Cis/Gem/Nivo is my first option in cis-eligible patients in 1st line mUC

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DISCLOSURES

- **Research funding:** Pfizer, BMS
- **Advisory boards:** Pfizer, Novartis, Ipsen, BMS, Janssen, Astellas, Sanofi, Bayer, Clovis, Roche, MSD, Pierre Fabre, Merck
- **Clinical trial payments:** Pfizer, Bayer, Janssen, MSD, Clovis, Pharmacyclics, BMS, Sanofi, Astra Zeneca, Roche, Eisai, Aveo
- **Travel arrangements:** Janssen, Roche, Pfizer, BMS, Ipsen, Bayer

ALGORITHM 2025

METASTATIC UROTHELIAL CARCINOMA

QT (PLATINUM)

CR
PR
SD

AVELUMAB

PD

ATEZO
PEMBRO

PD

ENFORTUMAB
VEDOTIN

ERDAFITINIB (FGFRmut)

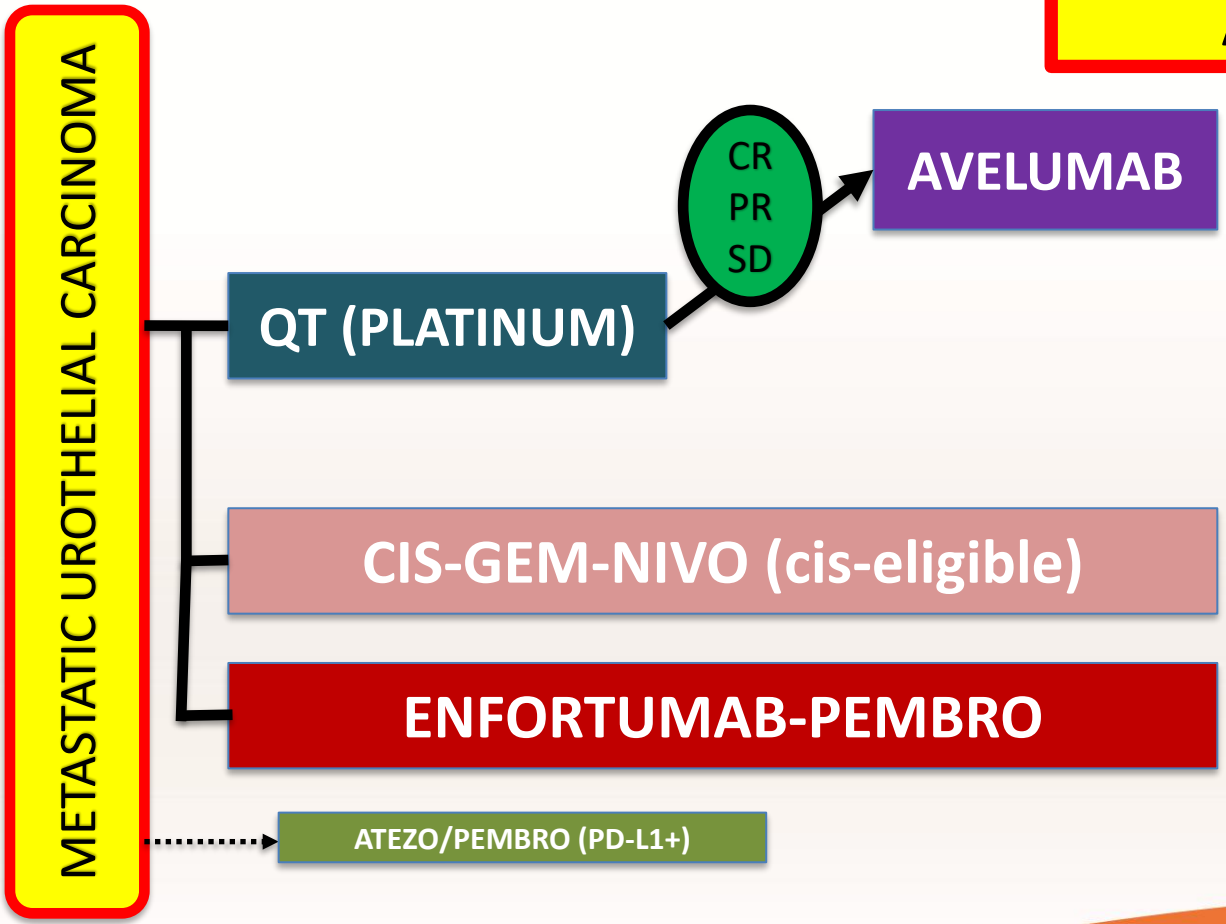
CIS-GEM-NIVO (cis-eligible)

ENFORTUMAB-PEMBRO

PD

ATEZO/PEMBRO (PD-L1+)

ALGORITHM 2025



Key inclusion criteria

- Age ≥ 18 years
- Previously untreated unresectable or mUC involving the renal pelvis, ureter, bladder, or urethra
- Cisplatin eligible
- ECOG PS of 0-1

Stratification factors:
- Tumor PD-L1 expression (≥ 1% vs < 1%)
- Liver metastases (yes vs no)

R

N = 304: **Combination phase** — NIVO 360 mg on D1 + Gemcitabine 1000 mg/m² on D1/D8 + Cisplatin 70 mg/m² on D1 Q3W (up to 6 cycles)[b] → 3 weeks → **Monotherapy phase** — NIVO 480 mg Q4W (until progression, unacceptable toxicity, withdrawal, or up to 24 months[c])

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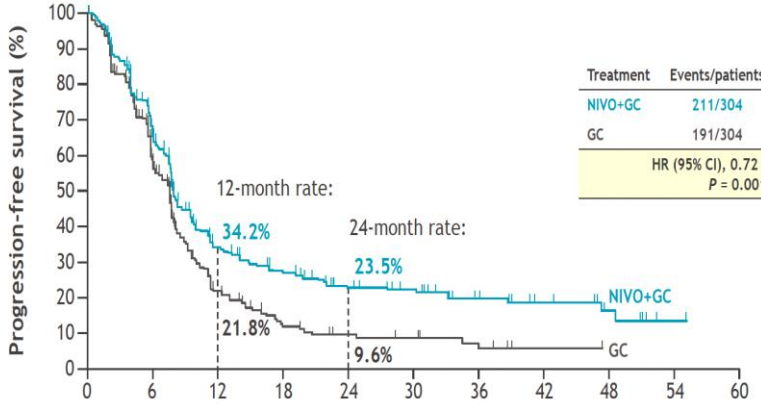
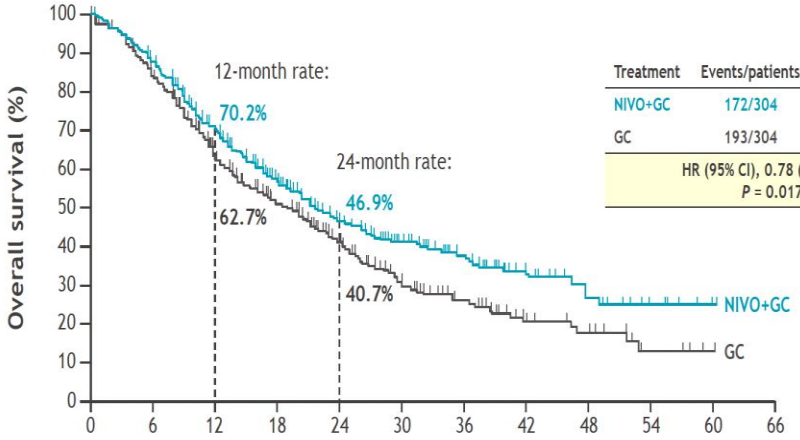
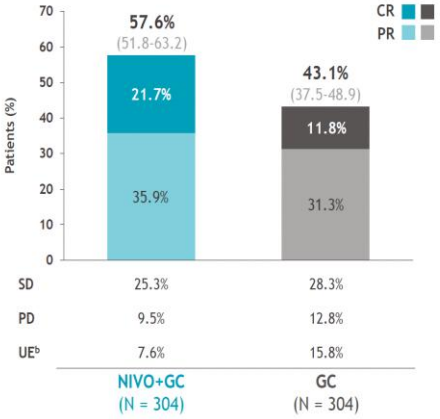


Treatment	Events/patients	Median PFS (95% CI), months
NIVO+GC	211/304	7.9 (7.6-9.5)
GC	191/304	7.6 (6.1-7.8)
HR (95% CI), 0.72 (0.59-0.88) *P* = 0.0012		



Treatment	Events/patients	Median OS (95% CI) months
NIVO+GC	172/304	21.7 (18.6-26.4)
GC	193/304	18.9 (14.7-22.4)
HR (95% CI), 0.78 (0.63-0.96) *P* = 0.0171		

ORR (95% CI) and BOR per BICR[a]

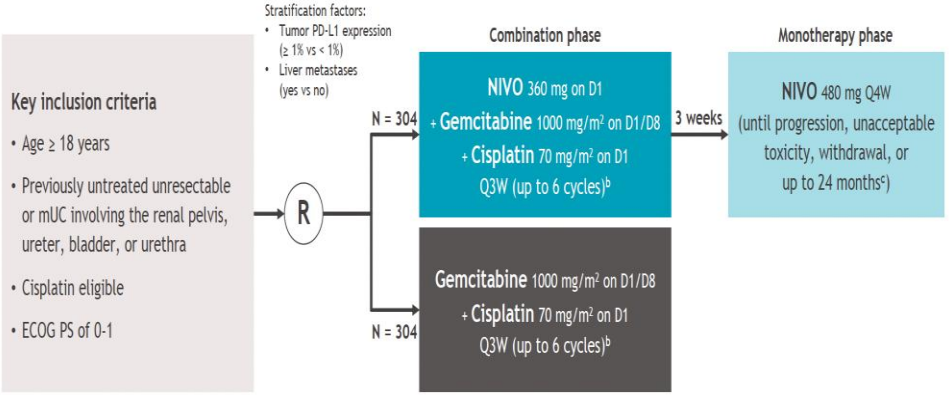


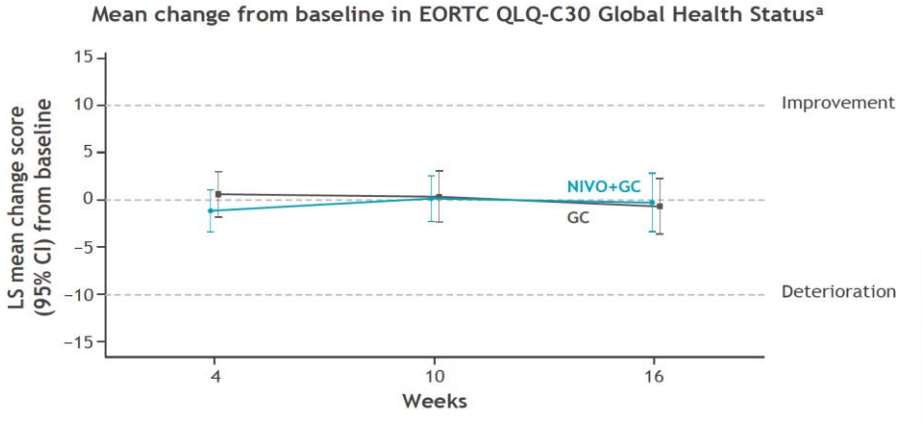
Time to and duration of responses

Any objective response[c]	NIVO+GC (n = 175)	GC (n = 131)
Median TTR (Q1-Q3), months	2.1 (2.0-2.3)	2.1 (2.0-2.2)
Median DoR (95% CI), months	9.5 (7.6-15.1)	7.3 (5.7-8.9)

Complete response[d]	NIVO+GC (n = 66)	GC (n = 36)
Median TTCR (Q1-Q3), months	2.1 (1.9-2.2)	2.1 (1.9-2.2)
Median DoCR (95% CI), months	37.1 (18.1-NE)	13.2 (7.3-18.4)

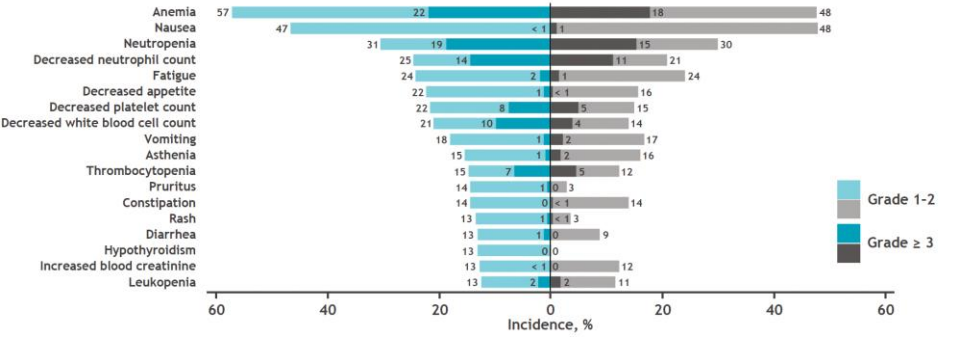
Van der Heijden MS et al. N Engl J Med 2023





Treatment-related AEs in all treated patients

Treatment-related AE, %a	NIVO+GC (n = 304) Any grade	NIVO+GC (n = 304) Grade ≥ 3b	GC (n = 288) Any grade	GC (n = 288) Grade ≥ 3b
Any	97	62	93	52
Leading to discontinuation	21	11	17	8



Van der Heijden MS et al. N Engl J Med 2023

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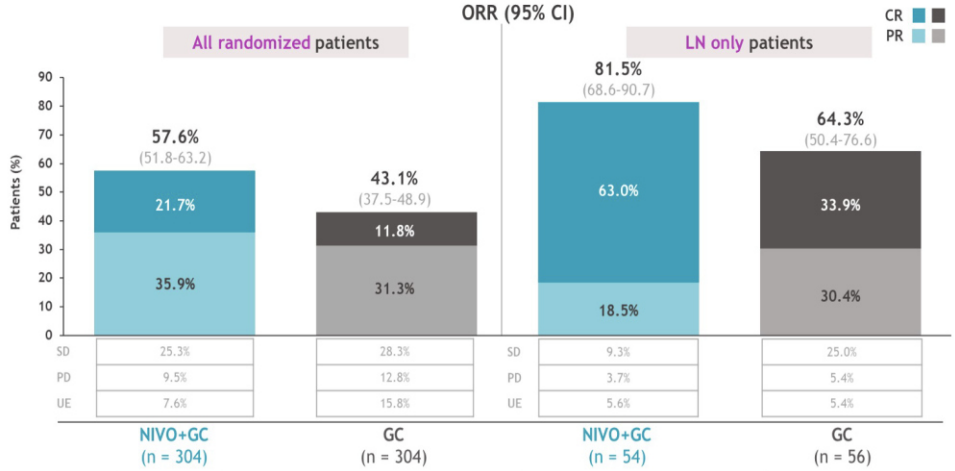
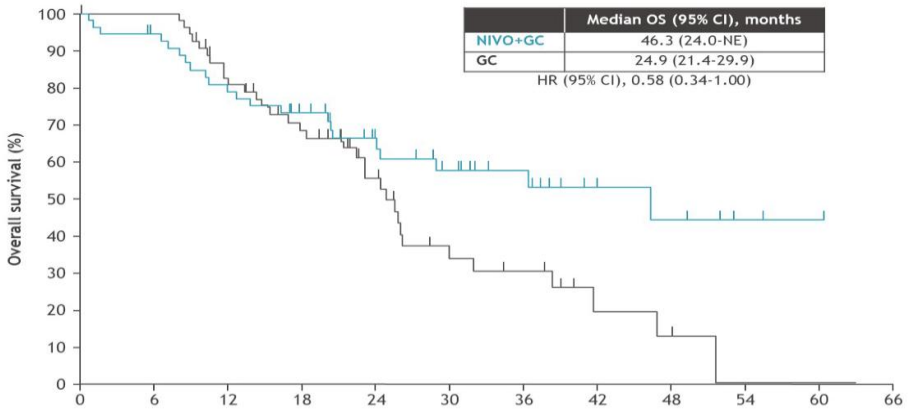
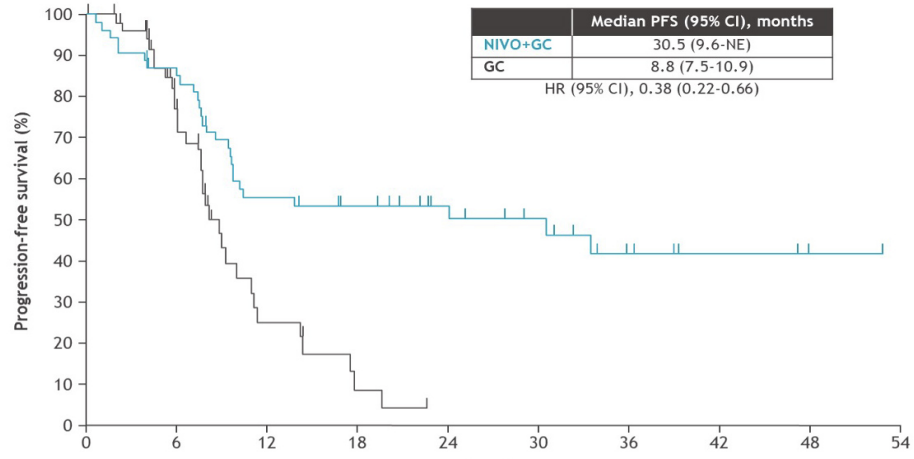






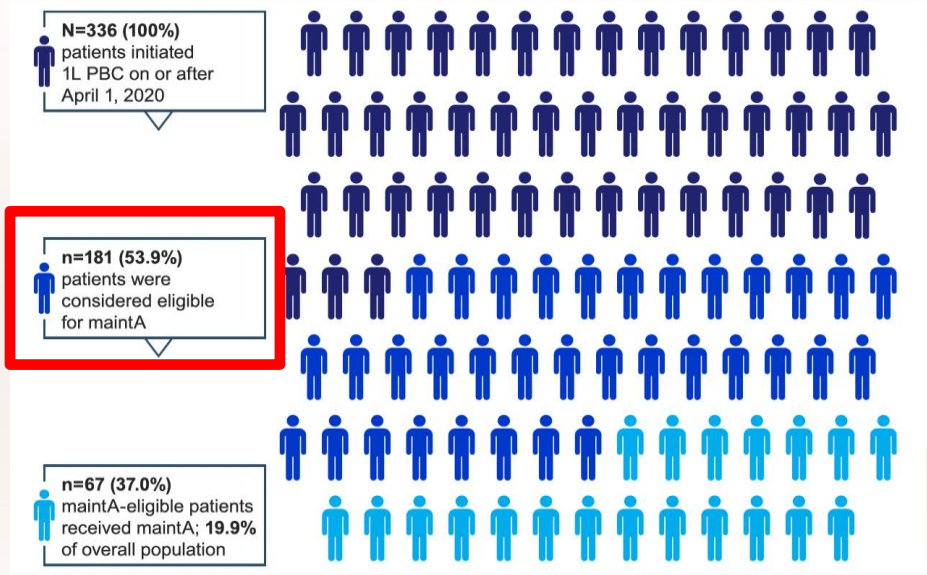
Galsky MD et al. ASCO 2024

ALGORITHM 2025

METASTATIC UROTHELIAL CARCINOMA

- QT (PLATINUM)
  - CR / PR / SD → AVELUMAB
    - What if I don't get a response to 1st-line chemo?
- CIS-GEM-NIVO (cis-eligible)
- ENFORTUMAB-PEMBRO
- ATEZO/PEMBRO (PD-L1+)

Real-World Treatment Patterns and Clinical Outcomes in Patients With Locally Advanced or Metastatic Urothelial Carcinoma by Eligibility for Maintenance Avelumab



Conclusion

Many patients are not eligible for maintenance avelumab following 1L treatment with PBC, and patient eligibility for maintenance avelumab cannot be assessed at initiation of 1L PBC. Patients who are ineligible for maintenance avelumab have a shorter OS than patients who are eligible for maintenance avelumab and, thus, real-world OS remains short for the overall 1L PBC–treated population. Consequently, the introduction of maintenance avelumab

Morgans AK et al. Clin Genitourin Cancer 2025

ALGORITHM 2025

METASTATIC UROTHELIAL CARCINOMA

QT (PLATINUM)

CR
PR
SD

AVELUMAB

What if I don't get a response to 1st-line chemo?

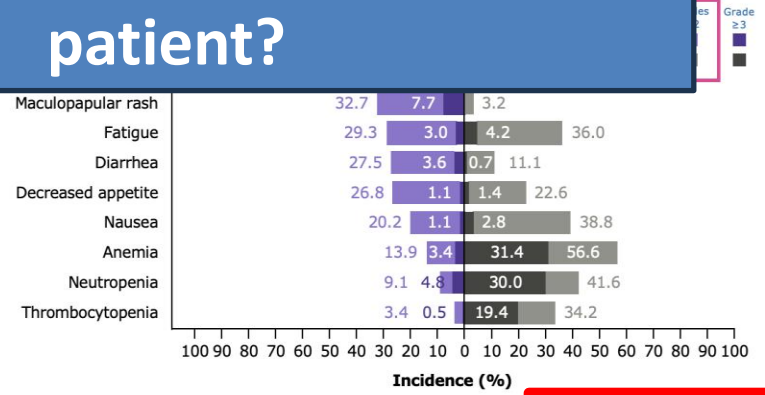
CIS-GEM-NIVO (cis-eligible)

What if I cause a serious toxicity and discontinue?

ENFORTUMAB-PEMBRO

ATEZO/PEMBRO (PD-L1+)

Do you need this highly-active, highly-toxic treatment for every patient?



Patients with any grade AE
- EV+pembro: 427 (97%)
- CT: 414 (95.6%)

TRAEs leading to discontinuation
- EV+pembro: 154 (35%)
- CT: 80 (18.5%)

TRAEs leading to interruption
- EV+pembro: 299 (68%)
- CT: 229 (52.9%)

TRAEs leading to dose reduction
- EV+pembro: 179 (40.7%)
- CT: 164 (37.9%)

TRAEs leading to death
- EV+pembro:* 4
- CT:† 4

TRAEs of special interest for EV, n (%)	EV+pembro (n=440)		CT (n=433)	
	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**
Ocular disorders	94 (21.4)	0	12 (2.8)	0
Hyperglycemia	57 (13.0)	27 (6.1)	3 (0.7)	0
Infusion-related reactions	9 (2.0)	0	9 (2.1)	0

EV-Ineligible criTeriA (EVITA) to identify patients who may not be optimal candidates for EV/P if they meet at least two of the criteria:

- Hemoglobin A1c ≥8% (if this parameter is not available it could be replaced by baseline glucose >150 mg/dl in 2 consecutive blood samples 1 wk apart).
- Grade ≥2 sensory or motor neuropathy.
- Any corneal or retinal abnormality.
- Creatinine clearance or glomerular filtration rate ≤45 ml/min.
- ECOG performance status score ≥2.

Powles T et al. NEJM 2024; Grande E et al. Eur Urol 2024

ALGORITHM 2025

METASTATIC UROTHELIAL CARCINOMA

QT (PLATINUM)

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AVELUMAB

What if I don't get a response to 1st-line chemo?

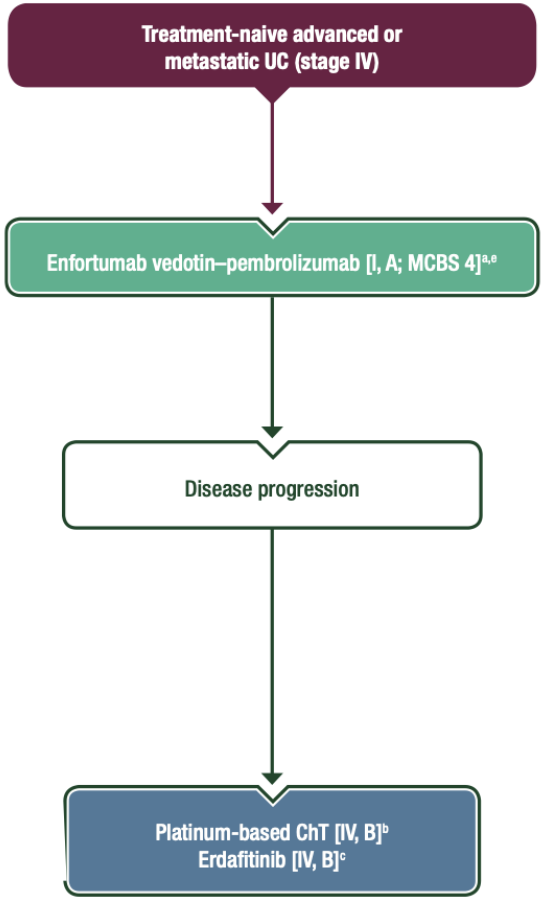
CIS-GEM-NIVO (cis-eligible)

What if I cause a serious toxicity and discontinue?

ENFORTUMAB-PEMBRO

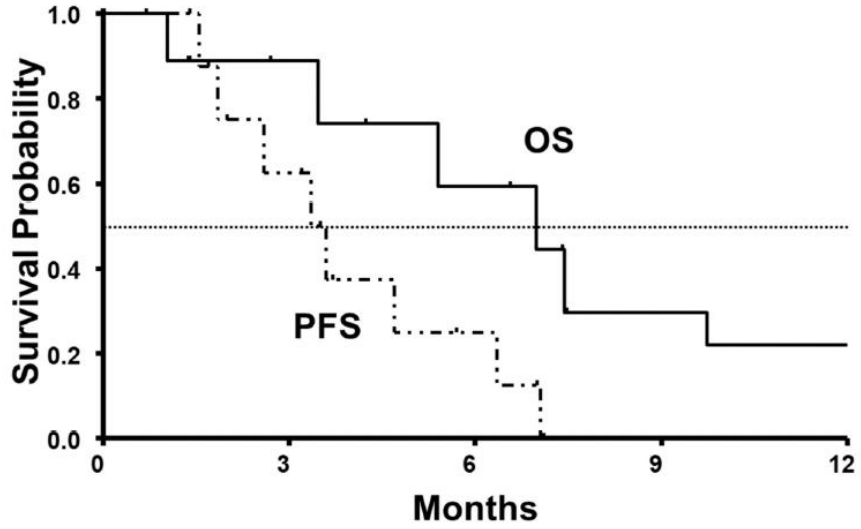
What will I use after progression?

ATEZO/PEMBRO (PD-L1+)



Second-Line Platinum-Based Chemotherapy (PBT) in Patients with Metastatic Urothelial Carcinoma (mUC) Treated withFirst-Line Pembrolizumab plus Enfortumab Vedotin (P/EV): A Single-Center, Retrospective Study

- **Progression-free survival (PFS): median 3.5 months (95% CI, 2.8 to 4.2)**
- **Overall survival (OS): median 7.4 months (95% CI, 5.3 to 9.5)**



Kim J et al. ASCO-GU 2025

CISPLATIN – GEMCITABINE - NIVOLUMAB

Increase of OS, PFS and RR

No increase in toxicity, no new toxicities

Make sure patients receive immunotherapy, chance of further treatment with EV

Patient selection (only cis-eligible)

Cis/Gem/Nivo is my first option in cis-eligible patients in 1st line mUC

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