received at least one dose of enfortumab vedotin 1.25 mg/kg in two phase 1 studies (EV-101 and EV-102), three phase 2 studies (EV-103, EV-201 and EV-203) and one phase 3 study (EV-301) (see Table 3 in section 4.8 of the SPC). Patients were exposed to enfortumab vedotin for a median duration of 4.7 months (range: 0.3 to 55.7 months). The most common adverse reactions with enfortumab vedotin were alopecia (47.7%), decreased appetite (47.2%), fatigue (46.8%), diarrhoea (39.1%), peripheral sensory neuropathy (38.5%), nausea (37.8%), pruritus (33.4%), dysgeusia (30.4%), anaemia (29.1%), weight decreased (25.2%), rash maculo-papular (23.6%), dry skin (21.8%), vomiting (18.7%), aspartate aminotransferase increased (17%), hyperglycaemia, (14.9%), dry eye (12.7%), alanine aminotransferase increased (12.7%) and rash (11.6%). The most common serious adverse reactions (≥2%) were diarrhoea (2.1%) and hyperglycaemia (2.1%). Twenty-one percent of patients permanently discontinued enfortumab vedotin for adverse reactions; the most common adverse reaction (≥2%) leading to dose discontinuation was peripheral sensory neuropathy (4.8%). Adverse reactions leading to dose interruption occurred in 62% of patients; the most common adverse reactions (≥2%) leading to dose interruption were peripheral sensory neuropathy (14.8%), fatigue (7.4%), rash maculo-papular (4%), aspartate aminotransferase increased (3.4%), alanine aminotransferase increased (3.2%), anaemia (3.2%), hyperglycaemia (3.2%), neutrophil count decreased (3%), diarrhoea (2.8%), rash (2.4%) and peripheral motor neuropathy (2.1%). Thirty-eight percent of patients required a dose reduction due to an adverse reaction; the most common adverse reactions (≥2%) leading to a dose reduction were peripheral sensory neuropathy (10.3%), fatigue (5.3%), rash maculo-papular (4.2%) and decreased appetite (2.1%). *Enfortumab vedotin in combination with pembrolizumab:* When enfortumab vedotin is administered in combination with pembrolizumab, refer to the SPC for pembrolizumab prior to initiation of treatment. The safety of enfortumab vedotin was evaluated in combination with pembrolizumab in 564 patients who received at least one dose of enfortumab vedotin 1.25 mg/kg in combination with pembrolizumab in one phase 2 study (EV-103) and one phase 3 study (EV-302) (see Table 3). Patients were exposed to enfortumab vedotin in combination with pembrolizumab for a median duration of 9.4 months (range: 0.3 to 34.4 months). The most common adverse reactions with enfortumab vedotin in combination with pembrolizumab were peripheral sensory neuropathy (53.4%), pruritus (41.1%), fatigue (40.4%), diarrhoea (39.2%), alopecia (38.5%), rash maculo-papular (36%), weight decreased (36%), decreased appetite (33.9%), nausea (28.4%), anaemia (25.7%), dysgeusia (24.3%), dry skin (18.1%), alanine aminotransferase increased (16.8%), hyperglycaemia (16.7%), aspartate aminotransferase increased (15.4%), dry eye (14.4%), vomiting (13.3%), rash macular (11.3%), hypothyroidism (10.5%) and neutropenia (10.1%). The most common serious adverse reactions (≥2%) were diarrhoea (3%) and pneumonitis (2.3%). Thirty-six percent of patients permanently discontinued enfortumab vedotin for adverse reactions; the most common adverse reactions (≥2%) leading to discontinuation were peripheral sensory neuropathy (12.2%) and rash maculo-papular (2%). Adverse reactions leading to dose interruption of enfortumab vedotin occurred in 72% of patients. The most common adverse reactions (≥2%) leading to dose interruption were peripheral sensory neuropathy (17%), rash maculo-papular (6.9%), diarrhoea (4.8%), fatigue (3.7%), pneumonitis (3.7%), hyperglycaemia (3.4%), neutropenia (3.2%), alanine aminotransferase increased (3%), pruritus (2.3%) and anaemia (2%). Adverse reactions leading to dose reduction of enfortumab vedotin occurred in 42.4% of patients. The most common adverse reactions (≥2%) leading to dose reduction were peripheral sensory neuropathy (9.9%), rash maculo-papular (6.4%), fatigue (3.2%), diarrhoea (2.3%) and neutropenia (2.1%). Summary of adverse reactions: Adverse reactions observed during clinical studies of enfortumab vedotin as monotherapy or in combination with pembrolizumab, or reported from post-marketing use of enfortumab vedotin are listed in this section according to Medical Dictionary for Regulatory Activities (MedDRA) system organ classification by frequency category. Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. Frequency categories are defined as follows: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data). *Infections and infestations:* (monotherapy and in combination with pembrolizumab) Common: Sepsis. *Blood and lymphatic system disorders:* (monotherapy and in combination with pembrolizumab) Very common: Anaemia. Not known[1]: Neutropenia, febrile neutropenia, neutrophil count decreased. *Endocrine disorders:* (in combination with pembrolizumab) Very common: Hypothyroidism. *Metabolism and nutrition disorders:* (monotherapy and in combination with pembrolizumab) Very common: Hyperglycaemia, decreased appetite. Not known[1]: Diabetic ketoacidosis. *Nervous system disorders:* (monotherapy and in combination with pembrolizumab) Very common: Peripheral sensory neuropathy, dysgeusia. (monotherapy) Common: Neuropathy peripheral, peripheral motor neuropathy, peripheral sensorimotor neuropathy, paraesthesia, hypoaesthesia, gait disturbance, muscular weakness. (in combination with pembrolizumab) Common: Peripheral motor neuropathy, peripheral sensorimotor neuropathy, paraesthesia, hypoaesthesia, gait disturbance, muscular weakness. (monotherapy) Uncommon: Demyelinating polyneuropathy, polyneuropathy, neurotoxicity, motor dysfunction, dysaesthesia, muscle atrophy, neuralgia, peroneal nerve palsy, sensory loss, skin burning sensation, burning sensation. (in combination with pembrolizumab) Uncommon: Neurotoxicity, dysaesthesia, myasthenia gravis, neuralgia, peroneal nerve palsy, skin burning sensation. *Eye disorders:* (monotherapy and in combination with pembrolizumab) Very common: Dry eye. *Respiratory, thoracic, and mediastinal disorders:* (in combination with pembrolizumab) Very common: Pneumonitis/ILD[2]. (monotherapy) Common: Pneumonitis/ILD[2]. *Gastrointestinal disorders:* (monotherapy and in combination with pembrolizumab) Very common: Diarrhoea, vomiting, nausea. *Skin and subcutaneous tissue disorders:* (monotherapy) Very common: Alopecia, pruritus, rash, rash maculo-papular, dry skin. (in combination with pembrolizumab) Very common: Alopecia, pruritus, rash maculo-papular, dry skin, rash macular. (monotherapy) Common: Drug eruption, skin exfoliation, conjunctivitis, dermatitis bullous, blister, stomatitis, palmar-plantar erythrodysesthesia syndrome, eczema, erythaema, rash erythaematous, rash macular, rash papular, rash pruritic, rash vesicular. (in combination with pembrolizumab) Common: Rash, skin exfoliation, conjunctivitis, dermatitis bullous, blister, stomatitis, palmar-plantar erythrodysesthesia syndrome, eczema, erythaema, rash erythaematous, rash papular, rash pruritic, rash vesicular, erythaema multiforme, dermatitis. (monotherapy) Uncommon: Dermatitis exfoliative generalised, erythaema multiforme, exfoliative rash, pemphigoid, rash maculovesicular, dermatitis, dermatitis allergic, dermatitis contact, intertrigo, skin irritation, stasis dermatitis, blood blister. (in combination with pembrolizumab) Uncommon: Drug eruption, dermatitis exfoliative generalised, exfoliative rash, pemphigoid, dermatitis contact, intertrigo, skin irritation, stasis dermatitis. (monotherapy and in combination with pembrolizumab) Not known[1]: TEN, SJS, epidermal necrosis, skin hyperpigmentation, skin discoloration, pigmentation disorder, symmetrical drug-related intertriginous and flexural exanthaema. *Musculoskeletal and connective tissue disorders:* (in combination with pembrolizumab) Common: Myositis. *General disorders and administration site conditions:* (monotherapy and in combination with pembrolizumab) Very common: Fatigue. (monotherapy and in combination with pembrolizumab) Common: Infusion site extravasation. *Investigations:* (monotherapy and in combination with pembrolizumab) Very common: Alanine aminotransferase increased, aspartate aminotransferase increased, weight decreased. (in combination with pembrolizumab) Common: Lipase increased. *Injury, poisoning and procedural complications:* (monotherapy and in combination with pembrolizumab) Common: Infusion related reaction.

[1]Based on global post-marketing experience.

[2]Includes: acute respiratory distress syndrome, autoimmune lung disease, immune-mediated lung disease, interstitial lung disease, lung opacity, organizing pneumonia, pneumonitis, pulmonary fibrosis, pulmonary toxicity and sarcoidosis.

Description of selected adverse reactions. *Immunogenicity:* A total of 697 patients were tested for immunogenicity to enfortumab vedotin1.25 mg/kg as monotherapy; 16 patients were confirmed to be positive at baseline for anti-drug antibody (ADA), and in patients that were negative at baseline (N=681), a total of 24 (3.5%) were positive post baseline. A total of 490 patients were tested for immunogenicity against enfortumab vedotin following enfortumab vedotin in combination with pembrolizumab; 24 patients were confirmed to be positive at baseline for ADA, and in patients that were negative at baseline (N=466), a total of 14 (3%) were positive post baseline. The incidence of treatment-emergent anti-enfortumab vedotin antibody formation was consistent when assessed following enfortumab vedotin administration as monotherapy and in combination with pembrolizumab. Due to the limited number of patients with antibodies against PADCEV, no conclusions can be drawn concerning a potential effect of immunogenicity on efficacy, safety or pharmacokinetics. *Skin reactions:* In clinical studies of enfortumab vedotin as monotherapy, skin reactions occurred in 57% (452) of the 793 patients treated with enfortumab vedotin 1.25 mg/kg. Severe (Grade 3 or 4) skin reactions occurred in 14% (108) of patients and a majority of these reactions included rash maculo-papular, stomatitis, rash erythematous, rash or drug eruption. The median time to onset of severe skin reactions was 0.7 months (range: 0.1 to 8.2 months). Serious skin reactions occurred in 4.3% (34) of patients. Of the patients who experienced skin reactions and had data regarding resolution (N=366), 61% had complete resolution, 24% had partial improvement, and 15% had no improvement at the time of their last evaluation. Of the 39% of patients with residual skin reactions at last evaluation, 38% had Grade ≥2 events. In clinical studies of enfortumab vedotin in combination with pembrolizumab, skin reactions occurred in 70% (392) of the 564 patients and a majority of these skin reactions included rash maculo-papular, rash macular and rash papular. Severe (Grade 3 or 4) skin reactions occurred in 17% (97) of patients (Grade 3: 16%, Grade 4: 1%). The median time to onset of severe skin reactions was 1.7 months (range: 0.1 to 17.2 months). Of the patients who experienced skin reactions and had data regarding resolution (N=391), 59% had complete resolution, 30% had partial improvement, and 10% had no improvement at the time of their last evaluation. Of the 41% of patients with residual skin reactions at last evaluation, 27% had Grade ≥2 events. *Pneumonitis/ILD:* In clinical studies of enfortumab vedotin as monotherapy, pneumonitis/ILD occurred in 26 (3.3%) of the 793 patients treated with enfortumab vedotin 1.25 mg/kg. Less than 1% of patients experienced severe (Grade 3 or 4) pneumonitis/ILD (Grade 3: 0.5%, Grade 4: 0.3%). Pneumonitis/ILD led to discontinuation of enfortumab vedotin in 0.5% of patients. There were no deaths from pneumonitis/ILD. The median time to onset of any grade pneumonitis/ILD was 2.7 months (range: 0.6 to 6.0 months) and the median duration for pneumonitis/ILD was 1.6 months (range: 0.1 to 43.0 months). Of the 26 patients who experienced pneumonitis/ILD, 8 (30.8%) had resolution of symptoms. In clinical studies of enfortumab vedotin in combination with pembrolizumab, pneumonitis/ILD occurred in 58 (10.3%) of the 564 patients. Severe (Grade 3 or 4) pneumonitis/ILD occurred in 20 patients (Grade 3: 3.0%, Grade 4: 0.5%). Pneumonitis/ILD led to discontinuation of enfortumab vedotin in 2.1% of patients. Two patients experienced a fatal event of pneumonitis/ILD. The median time to onset of any grade pneumonitis/ILD was 4 months (range: 0.3 to 26.2 months). *Hyperglycaemia:* In clinical studies of enfortumab vedotin as monotherapy, hyperglycaemia (blood glucose >13.9 mmol/L) occurred in 17% (133) of the 793 patients treated with enfortumab vedotin 1.25 mg/kg. Serious events of hyperglycaemia occurred in 2.5% of patients, 7% of patients developed severe (Grade 3 or 4) hyperglycaemia and 0.3% of patients experienced fatal events, one event each of hyperglycaemia and diabetic ketoacidosis. The incidence of Grade 3-4 hyperglycaemia increased consistently in patients with higher body mass index and in patients with higher baseline haemoglobin A1C (HbA1c). The median time to onset of hyperglycaemia was 0.5 months (range: 0 to 20.3). Of the patients who experienced hyperglycaemia and had data regarding resolution (N=106), 66% had complete resolution, 19% had partial improvement, and 15% had no improvement at the time of their last evaluation. Of the 34% of patients with residual hyperglycaemia at last evaluation, 64% had Grade ≥2 events. *Peripheral neuropathy:* In clinical studies of enfortumab vedotin as monotherapy, peripheral neuropathy occurred in 53% (422) of the 793 patients treated with enfortumab vedotin 1.25 mg/kg. Five percent of patients experienced severe (Grade 3 or 4) peripheral neuropathy including sensory and motor events. The median time to onset of Grade ≥2 peripheral neuropathy was 5 months (range: 0.1 to 20.2). Of the patients who experienced neuropathy and had data regarding resolution (N=340), 14% had complete resolution, 46% had partial improvement, and 41% had no improvement at the time of their last evaluation. Of the 86% of patients with residual neuropathy at last evaluation, 51% had Grade ≥2 events. *Ocular disorders:* In clinical studies of enfortumab vedotin as monotherapy, 30% of patients experienced dry eye during treatment with enfortumab vedotin 1.25 mg/kg. Treatment was interrupted in 1.5% of patients and 0.1% of patients permanently discontinued treatment due to dry eye. Severe (Grade 3) dry eye only occurred in 3 patients (0.4%). The median time to onset of dry eye was 1.7 months (range: 0 to 30.6 months). *Special populations:* Elderly: Enfortumab vedotin in combination with pembrolizumab has been studied in 173 patients <65 years and 391 patients ≥65 years. Generally, adverse event frequencies were higher in patients ≥65 years of age compared to <65 years of age, particularly for serious adverse events (56.3%, and 35.3%, respectively) and Grade ≥3 events (80.3% and 64.2%, respectively), similar to observations with the chemotherapy comparator. Prescribers should consult the full SPC in relation to other adverse reactions.

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).

Cost (excluding VAT): PADCEV 20 mg powder for concentrate for solution for infusion x 1 vial: £578
PADCEV 30 mg powder for concentrate for solution for infusion x 1 vial: £867

Legal classification: POM

Marketing Authorisation numbers:

PADCEV 20 mg powder for concentrate for solution for infusion PLGB 00166/0432.
PADCEV 30 mg powder for concentrate for solution for infusion PLGB 00166/0433.

Marketing Authorisation Holder:

Astellas Pharma Ltd. 300 Dashwood Lang Road, Bourne Business Park, Addlestone, United Kingdom, KT15 2NX.

Date of Preparation of Prescribing Information: February 2025

Job Bag Number: MAT-GB-PAD-2025-00017

Further information available from: Astellas Pharma Ltd, Medical Information 0800 783 5018. For full prescribing information, refer to the SPC, which may be found at: https://www.medicines.org.uk/emc.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Astellas Pharma Ltd. on 0800 783 5018.