KEYTRUDA® (pembrolizumab)

KEYTRUDA SC® (pembrolizumab) subcutaneous injection | 395 mg/2.4 mL 790 mg/4.8 mL

KEYTRUDA® (pembrolizumab) in combination with enfortumab vedotin▼ as a treatment option for patients with unresectable or metastatic urothelial carcinoma (u/mUC)

KEYTRUDA and KEYTRUDA SC, in combination with enfortumab vedotin, are each indicated for the first-line treatment of unresectable or metastatic urothelial carcinoma in adults[1-3]

The approved indications for KEYTRUDA SC have been established based on the MK-3475A-D77 study, which demonstrated non-inferior pharmacokinetics, and provides a descriptive analysis for the efficacy and safety profile of KEYTRUDA SC compared to KEYTRUDA.[1-3]

Please consult the SmPC and risk minimisation materials for further information to minimise the risks associated with the use of the medicine before making any prescribing decisions.

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Merck Sharp & Dohme (UK) Limited (Tel: 0208 154 8000)

For UK Healthcare professionals only.

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KEYTRUDA IV Prescribing Information [External link].
KEYTRUDA 395 mg solution for injection Prescribing Information [External link].
KEYTRUDA 790 mg solution for injection Prescribing Information [External link].

This is a photo of fictional patients and is for illustrative purposes only

MSD ONCOLOGY

1. KEYTRUDA IV Summary of Product Characteristics. MSD. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: May 2026. 2. KEYTRUDA 395 mg solution for injection Summary of Product Characteristics. MSD. Available at https://www.medicines.org.uk/emc/product/101749/smpc. Accessed May 2026. 3. KEYTRUDA 790 mg solution for injection Summary of Product Characteristics. MSD. Available at: https://www.medicines.org.uk/emc/product/101752/smpc. Accessed May 2026.

GB-PDO-03830 | May 2026

MSD

KEYTRUDA® (pembrolizumab)

DOSING | IV PI | SC PI 395 mg | SC PI 790 mg

Contents page

Click on the links below to navigate to any of the pages in this deck.
To access this page from any of the other pages in the deck, please press the ‘Home’ icon.

DoR, duration of response; ESMO, European Society for Medical Oncology; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; TRAE, treatment-related adverse event; u/mUC, unresectable/metastatic urothelial carcinoma; UC, urothelial carcinoma.

There is a significant unmet need in patients with unresectable/metastatic UC

For decades, platinum-based chemotherapy has been the first-line standard therapy for unresectable or metastatic UC;[1] however, treatment outcomes remain poor.[1,2]

Around

10%

of patients with u/mUC will survive their cancer for 5 years or more after diagnosis*[3]

New treatments are needed to improve outcomes for these patients

*Data is from 2019 and pertains to patients in England only.[3]
u/mUC, unresectable/metastatic urothelial carcinoma; UC, urothelial carcinoma.

1. Powles T, *et al. N Engl J Med* 2024;390:875–888. **2.** SEER cancer stat facts: Bladder cancer. Available at: https://seer.cancer.gov/statfacts/html/urinb.html. Accessed: May 2026. **3.** Cancer Research UK. Survival for bladder cancer. Available at: https://www.cancerresearchuk.org/about-cancer/bladder-cancer/survival. Accessed: May 2026.

KEYTRUDA in combination with enfortumab vedotin

For the first-line treatment of adult patients with unresectable or metastatic urothelial carcinoma.[1,2]

Indication

KEYTRUDA, in combination with enfortumab vedotin, is indicated for the first-line treatment of unresectable or metastatic urothelial carcinoma in adults.[1]

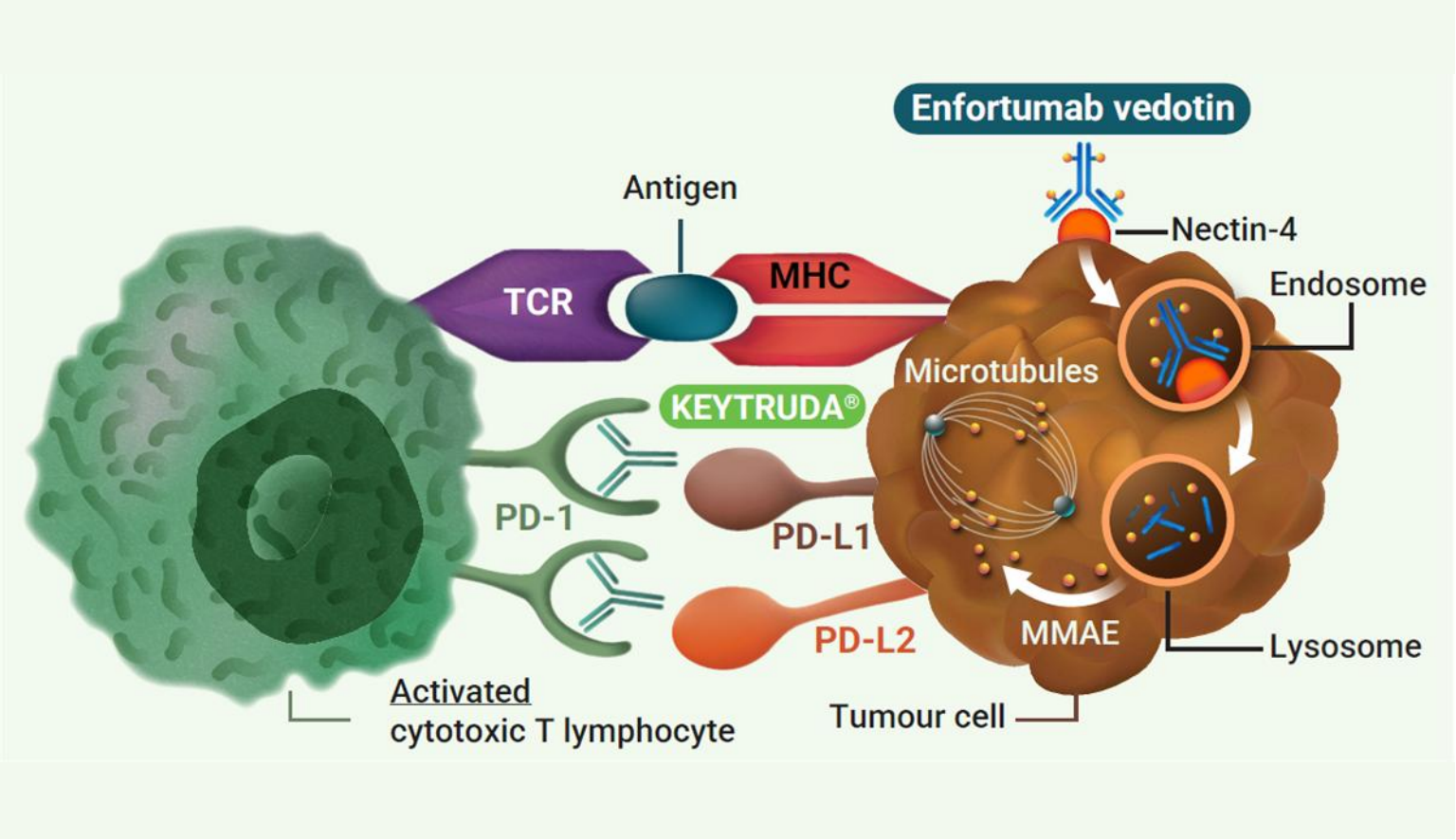
Enfortumab vedotin is an antibody–drug conjugate (ADC) composed of an anti-nectin-4 monoclonal antibody with payload monomethyl auristatin E (MMAE) attached via a protease-cleavable linker.[3]

Refer to the Summary of Product Characteristics and Risk Minimisation Materials available on the EMC website before prescribing, in order to help reduce the risks associated with KEYTRUDA.

ADC, antibody–drug conjugate; EMC, Electronic Medicines Compendium; MMAE, monomethyl auristatin E.

1. KEYTRUDA Summary of Product Characteristics. MSD. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: May 2026. **2.** Powles T, *et al. N Engl J Med* 2024;390:875–888. **3.** Heath EI & Rosenberg JE. *Nat Rev Urol* 2021;18:93–103.

KEYTRUDA mechanism of action[1,2]



- **KEYTRUDA** is a humanised monoclonal antibody that binds to the PD-1 receptor, blocking its interaction with the PD-L1 and PD-L2 ligands[1]
- **KEYTRUDA** enhances T-cell responses, including anti-tumour responses, by preventing the binding of PD-1 to PD-L1 and PD-L2. These ligands are expressed on antigen-presenting cells and can also be expressed by tumours or other cells in the tumour microenvironment[1]
- EV is an antibody–drug conjugate composed of an anti-nectin-4 monoclonal antibody with payload monomethyl auristatin E (MMAE) attached via a protease-cleavable linker[2]
- Upon binding to Nectin-4 on the cancer cell, EV is endocytosed and delivers the cytotoxic payload to induce cell death[2]

EV, enfortumab vedotin; MHC: major histocompatibility complex; MMAE: monomethyl auristatin; PD-1: programmed death 1; PD-L1: programmed death ligand 1; PD-L2: programmed death ligand 2; TCR: T-cell receptor.

1. KEYTRUDA Summary of Product Characteristics. MSD. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: May 2026. **2.** Heath EI & Rosenberg JE. *Nat Rev Urol* 2021;18:93–103.

KEYTRUDA+ EV is a recommended first-line treatment option for patients with advanced UC in 3 major guidelines[1–3]

National Institute for Health and Care Excellence (NICE)[1]

KEYTRUDA + EV can be used as an option for untreated unresectable or metastatic urothelial cancer in adults when platinum-based chemotherapy is suitable.

European Society for Medical Oncology (ESMO)[2]

ESMO guidelines recommend **KEYTRUDA + EV as the preferred first-line therapy for advanced or metastatic UC**, irrespective of platinum eligibility [I,A].[a,b]

European Association of Urology (EAU)[3]

EAU guidelines include a **strong recommendation** for the use of **KEYTRUDA + EV as first-line treatment** in patients with **metastatic UC** who are eligible for combination therapy.[c]

[a]ESMO levels of evidence include: **I:** evidence from at least 1 large randomised, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomised trials without heterogeneity; **II:** Small randomised trials or large randomised trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity; **III:** Prospective cohort studies; **IV:** Retrospective cohort studies or case-control studies; **V:** Studies without control group, case reports, expert opinions.[2] [b]ESMO grades of recommendation include: **A:** Strong evidence for efficacy with a substantial clinical benefit; strongly recommended; **B:** Strong or moderate evidence for efficacy but with a limited clinical benefit; generally recommended; **C:** Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs, etc.); optional; **D:** Moderate evidence against efficacy or for adverse outcome; generally not recommended; **E:** Strong evidence against efficacy or for adverse outcome; never recommended.[2] [c]EAU grades of recommendation include strong recommendations (typically indicate a high degree of evidence quality and/or a favourable balance of benefit to harm and patient preference) and weak recommendation (typically indicate availability of lower quality evidence, and/or equivocal balance between benefit and harm, and uncertainty or variability of patient preference).[3]

EAU, European Association of Urology; ESMO, European Society for Medical Oncology; EV, enfortumab vedotin; NICE, National Institute for Health and Care Excellence; UC, urothelial carcinoma.

1. Enfortumab vedotin with pembrolizumab for untreated unresectable or metastatic urothelial cancer when platinum-based chemotherapy is suitable. NICE technology appraisal guidance. 2025. Accessed May 2026. **2.** Powles T, *et al. Ann Oncol* 2024;35:485–490. **3.** Witjes JA, *et al.* European Association of Urology. Limited update April 2024. Available at: https://d56bochluxqnz.cloudfront.net/ documents/full-guideline/EAU-Guidelines-on-Muscle-Invasive-and-Metastatic-Bladder-Cancer-2024.pdf. Accessed May 2026.

ESMO/EAU recommendation levels[1,2]

ESMO levels of evidence[1]

I: Evidence from at least 1 large randomised, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomised trials without heterogeneity.
II: Small randomised trials or large randomised trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity.
III: Prospective cohort studies.
IV: Retrospective cohort studies or case-control studies.
V: Studies without control group, case reports, expert opinions.

ESMO grades of recommendation of evidence[1]

A: Strong evidence for efficacy with a substantial clinical benefit; strongly recommended.
B: Strong or moderate evidence for efficacy but with a limited clinical benefit; generally recommended.
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D: Moderate evidence against efficacy or for adverse outcome; generally not recommended.
E: Strong evidence against efficacy or for adverse outcome; never recommended.

EAU grades of recommendation[2]

Strong recommendations: Typically indicate a high degree of evidence quality and/or a favourable balance of benefit to harm and patient preference.
Weak recommendations: Typically indicate availability of lower quality evidence, and/or equivocal balance between benefit and harm, and uncertainty or variability of patient preference.

EAU, European Association of Urology; ESMO, European Society for Medical Oncology.
1. Powles T, *et al. Ann Oncol* 2024;35:485–490. **2.** Witjes JA, *et al*. European Association of Urology. Limited update April 2024. Available at: https://d56bochluxqnz.cloudfront.net/ documents/full-guideline/EAU-Guidelines-on-Muscle-Invasive-and-Metastatic-Bladder-Cancer-2024.pdf. Accessed May 2026.

KEYNOTE-A39 / EV-302

An open-label, multicentre, randomised, active-controlled Phase III study of KEYTRUDA + EV vs platinum-based chemotherapy (gemcitabine + either cisplatin or carboplatin) in previously untreated, u/mUC[1]

The indication of KEYTRUDA in combination with enfortumab vedotin, is for the treatment of unresectable or metastatic urothelial carcinoma in adults.[2]

EV, enfortumab vedotin; u/mUC, unresectable or metastatic urothelial carcinoma.

1. Powles T, *et al. N Engl J Med* 2024;390:875–888. **2.** KEYTRUDA Summary of Product Characteristics. MSD. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: May 2026.

KEYNOTE-A39 data presentation overview

Powles T, *et al. N Engl J Med*[1]

Abstract presented at ESMO Annual Congress 2023[3]

7 March 2024

Initial analysis
with 17.2 months median follow-up

Data cut-off: 8 August 2023

Because the results of the interim analysis of overall survival were significant, the interim analysis was considered to be the final analysis.

Powles T, *et al. Ann Oncol*[2]

Abstract presented at ASCO Genitourinary Cancers Symposium[4]

13–15 February 2025

Exploratory analysis
with 1 year of additional follow-up
(29.1 months median follow-up)

Data cut-off: 8 August 2024

ASCO, American Society of Clinical Oncology; ESMO, European Society of Medical Oncology; EV, enfortumab vedotin.

1. Powles T, *et al. N Engl J Med.* 2024;390:875–888 (plus supplementary appendix and protocol); 2. Powles T, et al. *Ann Oncol.* 2025;36(10)1212–121; 3. Powles T et al. Abstract LBA6. Presented at ESMO 2023. October 20-24, Madrid, Spain; 4. Powles et al. Abstract 664. Presented at ASCO GU 2025, February 13-15, San Francisco, CA.

KEYNOTE-A39 / EV-302: Study design[1]

A randomised, multicentre, open-label, active-controlled Phase III study across 25 countries

Patients with previously untreated, locally advanced or metastatic UC, eligible for platinum-based chemotherapy[a]

N=886

R 1:1

KEYTRUDA + EV (n=442)
≤35 cycles for KEYTRUDA
- KEYTRUDA 200 mg IV (Day 1/21-day cycle)
- EV 1.25 mg/kg IV (Day 1+8/21-day cycle)

Platinum-based chemotherapy (n=444)
(gemcitabine + either cisplatin or carboplatin)[e]
≤6 cycles
- Gem 1000 mg/m^2 IV (Day 1+8/21-day cycle)
- Cis 70 mg/m^2 IV (Day 1/21-day cycle)
- Carb AUC 4.5 or 5 mg/mL/min IV (Day 1/21-day cycle)

Treatment continued until disease progression, unacceptable toxicity, or for KEYTRUDA, a maximum of 35 cycles (up to approximately 2 years)[f]

Dual primary endpoints:
- PFS, OS

Select secondary endpoints:
- ORR,[g] DoR,

PFS, ORR and DoR were assessed by BICR according to RECIST v1.1

Key inclusion criteria:
- Eligible for cisplatin or carboplatin-containing chemotherapy
- PD-L1 inhibitor-naïve
- GFR ≥30 mL/min[b]
- ECOG PS ≤2[c]

Key exclusion criteria:
- Previous PD-1 or PD-L1 inhibitor therapy or other systemic therapy[d]
- Previous autoimmune disease that required systemic treatment in the previous 2 years
- Ongoing Grade ≥2 sensory or motor neuropathy or CNS metastasis
- Uncontrolled diabetes

Stratification factors:
- Cisplatin eligibility (eligible/ineligible)
- PD-L1 expression (high/low)
- Liver metastases (present/absent)

Adapted from Powles T, et al. N Engl J Med 2024 (plus supplementary appendix and protocol).

[a]Ineligible for cisplatin if met any of the following: GFR clearance 30–59 mL/min, ECOG PS ≥2, Grade ≥2 hearing loss, or NYHA Class III heart failure; [b]Measured by the Cockcroft-Gault formula, Modification of Diet in Renal Disease, or 24-hour urine; [c]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; [d]Except for neoadjuvant or adjuvant chemotherapy after surgery with recurrence >12 months after the completion of therapy; [e]Maintenance therapy could be used following completion and/or discontinuation of platinum-containing therapy; [f]Treatment continuation was permitted beyond RECIST v1.1, defined progression if the treating investigator considered the patient to be deriving clinical benefit and the treatment was tolerated; [g]Defined as a complete or partial response according to RECIST v1.1.

AUC, area under curve; BICR, blinded independent central review; carb, carboplatin; cis, cisplatin; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EV, enfortumab vedotin; gem, gemcitabine; GFR, glomerular filtration rate; IV, intravenous; NYHA, New York Heart Association; ORR, objective response rate; OS, overall survival; PD-1, programmed death receptor-1; PD-L1, programmed death ligand-1; PFS, progression-free survival; R, randomised; RECIST v1.1, Response Evaluation Criteria In Solid Tumours v1.1; TTPP, time to pain progression; UC, urothelial carcinoma.

1. Powles T, *et al. N Engl J Med*. 2024;390(10):875–888 (plus supplementary appendix and protocol).

Dosing schedule[1]

KEYNOTE-A39: KEYTRUDA in combination with enfortumab vedotin
21-DAY DOSING CYCLE

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Enfortumab vedotin 1.25 mg/kg	✔							✔													
KEYTRUDA, 200 mg Q3W	✔																				

Patients received enfortumab vedotin 1.25 mg/kg (up to a maximum of 125 mg per dose) as an IV infusion over 30 minutes on Days 1 and 8 of a 21-day cycle, followed by KEYTRUDA 200 mg as an IV infusion on Day 1 of a 21-day cycle approximately 30 minutes after enfortumab vedotin. Patients were treated until disease progression or unacceptable toxicity. In the absence of disease progression or unacceptable toxicity. In the absence of disease progression, initiation of subsequent anticancer therapy or unacceptable toxicity, KEYTRUDA was continued for up to 2 years.

IV, intravenous; Q3W, every 3 weeks.

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

Subsequent therapy (initial analysis)[1,2]

	KEYTRUDA + EV (N=442)	Platinum-based chemotherapy (N=444)
	No. of patients (percent)	
Patients who remained on treatment	**144 (32.6)**	**0**
Patients who received subsequent anticancer therapies	**140 (31.7)**	**313 (70.5)**
First subsequent systemic therapy	128 (29.0)	294 (66.2)
Platinum-based therapy	110 (24.9)	17 (3.8)
PD-1/PD-L1 inhibitor-containing therapy	7 (1.6)	260 (58.6)
Maintenance therapy*, †	0	143 (32.2)
Avelumab	0	135 (30.4)
Other therapy	7 (1.6)	117 (26.4)

Among the patients in the KEYTRUDA + EV arm who received subsequent therapies, 78.6% (110/140) received platinum-based therapy as the first subsequent therapy.[1]

Adapted from Powles T, *et al.* 2024.[2]

*Included atezolizumab, avelumab, ipilimumab, M 6223, nivolumab, Nktr 255, and pembrolizumab.[2] †Maintenance therapy was permitted in the trial after platinum-based chemotherapy.[2]
EV, enfortumab vedotin; PD-1: programmed death 1; PD-L1: programmed death ligand 1.
1. Powles T, *et al*. *N Engl J Med*. 2024;390(10):875–888 (plus supplementary appendix). **2.** KEYTRUDA (pembrolizumab) Summary of Product Characteristics. Available from: https://www.medicines.org.uk/emc/product/2498/smpc (Last Accessed: May 2026).

Baseline patient population[1,2]

Both treatment arms were well-balanced for key baseline demographic and disease characteristics

Characteristic		KEYTRUDA + EV (n=442)	Platinum-based chemotherapy (n=444)
Median age, years (range)		69 (37–87)	69 (22–91)
Age ≥75 years, n (%)		102 (23.1)	108 (24.3)
Male, n (%)		344 (77.8)	336 (75.7)
White, n (%)		308 (69.7)	290 (65.3)
Geographic region, n (%)	North America	103 (23.3)	85 (19.1)
	Europe	172 (38.9)	197 (44.4)
	Rest of the world	167 (37.8)	162 (36.5)
ECOG PS n (%)*	0	223 (50.5)	215 (48.4)
	1	204 (46.2)	216 (48.6)
	2	15 (3.4)	11 (2.5)
Creatinine clearance, n (%)†	≥60 ml/min	249 (56.3)	257 (57.9)
	<60 ml/min	193 (43.7)	187 (42.1)
Metastatic disease at randomisation, n (%)		421 (95.2)	420 (94.6)
Lower tract as primary source of disease origin, n (%)		305 (69.0)	339 (76.4)
Upper tract as primary source of disease origin, n (%)		135 (30.5)	104 (23.4)

Characteristic		KEYTRUDA + EV (n=442)	Platinum-based chemotherapy (n=444)
Histologic type, n (%)	UC	379 (85.7)	373 (84.0)
	UC, mixed types	50 (11.3)	53 (11.9)
	Variant UC only	4 (0.9)	7 (1.6)
Site of metastasis	Lymph node only	103 (23.3)	104 (23.4)
	Visceral site	318 (71.9)	318 (71.6)
	Bone	81 (18.3)	102 (23.0)
	Liver	100 (22.6)	99 (22.3)
	Lung	170 (38.5)	157 (35.4)
PD-L1 CPS ≥10 (high), n (%)‡		254/438 (58.0)	254/439 (57.9)
Cisplatin eligible, n (%)		240 (54.3)	242 (54.5)

In the platinum-chemotherapy arm, those who were cisplatin-ineligible received carboplatin-based chemotherapy instead.

- 210 patients (23.7%) were aged 75 years or over

Adapted from Powles T, *et al.* 2024.[1,2]

Data cut-off date: 8 August 2023.
*ECOG PS scores range from 0–5, with higher scores indicating greater disability.[1] †Renal function criteria: normal (GFR ≥90 ml/min per 1.73 m^2); mild impairment (GFR 60–89 ml/min per 1.73 m^2); moderate impairment (GFR 30–59 ml/min per 1.73 m^2); severe impairment (GFR 15–29 ml/min per 1.73 m^2).[3] ‡High PD-L1 expression was defined as CPS ≥10.[4]
CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; EV, enfortumab vedotin; GFR, glomerular filtration rate; PD-L1, programmed death-ligand 1; UC, urothelial carcinoma.
1. Powles T, *et al. N Engl J Med* 2024;390:875–888. **2.** Powles T, *et al. N Engl J Med* 2024;390:875–888. Supplementary appendix. **3**. Levey AS, *et al. Kidney Int* 2020;97:1117–1129. **4**. Powles T, *et al. N Engl J Med* 2024;390:875–888. Protocol.

How does ‘platinum-eligibility’ differ from ‘cisplatin-eligibility’?

- Although the pivotal KEYNOTE-A39 trial excluded patients ineligible for platinum-based therapies, it included individuals eligible for cisplatin and/or carboplatin. This means that some participants were ineligible for cisplatin but still eligible for carboplatin.[1]
- Patients in the comparator arm received either cisplatin- or carboplatin-based chemotherapy, depending on whether they were eligible for cisplatin therapy or not[1,2]

KEYNOTE-A39 protocol: criteria for cisplatin-ineligibility[2]

Renal function	GFR <60 mL/min but ≥30 mL/min*
Prognostic factors	ECOG or WHO PS 2
NCI CTCAE	Grade ≥2 audiometric hearing loss
Heart failure classification	NYHA Class III heart failure

If a patient is eligible for either cisplatin or carboplatin, then they are potentially eligible for treatment with combination KEYTRUDA + EV[1–3]

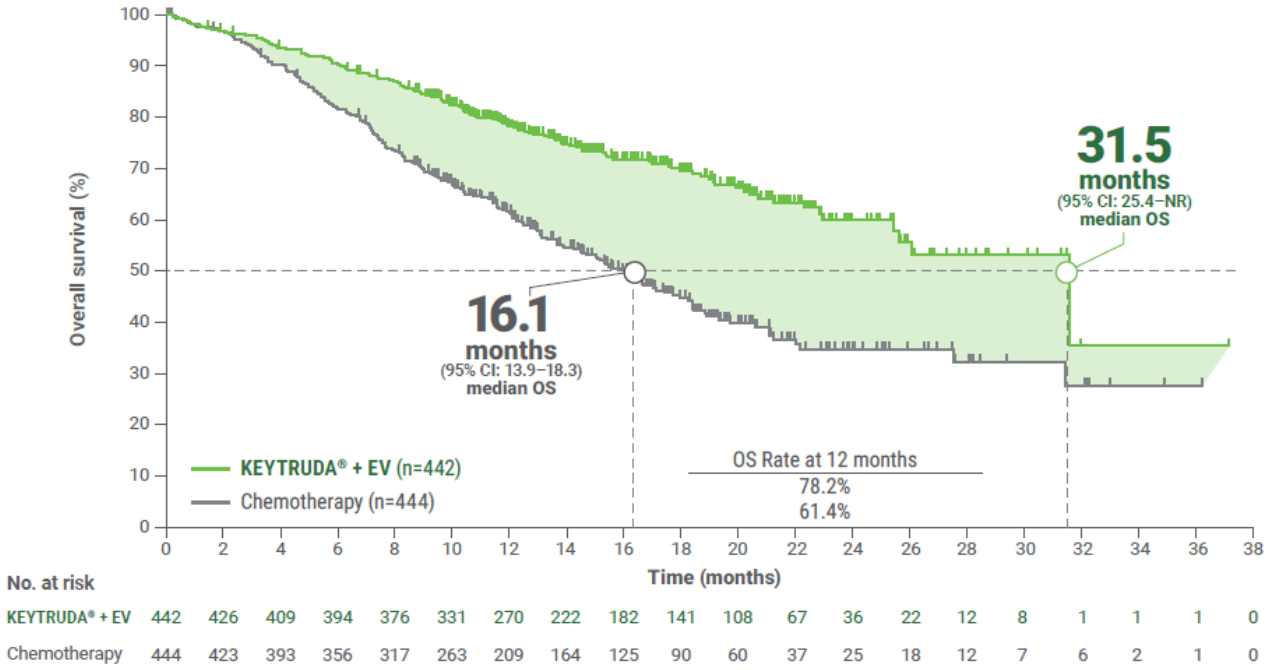
*Subjects with GFR ≥50 mL/min and no other cisplatin ineligibility criteria may be considered cisplatin-eligible based on the investigator's clinical judgement.[2]
CTCAE, Common Terminology Criteria for Adverse Events; ECOG, Eastern Cooperative Oncology Group; EV, enfortumab vedotin; GFR, glomerular filtration rate; NCI, National Cancer Institute; NYHA, New York Heart Association; PS, performance status; WHO, World Health Organisation.

1. Powles T, *et al. N Engl J Med* 2024;390:875–888. **2.** Powles T, *et al. N Engl J Med* 2024;390:875–888. Supplementary appendix. **3.** KEYTRUDA Summary of Product Characteristics. MSD. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: May 2026.

In the KEYNOTE-A39 initial analysis, there was a significant OS benefit with KEYTRUDA + EV vs platinum-based chemotherapy[1]

Kaplan-Meier estimates of OS (dual primary endpoint in the ITT population)

Median follow-up of 17.2 months[1]



No. at risk

KEYTRUDA® + EV	442	426	409	394	376	331	270	222	182	141	108	67	36	22	12	8	1	1	1	0
Chemotherapy	444	423	393	356	317	263	209	164	125	90	60	37	25	18	12	7	6	2	1	0

Adapted from Powles T, *et al.* 2024.[1]

KEYTRUDA + EV nearly doubled the median OS vs platinum-based chemotherapy in the 1L treatment of patients with u/mUC

53%

RELATIVE REDUCTION IN RISK OF DEATH
with KEYTRUDA + EV
vs platinum-based chemotherapy

Events: 30.1% (133/442) vs 50.9% (226/444)

HR: 0.47;† 95% CI: 0.38–0.58; p<0.001‡

Median OS

KEYTRUDA + EV
31.5 months
(95% CI: 25.4–NR)

vs

Platinum-based chemotherapy
16.1 months
(95% CI: 13.9–18.3)

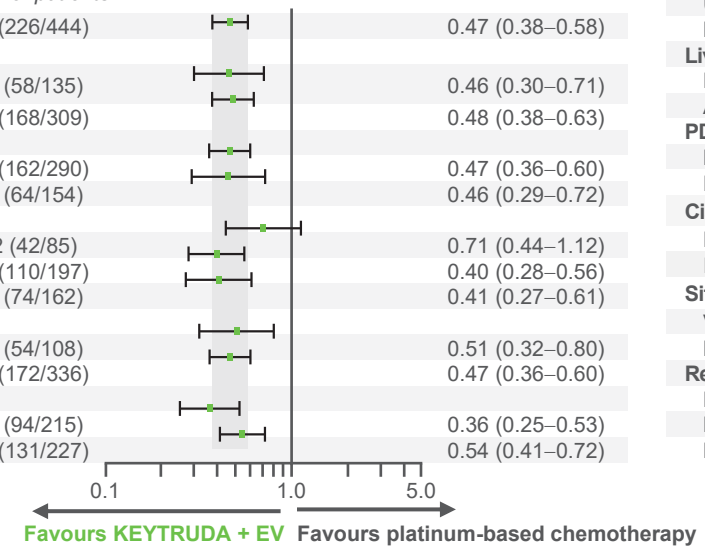
***Cut-off date: 8 August 2023.**[1] †Based on the stratified Cox proportional hazard regression model.[1] ‡Two-sided p-value based on stratified log-rank test.[1]
1L, first-line; CI, confidence interval; EV, enfortumab vedotin; HR, hazard ratio; ITT, intention-to-treat; NR, not reached; OS, overall survival; u/mUC, unresectable/metastatic urothelial carcinoma.

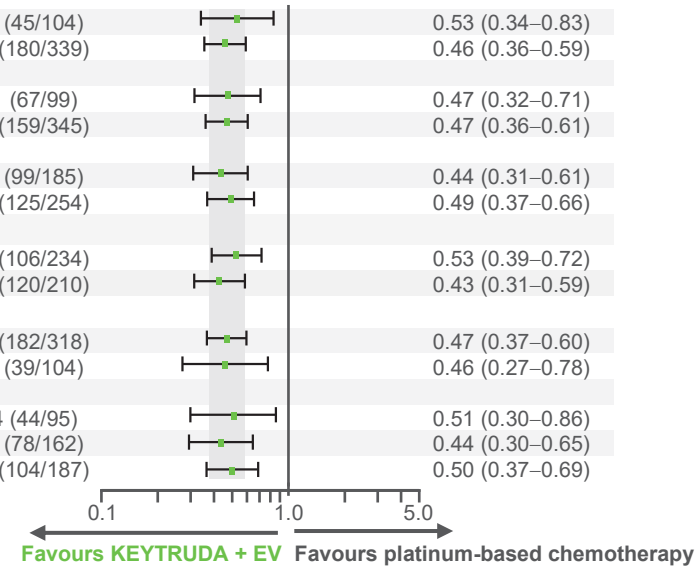
1. Powles T, *et al. N Engl J Med* 2024;390:875–888.

In the KEYNOTE-A39 initial analysis, OS favoured KEYTRUDA + EV across all prespecified patient subgroups[1]

Exploratory subgroup analysis of OS within the ITT population

Subgroup	KEYTRUDA + EV	Platinum-based chemotherapy	HR (95% CI)
	no. of events/no. of patients		
Overall	31.5 (133/442)	16.1 (226/444)	0.47 (0.38–0.58)
Age			
<65 years	NE (39/144)	19.7 (58/135)	0.46 (0.30–0.71)
≥65 years	31.5 (94/298)	14.6 (168/309)	0.48 (0.38–0.63)
Race			
White	26.1 (104/308)	15.3 (162/290)	0.47 (0.36–0.60)
Other	NE (29/134)	19.3 (64/154)	0.46 (0.29–0.72)
Geographic region			
North America	25.6 (40/103)	21.2 (42/85)	0.71 (0.44–1.12)
Europe	NE (56/172)	13.9 (110/197)	0.40 (0.28–0.56)
Rest of the world	NE (37/167)	16.4 (74/162)	0.41 (0.27–0.61)
Sex			
Female	25.4 (32/98)	14.6 (54/108)	0.51 (0.32–0.80)
Male	31.5 (101/344)	16.6 (172/336)	0.47 (0.36–0.60)
ECOG PS score			
0	NE (44/223)	18.4 (94/215)	0.36 (0.25–0.53)
1 or 2	25.4 (89/219)	13.1 (131/227)	0.54 (0.41–0.72)
Primary site of origin of disease			
Upper tract	NE (38/135)	18.4 (45/104)	0.53 (0.34–0.83)
Lower tract	31.5 (94/305)	15.6 (180/339)	0.46 (0.36–0.59)
Liver metastases			
Present	19.1 (43/100)	10.1 (67/99)	0.47 (0.32–0.71)
Absent	NE (90/342)	17.9 (159/345)	0.47 (0.36–0.61)
PD-L1 expression			
Low (CPS <10)	NE (53/184)	15.5 (99/185)	0.44 (0.31–0.61)
High (CPS ≥10)	31.5 (79/254)	16.6 (125/254)	0.49 (0.37–0.66)
Cisplatin eligibility status			
Eligible	31.5 (69/244)	18.4 (106/234)	0.53 (0.39–0.72)
Ineligible	NE (64/198)	12.7 (120/210)	0.43 (0.31–0.59)
Site of metastasis			
Visceral site	25.6 (108/318)	13.6 (182/318)	0.47 (0.37–0.60)
Lymph node only	NE (22/103)	27.5 (39/104)	0.46 (0.27–0.78)
Renal function			
Normal	26.1 (24/84)	18.4 (44/95)	0.51 (0.30–0.86)
Mild impairment	NE (42/165)	16.4 (78/162)	0.44 (0.30–0.65)
Moderate or severe impairment	31.5 (67/193)	13.3 (104/187)	0.50 (0.37–0.69)





In KEYNOTE-A39, formal statistical testing for these subgroups was not conducted. The study was not powered to detect differences in the treatment effect in these subgroups. **Therefore, results should be interpreted with caution and no conclusions should be drawn**

Adapted from Powles T, *et al.* 2024.[1]

***Cut-off date: 8 August 2023.**[1]

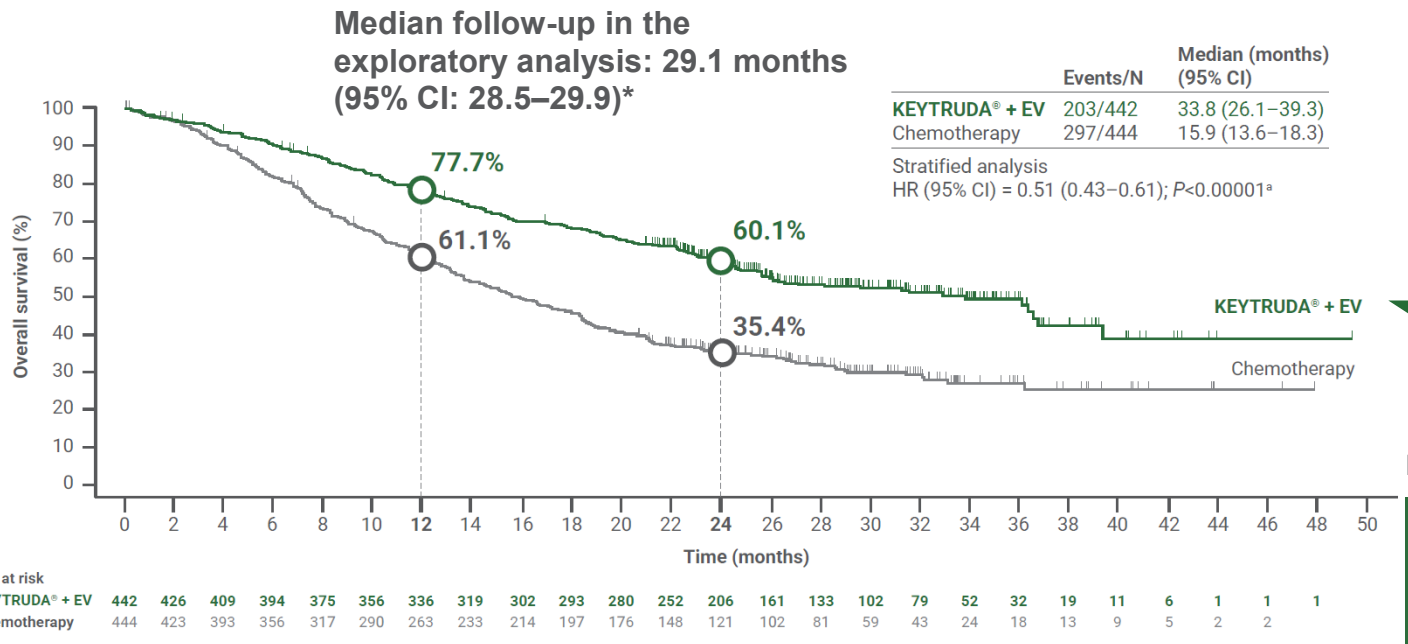
CI, confidence interval; CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; EV, enfortumab vedotin; HR, hazard ratio; ITT, intention-to-treat; no, number; OS, overall survival; PD-L1, programmed death-ligand 1.

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

An exploratory analysis of the KEYNOTE-A39 trial data showed that the OS benefit was maintained with KEYTRUDA + EV vs platinum-based chemotherapy[1,2]

LIMITATIONS: This analysis was exploratory in nature. No formal statistical testing was performed. Therefore, no conclusions can be drawn.

Kaplan-Meier estimates of OS (dual primary endpoint in the ITT population)[1]



	Events/N	Median (months) (95% CI)
KEYTRUDA® + EV	203/442	33.8 (26.1–39.3)
Chemotherapy	297/444	15.9 (13.6–18.3)

Stratified analysis
HR (95% CI) = 0.51 (0.43–0.61); *P*<0.00001[a]

49%

RELATIVE REDUCTION IN RISK OF DEATH
with KEYTRUDA + EV
vs platinum-based chemotherapy

Events: 45.8% (203/444) vs 66.9% (297/444)

HR: 0.51; 95% CI: 0.43–0.61; p<0.00001†

Median OS

KEYTRUDA + EV
33.8 months
(95% CI: 26.1–39.3)

vs

Platinum-based chemotherapy
15.9 months
(95% CI: 13.6–18.3)

Adapted from Powles T, *et al.* 2025.[1]

*1 year additional follow-up from final analysis (~2.5 years of median follow-up). **Cut-off date: 8 August 2024.**[1] †P-value is nominal and descriptive.[1]
CI, confidence interval; EV, enfortumab vedotin; HR, hazard ratio; ITT, intention-to-treat; OS, overall survival.

1. Powles T, *et al. Ann Oncol.* 2025;36:1212–1219. **2.** Powles T, *et al. N Engl J Med* 2024;390:875–888.

OS in key subgroups of the ITT population with 1 year of additional follow-up (follow-up analysis)[1]

Median follow-up: 29.1 months (95% CI: 28.5–29.9)

LIMITATIONS: This analysis was exploratory in nature. No formal statistical testing was performed. Therefore, no conclusions can be drawn.

	Median OS, months (events/N)		
	KEYTRUDA® + EV	Chemotherapy	HR (95% CI)
Overall	33.8 (203/442)	15.9 (297/444)	0.51 (0.43–0.61)
Age			
<65 years	39.3 (59/144)	18.7 (87/135)	0.43 (0.31–0.61)
≥65 years	27.1 (144/298)	14.6 (210/309)	0.54 (0.44–0.67)
Race			
White	26.1 (158/308)	15.1 (207/290)	0.52 (0.42–0.64)
Other	36.3 (45/134)	19.1 (90/154)	0.44 (0.30–0.63)
Region			
North America	25.7 (57/103)	21.0 (54/85)	0.67 (0.45–1.00)
Europe	25.6 (90/172)	14.6 (140/197)	0.52 (0.40–0.69)
Rest of world	NR (56/167)	15.5 (103/162)	0.39 (0.28–0.54)
Sex			
Female	25.4 (46/98)	14.6 (70/108)	0.55 (0.37–0.81)
Male	33.8 (157/344)	16.4 (227/336)	0.50 (0.41–0.62)
ECOG PS			
0	36.5 (77/223)	18.7 (136/215)	0.39 (0.30–0.52)
1-2	22.8 (126/219)	13.3 (160/227)	0.62 (0.49–0.79)
Primary disease site of origin			
Upper tract	36.5 (60/135)	18.3 (63/104)	0.54 (0.37–0.78)
Lower tract	32.9 (142/305)	15.6 (233/339)	0.50 (0.41–0.62)

	Median OS, months (events/N)		
	KEYTRUDA® + EV	Chemotherapy	HR (95% CI)
Overall	33.8 (203/442)	15.9 (297/444)	0.51 (0.43–0.61)
Liver metastases			
Present	19.1 (68/100)	10.1 (82/99)	0.56 (0.40–0.78)
Absent	39.3 (135/342)	18.3 (215/345)	0.50 (0.40–0.62)
PD-L1 expression			
Low (CPS <10)	31.2 (91/184)	15.1 (136/185)	0.47 (0.36–0.62)
High (CPS ≥10)	36.5 (111/254)	17.1 (158/254)	0.55 (0.43–0.70)
Cisplatin eligibility			
Eligible	36.7 (101/244)	18.7 (143/234)	0.54 (0.42–0.70)
Ineligible	25.6 (102/198)	12.7 (154/210)	0.50 (0.39–0.64)
Metastatic disease site			
Visceral metastases	25.7 (163/318)	13.5 (235/318)	0.51 (0.41–0.62)
Lymph node only	NR (34/103)	24.4 (54/104)	0.51 (0.33–0.79)
Renal function			
Normal	39.3 (33/84)	18.6 (61/95)	0.50 (0.32–0.77)
Mild	36.5 (69/165)	18.4 (101/162)	0.50 (0.37–0.69)
Moderate/severe	25.6 (101/193)	13.3 (135/187)	0.53 (0.41–0.69)

Adapted from Powles T, *et al.* 2025.[1]

Data cut-off date: 8 August 2024.

*As assessed by BICR according to RECIST v1.1.

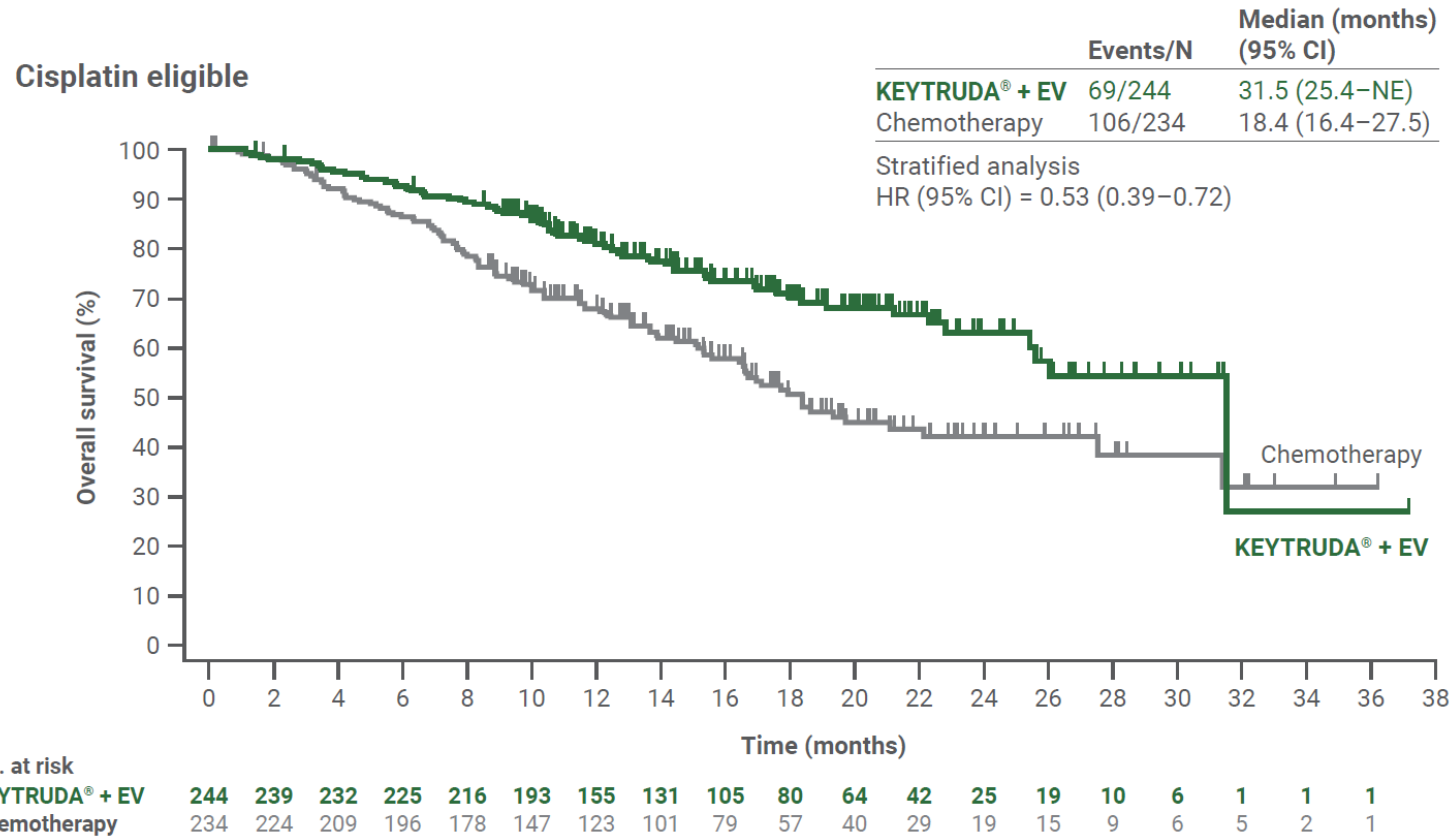
BICR, blinded independent central review; CI, confidence interval; CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; ESMO, European Society for Medical Oncology; EV, enfortumab vedotin; HR, hazard ratio; ITT, intention-to-treat; no, number; NR, not reached; OS, overall survival; PD-L1, programmed death ligand-1; PFS, progression free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumours v1.1.

1. Powles T, *et al. Ann Oncol.* 2025;36:1212–1219.

OS in the cisplatin eligible population (initial analysis)[1,2]

Median follow-up: 17.2 months

LIMITATIONS: This analysis was exploratory in nature. No formal statistical testing was performed. Therefore, no conclusions can be drawn.



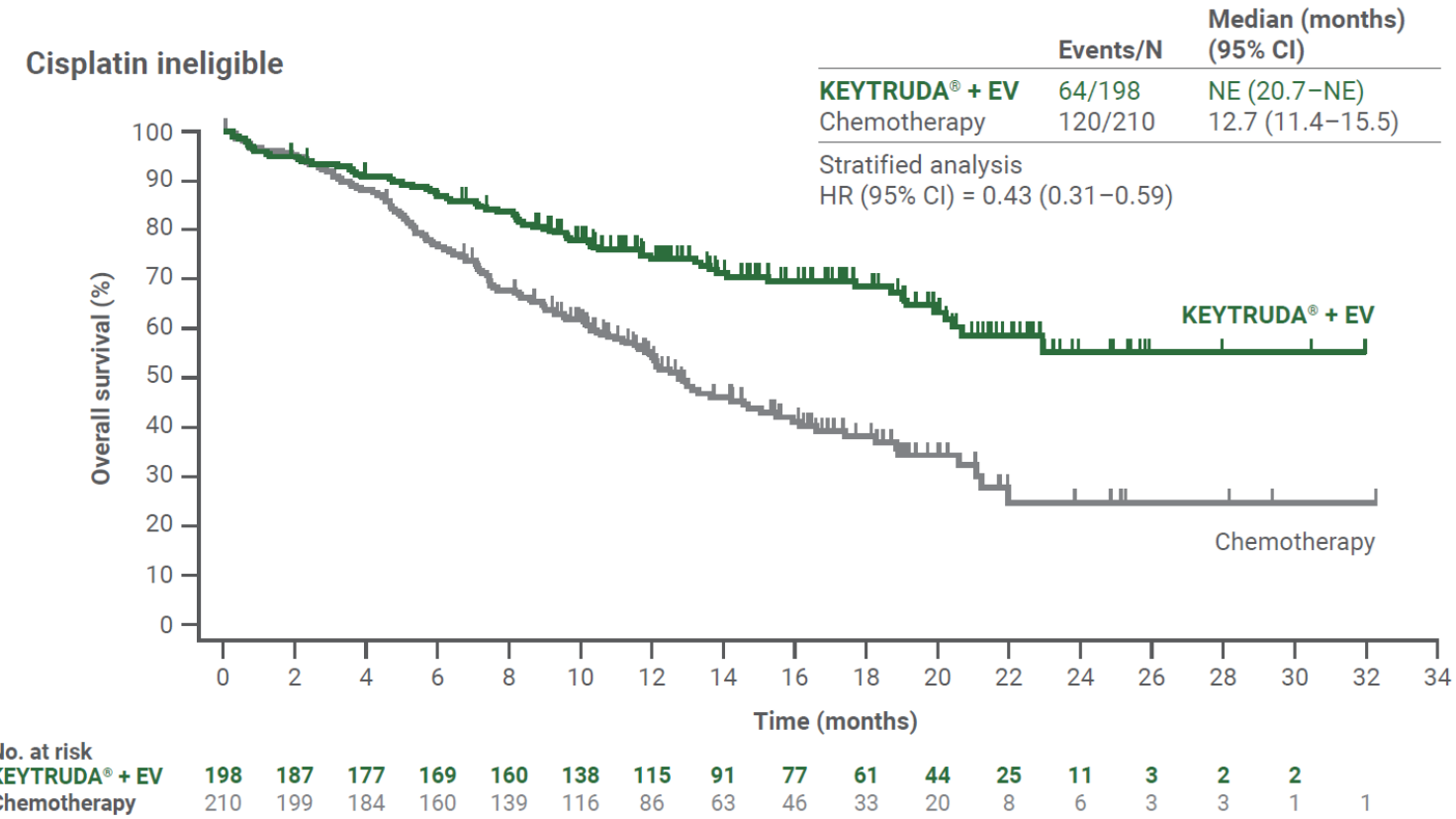
Adapted from Powles T, *et al.* 2024. Supplementary appendix.[2]

Data cut-off date: 8 August 2023.
CI, confidence interval; EV, enfortumab vedotin; HR, hazard ratio; NE, not estimable; OS, overall survival.
1. Powles T, *et al. N Engl J Med* 2024;390:875–888. **2.** Powles T, *et al. N Engl J Med* 2024;390:875–888. Supplementary appendix.

OS in the cisplatin ineligible population (initial analysis)[1,2]

Median follow-up: 17.2 months

LIMITATIONS: This analysis was exploratory in nature. No formal statistical testing was performed. Therefore, no conclusions can be drawn.



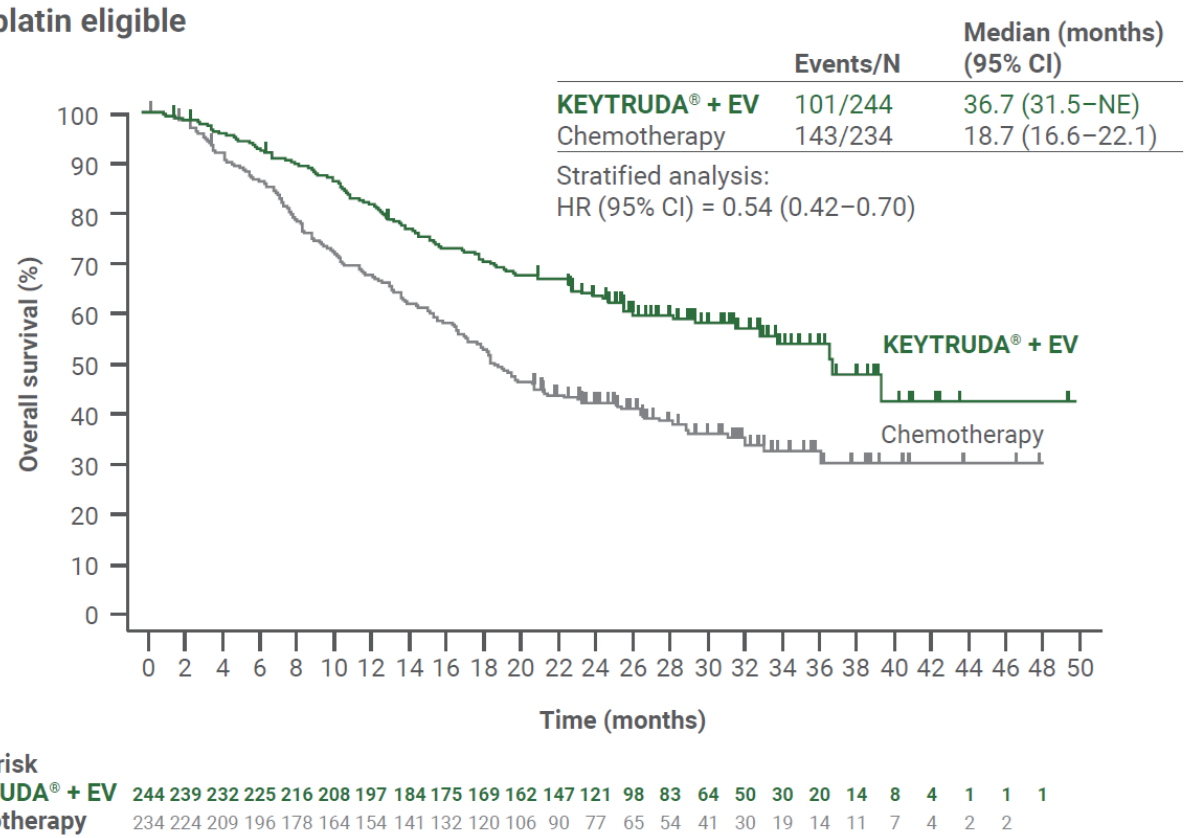
Adapted from Powles T, *et al.* 2024. Supplementary appendix.[2]

Data cut-off date: 8 August 2023.
CI, confidence interval; EV, enfortumab vedotin; HR, hazard ratio; NE, not estimable; OS, overall survival.
1. Powles T, *et al. N Engl J Med* 2024;390:875–888. **2.** Powles T, *et al. N Engl J Med* 2024;390:875–888. Supplementary appendix.

OS in the cisplatin eligible population (follow-up analysis)[1,2]

Median follow-up: 29.1 months (95% CI: 28.5–29.9)

LIMITATIONS: This analysis was exploratory in nature. No formal statistical testing was performed. Therefore, no conclusions can be drawn.



Adapted from Powles T, *et al.* 2025. Supplementary Appendix.[2]

Data cut-off date: 8 August 2023.

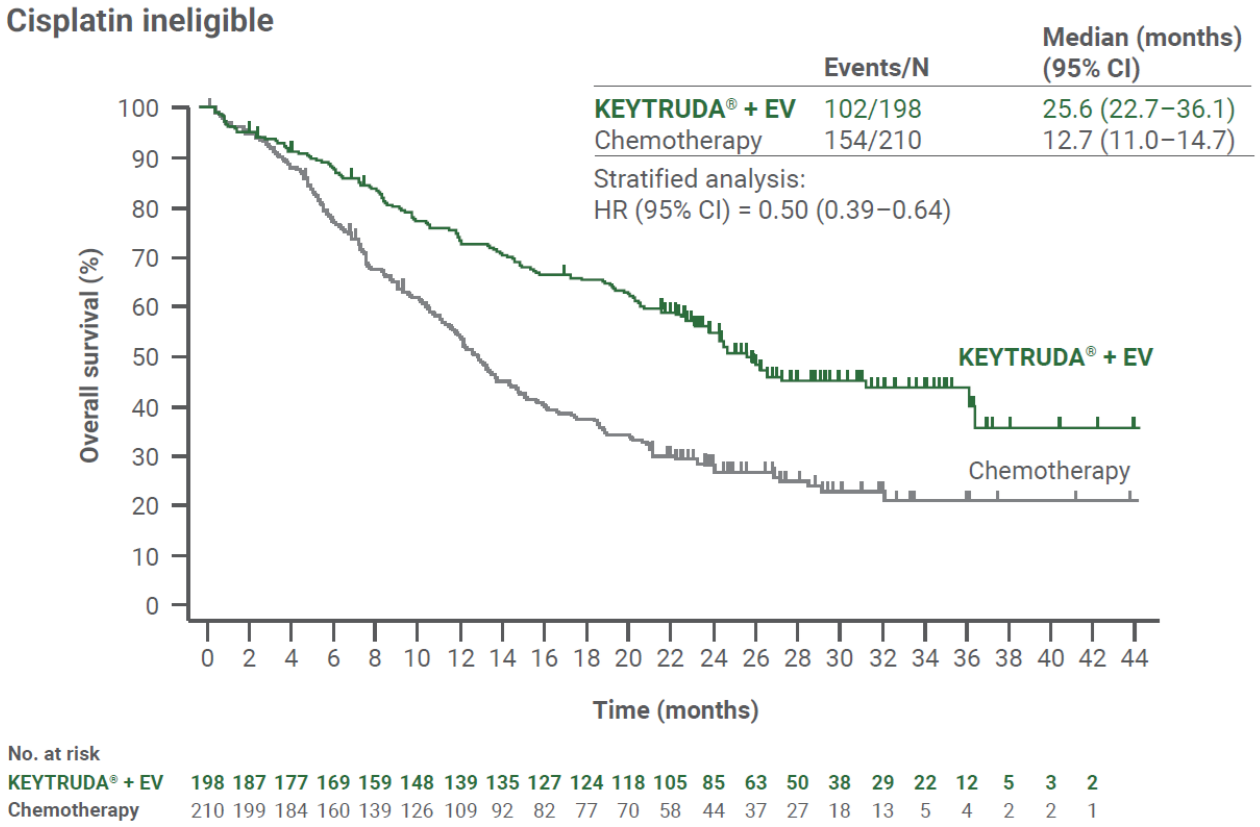
CI, confidence interval; EV, enfortumab vedotin; HR, hazard ratio; NE, not estimable; OS, overall survival.

1. Powles T, *et al. Ann Oncol.* 2025;36:1212–1219. **2. .** Powles T, *et al. Ann Oncol.* 2025;36:1212–1219. Supplementary Appendix.

OS in the cisplatin ineligible population (follow-up analysis)[1,2]

Median follow-up: 29.1 months (95% CI: 28.5–29.9)

LIMITATIONS: This analysis was exploratory in nature. No formal statistical testing was performed. Therefore, no conclusions can be drawn.



Adapted from Powles T, *et al.* 2025. Supplementary Appendix.[2]

Data cut-off date: 8 August 2023.

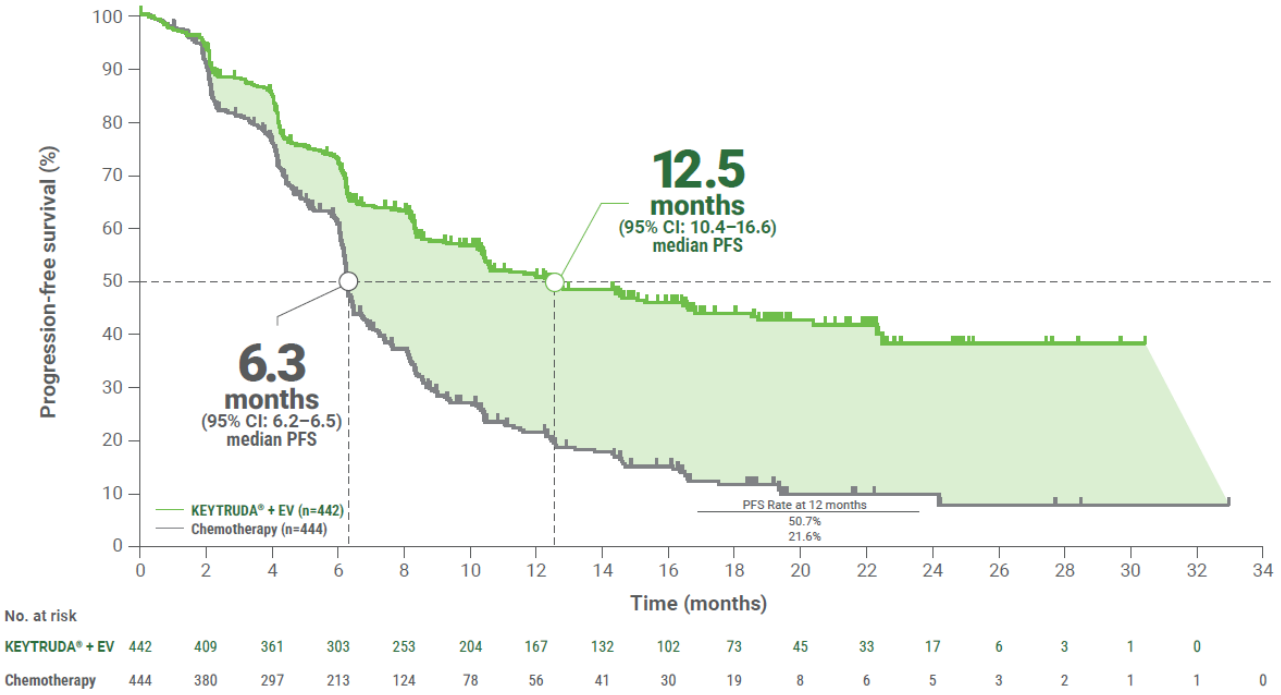
CI, confidence interval; EV, enfortumab vedotin; HR, hazard ratio; NE, not estimable; OS, overall survival.

1. Powles T, *et al. Ann Oncol.* 2025;36:1212–1219. **2.** . Powles T, *et al. Ann Oncol.* 2025;36:1212–1219. Supplementary Appendix.

In the KEYNOTE-A39 initial analysis, KEYTRUDA + EV significantly reduced the risk of disease progression or death vs platinum-based chemotherapy[1]

Kaplan-Meier estimates of PFS* (dual primary endpoint in the ITT population)

Median follow-up of 17.2 months[1]



No. at risk																	
KEYTRUDA® + EV	442	409	361	303	253	204	167	132	102	73	45	33	17	6	3	1	0
Chemotherapy	444	380	297	213	124	78	56	41	30	19	8	6	5	3	2	1	1	0

Adapted from Powles T, *et al.* 2024.[1]

KEYTRUDA + EV nearly doubled the median PFS vs platinum-based chemotherapy in the 1L treatment of u/mUC

55%

RELATIVE REDUCTION IN RISK OF DISEASE PROGRESSION OR DEATH with KEYTRUDA + EV vs platinum-based chemotherapy

Events: 50.5% (223/442) vs 69.1% (307/444)

HR: 0.45;‡ 95% CI: 0.38–0.54; p<0.001§

Median PFS

KEYTRUDA + EV
12.5 months
(95% CI: 10.4–16.6)

vs

Platinum-based chemotherapy
6.3 months
(95% CI: 6.2–6.5)

*As assessed by BICR according to RECIST v1.1.[1] †**Cut-off date: 8 August 2023.**[1] ‡Based on the stratified Cox proportional hazard regression model.[1] §Two-sided p-value based on stratified log-rank test.[1]
1L, first-line; BICR, blinded independent central review; CI, confidence interval; EV, enfortumab vedotin; HR, hazard ratio; ITT, intention-to-treat; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours; u/mUC, unresectable/metastatic urothelial carcinoma.

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

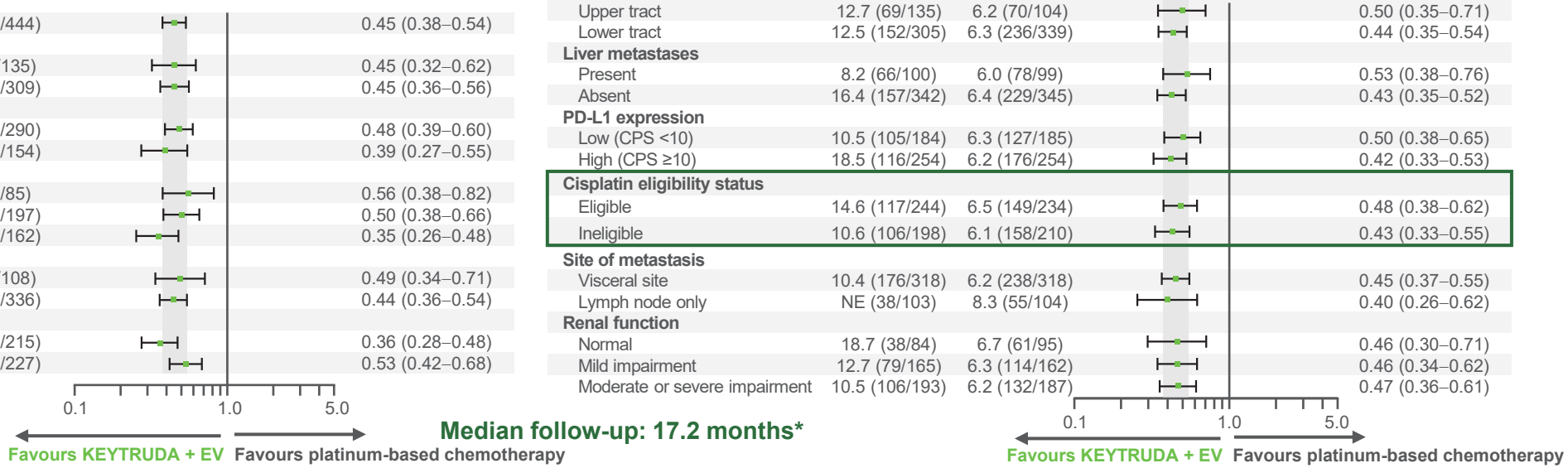
KEYTRUDA® (pembrolizumab)

DOSING | IV PI | SC PI 395 mg | SC PI 790 mg

In the KEYNOTE-A39 initial analysis, PFS favoured KEYTRUDA + EV across all prespecified patient subgroups[1]

Exploratory subgroup analysis of PFS within the ITT population

Subgroup	KEYTRUDA + EV	Platinum-based chemotherapy	HR (95% CI)
	no. of events/no. of patients		
Overall	12.5 (223/442)	6.3 (307/444)	0.45 (0.38–0.54)
Age			
<65 years	12.7 (75/144)	6.4 (88/135)	0.45 (0.32–0.62)
≥65 years	12.0 (148/298)	6.2 (219/309)	0.45 (0.36–0.56)
Race			
White	12.0 (148/298)	6.2 (207/290)	0.48 (0.39–0.60)
Other	22.3 (55/134)	6.5 (100/154)	0.39 (0.27–0.55)
Geographic region			
North America	12.0 (58/103)	6.3 (55/85)	0.56 (0.38–0.82)
Europe	10.4 (94/172)	6.3 (144/197)	0.50 (0.38–0.66)
Rest of the world	NE (71/167)	6.2 (108/162)	0.35 (0.26–0.48)
Sex			
Female	10.4 (55/98)	6.1 (74/108)	0.49 (0.34–0.71)
Male	14.6 (168/344)	6.3 (233/336)	0.44 (0.36–0.54)
ECOG PS score			
0	22.3 (93/223)	6.7 (146/215)	0.36 (0.28–0.48)
1 or 2	9.3 (130/219)	6.1 (161/227)	0.53 (0.42–0.68)
Primary site of origin of disease			
Upper tract	12.7 (69/135)	6.2 (70/104)	0.50 (0.35–0.71)
Lower tract	12.5 (152/305)	6.3 (236/339)	0.44 (0.35–0.54)
Liver metastases			
Present	8.2 (66/100)	6.0 (78/99)	0.53 (0.38–0.76)
Absent	16.4 (157/342)	6.4 (229/345)	0.43 (0.35–0.52)
PD-L1 expression			
Low (CPS <10)	10.5 (105/184)	6.3 (127/185)	0.50 (0.38–0.65)
High (CPS ≥10)	18.5 (116/254)	6.2 (176/254)	0.42 (0.33–0.53)
Cisplatin eligibility status			
Eligible	14.6 (117/244)	6.5 (149/234)	0.48 (0.38–0.62)
Ineligible	10.6 (106/198)	6.1 (158/210)	0.43 (0.33–0.55)
Site of metastasis			
Visceral site	10.4 (176/318)	6.2 (238/318)	0.45 (0.37–0.55)
Lymph node only	NE (38/103)	8.3 (55/104)	0.40 (0.26–0.62)
Renal function			
Normal	18.7 (38/84)	6.7 (61/95)	0.46 (0.30–0.71)
Mild impairment	12.7 (79/165)	6.3 (114/162)	0.46 (0.34–0.62)
Moderate or severe impairment	10.5 (106/193)	6.2 (132/187)	0.47 (0.36–0.61)



LIMITATIONS: In KEYNOTE-A39, formal statistical testing for these subgroups was not conducted. The study was not powered to detect differences in the treatment effect in these subgroups. **Therefore, results should be interpreted with caution and no conclusions should be drawn**

Adapted from Powles T, *et al.* 2024.[1]

***Cut-off date: 8 August 2023.**[1]

CI, confidence interval; CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; EV, enfortumab vedotin; HR, hazard ratio; ITT, intention-to-treat; no, number; PD-L1, programmed death-ligand 1; PFS, progression-free survival.

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

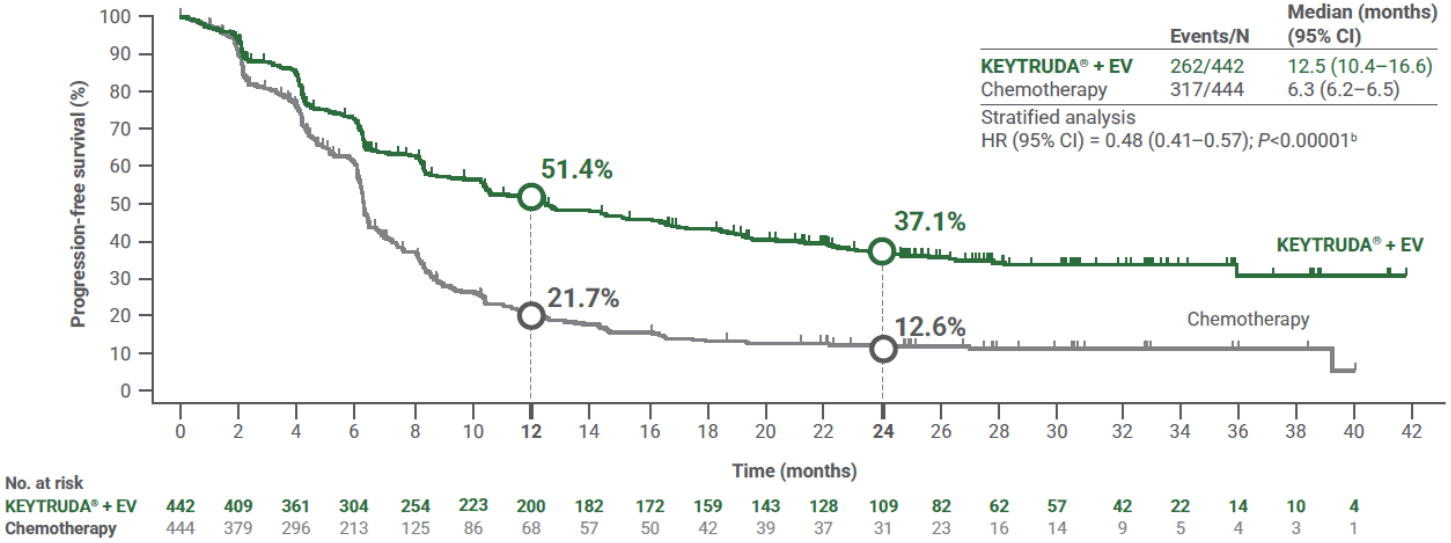
An exploratory analysis of the KEYNOTE-A39 trial data showed that the PFS benefit was maintained with KEYTRUDA + EV vs platinum-based chemotherapy[1,2]

LIMITATIONS: This analysis was exploratory in nature. No formal statistical testing was performed. Therefore, no conclusions can be drawn.

Kaplan-Meier estimates of PFS* (dual primary endpoint in the ITT population)[1]

Median follow-up in the exploratory analysis: 29.1 months (95% CI: 28.5–29.9)*

PFS[a] in the overall population[2]



	Events/N	Median (months) (95% CI)
KEYTRUDA® + EV	262/442	12.5 (10.4–16.6)
Chemotherapy	317/444	6.3 (6.2–6.5)

Stratified analysis
HR (95% CI) = 0.48 (0.41–0.57); *P*<0.00001[b]

No. at risk																				
KEYTRUDA® + EV	442	409	361	304	254	223	200	182	172	159	143	128	109	82	62	57	42	22	14	10	4
Chemotherapy	444	379	296	213	125	86	68	57	50	42	39	37	31	23	16	14	9	5	4	3	1

52%

RELATIVE REDUCTION IN RISK OF DISEASE PROGRESSION OR DEATH with KEYTRUDA + EV vs platinum-based chemotherapy

Events: 59.0% (262/444) vs 71.4% (317/444)

HR: 0.48; 95% CI: 0.41–0.57; p<0.00001†

Median PFS

KEYTRUDA + EV
12.5 months
(95% CI: 10.4–16.6)

vs

Platinum-based chemotherapy
6.3 months
(95% CI: 6.2–6.5)

Adapted from Powles T, *et al.* 2025.[1]

*As assessed by BICR according to RECIST v1.1. 1 year additional follow-up from final analysis (~2.5 years of median follow-up). **Cut-off date: 8 August 2024.**[1] †P-value is nominal and descriptive.[1]
BICR, blinded independent central review; CI, confidence interval; EV, enfortumab vedotin; HR, hazard ratio; ITT, intention-to-treat; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours.

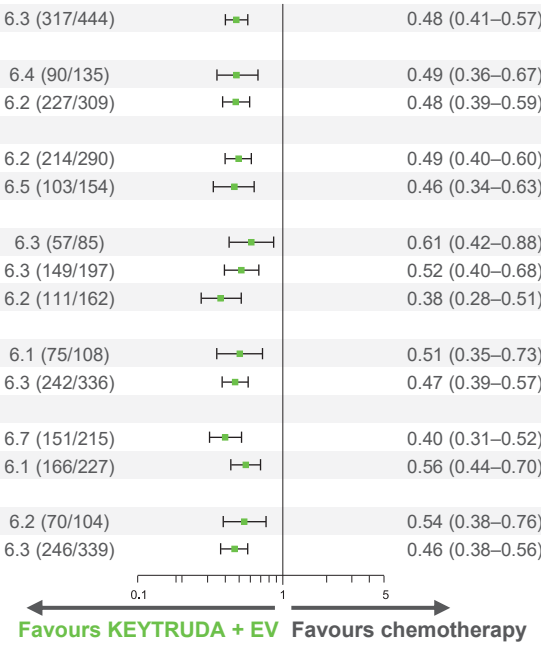
1. Powles T, *et al. Ann Oncol.* 2025;36:1212–1219 . **2.** Powles T, *et al. N Engl J Med* 2024;390:875–888.

PFS in key subgroups of the ITT population with 1 year of additional follow-up (follow-up analysis)[1,*]

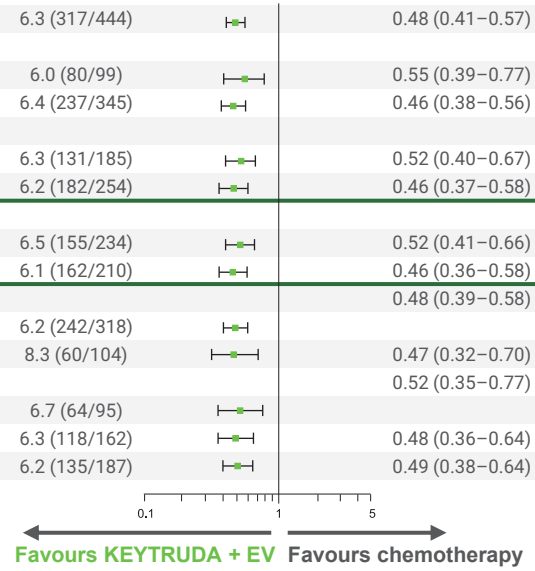
Median follow-up: 29.1 months (95% CI: 28.5–29.9)

LIMITATIONS: This analysis was exploratory in nature. No formal statistical testing was performed. Therefore, no conclusions can be drawn.

Subgroup	KEYTRUDA + EV *no. of events/no. of patients*	Chemotherapy *no. of events/no. of patients*	HR (95% CI)
Overall	12.5 (262/442)	6.3 (317/444)	0.48 (0.41–0.57)
Age			
<65 years	14.6 (87/144)	6.4 (90/135)	0.49 (0.36–0.67)
≥65 years	12.3 (175/298)	6.2 (227/309)	0.48 (0.39–0.59)
Race			
White	10.5 (191/308)	6.2 (214/290)	0.49 (0.40–0.60)
Other	19.2 (71/134)	6.5 (103/154)	0.46 (0.34–0.63)
Geographic region			
North America	10.3 (72/103)	6.3 (57/85)	0.61 (0.42–0.88)
Europe	10.4 (102/172)	6.3 (149/197)	0.52 (0.40–0.68)
Rest of the world	19.3 (88/167)	6.2 (111/162)	0.38 (0.28–0.51)
Sex			
Female	10.4 (59/98)	6.1 (75/108)	0.51 (0.35–0.73)
Male	14.0 (203/344)	6.3 (242/336)	0.47 (0.39–0.57)
ECOG PS score			
0	17.3 (121/223)	6.7 (151/215)	0.40 (0.31–0.52)
1 or 2	9.3 (141/219)	6.1 (166/227)	0.56 (0.44–0.70)
Primary disease site of origin			
Upper tract	12.3 (81/135)	6.2 (70/104)	0.54 (0.38–0.76)
Lower tract	12.8 (179/305)	6.3 (246/339)	0.46 (0.38–0.56)



Subgroup	KEYTRUDA + EV *no. of events/no. of patients*	Chemotherapy *no. of events/no. of patients*	HR (95% CI)
Overall	12.5 (262/442)	6.3 (317/444)	0.48 (0.41–0.57)
Liver metastases			
Present	8.1 (74/100)	6.0 (80/99)	0.55 (0.39–0.77)
Absent	16.4 (188/342)	6.4 (237/345)	0.46 (0.38–0.56)
PD-L1 expression			
Low (CPS <10)	10.5 (122/184)	6.3 (131/185)	0.52 (0.40–0.67)
High (CPS ≥10)	16.4 (138/254)	6.2 (182/254)	0.46 (0.37–0.58)
Cisplatin eligibility			
Eligible	15.0 (140/244)	6.5 (155/234)	0.52 (0.41–0.66)
Ineligible	10.6 (122/198)	6.1 (162/210)	0.46 (0.36–0.58)
Metastatic disease site			0.48 (0.39–0.58)
Visceral site	10.4 (203/318)	6.2 (242/318)	
Lymph node only	22.1 (50/103)	8.3 (60/104)	0.47 (0.32–0.70)
Renal function			0.52 (0.35–0.77)
Normal	18.7 (47/84)	6.7 (64/95)	
Mild impairment	12.7 (91/165)	6.3 (118/162)	0.48 (0.36–0.64)
Moderate or severe impairment	10.5 (124/193)	6.2 (135/187)	0.49 (0.38–0.64)



Adapted from Powles T, *et al.* 2025.[1]

Data cut-off date: 8 August 2024.

*As assessed by BICR according to RECIST v1.1.

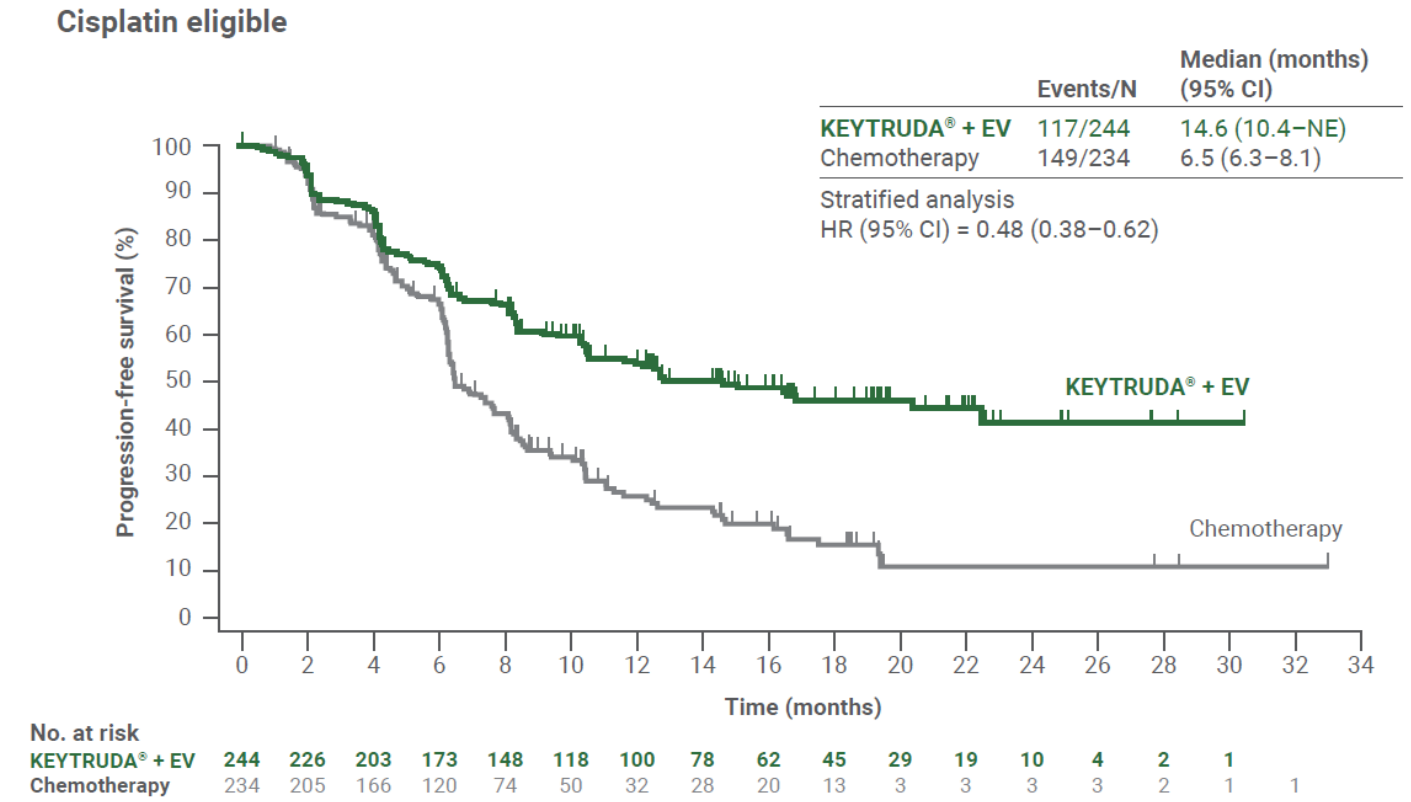
BICR, blinded independent central review; CI, confidence interval; CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; EV, enfortumab vedotin; HR, hazard ratio; ITT, intention-to-treat; no, number; PD-L1, programmed death ligand-1; PFS, progression free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumours v1.1.

1. Powles T, *et al. Ann Oncol.* 2025;36:1212–1219.

PFS* in the cisplatin-eligible population (initial analysis)[1,2]

Median follow-up: 17.2 months

LIMITATIONS: This analysis was exploratory in nature. No formal statistical testing was performed. Therefore, no conclusions can be drawn.



Adapted from Powles T, *et al.* 2024. Supplementary appendix.[2]

Data cut-off date: 8 August 2023.
*As assessed by BICR according to RECIST v1.1.
CI, confidence interval; EV, enfortumab vedotin; HR, hazard ratio; NE, not estimable; PFS, progression-free survival.
1. Powles T, *et al. N Engl J Med* 2024;390:875–888. **2.** Powles T, *et al. N Engl J Med* 2024;390:875–888. Supplementary appendix.

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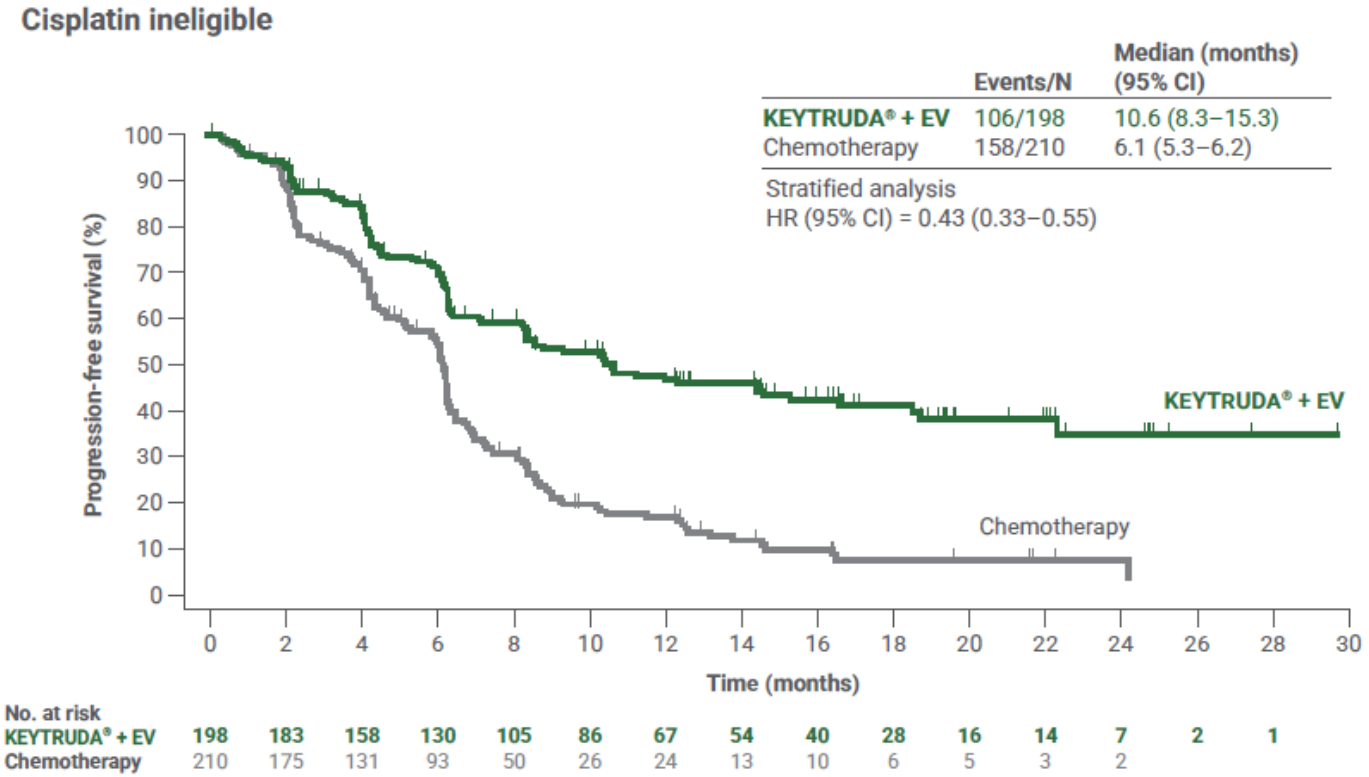


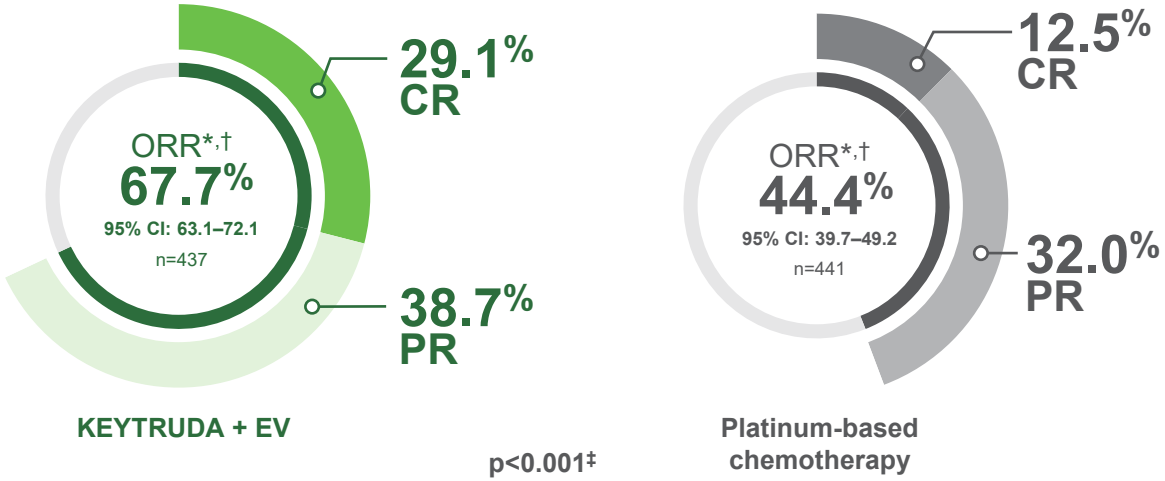
Adapted from Powles T, *et al.* 2024. Supplementary appendix.[2]

Data cut-off date: 8 August 2023.
*As assessed by BICR according to RECIST v1.1.
CI, confidence interval; EV, enfortumab vedotin; HR, hazard ratio; PFS, progression-free survival.
1. Powles T, *et al. N Engl J Med* 2024;390:875–888. **2.** Powles T, *et al. N Engl J Med* 2024;390:875–888. Supplementary appendix.

In the KEYNOTE-A39 initial analysis, a significant ORR benefit was demonstrated with KEYTRUDA + EV vs platinum-based chemotherapy*[1,2]

Secondary endpoint

Treatment response rates within the ITT population



ORR favoured KEYTRUDA + EV across all prespecified patient subgroups[4]

Median follow-up: 17.2 months§

29.1% had a complete response with KEYTRUDA + EV
vs **12.5%** with platinum-based chemotherapy

Events: 29.1% (127/437) vs 12.5% (55/441)

Disease control rate (achieved stable disease or better)[1,3]

KEYTRUDA + EV	vs	Platinum-based chemotherapy
86.0%		78.0%

KEYTRUDA + EV **more than doubled the complete response rate** vs platinum-based chemotherapy

Adapted from Powles T, *et al.* 2024.[1]

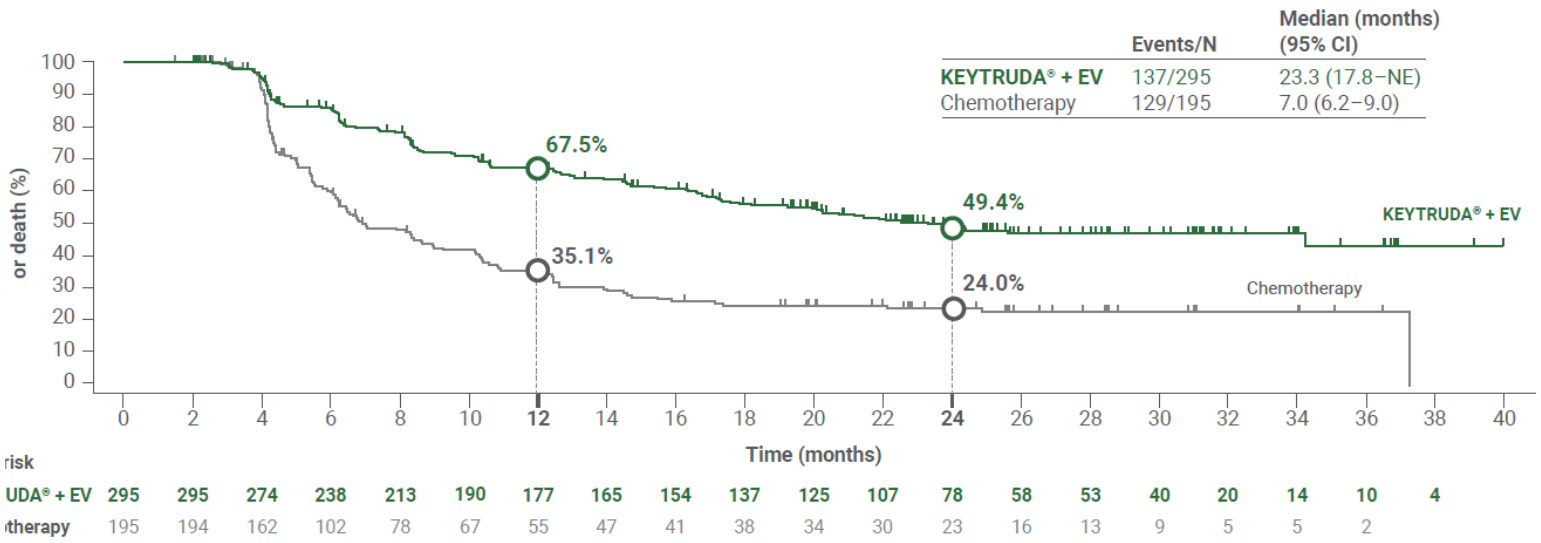
*As assessed by BICR according to RECIST v1.1.[1] †Includes only patients with measurable disease at baseline. Based on patients with a best overall response as confirmed complete or partial response.[1] ‡Two-sided p-value based on Cochran-Mantel-Haenszel test stratified by PD-L1 expression, cisplatin eligibility and liver metastases.[1] §**Cut-off date: 8 August 2023.**[1]
BICR, blinded independent central review; CI, confidence interval; CR, complete response; EV, enfortumab vedotin; ITT, intention-to-treat; ORR, objective response rate; PD-L1, programmed death-ligand 1; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumours.
1. Powles T, *et al. N Engl J Med* 2024;390:875–888. **2.** Powles T, *et al. N Engl J Med* 2024;390:875–888. Protocol. **3.** MSD. Company Core Data Sheet. S-CCDS-MK3475-IV-072024. **4.** Powles T, *et al. N Engl J Med* 2024;390:875–888. Supplementary appendix.

An exploratory analysis of the KEYNOTE-A39 trial data showed that the DoR benefit of KEYTRUDA + EV vs platinum-based chemotherapy* was maintained[1,2]

Secondary endpoint analysis

LIMITATIONS: This analysis was exploratory in nature. No formal statistical testing was performed. Therefore, no conclusions can be drawn.

Duration of response (CR or PR) by BICR



Median follow-up in the exploratory analysis: 29.1 months (95% CI: 28.5–29.9)†

Among responders, the probability of maintained response at 24 months was **~50% with KEYTRUDA + EV[1]**

Median DoR:

- **KEYTRUDA + EV: 23.3 months (17.8–NE)**
- **Platinum-based chemotherapy: 7.0 months (6.2–9.0)[1]**

Adapted from Powles T, *et al.* 2025.[1]

*As assessed by BICR according to RECIST v1.1.[1] †1 year additional follow-up from final analysis (~2.5 years of median follow-up). **Cut-off date: 8 August 2024.**[1] ‡P-value is nominal and descriptive.[1]
BICR, blinded independent central review; DoR, duration of response; EV, enfortumab vedotin; NE, non-estimable.

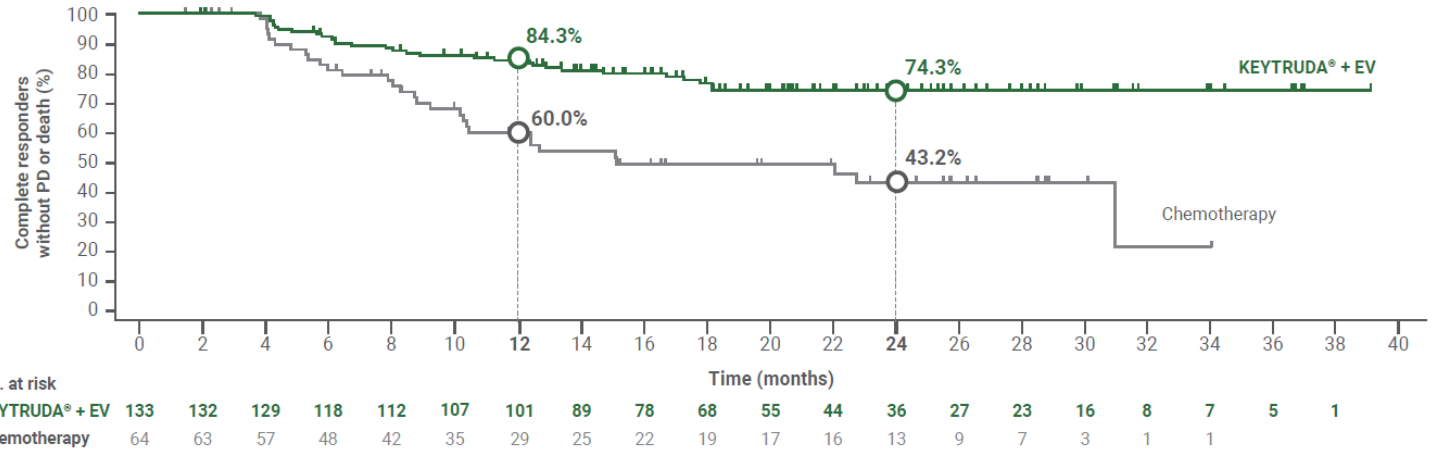
1. Powles T, *et al. Ann Oncol.* 2025;36:1212–1219. **2.** Powles T, *et al. N Engl J Med* 2024;390:875–888.

In the exploratory analysis, the probability of a maintained CR at 24 months was higher with KEYTRUDA + EV vs platinum-based chemotherapy*[1,2]

LIMITATIONS: This analysis was exploratory in nature. No formal statistical testing was performed. Therefore, no conclusions can be drawn.

Duration of confirmed CR† by BICR

	Events/N	Median (months) (95% CI)
KEYTRUDA® + EV	30/133	NR (NE, NE)
Chemotherapy	30/64	15.2 (10.3, NE)



For patients who had a cCR:[3]

Estimated 24-month PFS rate: 78.2% for KEYTRUDA + EV vs 53.7% for platinum-based chemotherapy

Estimated 24-month OS rate: 95.4% for KEYTRUDA + EV vs 85.8% for platinum-based chemotherapy

With 29.1 months (95% CI: 28.5–29.9) of median follow-up:‡

Probability of maintained CR at 24 months was 74.3% with KEYTRUDA + EV vs 43.3% with platinum-based chemotherapy[1]

Median DoCR:

- **KEYTRUDA + EV: NR (NE–NE)**
- **Platinum-based chemotherapy: 15.2 months (10.3–NE)**
- **Events: 22.6% (30/133) vs 46.9% (30/64)**

Adapted from Powles T, *et al.* 2025.[1]

*As assessed by BICR according to RECIST v1.1.[1] †For patients with a best overall response of confirmed CR.[1] ‡1 year additional follow-up from final analysis (~2.5 years of median follow-up). **Cut-off date: August 8 2024.**[1]
BICR, blinded independent central review; cCR, confirmed complete response; CI, confidence interval; CR, complete response; DoCR, duration of complete response; EV, enfortumab vedotin; NE, non-estimable; NR, not reached; OS, overall survival; PD, progressive disease; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours.

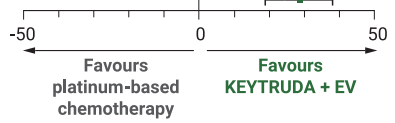
1. Powles T, *et al. Ann Oncol.* 2025;36:1212–1219. **2.** Powles T, *et al. N Engl J Med* 2024;390:875–888; 3. Gupta S, et al. *JCO* 2025; 43(16):4502 (DOI: 10.1200/JCO.2025.43.16_suppl.4502)

ORR subgroup analysis (secondary endpoint)[1,2]

Median follow-up: 17.2 months

LIMITATIONS: This analysis was exploratory in nature. No formal statistical testing was performed. Therefore, no conclusions can be drawn.

Subgroup	KEYTRUDA + EV *no. of events/no. of patients*	Platinum-based chemotherapy	Absolute difference, % (95% CI)
Overall	296/437 (67.7)	196/441 (44.4)	23.3 (16.8–29.6)
Age			
<65 years	98/142 (69.0)	70/134 (52.2)	16.8 (5.3–27.9)
≥65 years	198/295 (67.1)	126/307 (41.0)	26.1 (18.2–33.6)
Race			
White	204/307 (66.4)	130/289 (45.0)	21.5 (13.6–29.1)
Other	92/130 (70.8)	66/152 (43.4)	27.3 (15.9–38.0)
Geographic region			
North America	66/103 (64.1)	42/85 (49.4)	14.7 (0.4–28.4)
Europe	112/171 (65.5)	91/196 (46.4)	19.1 (8.9–28.8)
Rest of the world	118/163 (72.4)	63/160 (39.4)	33.0 (22.5–42.8)
Sex			
Female	64/97 (66.0)	44/107 (41.1)	24.9 (11.2–37.6)
Male	232/340 (68.2)	152/334 (45.5)	22.7 (15.3–29.9)
ECOG PS score			
0	161/222 (72.5)	106/213 (49.8)	22.8 (13.7–31.5)
1 or 2	135/215 (62.8)	89/226 (39.4)	23.4 (14.2–32.3)
Primary site of origin of disease			
Upper tract	90/133 (67.7)	42/103 (40.8)	26.9 (14.2–38.8)
Lower tract	205/302 (67.9)	154/337 (45.7)	22.2 (14.6–29.5)
Liver metastases			
Present	60/100 (60.0)	41/99 (41.4)	18.6 (4.7–31.8)
Absent	236/337 (70.0)	155/342 (45.3)	24.7 (17.4–31.8)
PD-L1 expression			
Low (CPS <10)	114/180 (63.3)	75/183 (41.0)	22.3 (12.1–32.1)
High (CPS ≥10)	180/253 (71.1)	118/253 (46.6)	24.5 (16.0–32.6)
Cisplatin eligibility			
Eligible	172/243 (70.8)	123/232 (53.0)	17.8 (9.1–26.2)
Ineligible	124/194 (63.9)	73/209 (34.9)	29.0 (19.4–38.0)
Site of metastasis			
Visceral metastases	202/315 (64.1)	126/318 (39.6)	24.5 (16.8–31.9)
Lymph node only	79/102 (77.5)	55/103 (53.4)	24.1 (11.1–36.3)
Renal function			
Normal	58/84 (69.0)	53/95 (55.8)	13.3 (-1.0–26.9)
Mild impairment	111/163 (68.1)	72/160 (45.0)	23.1 (12.4–33.3)
Moderate or severe impairment	127/190 (66.8)	71/186 (38.2)	28.7 (18.7–38.0)



Adapted from Powles T, *et al.* 2024. Supplementary appendix.[2]

Cut-off date: August 8 2023.[1]

CI, confidence interval; CPS, complete positive score; ECOG PS, Eastern Cooperative Oncology Guidelines Performance Status; EV, enfortumab vedotin; NE, non-estimable; PD-L1, programmed death ligand-1; RECIST, Response Evaluation Criteria in Solid Tumours.

1. Powles T, *et al. Ann Oncol.* 2025;36:1212–1219. **2.** Powles T, *et al. N Engl J Med* 2024;390:875–888.

KEYNOTE-A39 initial analysis: Summary of AEs in the as-treated population (initial analysis)[1,2]

The safety analysis included all patients who received any dose of trial treatment.

Summary of adverse events (AEs)* **Median follow-up: 17.2 months†**

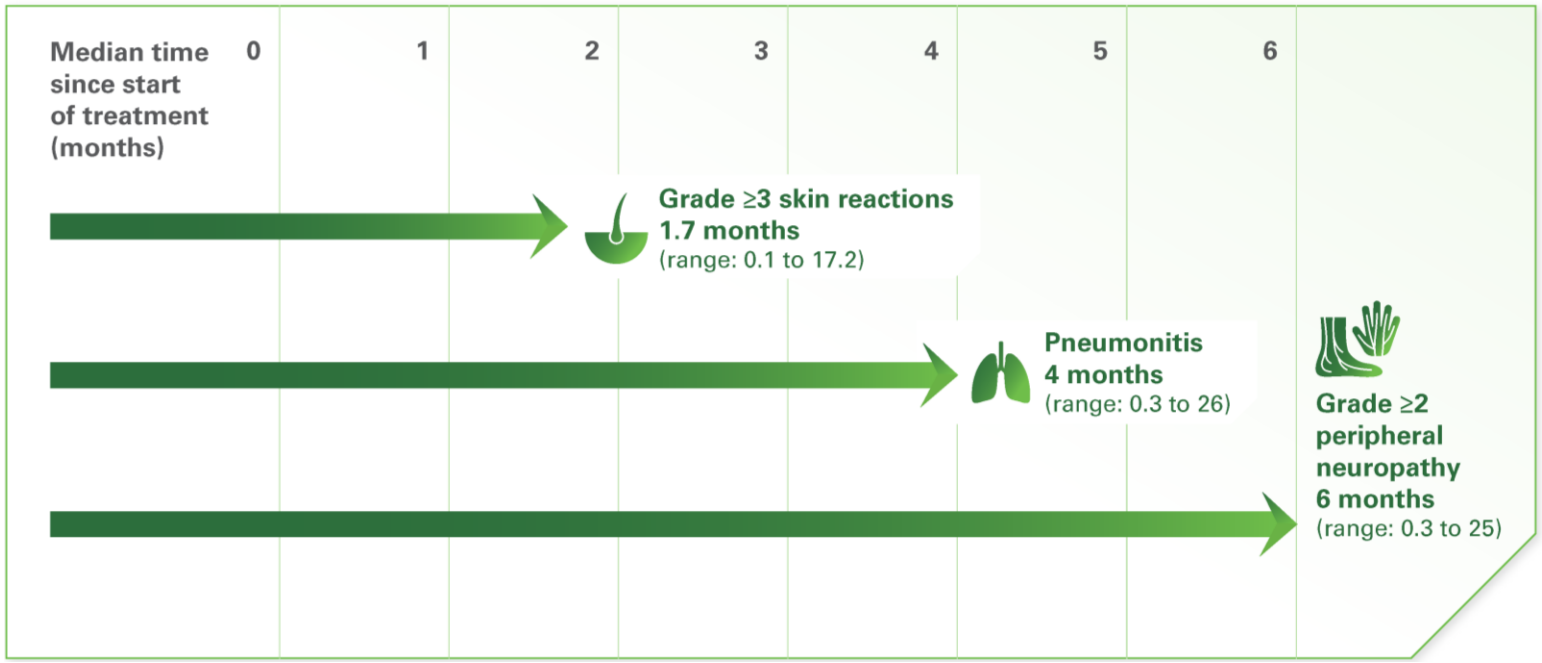
AE, % (n)	KEYTRUDA + EV (n=440)	Platinum-based chemotherapy (n=433)
Any grade, any cause	439 (99.8)	427 (98.6)
Treatment-related	427 (97.0)	414 (95.6)
Grade ≥3, treatment-related	246 (55.9)	301 (69.5)
Treatment-related AE leading to death (Grade 5)	4 (0.9)	4 (0.9)
Serious, treatment-related	122 (27.7)	85 (19.6)
Led to dose interruption of any study drug	299 (68.0)	229 (52.9)
Led to dose interruption of KEYTRUDA	218 (49.5)	N/A
Led to dose interruption of EV	266 (60.5)	N/A
Led to discontinuation of any study drug	154 (35.0)	80 (18.5)
Led to discontinuation of KEYTRUDA	94 (21.4)	N/A
Led to discontinuation of EV	130 (29.5)	N/A

AEs experienced by patients treated with combination KEYTRUDA + EV during KEYNOTE-A39 were generally similar to those observed in patients receiving either component as a monotherapy[1,2]

Adapted from Powles T, *et al.* 2024.[1,2]

*Determined by the investigator as reasonably related to treatment. AEs were graded according to the NCI CTCAE v4.03.[1,2] †**Cut-off date: 8 August 2023.**[1] ‡Multiple organ dysfunction syndrome, immune-mediated lung disease, diarrhoea and asthenia; 1 patient each.[1] §Sepsis, febrile neutropenia, neutropenic sepsis and myocardial infarction; 1 patient each.[1]
AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events; EV, enfortumab vedotin; NCI, National Cancer Institute.
1. Powles T, *et al. N Engl J Med* 2024;390:875–888. **2.** Powles T, *et al. N Engl J Med* 2024;390:875–888. Supplementary appendix.

Median time to onset for select AEs in patients receiving KEYTRUDA® + EV: KEYNOTE-A39 and EV-103 trials (dose escalation cohorts A and K)[1]



Adapted from Brower B, *et al.* 2024.[1]

Median duration of treatment at the time of data cutoff (months)[2]

- **KEYTRUDA + EV:** 9.4 (range: 0.3–31.9)
- **KEYTRUDA:** 8.5 (range: 0.3–28.5)
- **EV:** 7.0 (range: 0.3–31.9)

Median number of cycles[2]

- **KEYTRUDA + EV:** 12 (range: 1–46)
- **KEYTRUDA:** 11 (range: 1–35)
- **EV:** 9 (range: 1–46)

Among patients with u/mUC receiving KEYTRUDA + EV, AEs were generally similar to those observed in patients receiving KEYTRUDA or EV as monotherapy. The incidence of rash maculo-papular was 36% all Grades (10% Grades 3-4), which is higher than observed in pembrolizumab monotherapy.[3]

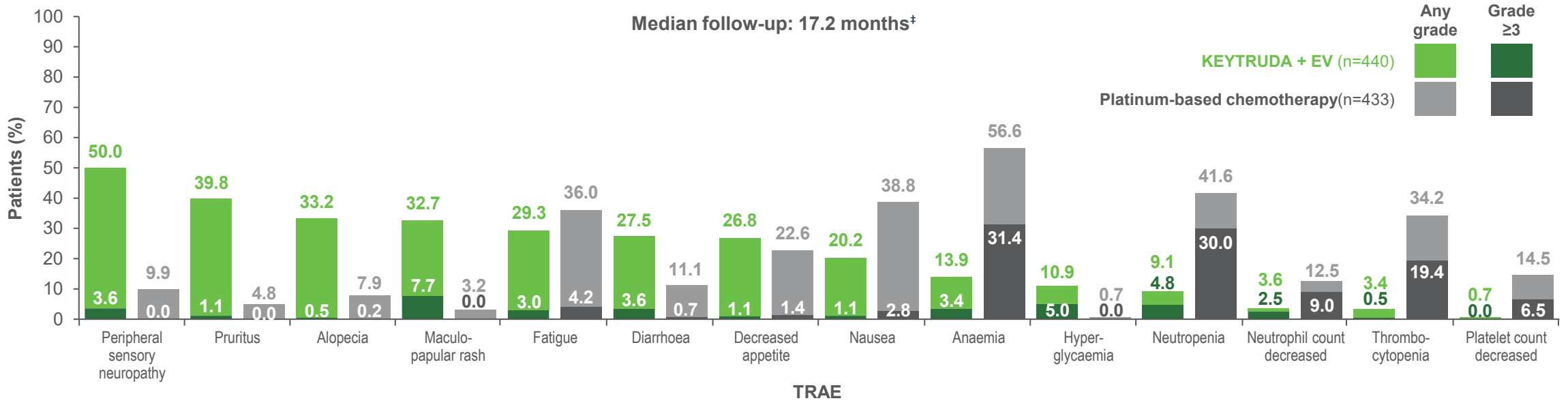
Cut-off date: August 8 2023.[2]
An AE may occur at any timepoint. Data reflect patients with urothelial cancer who received at least one dose of KEYTRUDA + EV from KEYNOTE-A39 and EV-103 (N=564). Grading based on NCI CTCAE Version 4.03.
AE, adverse event; EV enfortumab vedotin; u/mUC, unresectable or metastatic urothelial carcinoma.

1. Brower B, *et al. Front Oncol.* 2024;14:1326715. **2.** Powles T, *et al. N Engl J Med* 2024;390:875–888. **3.** KEYTRUDA Summary of Product Characteristics. MSD. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: May 2026.

KEYNOTE-A39 initial analysis: Treatment-related adverse events (TRAEs)[1,2]

The safety analysis included all patients who received any dose of trial treatment.

Any grade TRAEs occurring in ≥20% of patients and Grade ≥3 TRAEs occurring in ≥5% of patients in either treatment group*†



Adapted from Powles T, *et al.* 2024.[1]

*TRAEs are those for which there is a reasonable possibility that they were caused by the trial treatment, as assessed by the investigator. This analysis included all the patients who had received any dose of the trial treatment.[1] †Adverse events were graded according to the NCI CTCAE, version 4.03.[1] ‡**Cut-off date: 8 August 2023.**[1]

CTCAE, Common Terminology Criteria for Adverse Events; EV, enfortumab vedotin; NCI, National Cancer Institute.

1. Powles T, *et al. N Engl J Med* 2024;390:875–888. **2.** Powles T, *et al. N Engl J Med* 2024;390:875–888. Supplementary appendix.

KEYTRUDA treatment-emergent adverse events (TEAEs) of special interest[1]

	KEYTRUDA + EV (N=440) n (%)		Platinum-based chemotherapy (N=433) n (%)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Severe skin reactions	75 (17.0)	52 (11.8)	2 (0.5)	0
Hypothyroidism	47 (10.7)	2 (0.5)	3 (0.7)	0
Pneumonitis	42 (9.5)	16 (3.6)	1 (0.2)	1 (0.2)
Hyperthyroidism	20 (4.5)	1 (0.2)	2 (0.5)	0
Hepatitis	14 (3.2)	8 (1.8)	2 (0.5)	0
Colitis	12 (2.7)	7 (1.6)	0	0
Gastritis	9 (2.0)	0	3 (0.7)	0
Adrenal insufficiency	7 (1.6)	2 (0.5)	0	0
Infusion reactions	6 (1.4)	0	6 (1.4)	1 (0.2)
Pancreatitis	5 (1.1)	4 (0.9)	1 (0.2)	1 (0.2)
Myositis	4 (0.9)	1 (0.2)	2 (0.5)	2 (0.5)
Nephritis	4 (0.9)	1 (0.2)	0	0
Myocarditis	3 (0.7)	1 (0.2)	0	0
Hypophysitis	3 (0.7)	0	0	0
Thyroiditis	3 (0.7)	0	0	0
Arthritis	2 (0.5)	0	0	0
Optic neuritis	2 (0.5)	0	0	0
Cholangitis sclerosing	1 (0.2)	1 (0.2)	0	0
Encephalitis	1 (0.2)	1 (0.2)	0	0
Sarcoidosis	1 (0.2)	1 (0.2)	0	0
Type 1 diabetes mellitus	1 (0.2)	1 (0.2)	0	0
Uveitis	1 (0.2)	0	0	0

Adapted from Powles T, *et al. N Engl J Med* 2024 (plus supplementary appendix).

EV, enfortumab vedotin.

1. Powles T, *et al. N Engl J Med.* 2024;390:875–888 (plus supplementary appendix).

EV TRAEs of special interest[1]

In the KEYTRUDA + EV arm, the most common TRAEs of special interest of Grade ≥3 that have been previously associated with EV were skin reactions (15.5%), peripheral neuropathy (6.8%) and hyperglycaemia (6.1%)

	KEYTRUDA + EV (N=440) n (%)		Platinum-based chemotherapy (N=433) n (%)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Skin reactions	294 (66.8)	68 (15.5)	60 (13.9)	1 (0.2)
Peripheral neuropathy	278 (63.2)	30 (6.8)	53 (12.2)	0 (0.0)
Sensory events	260 (59.1)	19 (4.3)	51 (11.8)	0 (0.0)
Motor events	44 (10.0)	12 (2.7)	5 (1.2)	0 (0.0)
Ocular disorders	94 (21.4)	0 (0.0)	12 (2.8)	0 (0.0)
Dry eye	82 (18.6)	0 (0.0)	8 (1.8)	0 (0.0)
Hyperglycaemia	57 (13.0)	27 (6.1)	3 (0.7)	0 (0.0)
Infusion-related reactions	9 (2.0)	0 (0.0)	9 (2.1)	0 (0.0)

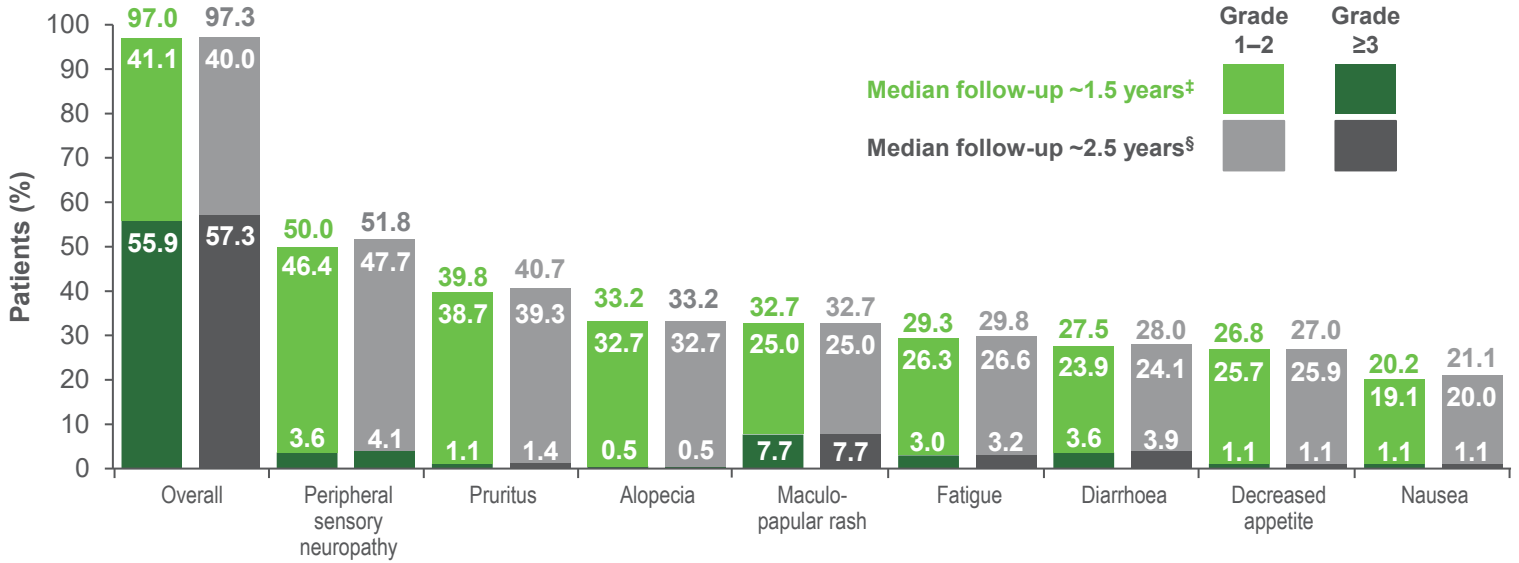
Adapted from Powles T, *et al. N Engl J Med* 2024 (plus supplementary appendix).

EV, enfortumab vedotin; TRAEs, treatment-related adverse events.

1. Powles T, *et al. N Engl J Med.* 2024;390:875–888 (plus supplementary appendix).

With an additional year of follow-up, TRAEs in KEYNOTE-A39 remained consistent with the primary analysis[1,2]

Most frequent (≥20%) TRAEs with KEYTRUDA + EV *†,[1]



- No new safety signals were observed with KEYTRUDA + EV after an additional 1-year follow-up[1]
- Frequency and grade of TRAEs remained consistent with the primary analysis[2]
- Rates of TRAEs of special interest for KEYTRUDA + EV were consistent with those in the primary KEYNOTE-A39 analysis[1,2]

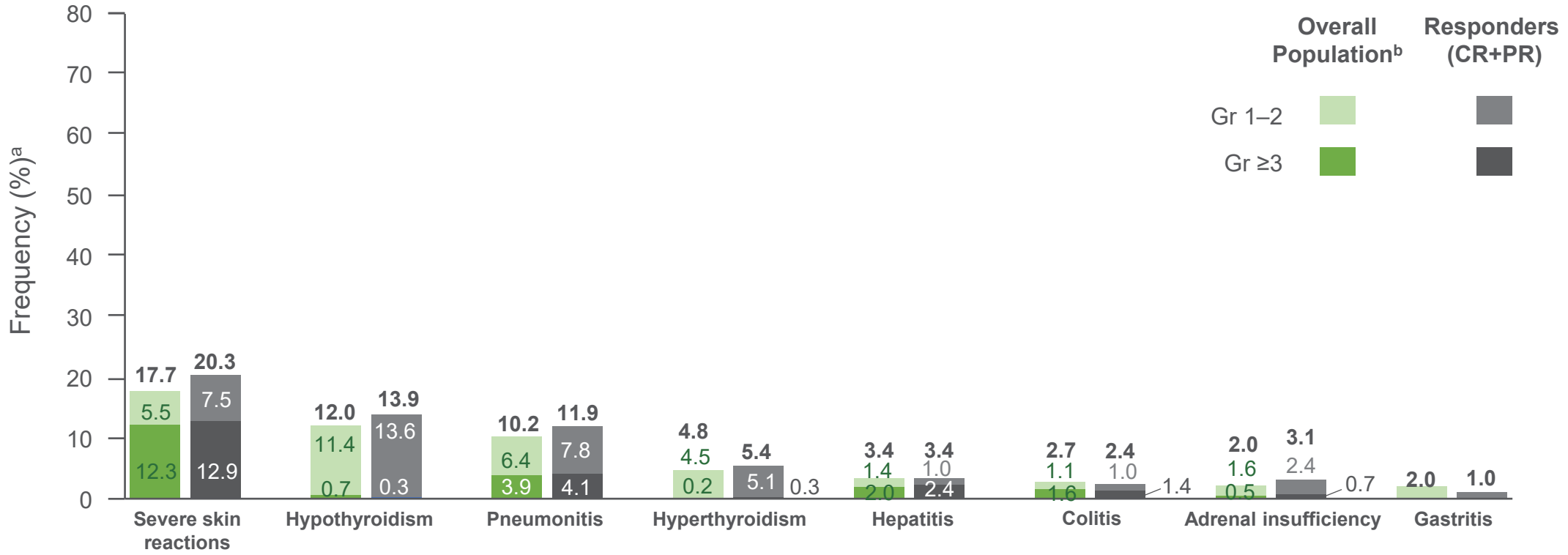
Adapted from Powles T, *et al.* 2025.[1]

*TRAEs are those for which there is a reasonable possibility that they were caused by the trial treatment, as assessed by the investigator. This analysis included all the patients who had received any dose of the trial treatment.[1,2] †Adverse events were graded according to the NCI CTCAE, version 4.03.[1,2] ‡**Cut-off date: 8 August 2023.**[2] §1 year additional follow-up from final analysis. **Cut-off date: 8 August 2024.**[1]
EV, enfortumab vedotin; TRAEs, treatment-related adverse events.

1. Powles T, *et al. Ann Oncol.* 2025;36:1212–1219. **2.** Powles T, *et al. N Engl J Med* 2024;390:875–888.

TEAEs of special interest for KEYTRUDA (follow-up analysis)[1]

KEYTRUDA's safety profile for responders (CR+PR) was generally consistent with the overall population



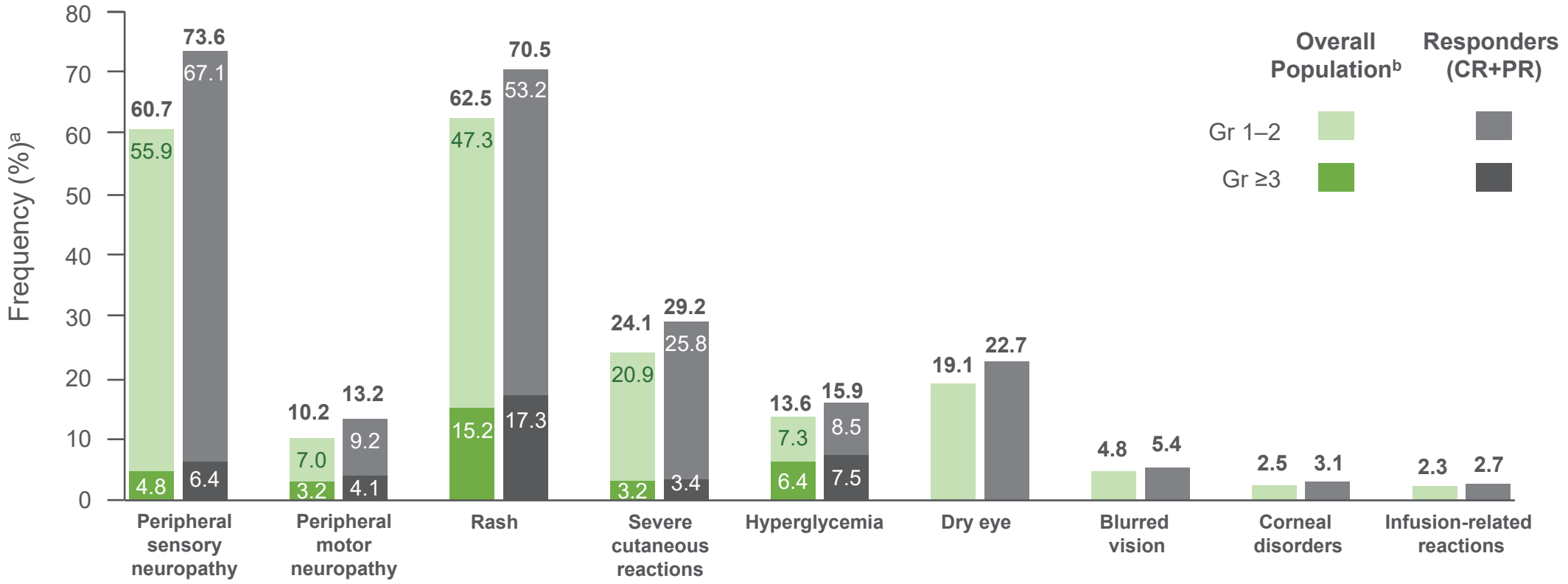
Adapted from Gupta S, *et al.* ASCO 2025.

Data cutoff: August 8, 2024. NCT04223856. Percentages have been rounded and may not equal total.
[a]AEs of special interest for P that occurred in ≥2% of patients in the EV+P arm are shown by medical concept; [b]Overall population refers to evaluable patients in the safety analysis set.
AE, adverse event; CR, complete response; EV, enfortumab vedotin; Gr, grade; P, pembrolizumab; PR, partial response; TEAEs, treatment-emergent adverse events.

1. Gupta S, et al. *Abstract* 4502. Presented at ASCO 2025, May 30-June 3, Chicago, IL

TRAEs of special interest for EV (follow-up analysis)[1]

EV's safety profile for responders (CR+PR) was generally consistent with the overall population



Adapted from Gupta S, *et al.* ASCO 2025.

Data cutoff: August 8, 2024. NCT04223856. Percentages have been rounded and may not equal total

[a]AEs of special interest for P that occurred in ≥2% of patients in the EV+P arm are shown by medical concept; [b]Overall population refers to evaluable patients in the safety analysis set.

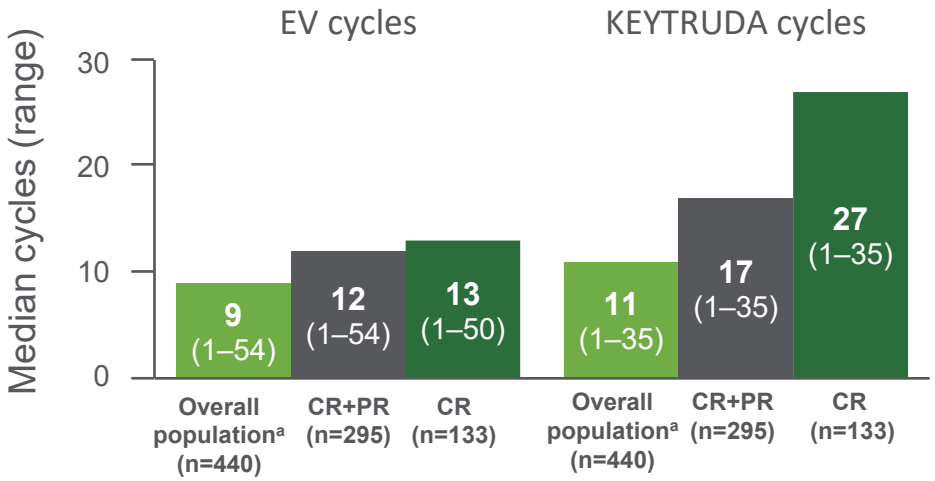
AE, adverse event; CR, complete response; EV, enfortumab vedotin; Gr, grade; P, pembrolizumab; PR, partial response; TRAEs, treatment-related adverse events.

1. Gupta S, et al. *Abstract* 4502. Presented at ASCO 2025, May 30-June 3, Chicago, IL

Safety and exposure: Overall and in responders (CR+PR; CR) (follow-up analysis)[1]

With longer treatment duration in responders (CR+PR or CR), no worsening of safety was seen with KEYTRUDA + EV
Median follow-up: 29.1 months (95% CI: 28.5–29.9)

Median cycles in KEYTRUDA + EV arm



Safety summary

Patients with TRAE, n (%)	Overall population (safety analysis set)		Responders (CR+PR)		Patients with CR	
	KEYTRUDA + EV (n=440)	Chemo-therapy (n=433)	KEYTRUDA + EV (n=295)	Chemo-therapy (n=195)	KEYTRUDA + EV (n=133)	Chemo-therapy (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 (66.2)	82 (61.7)	46 (71.9)

Adapted from Gupta S, *et al.* ASCO 2025.

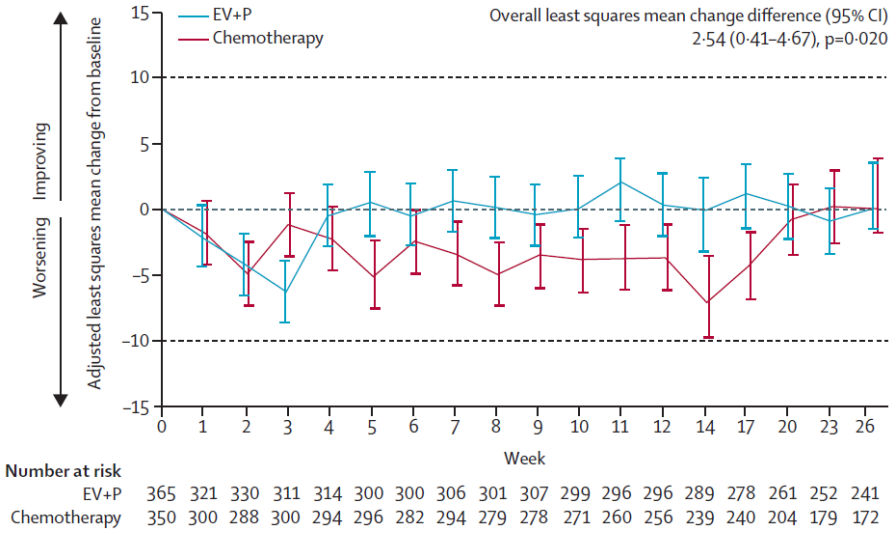
- In the overall population[a], KEYTRUDA + EV treatment was given for a median of 12 cycles (range, 1-54)
- For responders (CR+PR), KEYTRUDA + EV treatment duration was longer (median cycles, 19 [range, 1-54]), and among patients with CR, KEYTRUDA + EV was given for a median of 30 cycles (range, 1-50)

Data cutoff: August 8, 2024. NCT04223856.
[a]Overall population refers to evaluable patients in the safety analysis set.
CR, complete response; EV, enfortumab vedotin; P, pembrolizumab; PR, partial response; TRAE, treatment-related adverse event.
1. Gupta S, et al. *Abstract* 4502. Presented at ASCO 2025, May 30-June 3, Chicago, IL.

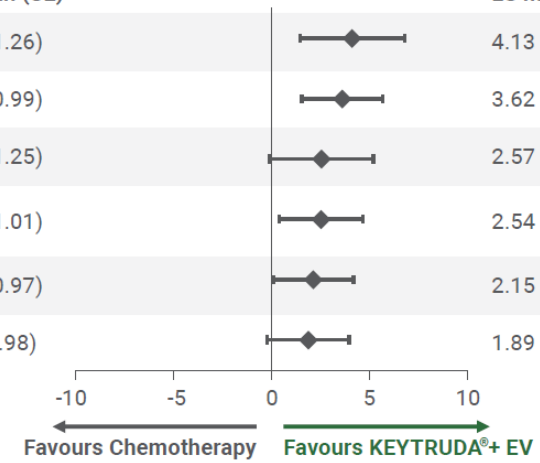
Change in EORTC QLQ-C30 functioning domains[1]

Patients in the KEYTRUDA + EV arm demonstrated a trend towards improved functioning across all domains compared with patients in the Chemotherapy arm, based on change from baseline during the first 26 weeks.

LIMITATIONS: This analysis was exploratory in nature. No formal statistical testing was performed. Therefore, no conclusions can be drawn



Functioning domain	KEYTRUDA®+ EV LS mean (SE)	Chemotherapy LS mean (SE)	KEYTRUDA®+ EV – 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
Global health status/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



Adapted from Gupta S, et al. Lancet Oncol. 2025.[1]

CI: confidence interval; EORTC QLC-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; EV: enfortumab vedotin; LS: least squares; PRO: patient-reported outcomes; QoL: quality of life; SE: standard error.

1. Gupta S, et al. *Lancet Oncol*. 2025;26:795–805.

SUMMARY: First-line KEYTRUDA + EV significantly improved OS, PFS and ORR vs platinum-based chemotherapy in patients with u/mUC[1–3]

Improved efficacy in the initial analysis was maintained with 1-year additional follow-up (~2.5 years median follow-up):

- KEYTRUDA + EV extended OS and PFS vs platinum-based chemotherapy, including across prespecified subgroups
- The chance of achieving a CR more than doubled with KEYTRUDA + EV vs platinum-based chemotherapy

Manageable safety profile

- Frequency and grade of TRAEs and AEs of special interest with KEYTRUDA + EV remained consistent with previously observed AEs
- **No new safety signals identified** during an extended follow-up analysis (median follow-up ~2.5 years)
- The safety profile of KEYTRUDA SC was consistent with the known safety profile of KEYTRUDA, with an addition of injection site reactions, which occurred in 2.4% of patients receiving KEYTRUDA SC; all were Grade 1[4]

These data support the use of KEYTRUDA + EV for the first-line treatment of patients with u/mUC[4]

The indication of KEYTRUDA in combination with enfortumab vedotin, is for the treatment of unresectable or metastatic urothelial carcinoma in adults.[4]

AE, adverse event; CR, complete response; EV, enfortumab vedotin; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; SC, subcutaneous; SOC, standard of care; TRAE, treatment-related adverse event; u/mUC, unresectable/metastatic urothelial carcinoma; UC, urothelial carcinoma.

1. Powles T, *et al. N Engl J Med* 2024;390:875–888. **2.** Powles T, *et al. N Engl J Med* 2024;390:875–888. Supplementary appendix. **3.** Powles T, *et al. Ann Oncol.* 2025;36:1212–1219. **4.** KEYTRUDA SC 395 mg and 790 mg Summary of Product Characteristics. MSD. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed: May 2026.

KEYTRUDA® (pembrolizumab)

DOSING | IV PI | SC PI 395 mg | SC PI 790 mg

Meet Victor*

Victor

69-year-old retired shop owner

Victor first noticed he had less energy when he was gardening. He reached out to his doctor when he noticed pain while urinating. After a diagnostic work-up from his GP and urologist, a diagnosis of mUC (with metastases to the liver) was made.[1]

Presentation

Upper abdominal pain, pain with urination, unintentional weight loss[1]

Diagnosis

- Stage IVB (T3, N1, M1b) mUC[1,2]
- ECOG PS: 1[1]
- CrCl: 70 mL/min[3]
- **Treatment eligibility: platinum-eligible**

Comorbidities

Hypertension, hypercholesterolemia, controlled type 2 diabetes (HbA1c: 6.7%)

Victor may benefit from KEYTRUDA + EV

How would you manage this patient with metastatic UC?

***Patient cases are fictitious, based on clinical examples. Images are illustrative of the range of patients diagnosed with UC.**

CrCl, creatinine clearance; ECOG PS, Eastern Cooperative Oncology Group performance status; EV, enfortumab vedotin; GP, general practitioner; HbA1c, glycated haemoglobin; N1, single regional lymph node metastasis in the true pelvis (perivesical, obturator, internal and external iliac, or sacral lymph node);[3] M1b, non–lymph node distant metastases;[3] mUC, metastatic urothelial carcinoma; T3, tumour invades perivesical tissue;[3] UC, urothelial carcinoma.

1. Witjes JA, *et al. Eur Urol* 2024;85:17–31. **2.** Leslie SW, Soon-Sutton TL, *et al.* Bladder cancer. NCBI Bookshelf. Last updated 15 August 2024. Available at: https://www.ncbi.nlm.nih.gov/books/NBK536923/. Accessed: May 2026. **3** Powles T, *et al. N Engl J Med* 2024;390:875–888

KEYTRUDA®
(pembrolizumab)

DOSING | IV PI | SC PI 395 mg | SC PI 790 mg

Meet Kate*

Kate

71-year-old retired teacher

Kate noticed she was slowing down and getting tired more frequently. She contacted her doctor after she noticed blood in her urine – her mUC diagnosis followed less than a month later.[1]

Presentation

Unintentional weight loss, painless visible haematuria, pelvic pain[1]

Diagnosis

- Stage IVA (T3, N1, M1a) mUC, in lymph nodes only[1,2]
- ECOG PS: 2[1]
- CrCl: 61 mL/min[3]
- **Treatment eligibility: platinum-eligible**

Comorbidities

Depression, controlled hypertension

Kate may benefit from KEYTRUDA + EV

How would you manage this patient with metastatic UC?

***Patient cases are fictitious, based on clinical examples. Images are illustrative of the range of patients diagnosed with UC.**
CrCl, creatinine clearance; ECOG PS, Eastern Cooperative Oncology Group performance status; EV, enfortumab vedotin; N1, single regional lymph node metastasis in the true pelvis (perivesical, obturator, internal and external iliac, or sacral lymph node);[3] M1a, distant metastasis limited to lymph nodes beyond the common iliacs;[3] mUC, metastatic urothelial carcinoma; T3, tumour invades perivesical tissue;[3] UC, urothelial carcinoma.

1. Witjes JA, *et al. Eur Urol* 2024;85:17–31. **2.** Leslie SW, Soon-Sutton TL, *et al.* Bladder cancer. NCBI Bookshelf. Last updated 15 August 2024. Available at: https://www.ncbi.nlm.nih.gov/books/NBK536923/. Accessed: May 2026. **3.** Powles T, *et al. N Engl J Med* 2024;390:875–888

KEYTRUDA SC and KEYTRUDA offer flexibility in dosing and treatment administration[1–3]

KEYTRUDA SC®

Administered subcutaneously[1,2]

In thigh or abdomen[1,2]

Over 1 minute for 395 mg /2.4 mL **Q3W**[1]

OR

Over 2 minutes for 790 mg /4.8 mL **Q6W**[2]

The approved indications for KEYTRUDA SC have been established based on the MK-3475A-D77 study, which demonstrated non-inferior pharmacokinetics, and provides a descriptive analysis for the efficacy and safety profile of KEYTRUDA SC compared to KEYTRUDA.[1,2]

KEYTRUDA®

Administered as an IV infusion[3]

Over 30 minutes[3]

200 mg Q3W or 400 mg Q6W[3]

The 200 mg Q3W regimen has been assessed in phase 2 and 3 registration studies across a multitude of indications of KEYTRUDA. An exposure response evaluation, using modelling and simulation, led to the approval of the 400 mg Q6W dosing for monotherapy and combination therapy.[3]

Patients have the option to switch from KEYTRUDA to KEYTRUDA SC, or from KEYTRUDA SC to KEYTRUDA, at their next scheduled dose[1–3]

KEYTRUDA should be administered after enfortumab vedotin when given on the same day.

Please refer to the individual product SmPCs for full information about dosing, preparation and administration.

cHL, Classical Hodgkin lymphoma; IV, intravenous; Q3W, every 3 weeks; Q6W, every 6 weeks; SmPC, Summary of Product Characteristics.

1. KEYTRUDA (pembrolizumab) 395 mg Solution for Injection Summary of Product Characteristics; 2. KEYTRUDA (pembrolizumab) 790 mg Solution for Injection Summary of Product Characteristics; 3. KEYTRUDA (pembrolizumab) 25 mg/mL Concentrate for Solution for Infusion Summary of Product Characteristics.