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Treatment Updates in Metastatic Urothelial Cancer

Debates and Didactics in Hematology and Oncology

July 26, 2024
Sea Island, GA

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Disclosures

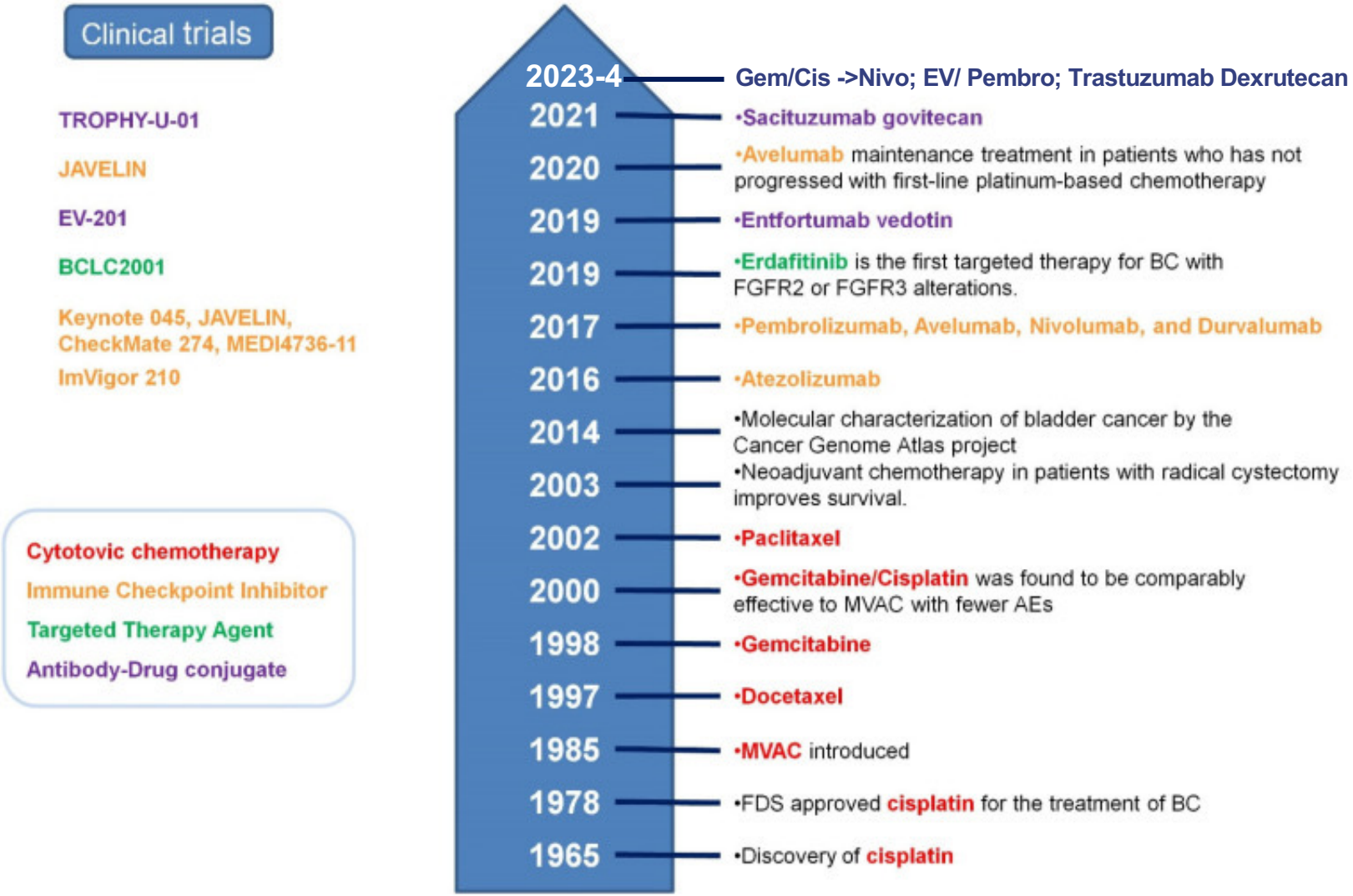
- Consultant:
  - Eisai
  - Bristol Myers-Squibb
  - Gilead

- Research funding to Institution:
  - Bristol Myers-Squibb
  - Immunomedics
  - AstraZeneca
  - Alkermes

Objectives

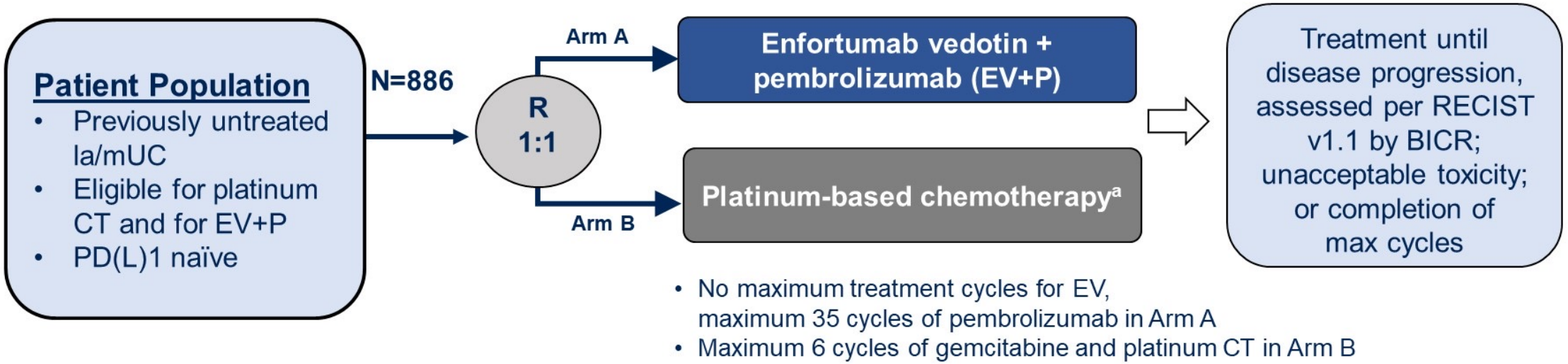
- Review of Treatment Landscape 2024
- Examine Novel 1st Line Treatment Data
- Recap Current Recommendations for Metastatic Setting
- Examine Sequencing of Agents in Select Patients

The Path From Cisplatin in Bladder Cancer



Adapted from: Bilim, V. et al. J Pers Med. 2022 Oct 20;12(10):1745

EV-302 Enfortumab Vedotin and Pembrolizumab in Metastatic Urothelial Carcinoma



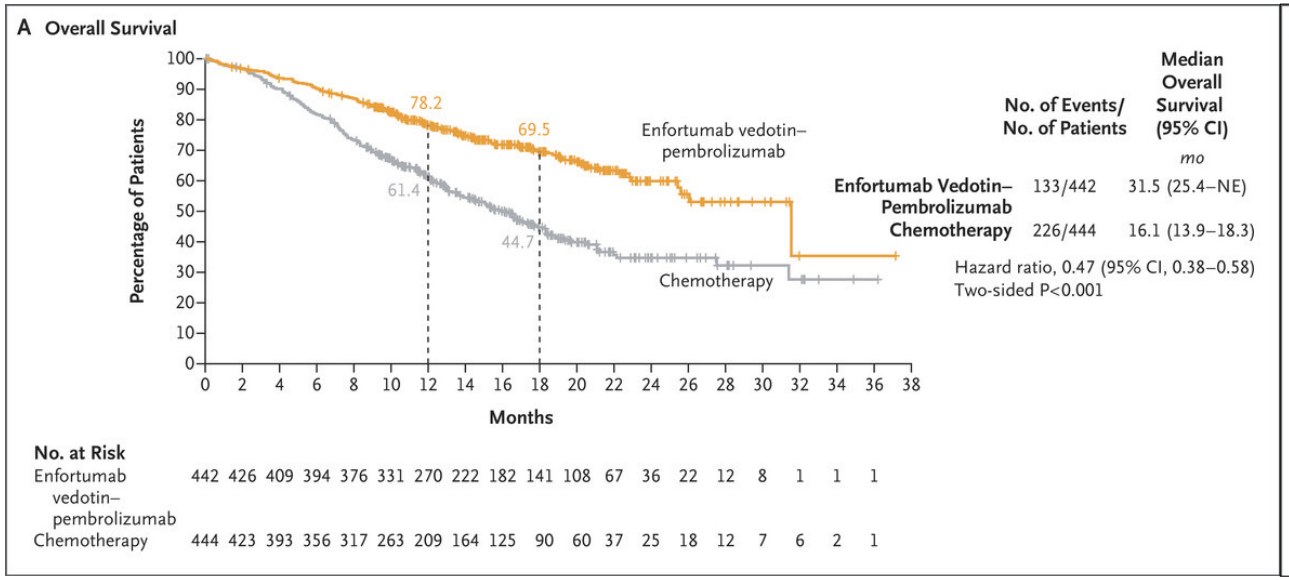
- No maximum treatment cycles for EV, maximum 35 cycles of pembrolizumab in Arm A
- Maximum 6 cycles of gemcitabine and platinum CT in Arm B

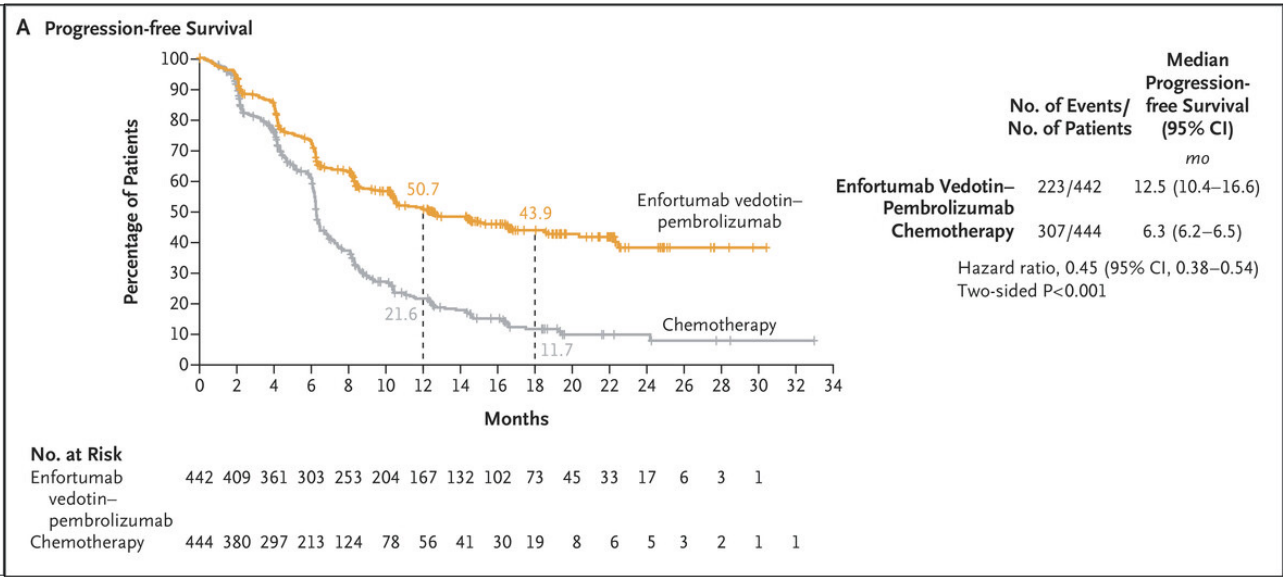
Efficacy and Safety Endpoints:
- Dual primary endpoints (PFS by BICR and OS)
- Pre-specified secondary endpoints: ORR by BICR, PFS and ORR per investigator, DOR, DCR, Safety

PRO Endpoints:
- Key secondary endpoints: Time to pain progression (TTPP), change from baseline in BPI-SF worst pain at week 26
- Other pre-specified PRO secondary endpoints were descriptive with no adjustment for multiplicity

Gupta, S. ASCO 2024

EV-302 Enfortumab Vedotin and Pembrolizumab in Metastatic Urothelial Carcinoma





Powles T, et al. Enfortumab Vedotin and Pembrolizumab in Untreated Advanced Urothelial Cancer. N Engl J Med. 2024 Mar 7;390(10)

EV-302 Enfortumab Vedotin and Pembrolizumab in Metastatic Urothelial Carcinoma

Variable	Enfortumab Vedotin–Pembrolizumab (N=437)	Chemotherapy (N=441)
Confirmed best overall response — no. (%)		
Complete response	127 (29.1)	55 (12.5)
Partial response	169 (38.7)	141 (32.0)
Stable disease	82 (18.8)	149 (33.8)
Progressive disease	38 (8.7)	60 (13.6)
Could not be evaluated†	0	4 (0.9)
No assessment‡	21 (4.8)	32 (7.3)
Confirmed overall response (95% CI) — %§	67.7 (63.1–72.1)	44.4 (39.7–49.2)
Median time to response (range) — mo	2.1 (1.3–12.3)	2.1 (1.6–8.3)
Median duration of response (95% CI) — mo	Not reached (20.2–NE)	7.0 (6.2–10.2)

Powles T, et al. Enfortumab Vedotin and Pembrolizumab in Untreated Advanced Urothelial Cancer. N Engl J Med. 2024 Mar 7;390(10):875-888.

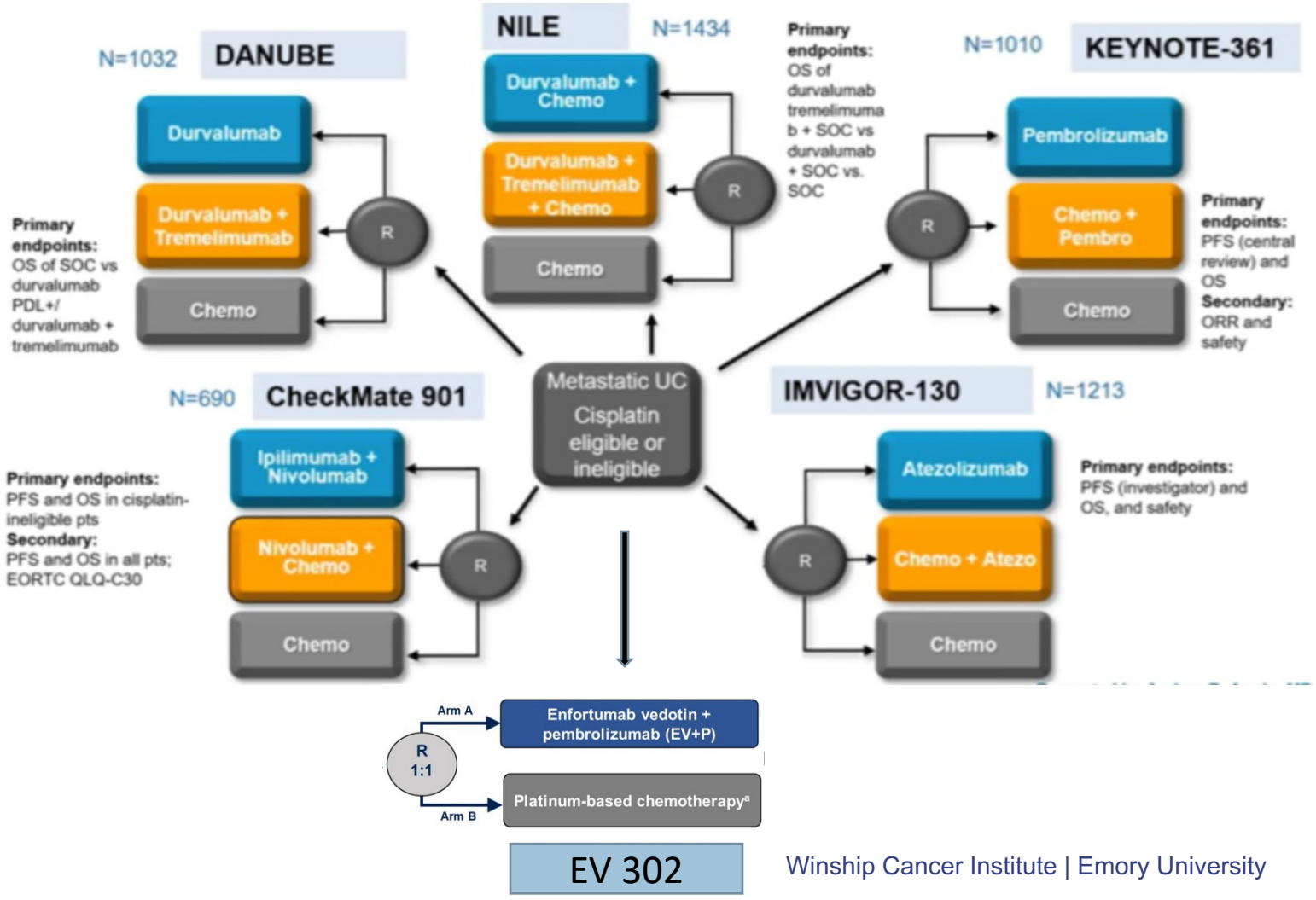
EV-302 Enfortumab Vedotin and Pembrolizumab in Metastatic Urothelial Carcinoma: Adverse Events

Adverse Event	Enfortumab Vedotin–Pembrolizumab (N=440)		Chemotherapy (N=433)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
	Number of patients (percent)			
Any adverse event	427 (97.0)	246 (55.9)	414 (95.6)	301 (69.5)
Peripheral sensory neuropathy	220 (50.0)	16 (3.6)	43 (9.9)	0
Pruritus	175 (39.8)	5 (1.1)	21 (4.8)	0
Alopecia	146 (33.2)	2 (0.5)	34 (7.9)	1 (0.2)
Maculopapular rash	144 (32.7)	34 (7.7)	14 (3.2)	0
Fatigue	129 (29.3)	13 (3.0)	156 (36.0)	18 (4.2)
Diarrhea	121 (27.5)	16 (3.6)	48 (11.1)	3 (0.7)
Decreased appetite	118 (26.8)	5 (1.1)	98 (22.6)	6 (1.4)
Nausea	89 (20.2)	5 (1.1)	168 (38.8)	12 (2.8)
Anemia	61 (13.9)	15 (3.4)	245 (56.6)	136 (31.4)
Hyperglycemia	48 (10.9)	22 (5.0)	3 (0.7)	0
Neutropenia	40 (9.1)	21 (4.8)	180 (41.6)	130 (30.0)
Neutrophil count decreased	16 (3.6)	11 (2.5)	54 (12.5)	39 (9.0)
Thrombocytopenia	15 (3.4)	2 (0.5)	148 (34.2)	84 (19.4)
Platelet count decreased	3 (0.7)	0	63 (14.5)	28 (6.5)

Powles T, et al. Enfortumab Vedotin and Pembrolizumab in Untreated Advanced Urothelial Cancer. N Engl J Med. 2024 Mar 7;390(10)

Best Practice in Metastatic UC Patients?

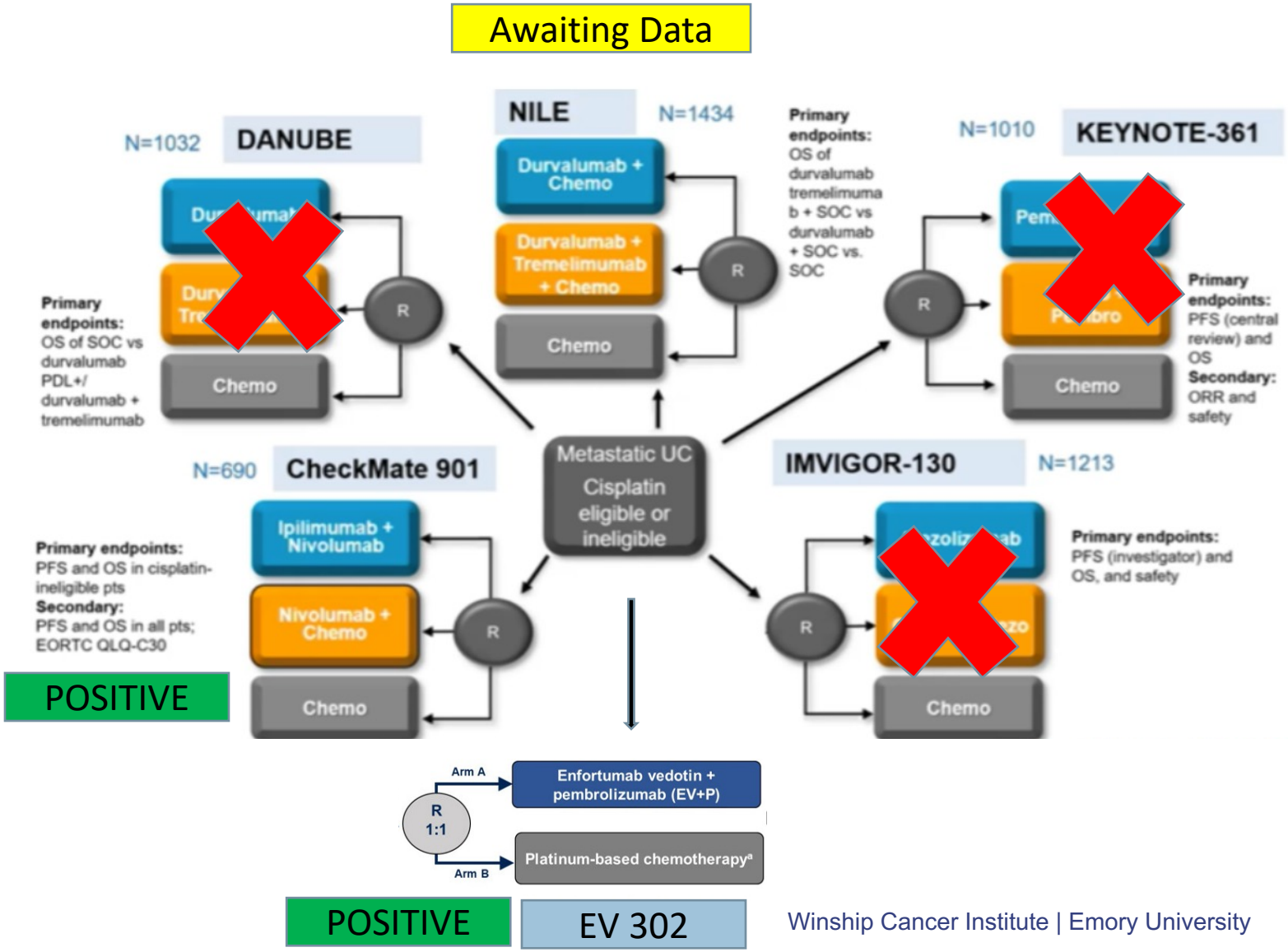
- Chemo + IO Upfront? IO Combos?
- Chemo → IO Maintenance?



Adapted from Apolo, A. ESMO 2023

Best Practice in Metastatic UC Patients?

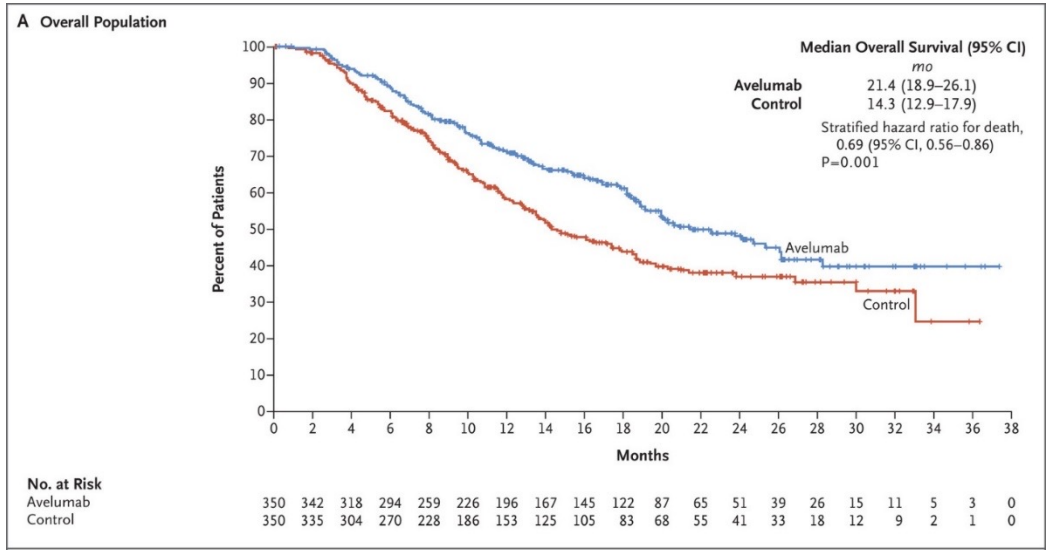
- Chemo + IO Upfront? IO Combos?
- Chemo → IO Maintenance?

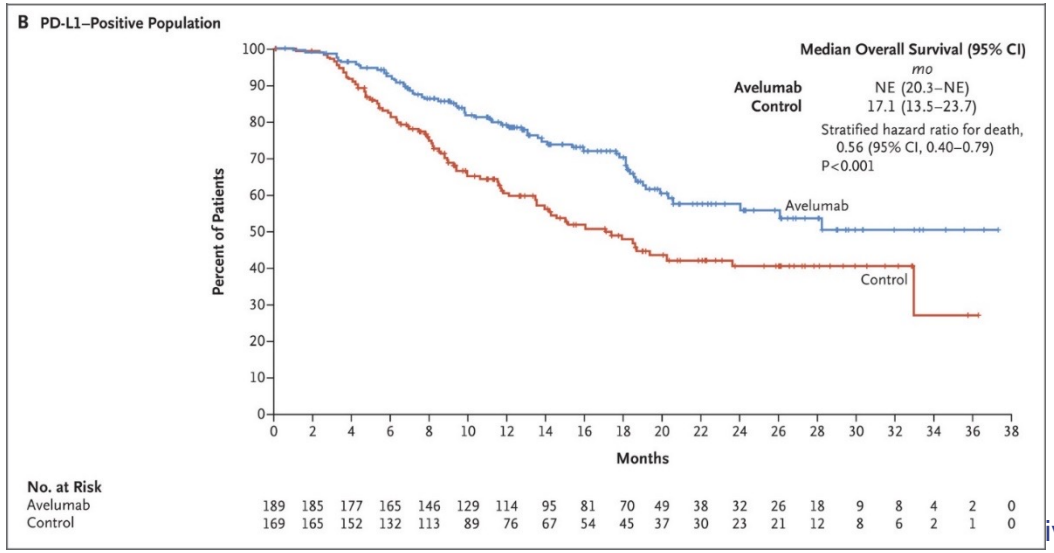


Adapted from Apolo, A. ESMO 2023

Best Practice in Metastatic UC Patients?

- Chemo + IO Upfront?
- Chemo (+/- IO)→ IO Maintenance?
  - ***Javelin Bladder 100***
  - ***CheckMate-901****

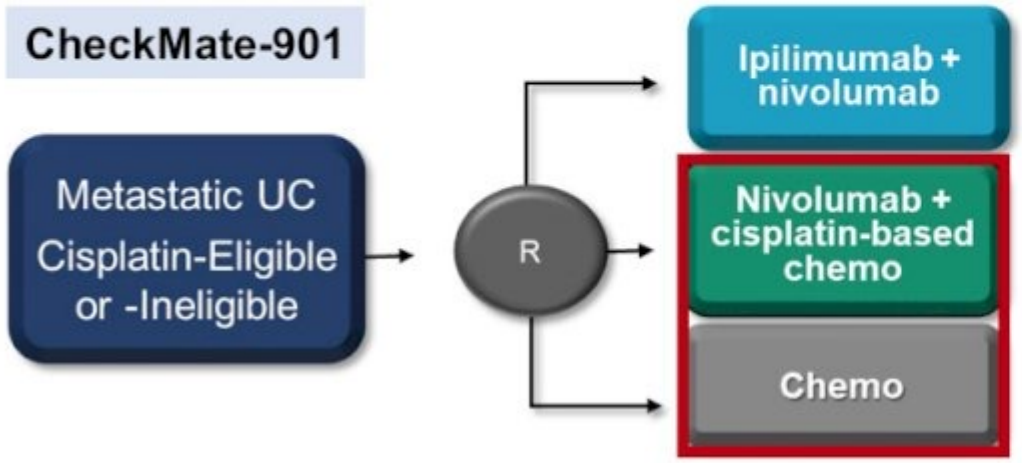


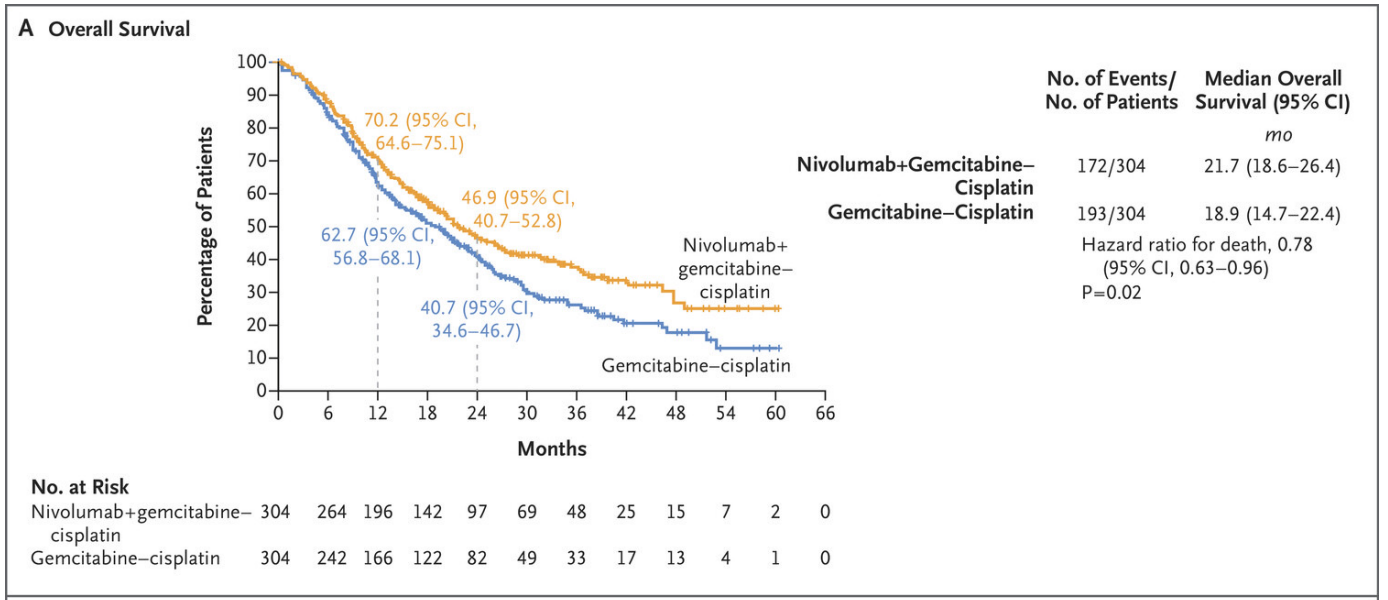


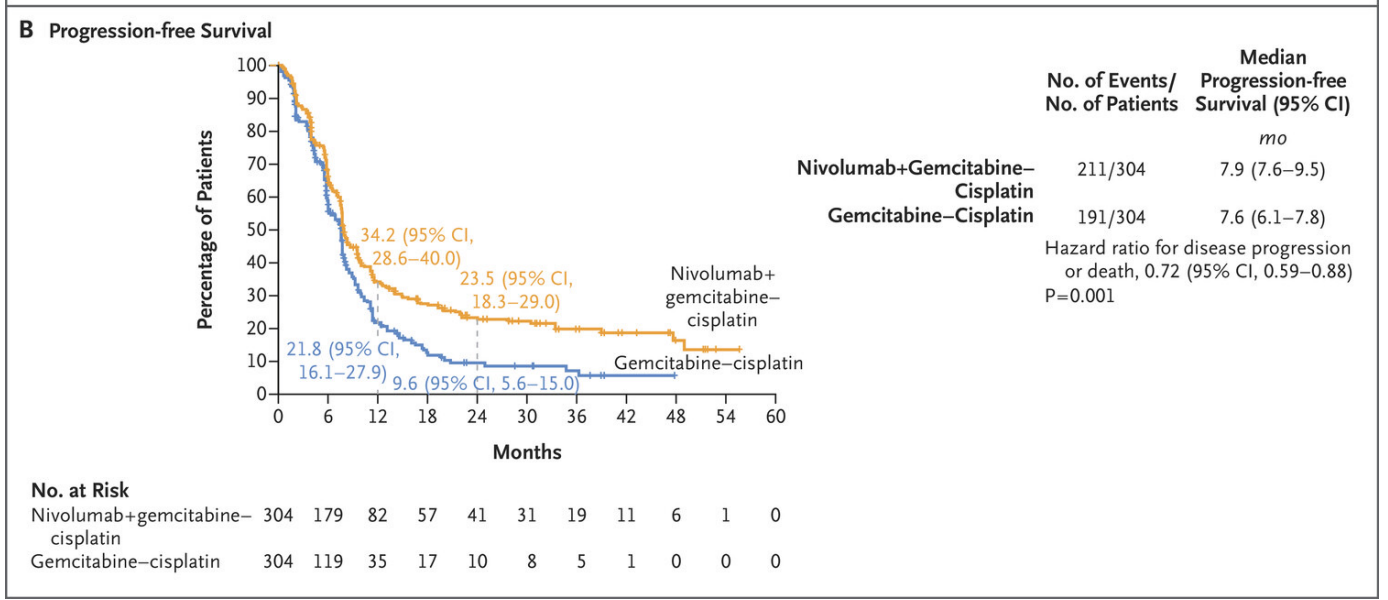
PD-L1 +

Powles, T, et al. N Engl J Med 2020; 383:1218-1230

CheckMate- 901: Nivolumab + Cisplatin Based Chemo







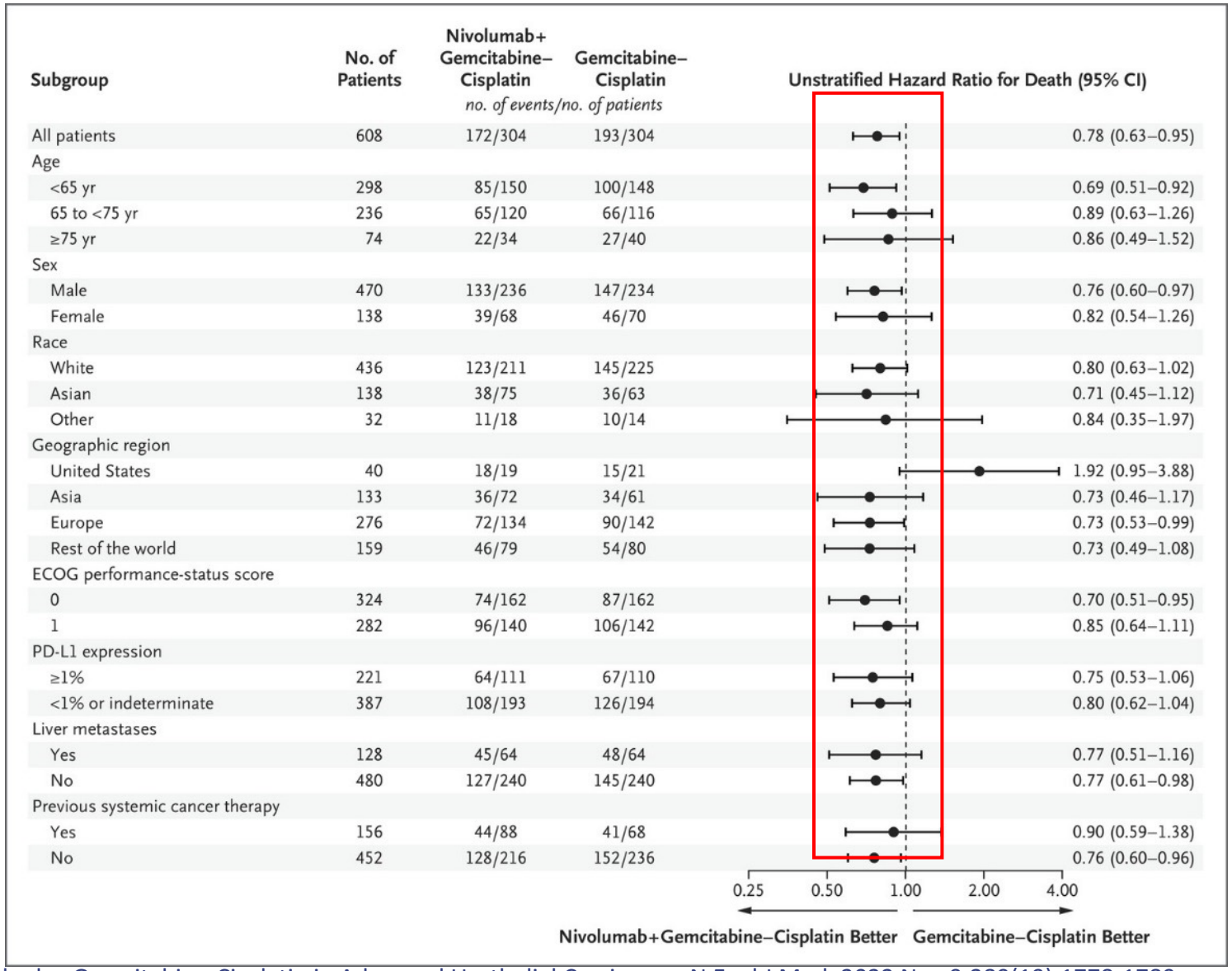
van der Heijden MS et al. Nivolumab plus Gemcitabine-Cisplatin in Advanced Urothelial Carcinoma. N Engl J Med. 2023 Nov 9;389(19):1778-1789

CheckMate- 901: Nivolumab + Cisplatin Based Chemo

Variable	Nivolumab plus Gemcitabine–Cisplatin (N=304)	Gemcitabine–Cisplatin Alone (N=304)
Objective response — % (95% CI)	57.6 (51.8–63.2)	43.1 (37.5–48.9)
Confirmed best overall response — no. (%)		
Complete response	66 (21.7)	36 (11.8)
Partial response	109 (35.9)	95 (31.2)
Stable disease	77 (25.3)	86 (28.3)
Progressive disease	29 (9.5)	39 (12.8)
Unevaluable	23 (7.6)	48 (15.8)
Median time until objective response (IQR) — mo		
Any objective response	2.1 (2.0–2.3)	2.1 (2.0–2.2)
Complete response	2.1 (1.9–2.2)	2.1 (1.9–2.2)
Median duration of objective response (95% CI) — mo		
Any objective response	9.5 (7.6–15.1)	7.3 (5.7–8.9)
Complete response	37.1 (18.1–NE)	13.2 (7.3–18.4)

van der Heijden MS et al. Nivolumab plus Gemcitabine-Cisplatin in Advanced Urothelial Carcinoma. N Engl J Med. 2023 Nov 9;389(19):1778-1789

CheckMate- 901: Nivolumab + Cisplatin Based Chemo Forest Plots and AEs



Subgroup	No. of Patients	Nivolumab+ Gemcitabine–Cisplatin	Gemcitabine–Cisplatin	Unstratified Hazard Ratio for Death (95% CI)
		no. of events/no. of patients		
All patients	608	172/304	193/304	0.78 (0.63–0.95)
Age				
<65 yr	298	85/150	100/148	0.69 (0.51–0.92)
65 to <75 yr	236	65/120	66/116	0.89 (0.63–1.26)
≥75 yr	74	22/34	27/40	0.86 (0.49–1.52)
Sex				
Male	470	133/236	147/234	0.76 (0.60–0.97)
Female	138	39/68	46/70	0.82 (0.54–1.26)
Race				
White	436	123/211	145/225	0.80 (0.63–1.02)
Asian	138	38/75	36/63	0.71 (0.45–1.12)
Other	32	11/18	10/14	0.84 (0.35–1.97)
Geographic region				
United States	40	18/19	15/21	1.92 (0.95–3.88)
Asia	133	36/72	34/61	0.73 (0.46–1.17)
Europe	276	72/134	90/142	0.73 (0.53–0.99)
Rest of the world	159	46/79	54/80	0.73 (0.49–1.08)
ECOG performance-status score				
0	324	74/162	87/162	0.70 (0.51–0.95)
1	282	96/140	106/142	0.85 (0.64–1.11)
PD-L1 expression				
≥1%	221	64/111	67/110	0.75 (0.53–1.06)
<1% or indeterminate	387	108/193	126/194	0.80 (0.62–1.04)
Liver metastases				
Yes	128	45/64	48/64	0.77 (0.51–1.16)
No	480	127/240	145/240	0.77 (0.61–0.98)
Previous systemic cancer therapy				
Yes	156	44/88	41/68	0.90 (0.59–1.38)
No	452	128/216	152/236	0.76 (0.60–0.96)

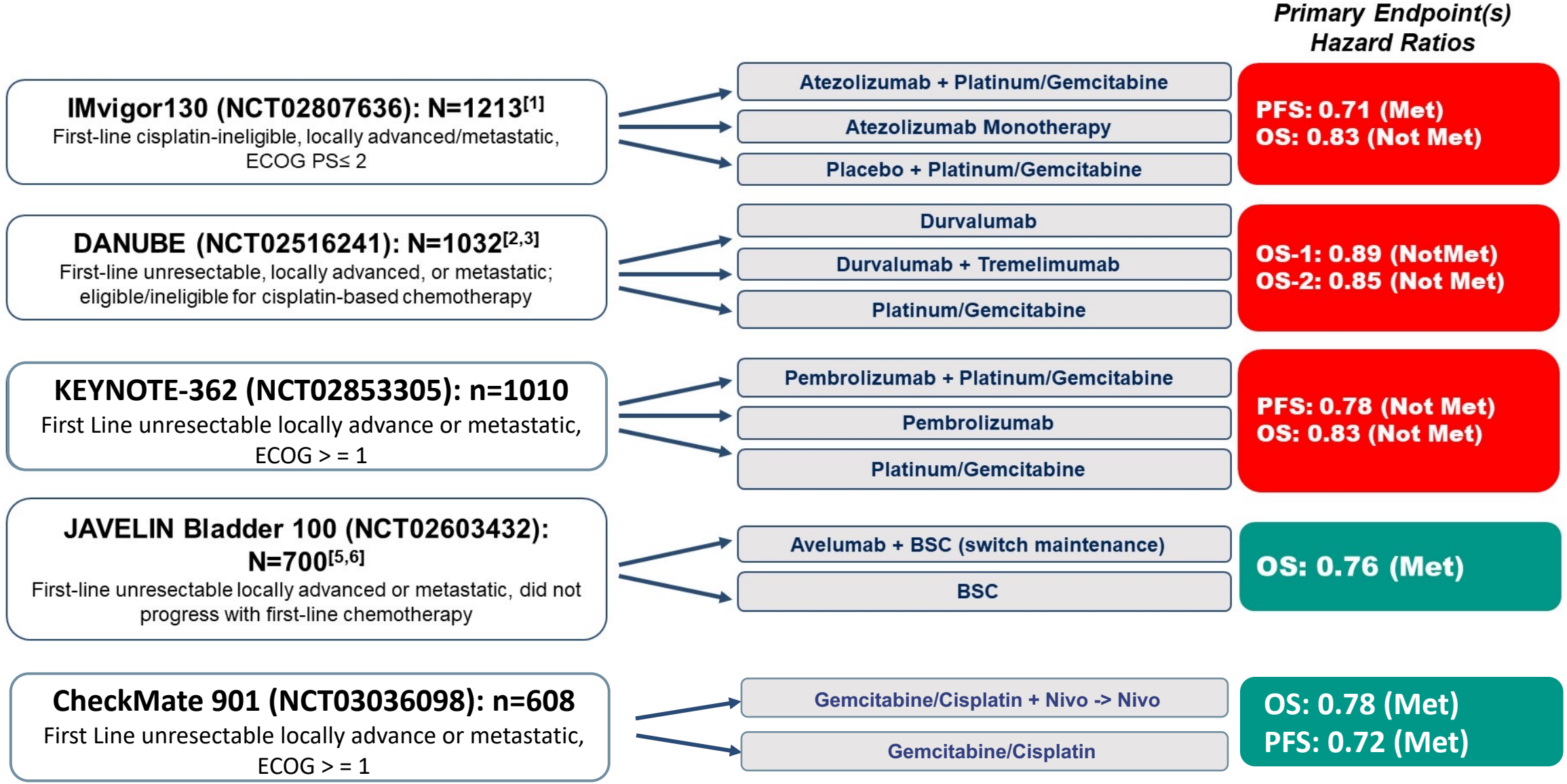
van der Heijden MS et al. Nivolumab plus Gemcitabine-Cisplatin in Advanced Urothelial Carcinoma. N Engl J Med. 2023 Nov 9;389(19):1778-1789

CheckMate- 901: Nivolumab + Cisplatin Based Chemo AEs

Adverse Event	Nivolumab plus Gemcitabine–Cisplatin (N=304)		Gemcitabine–Cisplatin Alone (N=288)	
	Any Grade	Grade ≥3†	Any Grade	Grade ≥3†
	number of patients (percent)			
Any adverse event	296 (97.4)	188 (61.8)	267 (92.7)	149 (51.7)
Anemia	174 (57.2)	67 (22.0)	137 (47.6)	51 (17.7)
Nausea	142 (46.7)	1 (0.3)	138 (47.9)	3 (1.0)
Neutropenia	93 (30.6)	57 (18.8)	86 (29.9)	44 (15.3)
Decreased neutrophil count	75 (24.7)	44 (14.5)	60 (20.8)	32 (11.1)
Fatigue	74 (24.3)	6 (2.0)	69 (24.0)	4 (1.4)
Decreased appetite	68 (22.4)	4 (1.3)	45 (15.6)	1 (0.3)
Decreased platelet count	66 (21.7)	23 (7.6)	43 (14.9)	14 (4.9)
Decreased white-cell count	64 (21.1)	30 (9.9)	40 (13.9)	11 (3.8)
Vomiting	55 (18.1)	4 (1.3)	48 (16.7)	6 (2.1)
Asthenia	47 (15.5)	3 (1.0)	46 (16.0)	5 (1.7)
Thrombocytopenia	45 (14.8)	20 (6.6)	35 (12.2)	13 (4.5)
Pruritus	44 (14.5)	2 (0.7)	8 (2.8)	0
Constipation	44 (14.5)	0	40 (13.9)	1 (0.3)
Rash	41 (13.5)	2 (0.7)	10 (3.5)	1 (0.3)
Diarrhea	40 (13.2)	4 (1.3)	25 (8.7)	0
Hypothyroidism	40 (13.2)	0	0	0
Increased blood creatinine	39 (12.8)	1 (0.3)	35 (12.2)	0
Leukopenia	38 (12.5)	7 (2.3)	33 (11.5)	5 (1.7)

van der Heijden MS et al. Nivolumab plus Gemcitabine-Cisplatin in Advanced Urothelial Carcinoma. N Engl J Med. 2023 Nov 9;389(19):1778-1789

Combination IO & Chemotherapy in 1L Settings by Trial



1. Galsky. Lancet. 2020;395:1547. 2. Powles. ESMO 2020. Abstr 6790. 3. Powles. Lancet Oncol. 2020;21:1574. 4. Powles. Lancet Oncol. 2021;22:931. 5. Powles. NEJM. 2020;383:1218. 6. Powles. ASCO 2020. Abstr LBA1

Adapted from Necchi, et al. ASCO 2023

1st Line Systemic Therapy Trials in UC

Regimen	CR Rate	RR	Median OS	Hazard Ratio
EV + Pembo (EV-302) N Engl J Med. 2024 Mar 7;390(10)	29.1%	67.7%	31.5 mos (25.4-NE)	0.47 P <0.001
Gem/Cis/Nivo ->Nivo (CheckMate 901) N Engl J Med. 2023 Nov 9;389(19):1778-1789	21.7%	57.6%	21.7 mos (18.6-26.4)	0.78 P=0.02
Cis/Carbo + Gem -> Avelumab (Javelin Bladder 100) N Engl J Med. 2020 Sep 24;383(13):1218-1230; J Clin Oncol 2023 Jul 1;41(19):3486-3492	25.7%*	72%*	23.8mos (18.9-26.1)	0.76 P<0.0036

1st Line Systemic Therapy

National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2024
Bladder Cancer

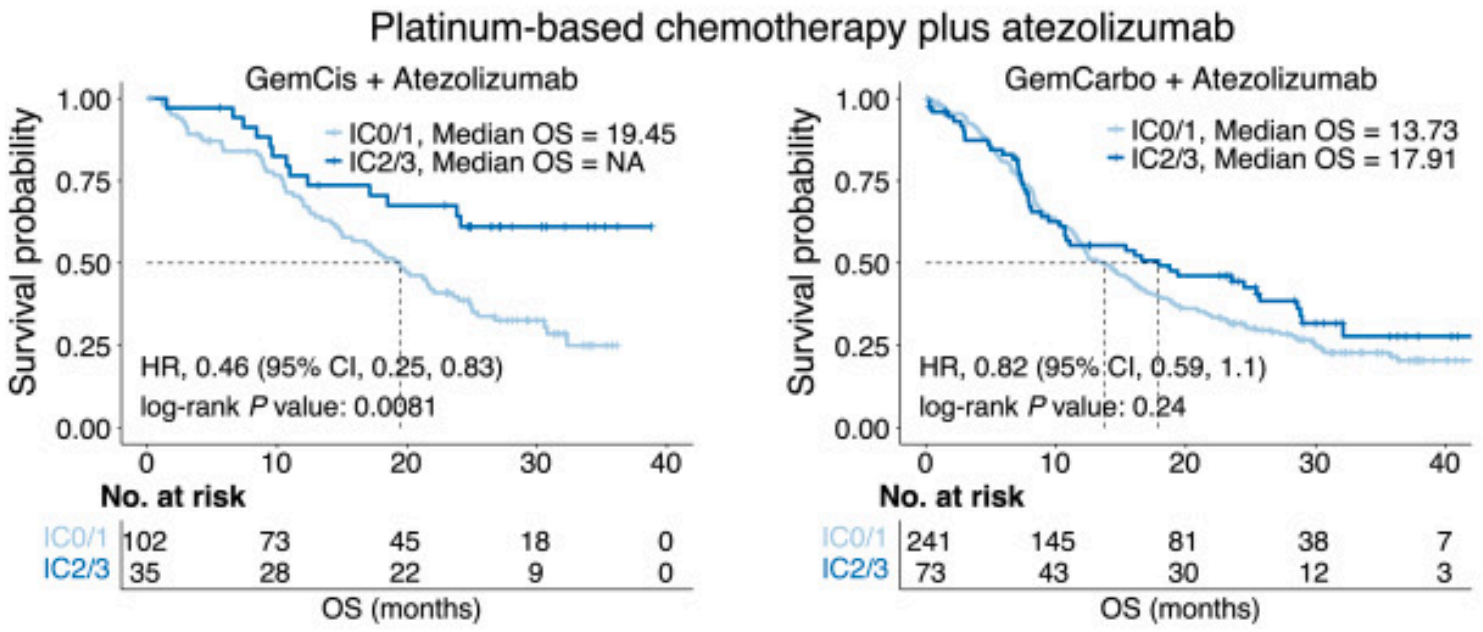
NCCN Guidelines Index
Table of Contents
Discussion

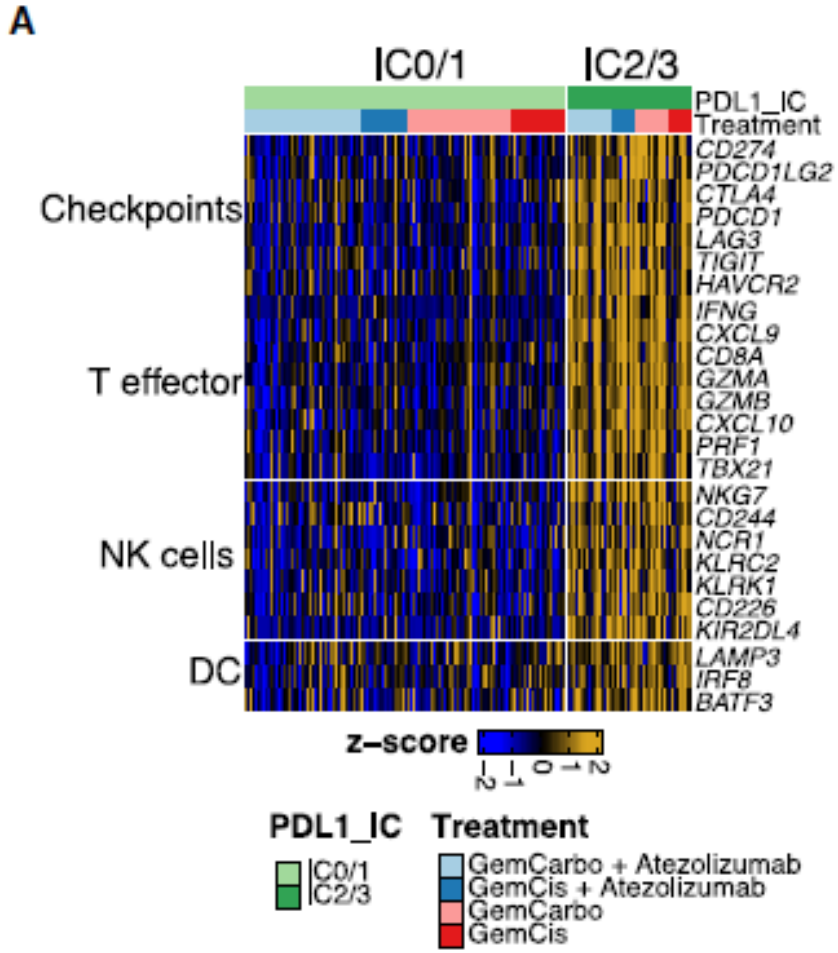
PRINCIPLES OF SYSTEMIC THERAPY

First-Line Systemic Therapy for Locally Advanced or Metastatic Disease (Stage IV)	
Cisplatin eligible	**Preferred regimens** • Pembrolizumab and enfortumab vedotin-ejfv[15] (category 1) **Other recommended regimens** • Gemcitabine and cisplatin[4] (category 1) followed by avelumab maintenance therapy (category 1)[a,13] • Nivolumab, gemcitabine, and cisplatin (category 1) followed by nivolumab maintenance therapy[14] (category 1) **Useful under certain circumstances** • DDMVAC with growth factor support (category 1)[2,8] followed by avelumab maintenance therapy (category 1)[a,13]
Cisplatin ineligible	**Preferred regimens** • Pembrolizumab and enfortumab vedotin-ejfv[15,17] (category 1) **Other recommended regimens** • Gemcitabine and carboplatin[16] followed by avelumab maintenance therapy (category 1)[a,13]
	Useful under certain circumstances • Gemcitabine[18] • Gemcitabine and paclitaxel[19] • Ifosfamide, doxorubicin, and gemcitabine[21] (for patients with good kidney function and good performance status) • Pembrolizumab[22] (for the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for any platinum-containing chemotherapy) • Atezolizumab[20] (only for patients whose tumors express PD-L1[b] or who are not eligible for any platinum-containing chemotherapy regardless of PD-L1 expression) (category 2B)

NCCN, Bladder Cancer 2024.

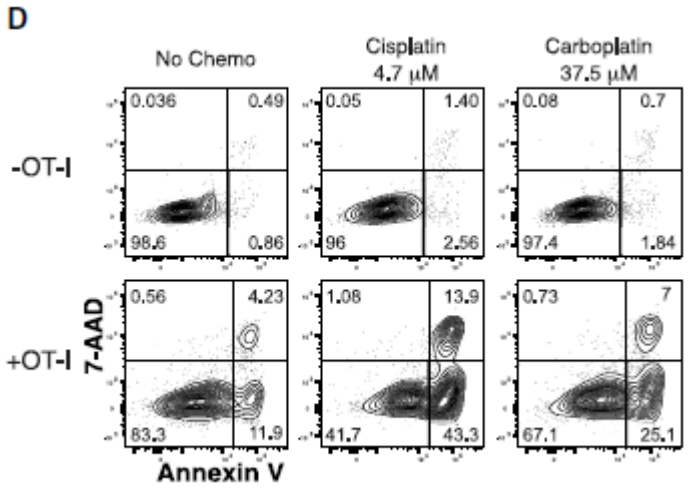
Improved outcomes with cisplatin- versus carboplatin-based chemotherapy in urothelial cancer: Imvigor I30

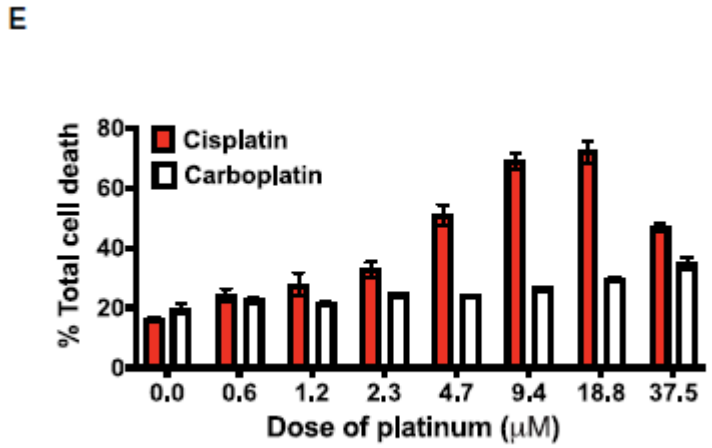


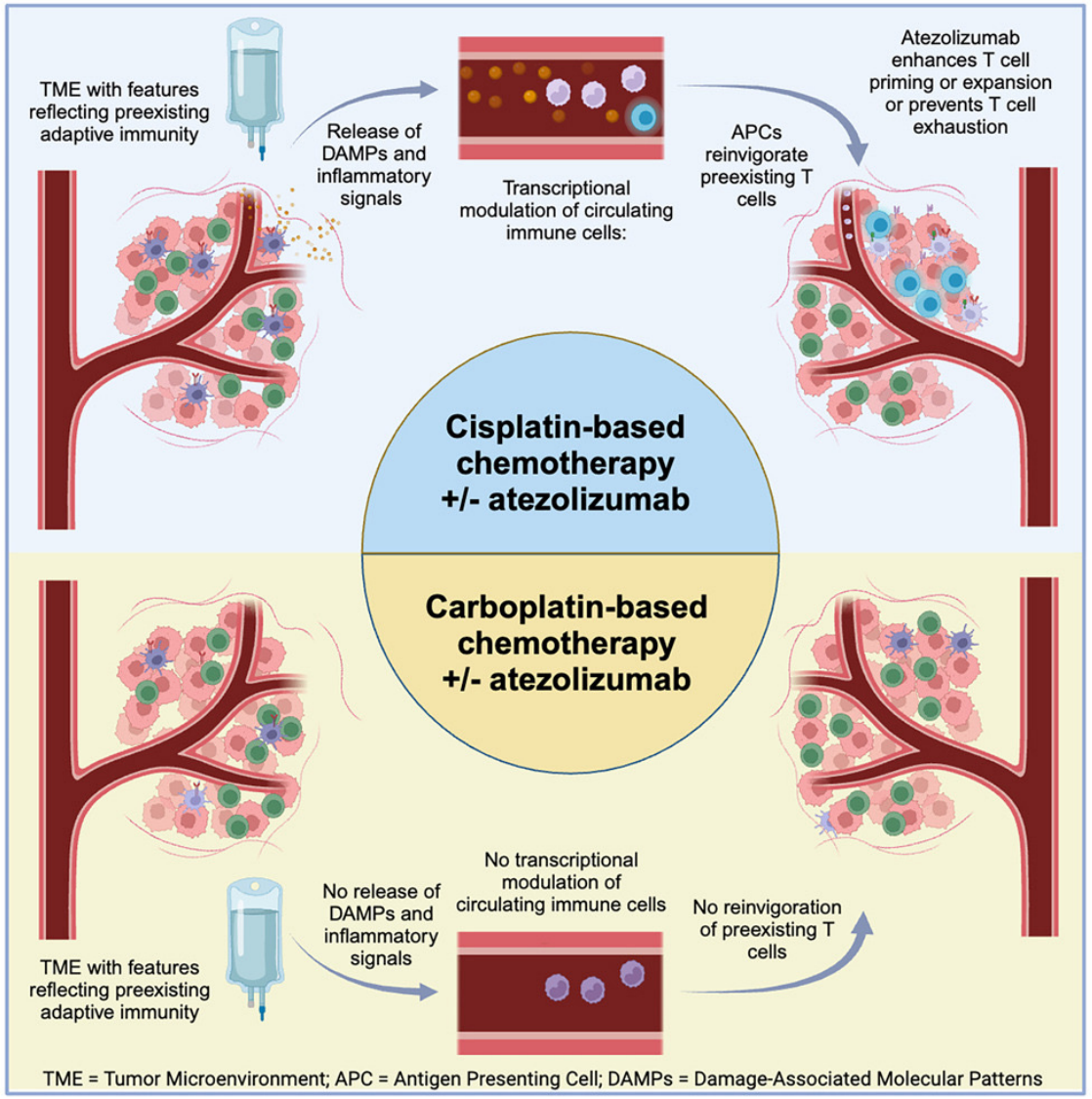


Galsky MD, et al. Cell Rep Med. 2024 Feb 20;5(2):101393

Cisplatin Enhances Adaptive Immunity, Inflammatory Responses and Cytotoxicity in Urothelial Cancer cells







Galsky MD, et al. Cell Rep Med. 2024 Feb 20;5(2):101393

Trophy U-01 Cohort 1 – Sacituzumab Govitecan Status Post Platinum and CPI Based Therapies

Cohort 1
(*N* = 113)
Patients with locally advanced unresectable or mUC (UC-predominant histology) who progressed after prior platinum-based and CPI-based therapies

→

SG 10 mg/kg IV
Days 1 and 8, every 21-day cycle

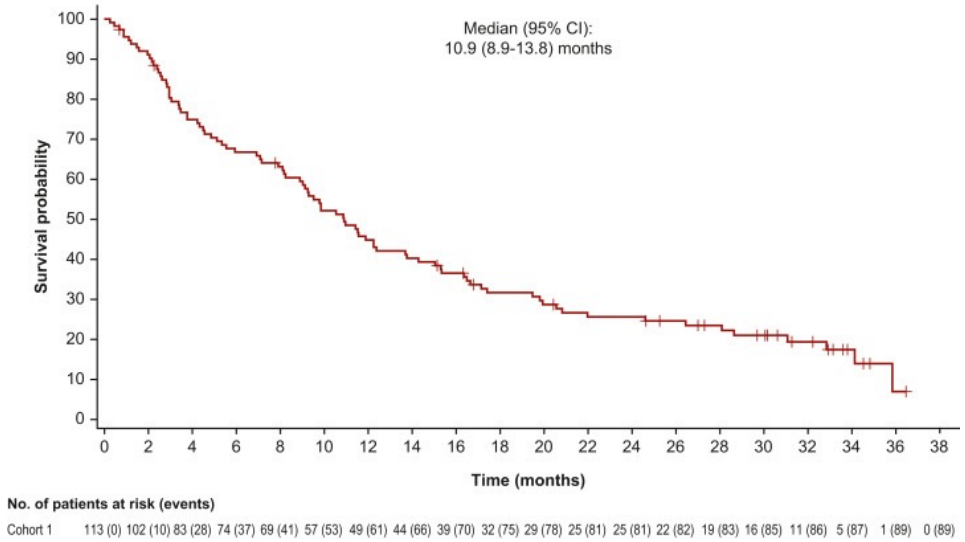
Continue treatment until loss of clinical benefit or unacceptable toxicity

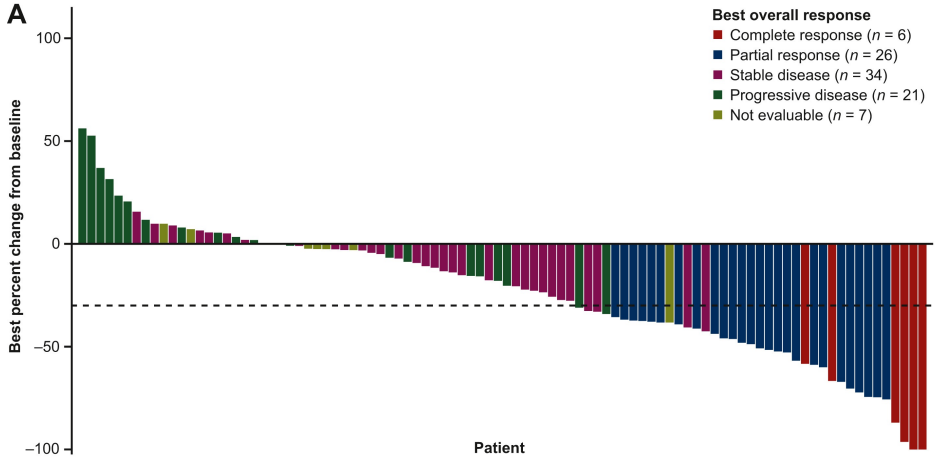
→

Primary objective
ORR by central review (RECIST 1.1)

Secondary objectives
Safety or tolerability
DOR
PFS
OS

ORR = 28%

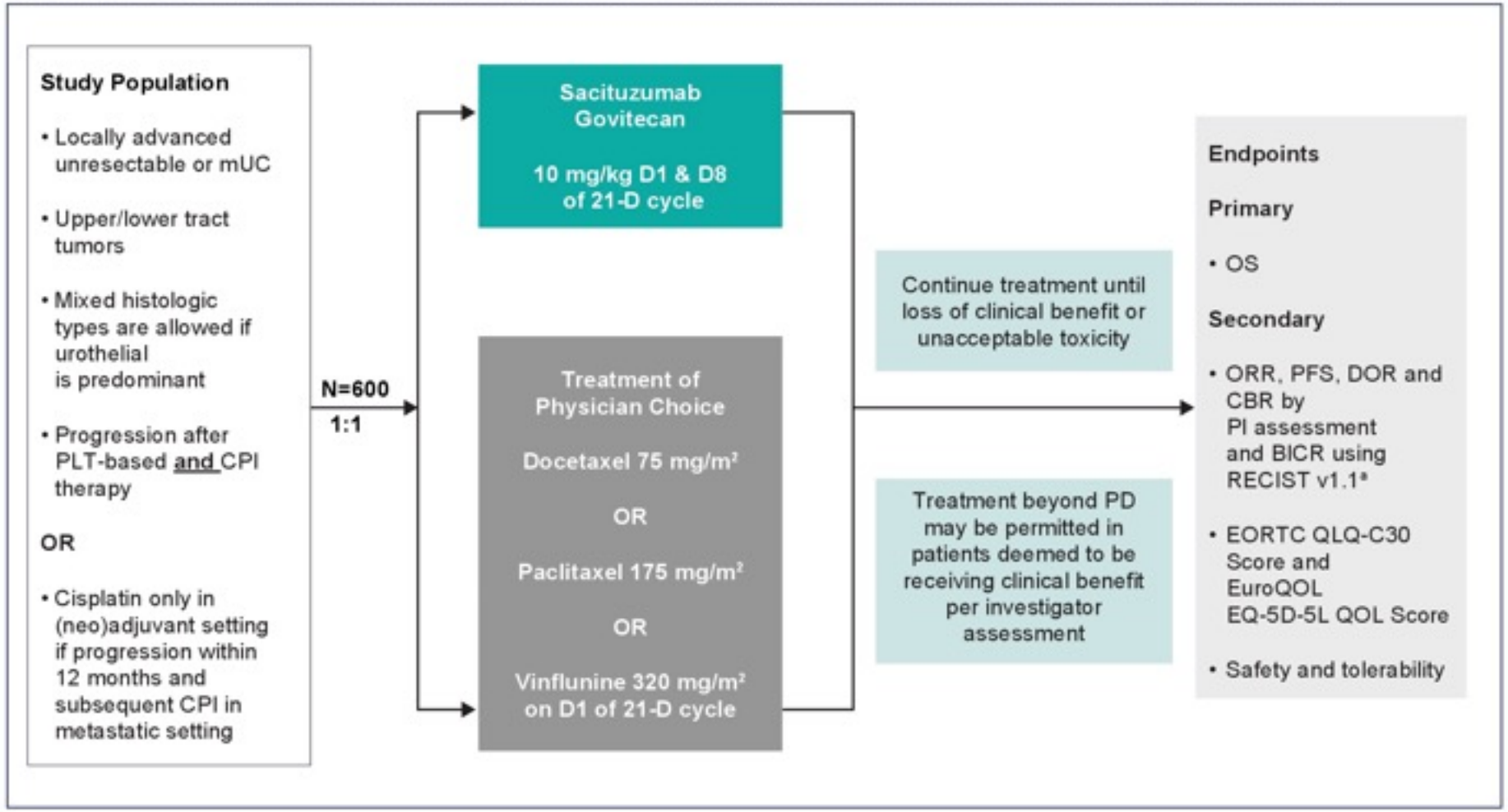




Loriot Y, et al. Ann Oncol. 2024 Apr;35(4):392-401.

Study of Sacituzumab Govitecan (IMMU-132) in Metastatic or Locally Advanced Unresectable Urothelial Cancer (TROPiCS-04)

Figure 3. TROPiCS-04: A Phase 3 Confirmatory Study of SG in mUC Progressing After Prior PLT-Based and CPI Therapies (NCT:04527991)



[a]Assessed every 6 weeks for the first 12 months and every 9 weeks thereafter until there is evidence of progressive disease (PD), including patients who discontinue prematurely due to toxicity.
BICR, blinded independent central review; CBR, clinical benefit rate; CPI, checkpoint inhibitor; D, day; DOR, duration of response; EORTC QLQ-C30, European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30; EuroQOL EQ-5D-5L QOL, European Quality of Life 5-dimensions 5-levels; mUC, metastatic urothelial carcinoma; ORR, objective response rate; OS, overall survival; PD-1, programmed death-1; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PI, Principal Investigator; PLT, platinum; QOL, quality of life; RECIST, Response Evaluation Criteria in Solid Tumors.

Vulsteke, C. GU ASCO 2022.

Study of Sacituzumab Govitecan (IMMU-132) in Metastatic or Locally Advanced Unresectable Urothelial Cancer (TROPiCS-04)

Press Releases

Company Provides Update on Phase 3 TROPiCS-04 Study

FOSTER CITY, Calif.--(BUSINESS WIRE)-- Company today announced topline results from the confirmatory Phase 3 TROPiCS-04 study in locally advanced or metastatic urothelial cancer (mUC). The TROPiCS-04 study evaluated sacituzumab govitecan-hziy vs. single-agent chemotherapy (treatment of physicians' choice, TPC) in patients with mUC who have previously received platinum-containing chemotherapy and anti-PD-(L)1 therapy.

The study did not meet the primary endpoint of overall survival (OS) in the intention-to-treat (ITT) population. A numerical improvement in OS favoring sacituzumab govitecan-hziy was observed, and trends in improvement for select pre-specified subgroups and secondary endpoints of progression-free survival (PFS) and overall response rate (ORR) were also shown. The pre-specified subgroup analyses were not alpha-controlled for formal statistical testing. These data will be presented at an upcoming medical meeting.

In the overall study population, there was a higher number of deaths due to adverse events with sacituzumab govitecan-hziy compared to TPC, which were primarily observed early in treatment and related to neutropenic complications, including infection. Company will further investigate these data, and is working to reiterate to treating physicians the importance of granulocyte-colony stimulating factor (G-CSF) use for the prevention of neutropenic complications. Sacituzumab govitecan-hziy has a Boxed Warning for severe or life-threatening neutropenia; please see below for Important Safety Information.

- Did not reach primary endpoint of OS
- Higher number of grade 5 AEs, notably neutropenia

https://www.gilead.com/news-and-press/press-room/press-releases/2024/5/gilead-provides-update-on-phase-3-tropics-04-study

Subsequent Therapies In Metastatic Urothelial CA

National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2024
Bladder Cancer

NCCN Guidelines Index
Table of Contents
Discussion

PRINCIPLES OF SYSTEMIC THERAPY

Second-Line Systemic Therapy for Locally Advanced or Metastatic Disease (Stage IV) (post-platinum or other chemotherapy)[c] Participation in clinical trials of new agents is recommended.	
Preferred regimen • Pembrolizumab (category 1 post-platinum)[24]	**Other recommended regimens** • Paclitaxel[30] or docetaxel[31] • Gemcitabine[18] • Pembrolizumab and enfortumab vedotin-ejfv (category 2B)[17]
Alternative preferred regimens • Immune checkpoint inhibitor ▸ Nivolumab[25] ▸ Avelumab[26,27] • Erdafitinib[d,28] • Enfortumab vedotin-ejfv[e,29]	**Useful in certain circumstances based on prior medical therapy** • Ifosfamide, doxorubicin, and gemcitabine[22] • Gemcitabine and paclitaxel[19] • Gemcitabine and cisplatin[4] • DDMVAC with growth factor support[2]

Second-Line Systemic Therapy for Locally Advanced or Metastatic Disease (Stage IV) (post-checkpoint inhibitor) Participation in clinical trials of new agents is recommended.	
Preferred regimens for cisplatin ineligible, chemotherapy naïve • Enfortumab vedotin-ejfv[29] • Gemcitabine and carboplatin • Erdafitinib[d,28]	**Other recommended regimens** • Paclitaxel or docetaxel[31] • Gemcitabine[18]
Preferred regimens for cisplatin eligible, chemotherapy naïve • Gemcitabine and cisplatin[4] • DDMVAC with growth factor support[2] • Erdafitinib[d,28]	**Useful in certain circumstances based on prior medical therapy** • Ifosfamide, doxorubicin, and gemcitabine[22] • Gemcitabine and paclitaxel[19]

Subsequent-Line Systemic Therapy for Locally Advanced or Metastatic Disease (Stage IV)[f,g] Participation in clinical trials of new agents is recommended.		
Preferred regimens • Enfortumab vedotin-ejfv (category 1)[32,33] • Erdafitinib[d,28] (category 1)	**Other recommended regimens** • Sacituzumab govitecan-hziy[34] • Gemcitabine[18] • Paclitaxel[30] or docetaxel[31] • Ifosfamide, doxorubicin, and gemcitabine[22] • Gemcitabine and paclitaxel[19] • Gemcitabine and cisplatin[4] • DDMVAC with growth factor support[2]	**Useful in Certain Cirumstances regimens** • Fam-trastuzumab deruxtecan-nxki (HER2-positive, IHC 3+)[43]

NCCN, Bladder Cancer 2024.

THOR Phase 3 Study: Erdafitinib vs. Chemo in FGFR Mutated UC

Cohort 1

Key eligibility criteria
- Age ≥18 years
- Metastatic or unresectable UC
- Confirmed disease progression
- Prior tx with anti–PD-(L)1
- 1-2 lines of systemic tx
- Select *FGFR3/2alt* (mutation/fusion)[a]
- ECOG PS 0-2

1:1
N=266[b]
R

Erdafitinib
(n=136)
Once-daily erdafitinib 8 mg with pharmacodynamically guided uptitration to 9 mg

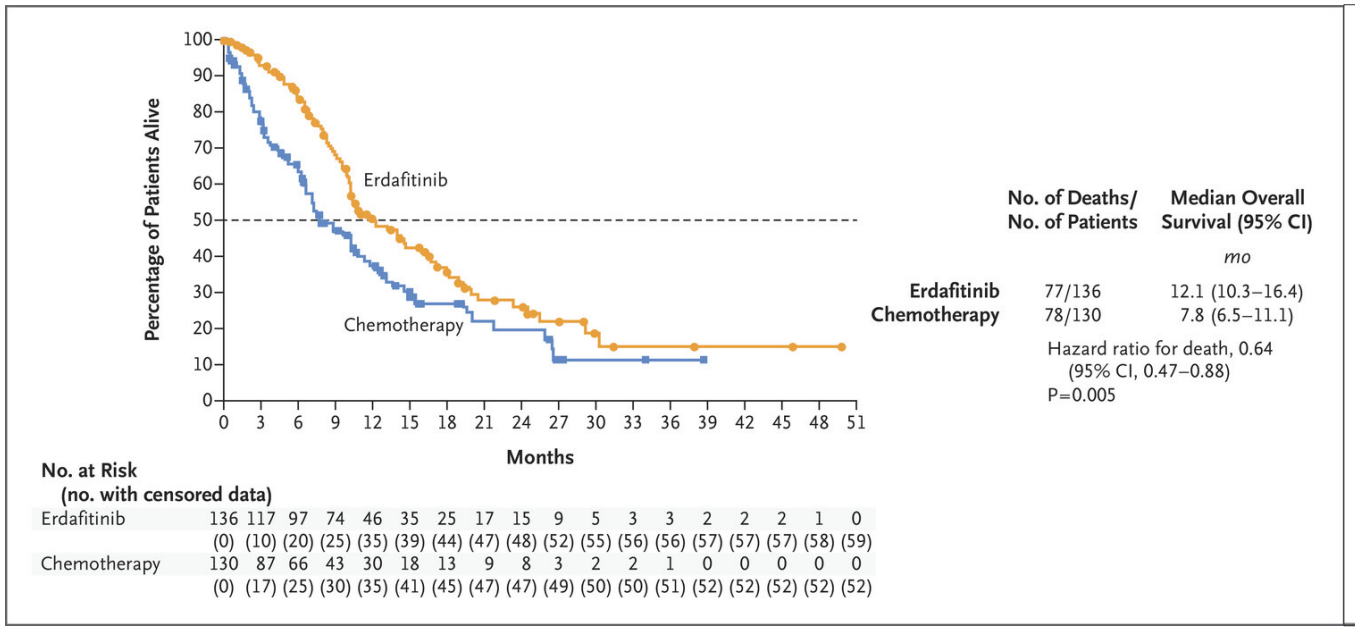
Chemotherapy of Choice
(n=130)
docetaxel or vinflunine once every 3 weeks

Stratification factors: region (North America vs European Union vs rest of world), ECOG PS (0 or 1 vs 2), and disease distribution (presence vs absence of visceral [lung, liver, or bone] metastases)

Primary end point:
- OS

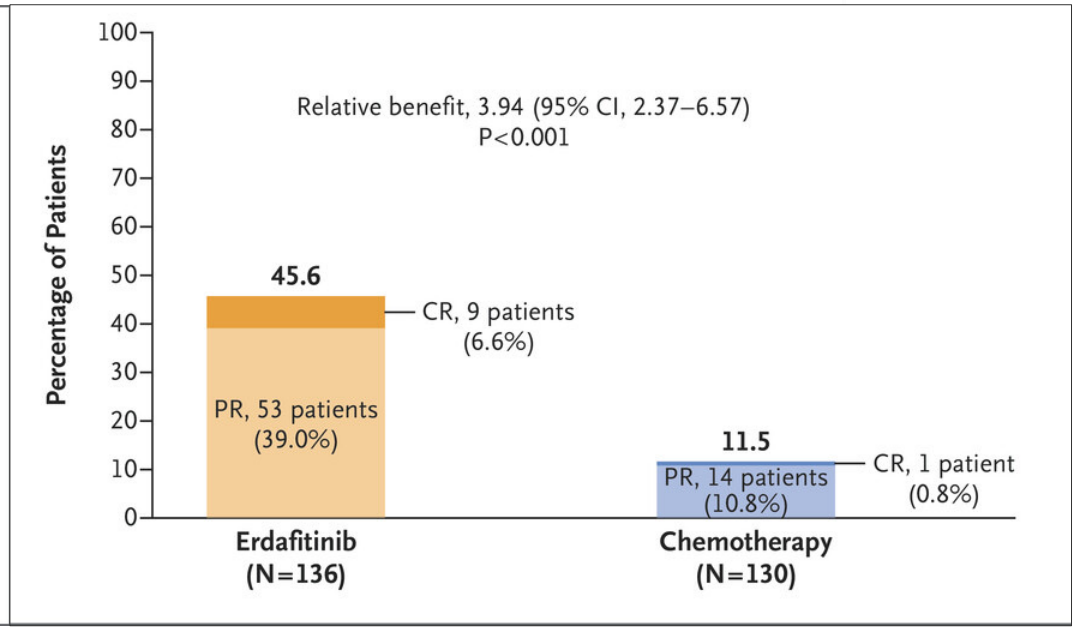
Key secondary end points:
- PFS
- ORR
- Safety

NCT03390504



	No. of Deaths/ No. of Patients	Median Overall Survival (95% CI)
		mo
Erdafitinib	77/136	12.1 (10.3–16.4)
Chemotherapy	78/130	7.8 (6.5–11.1)

Hazard ratio for death, 0.64 (95% CI, 0.47–0.88)
P=0.005



Destiny – PanTumor02: A Phase 2 Study of T-Dxd for HER2-Expressing Solid Tumors

- Advanced solid tumors not eligible for curative therapy
- 2L+ patient population
- HER2 expression (IHC 3+ or 2+)
  - Local test or central test by HercepTest if local test not feasible (ASCO/CAP gastric cancer guidelines[1])[a]
- Prior HER2-targeting therapy allowed
- ECOG/WHO PS 0–1

T-DXd
5.4 mg/kg
q3w

n≈40 per cohort planned

(Cohorts with no objective responses in the first 15 patients were to be closed)

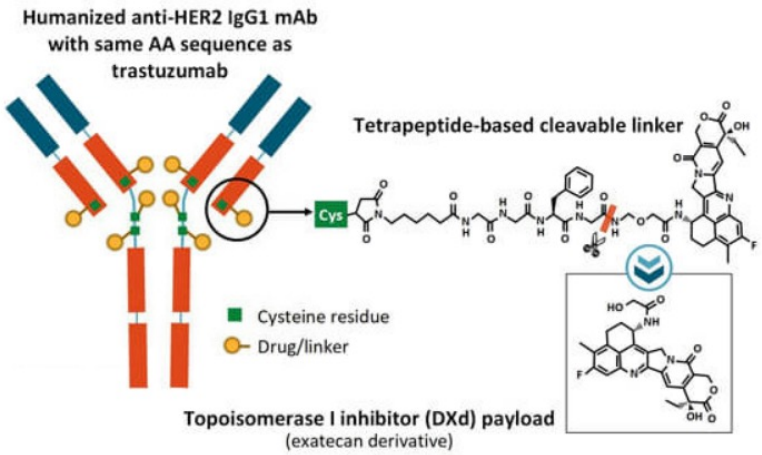
- Cervical cancer
- Endometrial cancer
- Ovarian cancer
- Biliary tract cancer
- Pancreatic cancer
- Bladder cancer
- Other tumors[b]

Primary endpoint
- Confirmed ORR (investigator)[c]

Secondary endpoints
- DOR[c]
- DCR[c]
- PFS[c]
- OS
- Safety

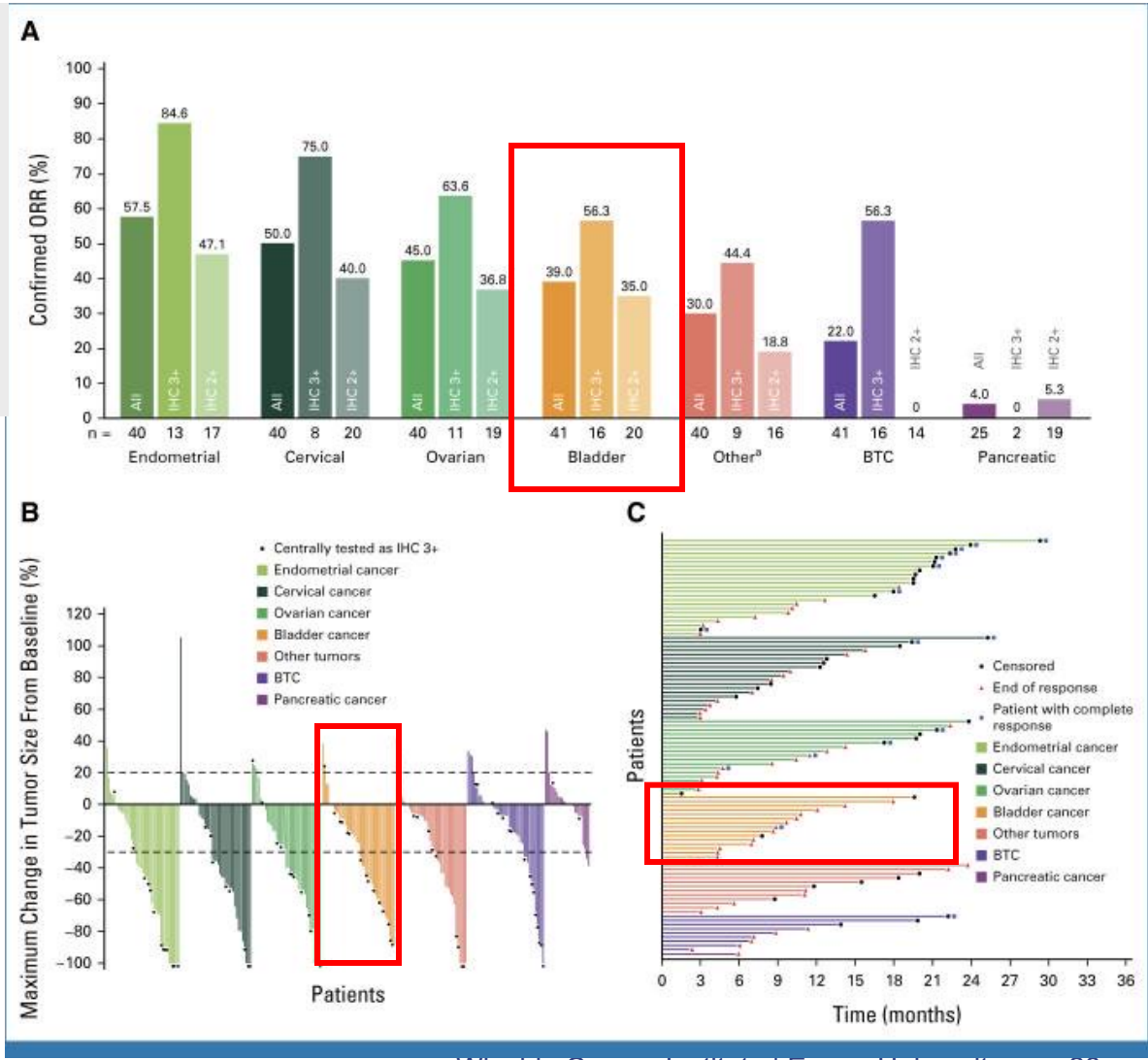
Data cut-off for analysis:
- Nov 16, 2022

HER2-Targeted ADC: Trastuzumab Deruxtecan



- High drug:antibody ratio: ~8
- Stable linker-payload
- Tumor-selectable cleavable linker
- High potency, membrane-permeable payload with short systemic half-life
- Bystander killing effect

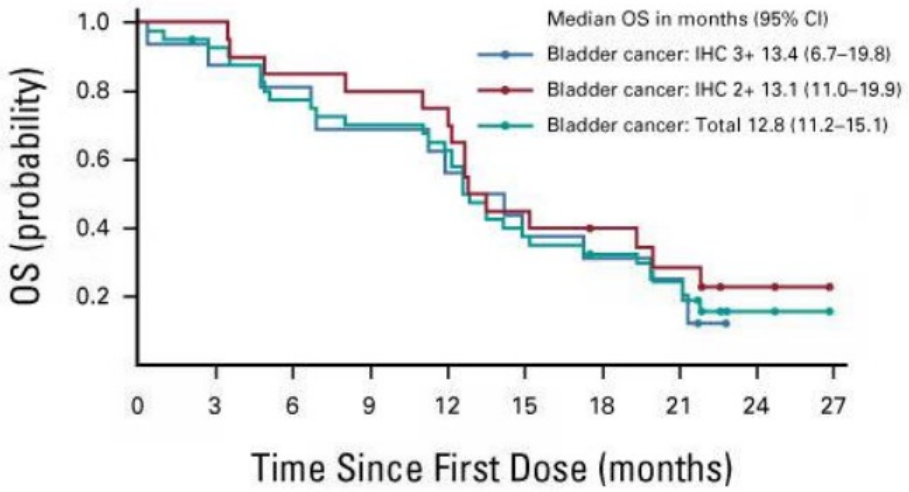
Nakada. Chem Pharm Bull (Tokyo). 2019;67:173. Trail. Pharmacol Ther. 2018;181:126. Ogitani. Cancer Sci. 2016;107:1039.



ASCO 2023; Meric-Bernstam F, et al. J Clin Oncol. 2024 Jan 1;42(1):47-58

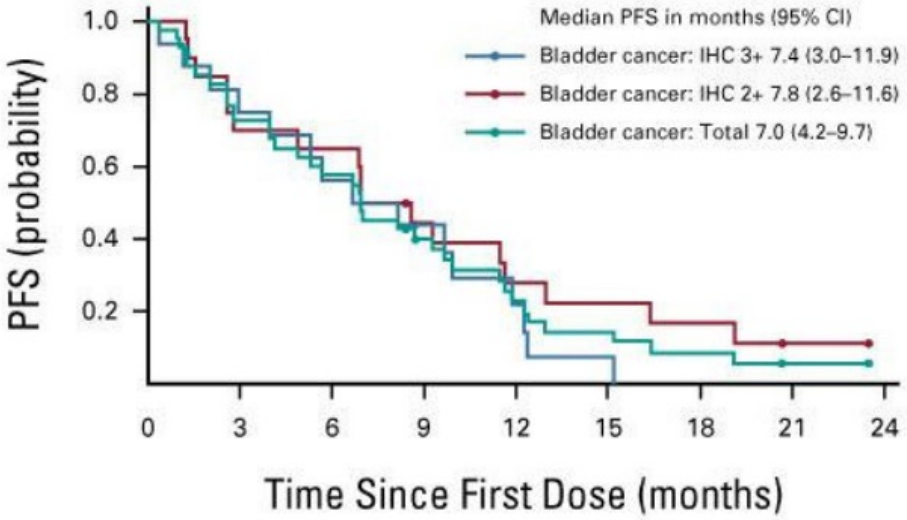
Destiny – PanTumor02: A Phase 2 Study of T-Dxd for HER2-Expressing Solid Tumors

D



No. at risk:										
Bladder cancer: IHC 3+	16	14	13	11	9	6	5	4	0	
Bladder cancer: IHC 2+	20	20	17	16	15	9	7	5	2	0
Bladder cancer: Total	41	37	31	28	25	15	12	9	2	0

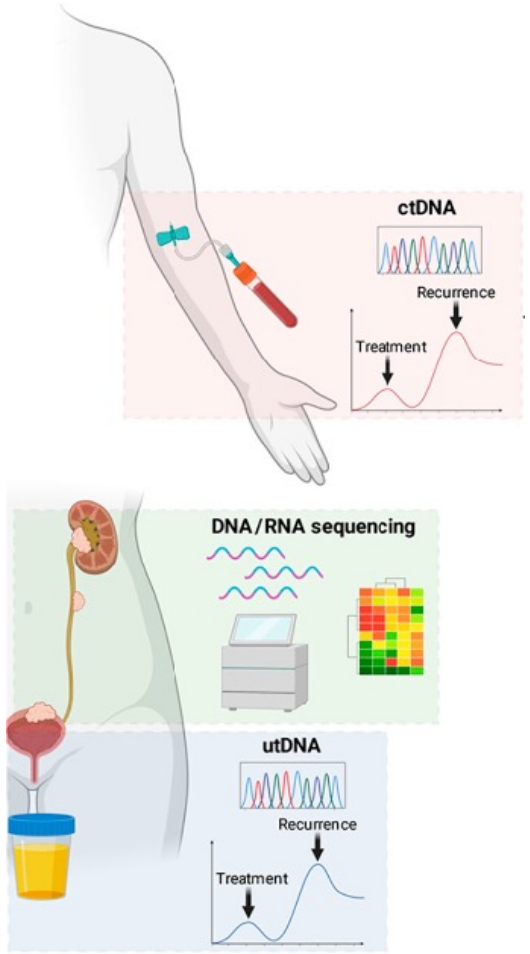
D

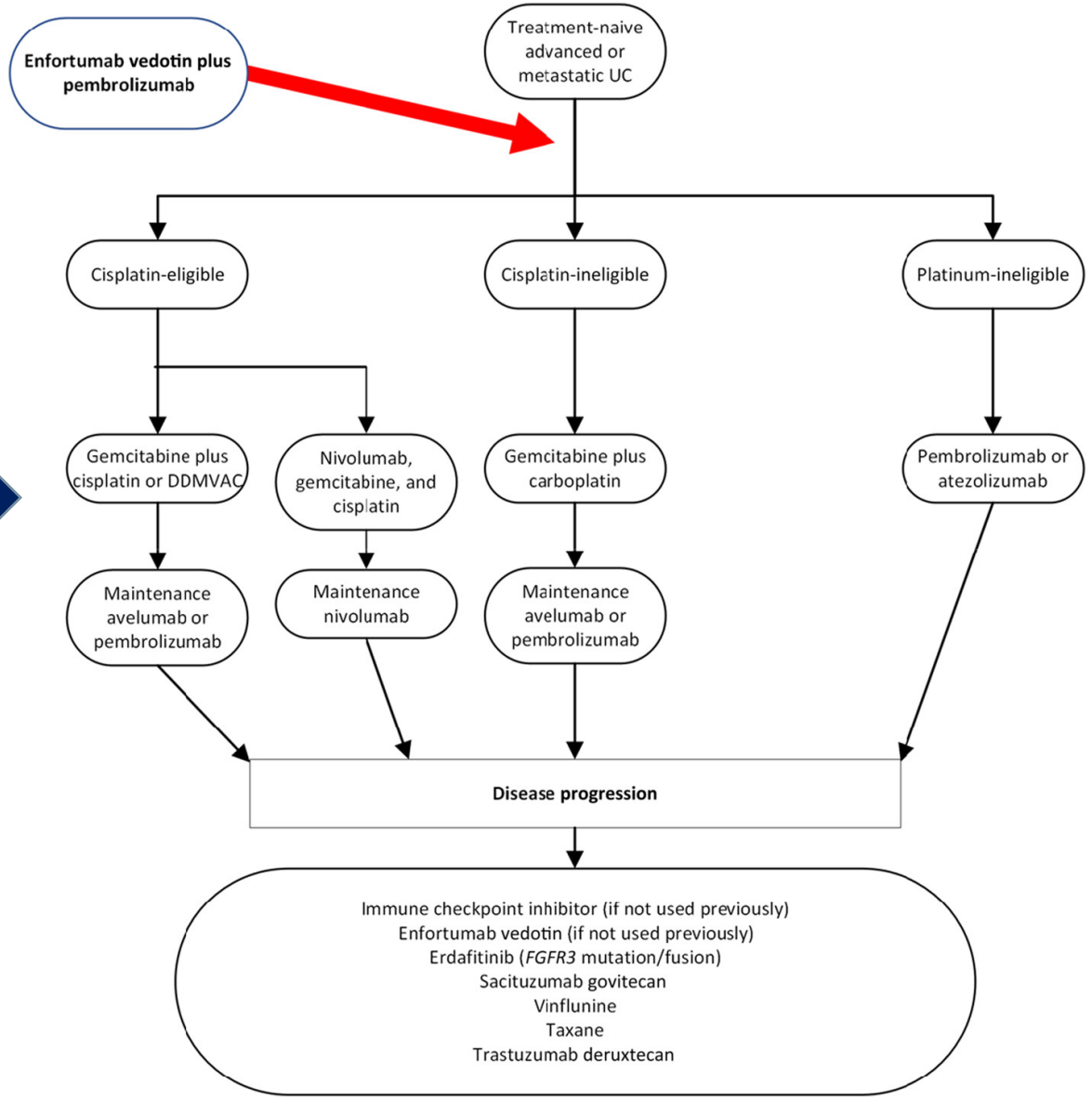


No. at risk:									
Bladder cancer: IHC 3+	16	12	9	6	3	1	0		
Bladder cancer: IHC 2+	20	14	13	8	5	4	3	1	0
Bladder cancer: Total	41	29	23	14	8	5	3	1	0

Meric-Bernstam F, et al. J Clin Oncol. 2024 Jan 1;42(1):47-58

1st Line Metastatic Urothelial Cancer 2024





Her 2 ADC + Check Point Inhibitor Combinations

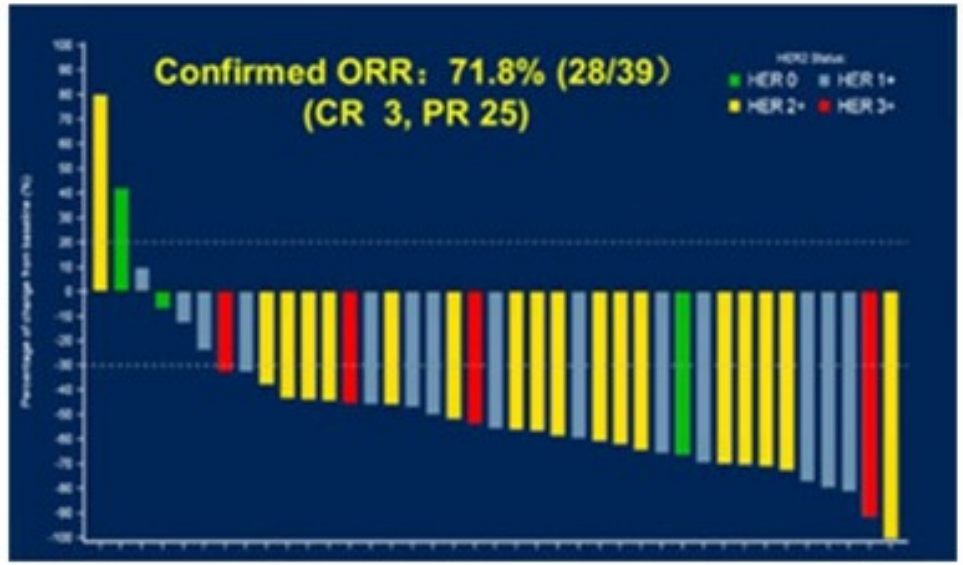
Disitimab Vedotin*

RC48 + toripalimab

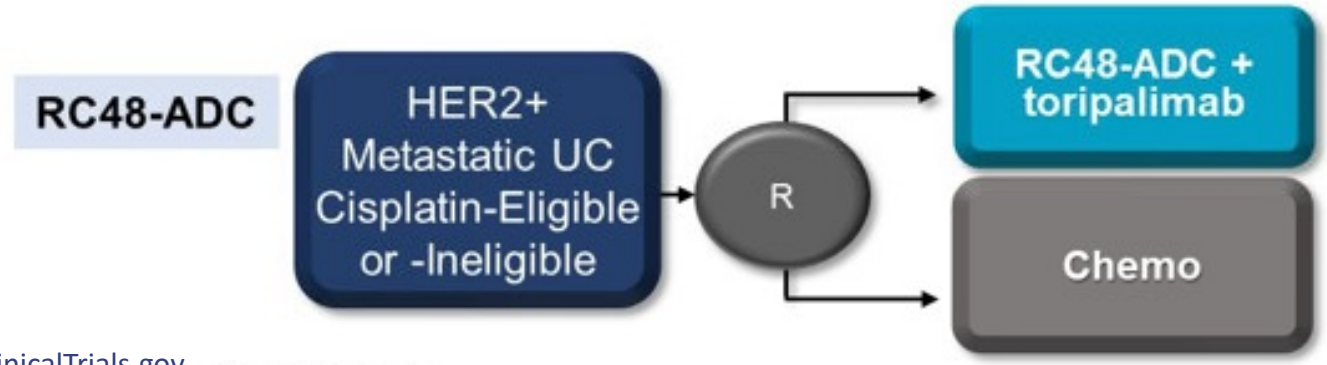
Phase II

ORR 71.8%

N=41



Phase III
N=452



Sheng, X. et al, ASCO 2023; Jan 1;27(1):43-51. ClinicalTrials.gov

Winship Advanced Urothelial Cancer Trials

First Line Non-Metastatic

Phase II / III
EA8192; ChemoXRT + Durvalumab
High Grade Upper Tract Urothelial Cancer Prior to Nephroureterectomy

First Line Metastatic

Phase 1/ 2
MK3475-04B: Pembrolizumab + EV in Combination With Investigational Agents Versus Pembrolizumab + EV

Phase 2
Winship5742-22; EV + Pembro in mUBC of Variant Histology
*Pts. may be untreated or having received any number of lines of prior therapy

≥ 2nd Line Metastatic/Advanced

Phase II
Winship 5200-20; Propranolol HCl + Pembrolizumab

Phase I/Ib
Winship 5259; Cabozantinib + Enfortumab Vedotin

SELECT COHORTS OPEN. PLEASE CONTACT CRC, KELSEA LOZADA
Phase II
Alliance
A031702 (ICONIC);
Ipilimumab, Cabo + Nivo

ACR-368-201: Phase 1b/2 Basket Study Of Acr-368 As Monotherapy And In Combination With Gemcitabine In Adult Subjects With Platinum -Resistant Urothelial Carcinoma Based On Acrivon Oncosignature® Status

Take Home Points:

- 1st line landscape has drastically changed
- Chemotherapy remains an active part of therapeutic toolbox
- Maintenance IO after chemotherapy likely enhances adaptive TME
- 2nd and subsequent line therapies will be highly patient specific
- Clinical trials remain viable options for patients

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  - Sagar Lonial, MD
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