Update in the Therapy of Bladder Cancer

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Disclosures

- **Guru Sonpavde, MD** declares the following financial relationships:
  - Speakers Bureau: Seagen, Gilead, Natera, Exelixis, Janssen, Astellas, Bayer, Pfizer, Merck, Aveo
  - Advisory Boards: EMD Serono, BMS, Merck, Seattle Genetics, Astellas, Janssen, Bicycle Therapeutics, Pfizer, Gilead, Scholar Rock, Eli Lilly, Loxo Oncology, Vial, Aktis, Daiichi-Sankyo
  - Consulting Fee: Syapse, Merck, Servier, Syncorp, Ellipses
  - Contracted Research: EMD Serono, Jazz Therapeutics, Bayer, Sumitomo Pharma, Blue Earth Diagnostics
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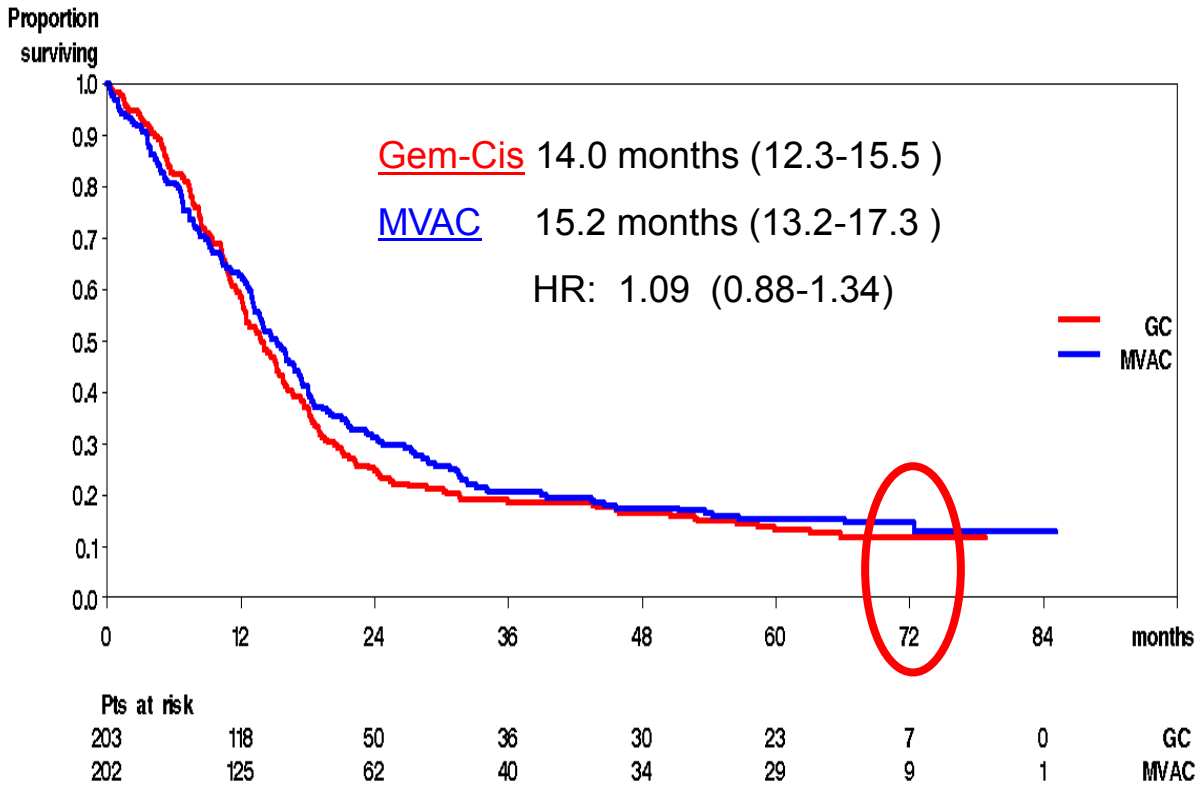
First-Line Chemotherapy for Metastatic Urothelial Carcinoma

1990s-2020

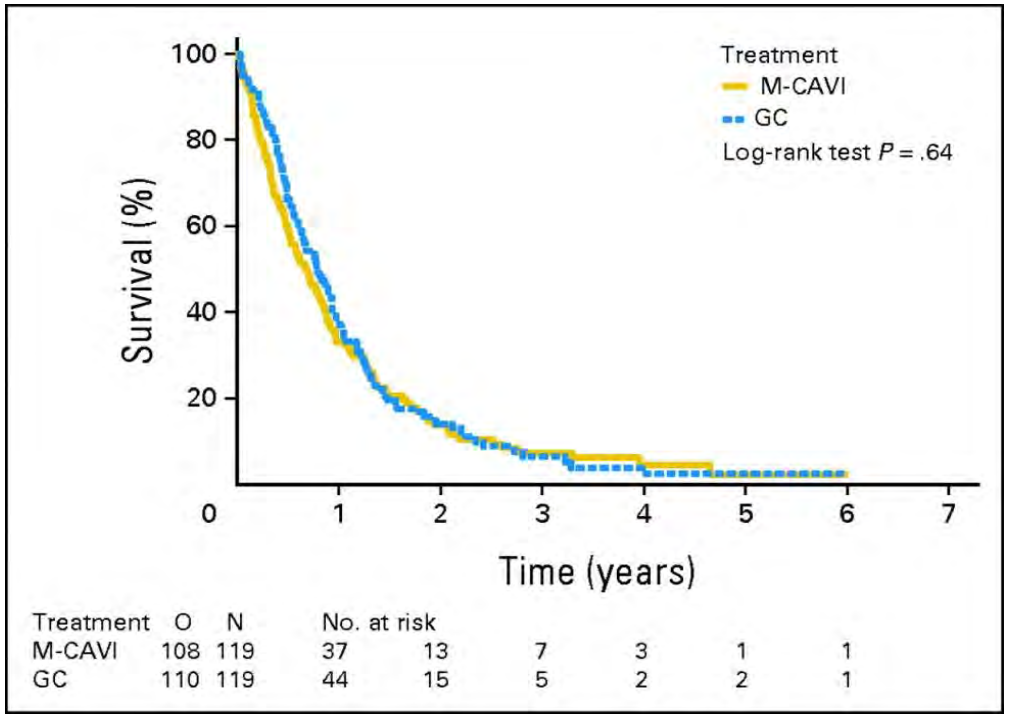
Cisplatin-eligible



von der Maase H, et al. *J Clin Oncol.* 2005;23(21):4602-4608;

Cisplatin-ineligible

ECOG PS=2
Cr Cl <60 mL/min
Neuropathy grade ≥2
CHF class ≥ 3
Hearing loss grade ≥2

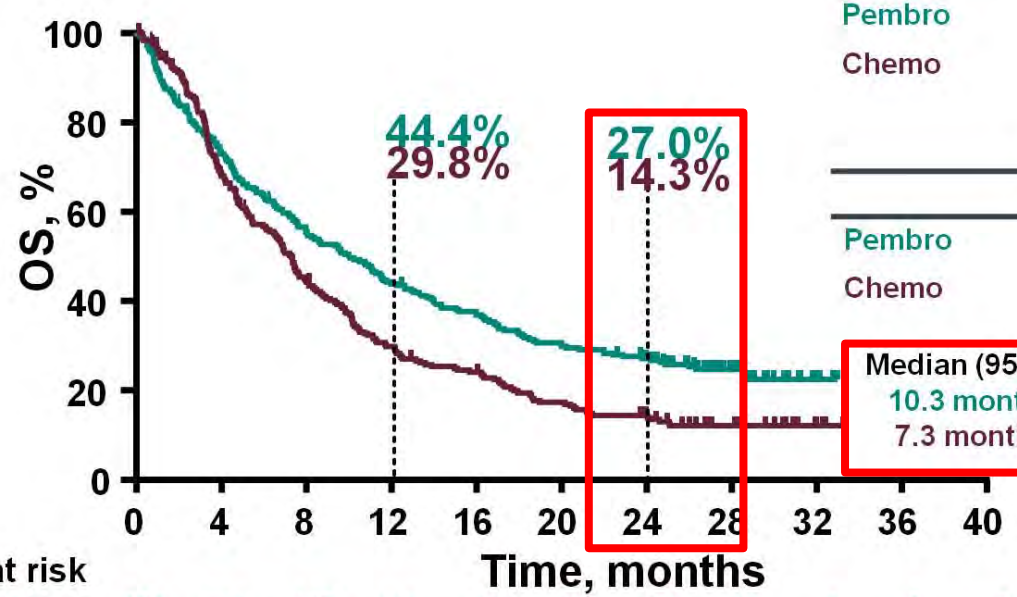


De Santis M, et al. *J Clin Oncol.* 2012;30(2):191–199.

Phase III KEYNOTE-045 trial

Pembrolizumab vs Chemotherapy for post-platinum progression

Overall Survival: Total



14.1 months of follow-up[1]

	Events, n	HR (95% CI)[a]	P[b]
Pembro	155	0.73 (0.59-0.91)	0.0022
Chemo	179		

27.7 months of follow-up

	Events, n	HR (95% CI)[a]	P[b]
Pembro	199	0.70 (0.57–0.85)	0.00017
Chemo	218		

Median (95% CI):
10.3 months (8.0–12.3)
7.3 months (6.1–8.1)

60.6% at 24 months in the chemotherapy arm received an immunotherapeutic agent, including those who received pembrolizumab as part of the cross over.

No. at risk

Pembro	270	194	147	116	98	80	67	32	6	0	0
Chemo	272	173	109	73	58	41	33	18	4	0	0

[a]Based on Cox regression model with treatment as a covariate stratified by ECOG performance status (0/1 vs 2), liver metastases (yes vs no), hemoglobin (<10 vs ≥10 g/dL), and time from completion of chemotherapy (<3 vs ≥3 months). [b]One-sided *P* value based on stratified log-rank test.
Data cutoff date: October 26, 2017.
1. Bellmunt J et al. *N Engl J Med*. 2017;376:1015-1026.

Bellmunt J, et al. N Engl J Med. 2017; Fradet Y, Ann Oncol 2019

Toxicities of pembrolizumab

Table 2. Adverse Events in the As-Treated Population.*

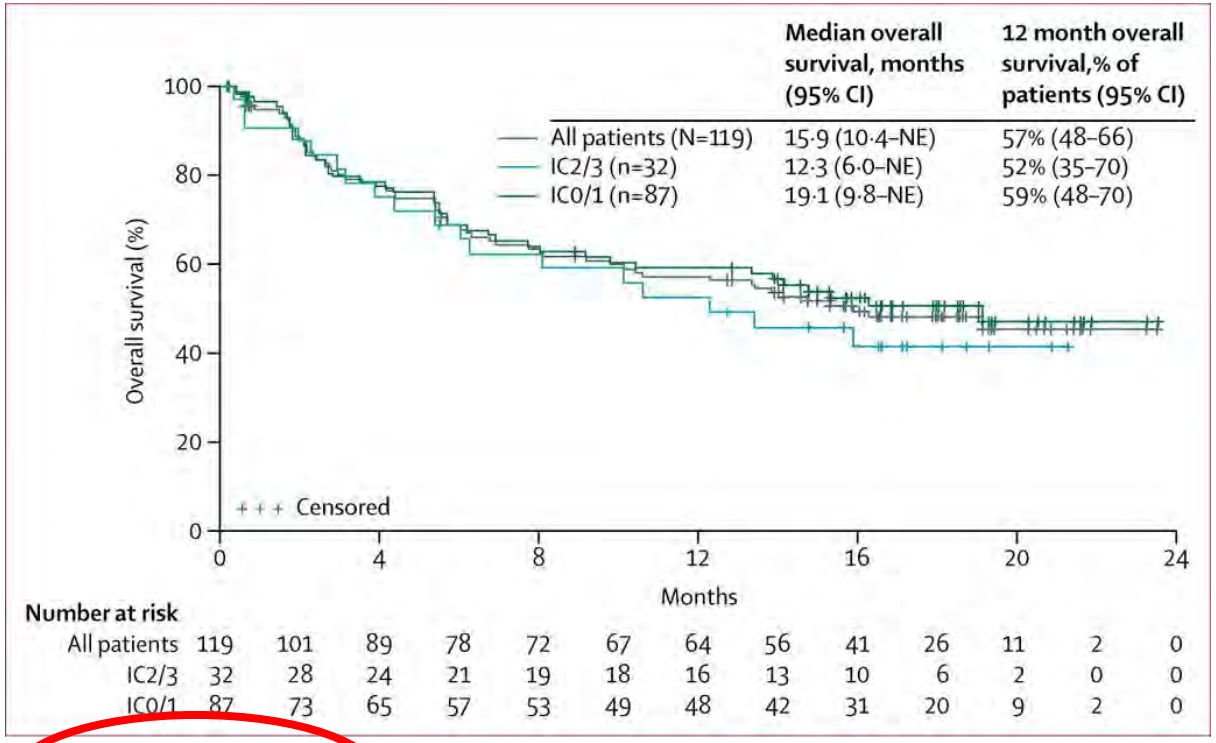
Event	Pembrolizumab Group (N=266)		Chemotherapy Group (N=255)	
	Any Grade	Grade 3, 4, or 5	Any Grade	Grade 3, 4, or 5
	number of patients (percent)			
Treatment-related event†				
Any event	162 (60.9)	40 (15.0)	230 (90.2)	126 (49.4)
Event leading to discontinuation of treatment	15 (5.6)	12 (4.5)	28 (11.0)	16 (6.3)
Event leading to death	4 (1.5)	4 (1.5)	4 (1.6)	4 (1.6)
Event occurring in ≥10% of patients in either group‡				
Pruritus	52 (19.5)	0	7 (2.7)	1 (0.4)
Fatigue	37 (13.9)	3 (1.1)	71 (27.8)	11 (4.3)
Nausea	29 (10.9)	1 (0.4)	62 (24.3)	4 (1.6)
Diarrhea	24 (9.0)	3 (1.1)	33 (12.9)	2 (0.8)
Decreased appetite	23 (8.6)	0	41 (16.1)	3 (1.2)
Asthenia	15 (5.6)	1 (0.4)	36 (14.1)	7 (2.7)
Anemia	9 (3.4)	2 (0.8)	63 (24.7)	20 (7.8)
Constipation	6 (2.3)	0	52 (20.4)	8 (3.1)
Peripheral sensory neuropathy	2 (0.8)	0	28 (11.0)	5 (2.0)
Neutrophil count decreased	1 (0.4)	1 (0.4)	36 (14.1)	31 (12.2)
Peripheral neuropathy	1 (0.4)	0	27 (10.6)	2 (0.8)
Neutropenia	0	0	39 (15.3)	34 (13.3)
[illegible]	0	0	96 (37.6)	2 (0.8)
Event of interest§				
Any event	45 (16.9)	12 (4.5)	19 (7.5)	4 (1.6)
Hypothyroidism	17 (6.4)	0	3 (1.2)	0
Hyperthyroidism	10 (3.8)	0	1 (0.4)	0
Pneumonitis	11 (4.1)	6 (2.3)	1 (0.4)	0
Colitis	6 (2.3)	3 (1.1)	1 (0.4)	0
Infusion reaction	2 (0.8)	0	10 (3.9)	0
Nephritis	2 (0.8)	2 (0.8)	0	0
Severe skin reaction	2 (0.8)	1 (0.4)	3 (1.2)	3 (1.2)
Thyroiditis	2 (0.8)	0	0	0
Adrenal insufficiency	1 (0.4)	1 (0.4)	0	0
Myositis	0	0	1 (0.4)	1 (0.4)

* The as-treated population included all the patients who received at least one dose of study treatment.
† Events were attributed to treatment by the investigator and are listed as indicated by the investigator on the case-report form. Although decreased neutrophil count and neutropenia may reflect the same condition, they were listed by the investigators as two distinct events; this was also the case for peripheral sensory neuropathy and peripheral neuropathy and for fatigue and asthenia.
‡ Events are listed in descending order of frequency in the pembrolizumab group.
§ The events of interest are those with an immune-related cause and are considered regardless of attribution to study treatment by the investigator. They are listed in descending order of frequency in the pembrolizumab group. In addition to the specific preferred terms listed, related terms were also included.

The NEW ENGLAND JOURNAL of MEDICINE

First-Line PD-1/PD-L1 Inhibitors for Cisplatin-Ineligible UC

Only pembro for platinum-ineligible mUC still US FDA approved (due to negative Phase III trials)

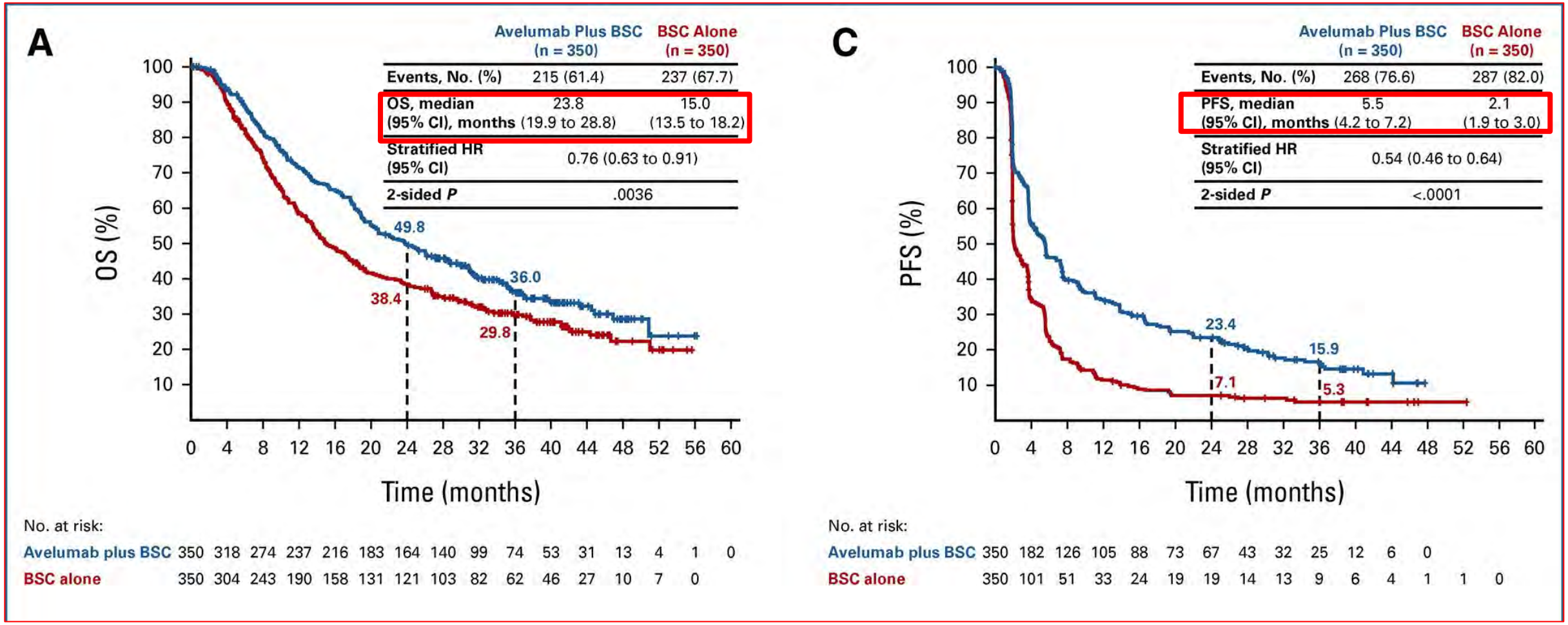


ORR 23% Median PFS 2.7 mo

	Total Population N = 370		
	n	%	95% CI
ORR	108	29	25-34
CR	27	7	5-10
PR	81	22	18-27
SD	67	18	14-22
PD	155	42	37-47

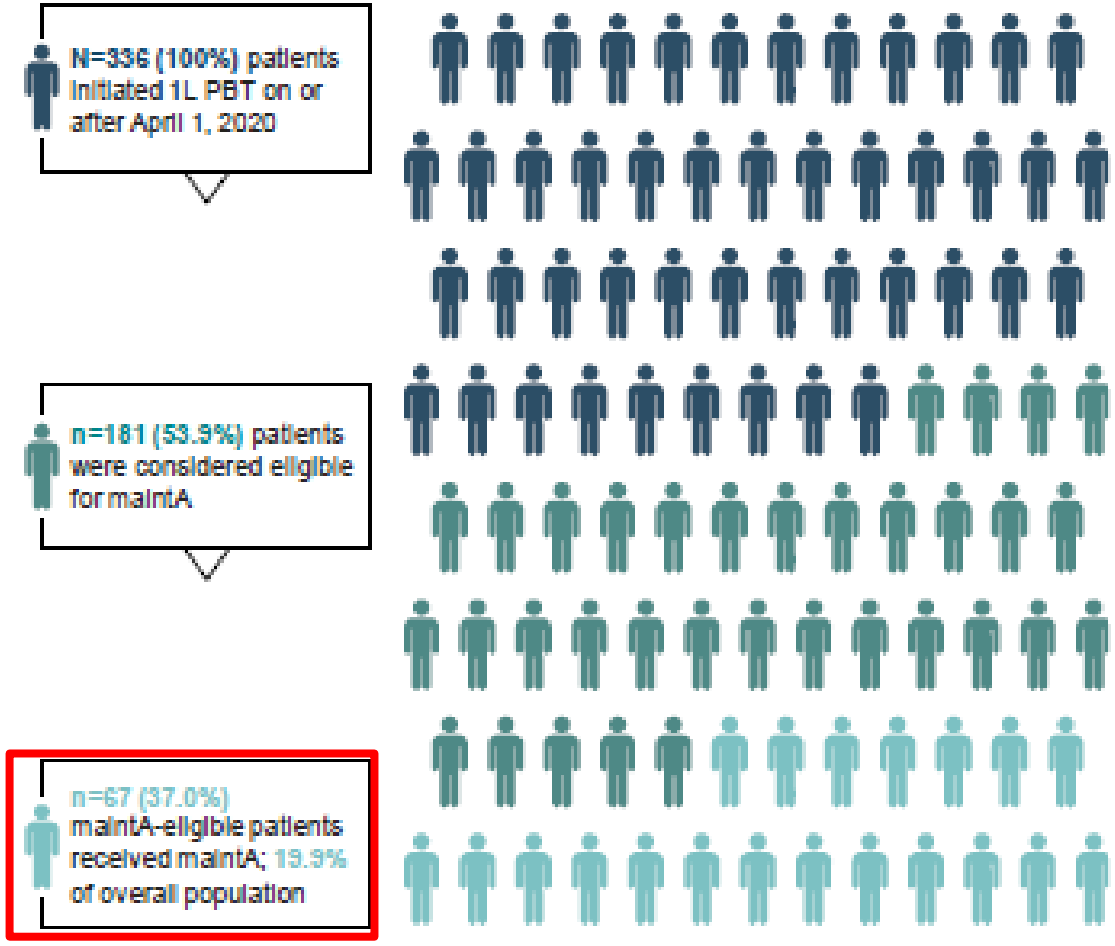
1. Balar AV, et al; for the IMvigor210 Study Group. Lancet. 2017;389(10064):67-76;
2. O'Donnell PH, et al. 2017 ASCO. Abstract 4502;
3. Balar AV; et al. Lancet Oncol. 2017;18:1483-1492.

Avelumab First-Line Maintenance for Advanced Urothelial Carcinoma: Results From the JAVELIN Bladder 100 Trial After ≥2 Years of Follow-Up



Powles T, et al. J Clin Oncol 2023 Jul 1;41(19):3486-3492.

Real world utilization of maintenance avelumab



Conclusions

These real-world data demonstrate that only about half of US patients with la/mUC treated with 1L PBT are eligible for maintA.

The most common reason for maintA ineligibility was disease progression or death following treatment with 1L PBT.

Among the total 1L PBT-treated population, only about 20% of patients received maintA.

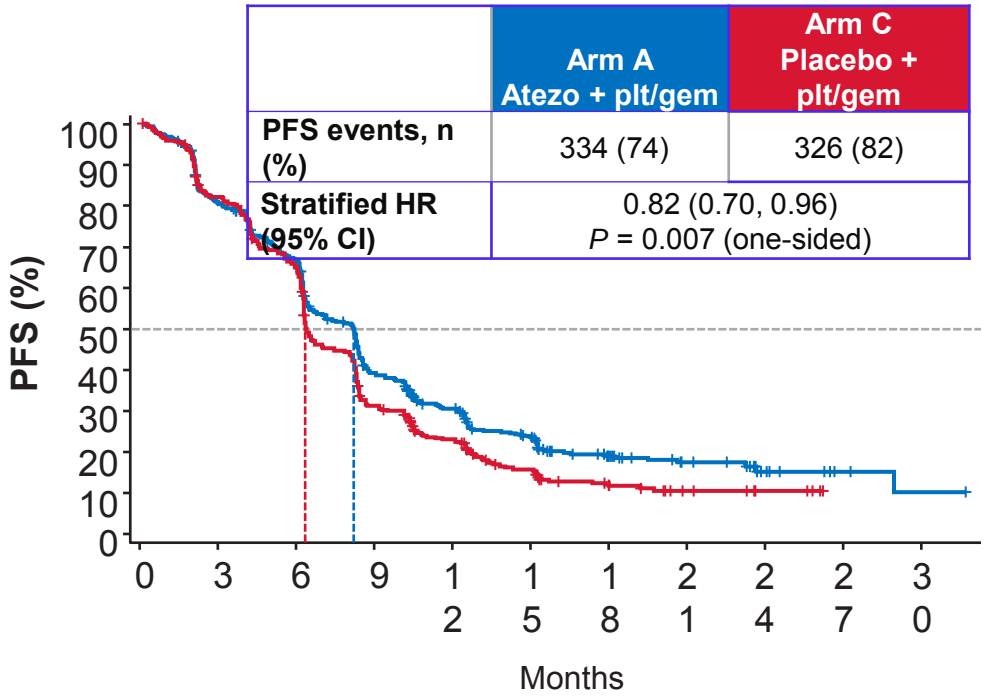
Patients ineligible for maintA had a higher mortality post–1L PBT and were almost three times more likely to die than patients eligible for maintA.

The limited proportion of patients eligible for or receiving maintA following 1L PBT highlights the ongoing unmet need for effective 1L therapies in patients with la/mUC.

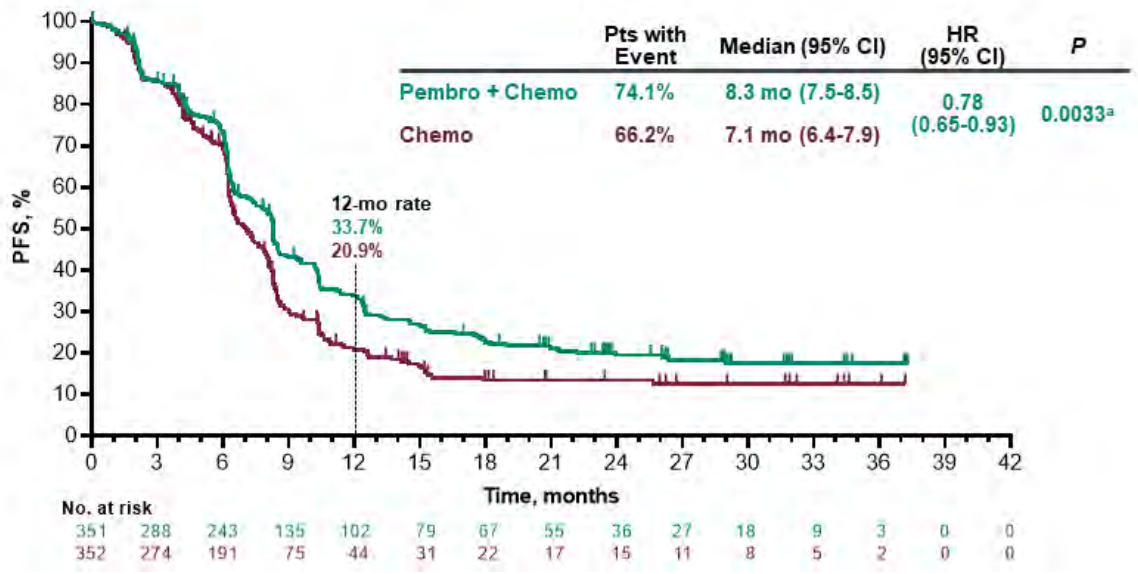
Morgans A, Sonpavde G, Shih V, et al. SUO November 2023

Platinum-based chemotherapy + ICI

First-line Phase III trials allowing cisplatin or carboplatin did not achieve improved survival



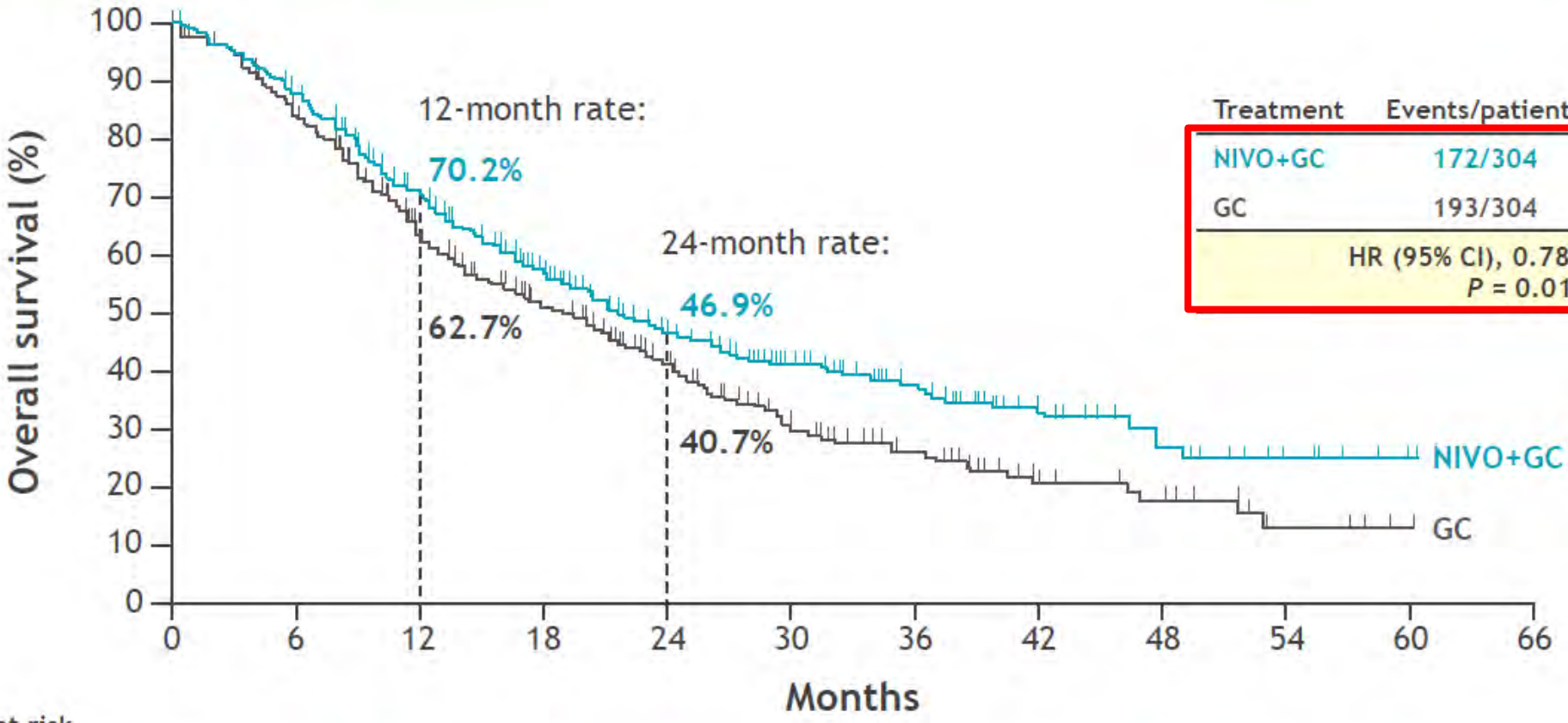
IMvigor130



KEYNOTE361

Galsky MD, et al. Lancet. 2020 May 16;395(10236):1547-1557.;
Powles T, et al. Lancet Oncol 2021

OS (primary endpoint) : CHECKMATE-901 Phase III trial



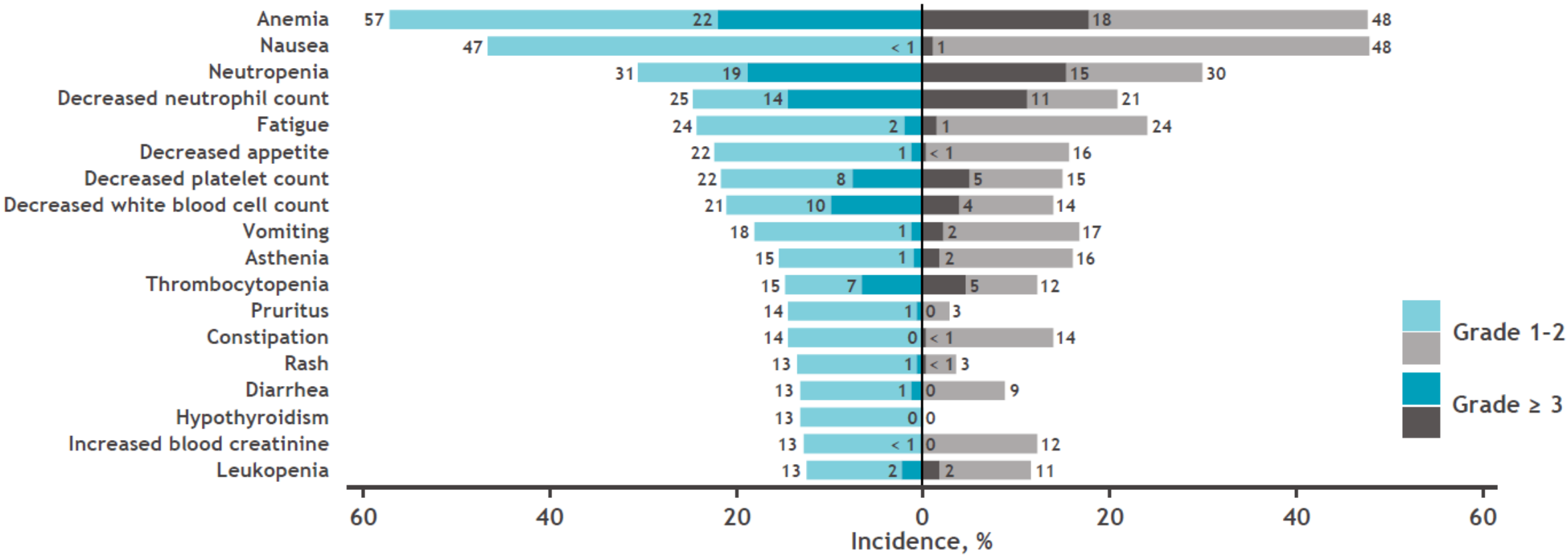
Treatment	Events/patients	Median OS (95% CI), months
NIVO+GC	172/304	21.7 (18.6-26.4)
GC	193/304	18.9 (14.7-22.4)
HR (95% CI), 0.78 (0.63-0.96) *P* = 0.0171		

No. at risk												
NIVO+GC	304	264	196	142	97	69	48	25	15	7	2	0
GC	304	242	166	122	82	49	33	17	13	4	1	0

Van Der Heijden*, Sonpavde G*, Powles T, et al. ESMO 2023, N Engl J Med 2023

Treatment-related AEs in all treated patients

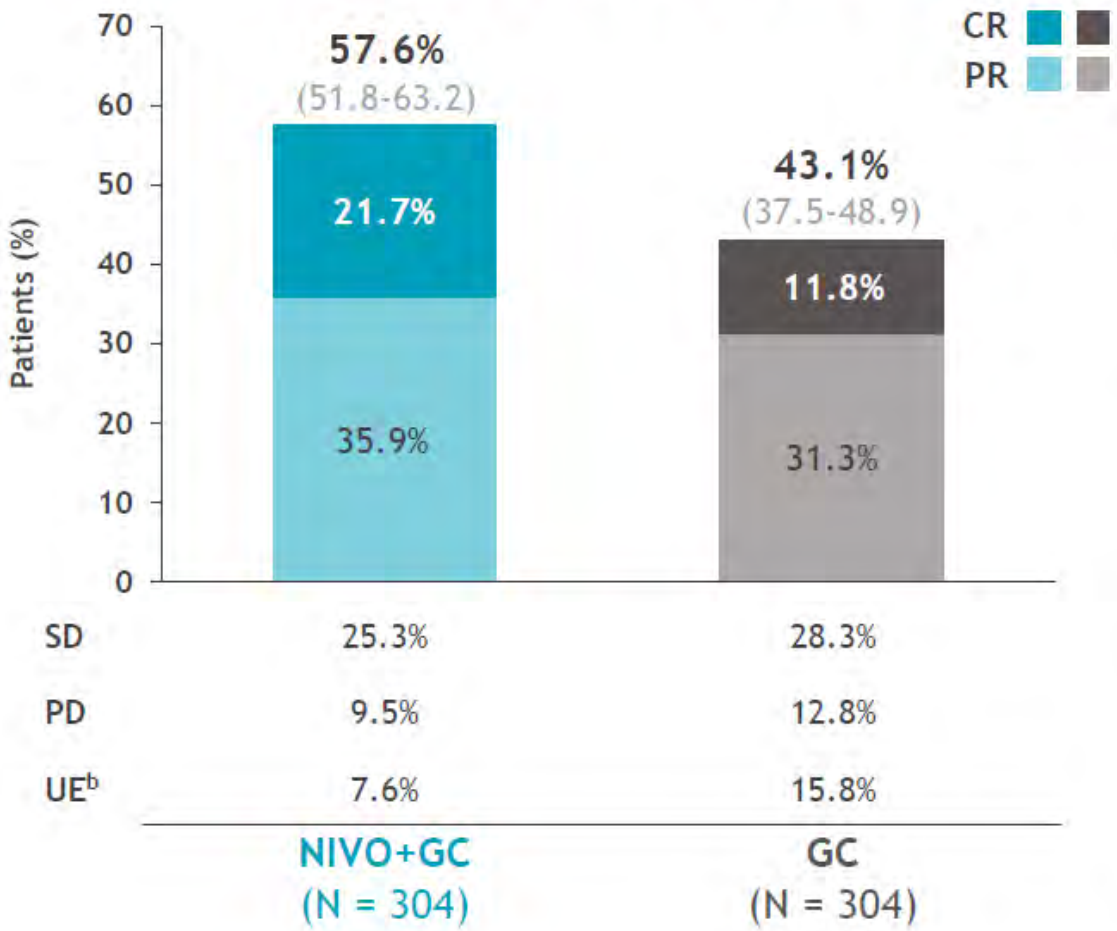
	NIVO+GC (n = 304)		GC (n = 288)	
Treatment-related AE, %[a]	Any grade	Grade ≥ 3[b]	Any grade	Grade ≥ 3[b]
Any	97	62	93	52
Leading to discontinuation	21	11	17	8



Van Der Heijden*, Sonpavde G*, Powles T, et al. ESMO 2023, N Engl J Med 2023

Objective response outcomes (exploratory endpoints)

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)

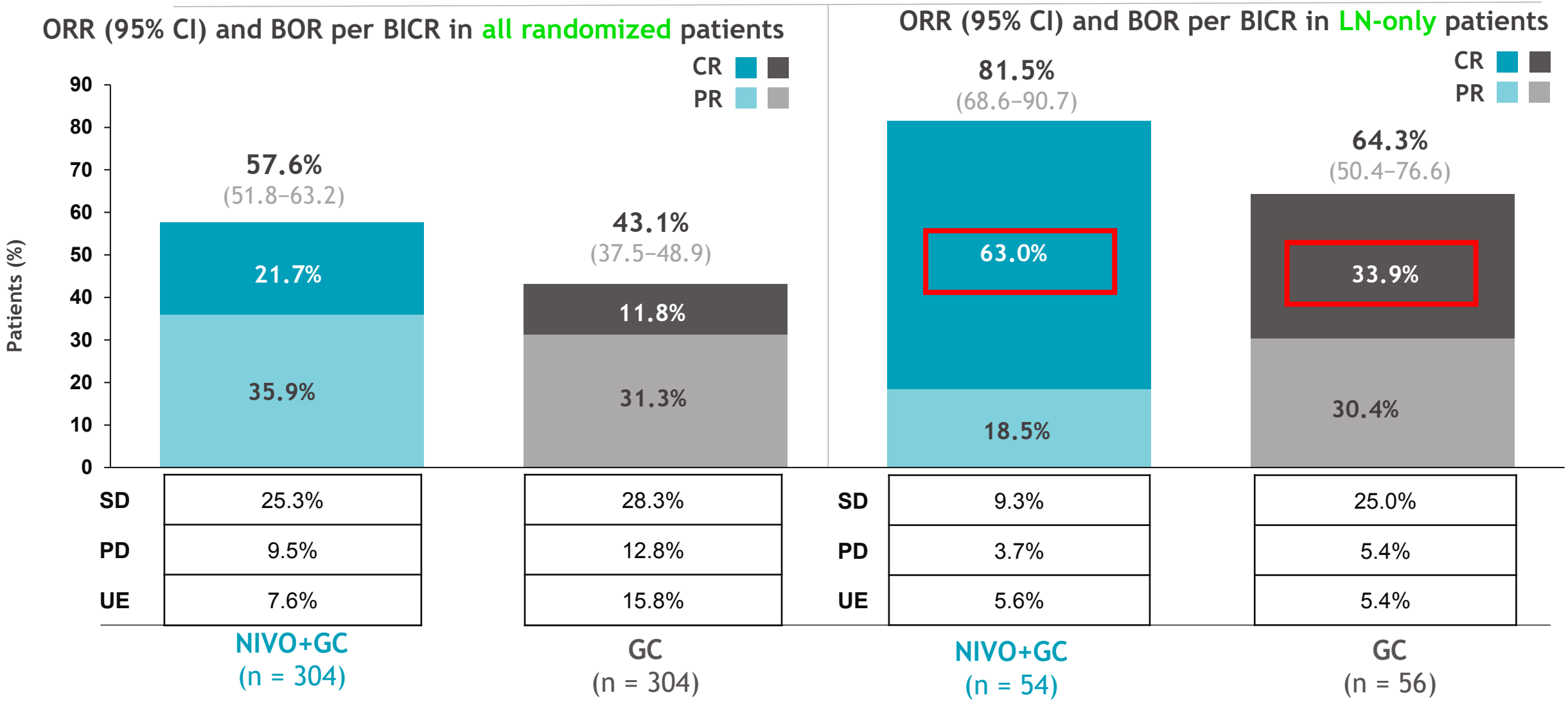
Complete response[d]	NIVO+GC (n = 66)	GC (n = 36)
Median TTCR (Q1-Q3), months	2.1 (1.9-2.2)	2.1 (1.9-2.2)
Median DoCR (95% CI), months	37.1 (18.1-NE)	13.2 (7.3-18.4)

Van Der Heijden*, Sonpavde G*, Powles T, et al. ESMO 2023, N Engl J Med 2023

Response per BICR: patients with LN-only mUC

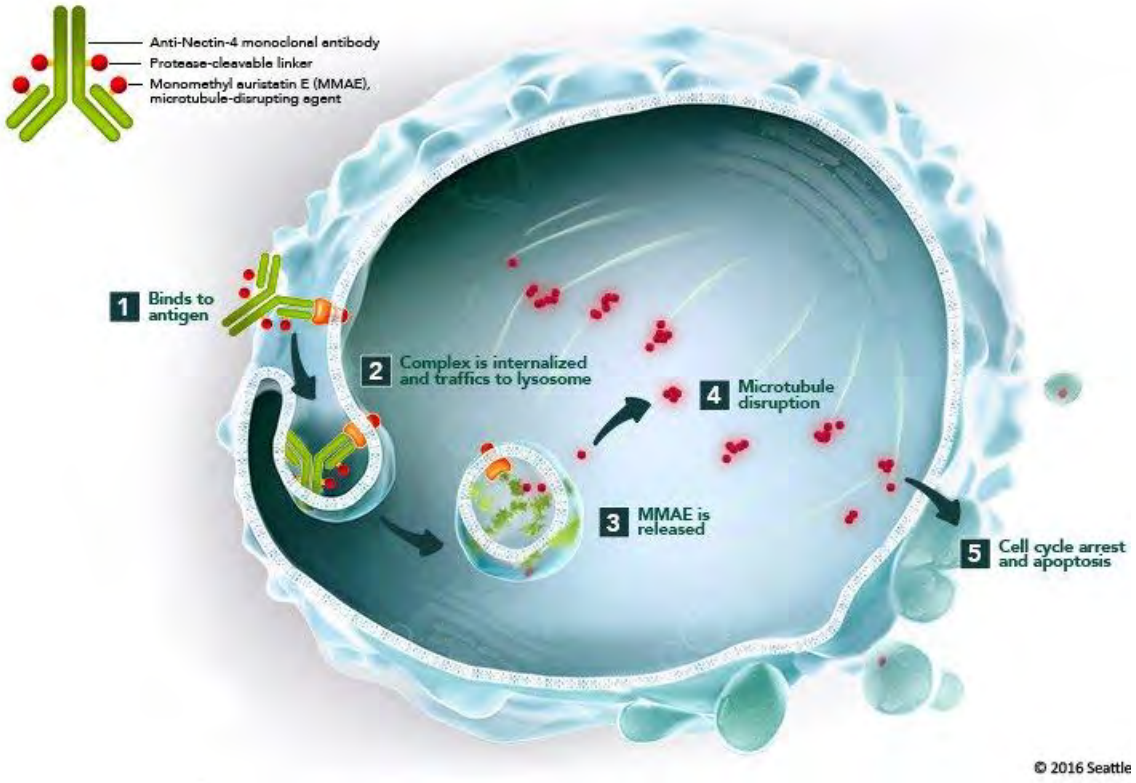
Galsky M, Sonpavde G, Powles T, et al. ASCO 24

- CR rates for NIVO+GC-treated patients with LN-only mUC were approximately twice that of GC-treated patients



Updated Results From the Enfortumab Vedotin Phase 1 (EV-101) Study in Patients With Metastatic Urothelial Cancer

J. Rosenberg,[1] S.S. Sridhar,[2] J. Zhang,[3] D. Smith,[4] J. Ruether,[5] T.W. Flaig,[6] J. Baranda,[7] J. Lang,[8] E.R. Plimack,[9] R. Sangha,[10] E. Heath,[11] J. Merchan,[12] D. Quinn,[13] S. Srinivas,[14] M. Milowsky,[15] C. Wu,[16] E. Gartner,[17] A. Melhem-Bertrandt,[16] D. Petrylak[18]



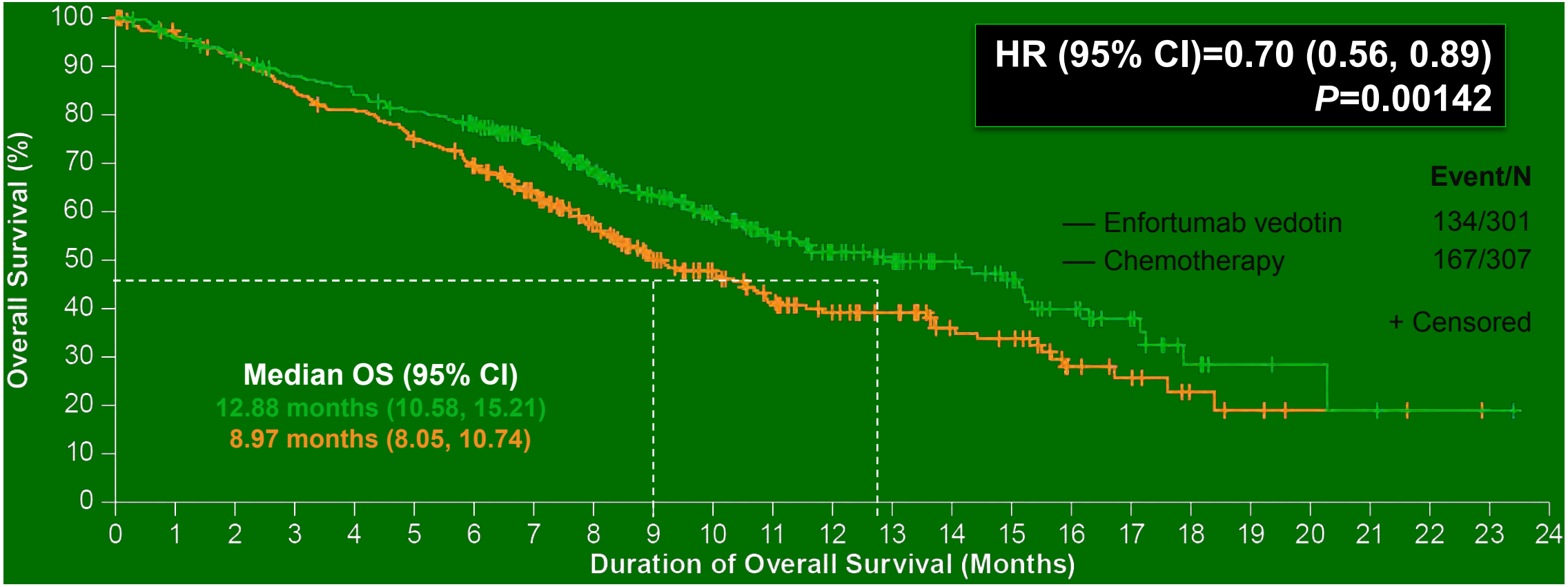
Monoclonal antibody **targeting Nectin-4**, conjugated by a protease-cleavable linker to the microtubule-disrupting agent **monomethyl auristatin E**

Nectin-4 is a transmembrane adhesion molecule, highly expressed in cancer, particularly UCC (93% in mUCC)

ORR 41% in chemo-treated mUC (n=112)

Rosenberg et al ASCO 2018

EV301: EV vs chemo post platinum & PD1/L1 inhibitor



Patients at risk (n)

Enfortumab vedotin	301	286	272	257	246	234	222	190	158	130	105	85	63	52	42	33	23	15	7	4	3	2	1	1	0
Chemotherapy	307	288	274	250	238	219	198	163	131	101	84	66	51	44	32	29	16	11	6	4	2	2	1	0	0

Data cut-off: July 15, 2020

EV301: Treatment-Related Adverse Events

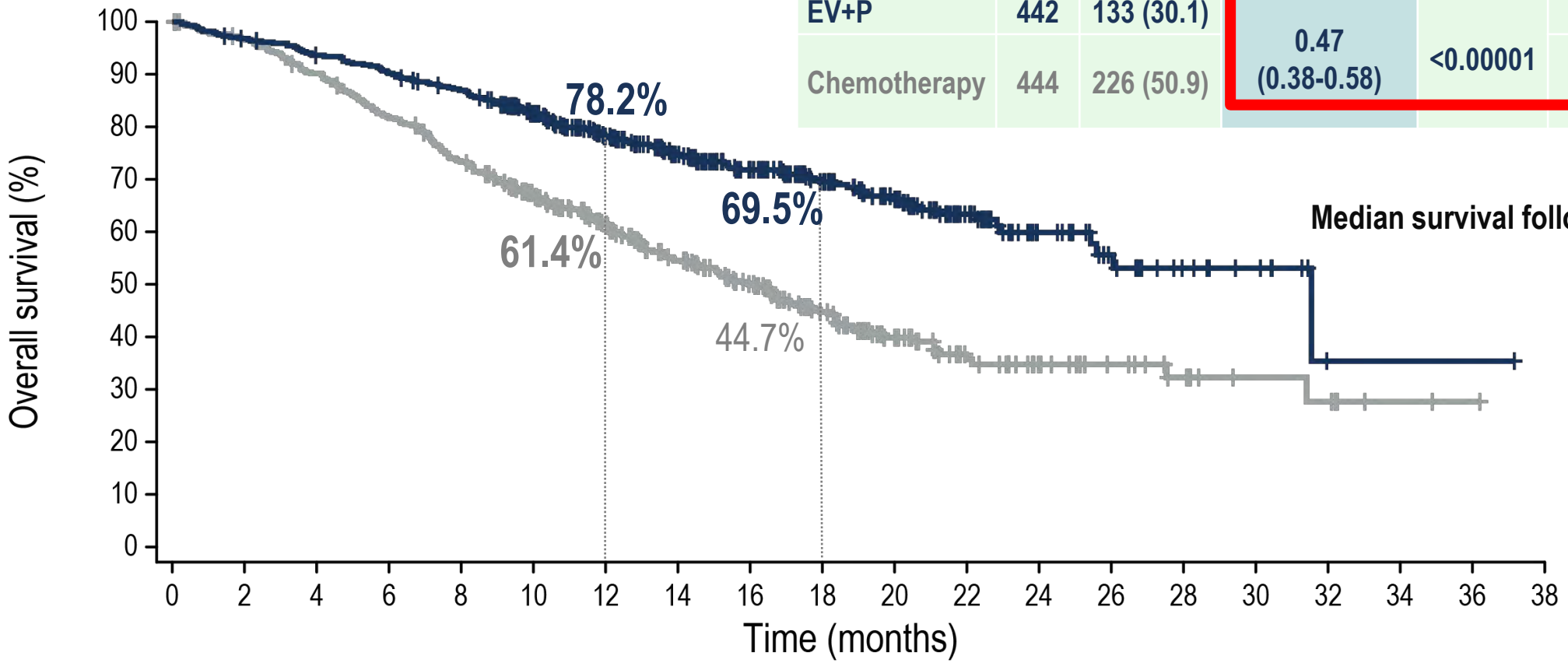
Table 2. Treatment-Related Adverse Events (Safety Population).*

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

Powles T et al. N Engl J Med2021;384:1125-1135

EV302 trial: Enfortumab-Vedotin + Pembrolizumab as first-line therapy for all-comers

	N	Events (%)	HR[a] (95% CI)	2-sided P value	mOS (95% CI), months
EV+P	442	133 (30.1)	0.47 (0.38-0.58)	<0.00001	31.5 (25.4-NR)
Chemotherapy	444	226 (50.9)			16.1 (13.9-18.3)



Median survival follow-up: 17.2 months

N at risk

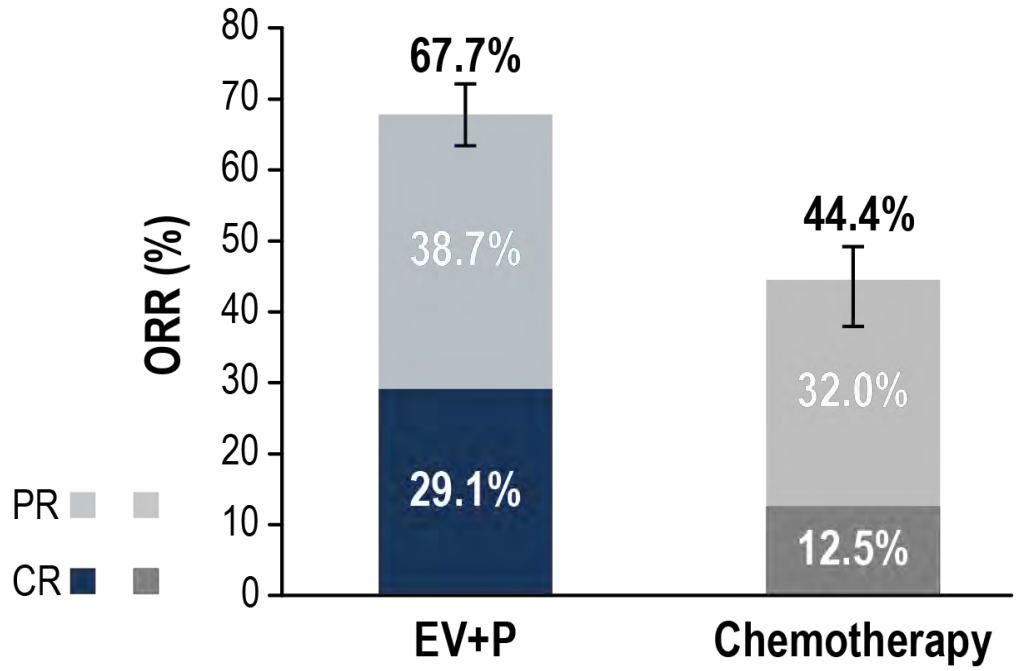
EV+P	442	426	409	394	376	331	270	222	182	141	108	67	36	22	12	8	1	1	1
Chemotherapy	444	423	393	356	317	263	209	164	125	90	60	37	25	18	12	7	6	2	1

Data cutoff: 08 Aug 2023

OS at 12 and 18 months was estimated using Kaplan-Meier method
mOS, median overall survival; NR, not reached
[a]Calculated using stratified Cox proportional hazards model. A hazard ratio <1 favors the EV+P arm

Powles et al. ESMO 2023; N Engl J Med 2024

EV302: Confirmed Overall Response per BICR



	EV+P (N=437)	Chemotherapy (N=441)
Confirmed ORR, n (%) (95% CI)	**296 (67.7) (63.1-72.1)**	**196 (44.4) (39.7-49.2)**
2-sided P value	<0.00001	
Best overall response[a], n (%)		
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)
Not evaluable/No assessment[b]	21 (4.8)	36 (8.2)

Median DOR (95% CI)	NR (20.2, NR)	7.0 (6.2, 10.2)

Data cutoff: 08 Aug 2023

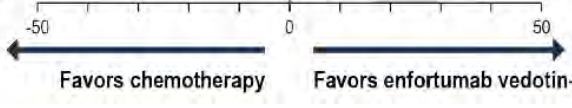
CR, complete response; DOR, duration of response; PR, partial response
[a]Best overall response according to RECIST v1.1 per BICR. CR or PR was confirmed with repeat scans ≥28 days after initial response
[b]Patients had either post-baseline assessment and the best overall response was determined to be not evaluable per RECIST v1.1 or no response assessment post-baseline

Powles et al. ESMO 2023; N Engl J Med 2024

EV-pembrolizumab: ORR in EV302 trial based on site of metastasis

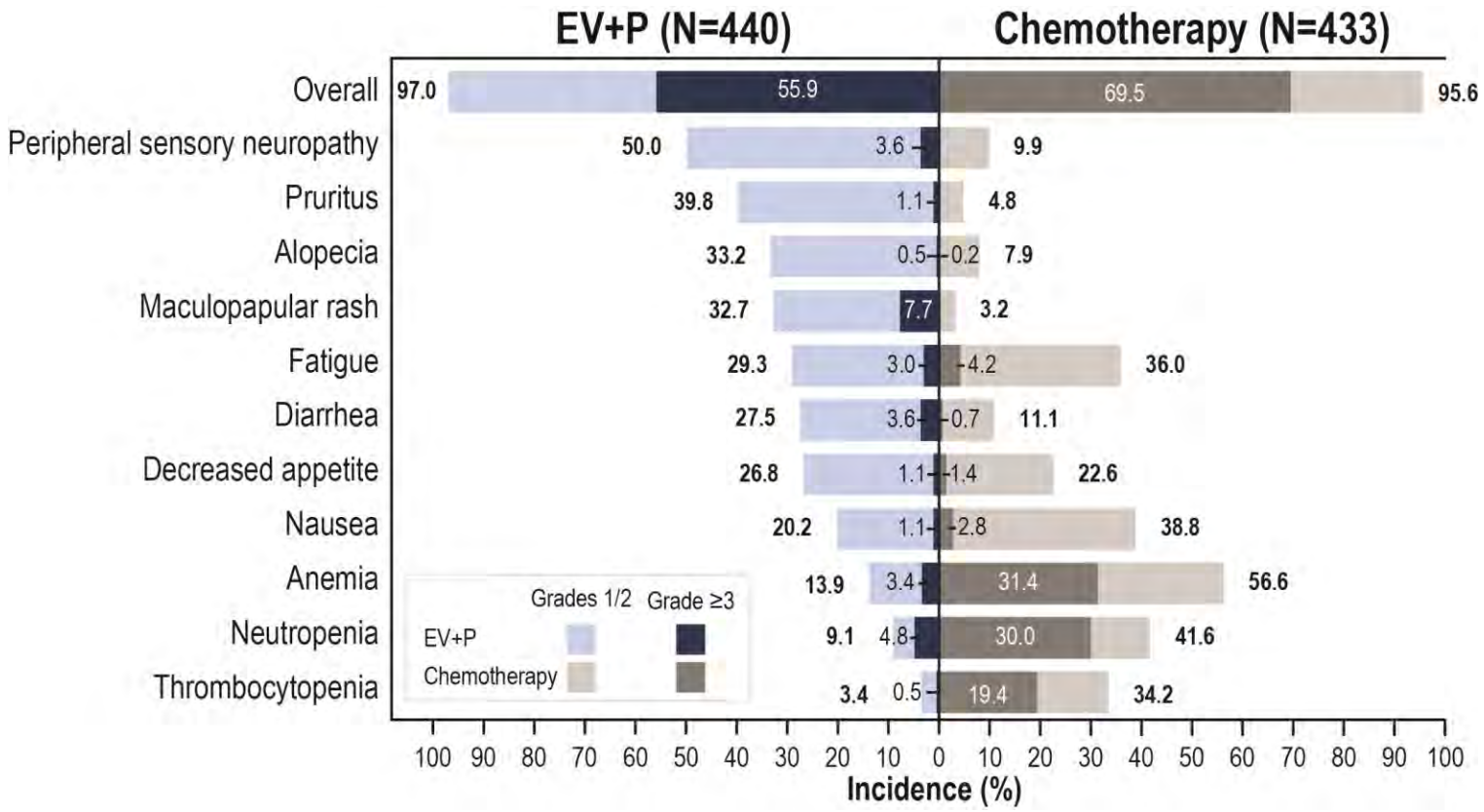
No striking differential activity in LN-only disease

Subgroup	Events/N: Enfortumab vedotin-pembrolizumab	Events/N: 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)
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 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			
0	161/222 (72.5)	106/213 (49.8)	22.8 (13.7–31.5)
1-2	135/215 (62.8)	89/226 (39.4)	23.4 (14.2–32.3)
Primary disease site of origin			
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)
Metastatic disease site			
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	111/163 (68.1)	72/160 (45.0)	23.1 (12.4–33.3)
Moderate/Severe	127/190 (66.8)	71/186 (38.2)	28.7 (18.7–38.0)



Powles et al. ESMO 23, NEJM 2024

EV302: Treatment-Related Adverse Events



Serious TRAEs:
- 122 (27.7%) EV+P
- 85 (19.6%) chemotherapy

TRAEs leading to death (per investigator):
EV+P: 4 (0.9%)
- Asthenia
- Diarrhea
- Immune-mediated lung disease
- Multiple organ dysfunction syndrome

Chemotherapy: 4 (0.9%)
- Febrile neutropenia
- Myocardial infarction
- Neutropenic sepsis
- Sepsis

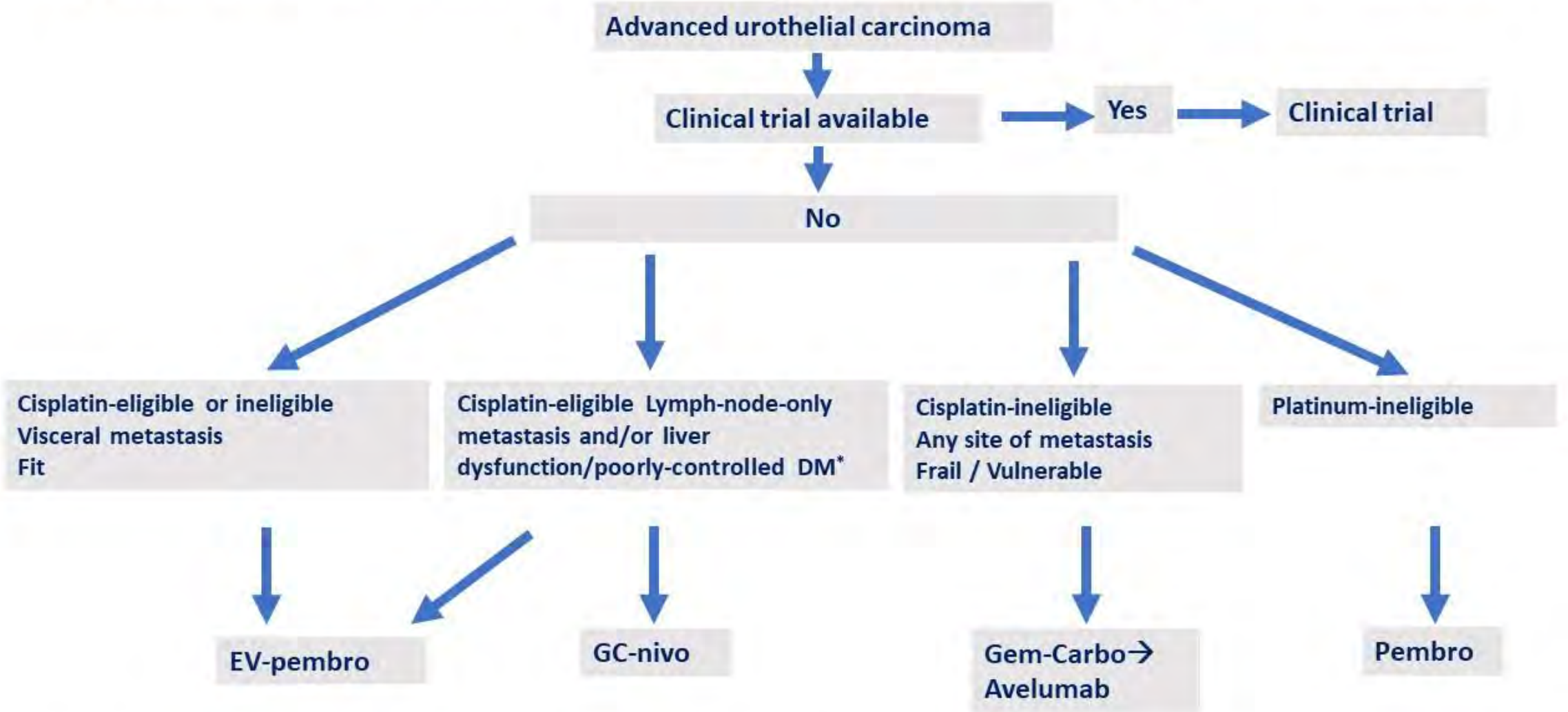
Median number of cycles (range): 12.0 (1,46) for EV+P; 6.0 (1,6) for chemotherapy

Data cutoff: 08 Aug 2023

TRAEs shown in figure are any grade by preferred term in ≥20% of patients for any grade in either arm
TRAEs, treatment-related adverse events

Powles et al. ESMO 2023; N Engl J Med 2024

Proposed schema for the first-line therapy of metastatic urothelial carcinoma



*All of these trials required satisfactory organ function and controlled comorbidities including DM, JAVELIN allowed Grade 2 neuropathy at baseline

Abbreviations: EV- Enfortumab Vedotin, pembro- Pembrolizumab, GC- Gemcitabine + Cisplatin, nivo- Nivolumab, Gem-Carbo- Gemcitabine + Carboplatin, DM- Diabetes Mellitus

Sonpavde G. ASCO Daily News April 2024

Updated Outcomes in TROPHY-U-01 Cohort 1, a Phase 2 Study of Sacituzumab Govitecan in Patients With Metastatic Urothelial Cancer Who Progressed After Platinum-Based Chemotherapy and a Checkpoint Inhibitor

Scott T. Tagawa,[1] Arjun V. Balar,[2] Daniel P. Petrylak,[3] Arash Rezazadeh Kalebasty,[4] Yohann Loriot,[5] Aude Fléchon,[6] Rohit K. Jain,[7] Neeraj Agarwal,[8] Manojkumar Bupathi,[9] Philippe Barthélémy,[10] Philippe Beuzeboc,[11] Phillip Palmbos,[12] Christos E. Kyriakopoulos,[13] Damien Pouessel,[14] Cora N. Sternberg,[1] Julia Tonelli,[15] Mitch Sierecki,[15] Huafeng Zhou,[15] and Petros Grivas[16]

Figure 1. Sacituzumab Govitecan Antibody-Drug Conjugate[6-8]

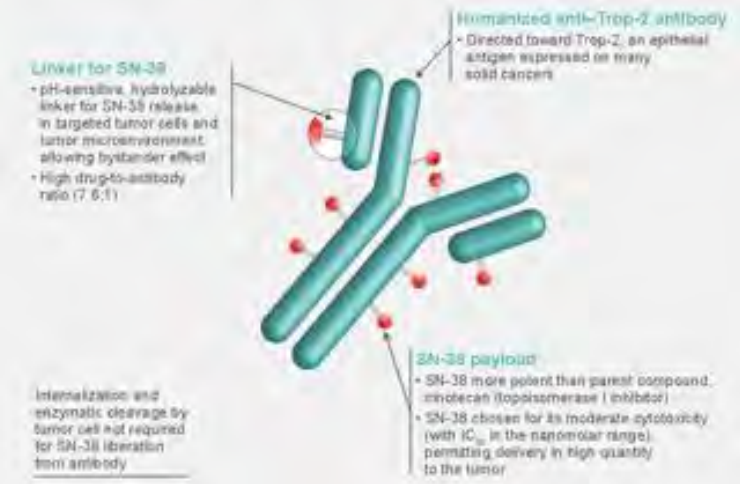


Table 1. Best Overall Response Rates

	Cohort 1 (N=113)
Best overall response, n (%)	
CR	6 (5)
PR	26 (23)
SD	37 (33)
PD	22 (19)
Not evaluable	8 (7)
Not assessed[a]	14 (12)
Objective response rate (CR + PR), n (%) [95% CI][b]	32 (28) [20.2-37.6]
Clinical benefit rate (CR + PR + SD ≥6 months), n (%) [95% CI]	43 (38) [29.1-47.7]

[a]Those patients had no post-baseline radiologic tumor assessments. [b]Primary endpoint.
CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease.

Figure 6. Progression-Free Survival

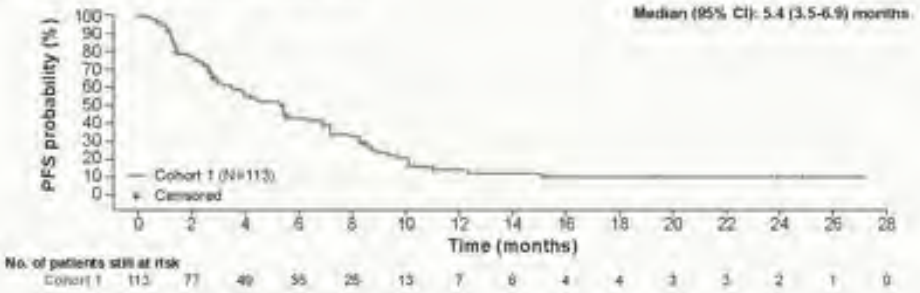
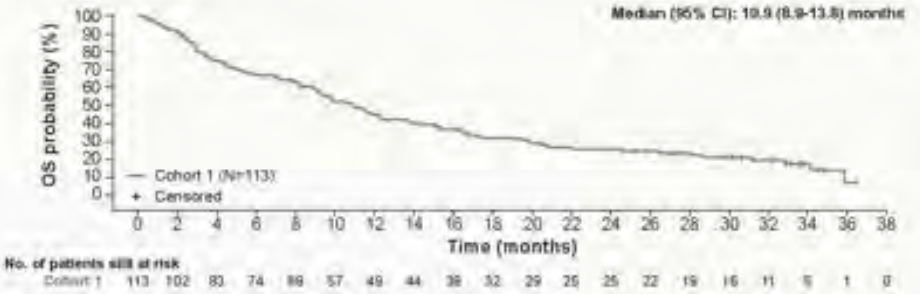
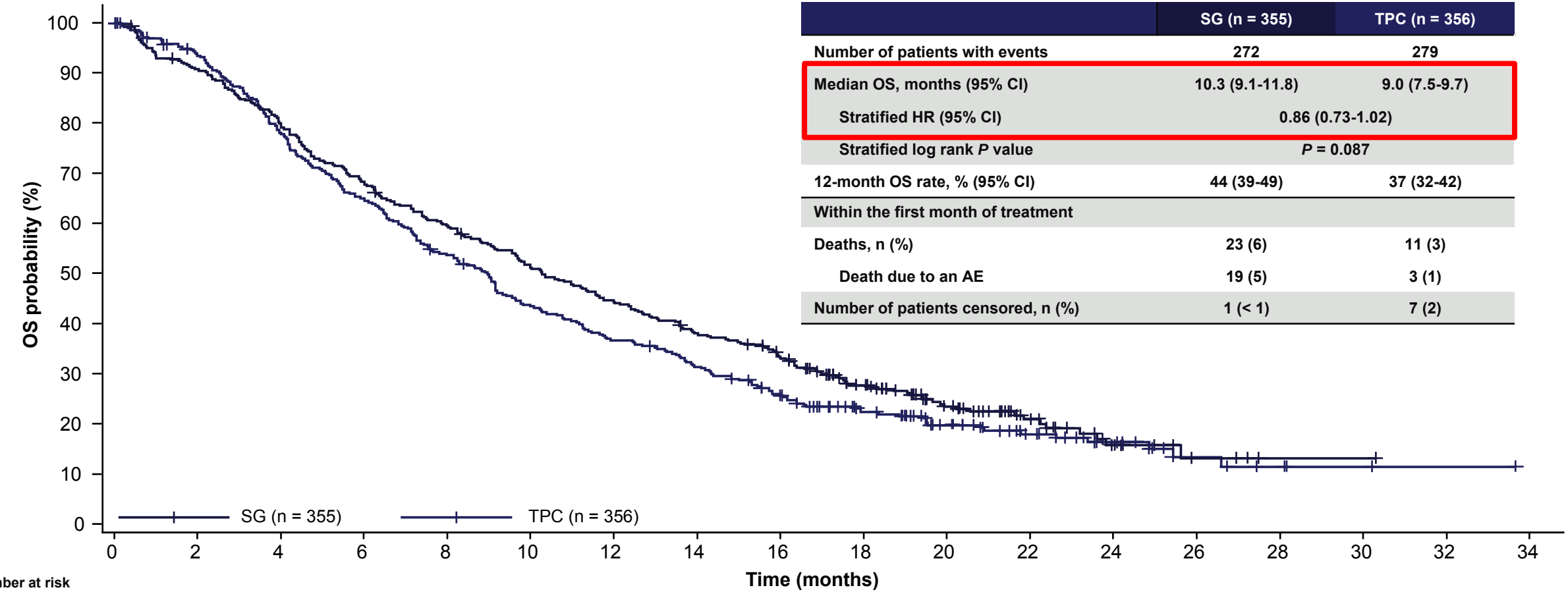


Figure 7. Overall Survival



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

TROPiCS-04: Overall Survival



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

Number at risk (events)

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

- While there was a trend toward favorable OS with SG, the primary end point of improved OS with SG vs TPC was not met

HR, hazard ratio; **OS**, overall survival; **SG**, sacituzumab govitecan; **TPC**, treatment of physician's choice.

Grivas P, et al. ESMO Asia, December 6-8, 2024, Singapore, Republic of Singapore

TROPiCS-04: G-CSF Use and Impact on AEs

Safety-Evaluable Patients, n (%)	SG n = 349	TPC n = 337
Any prophylaxis	128 (37)	87 (26)
Primary prophylaxis	74 (21)	73 (22)
Secondary prophylaxis	54 (15)	14 (4)
Therapeutic	106 (30)	33 (10)

- Primary prophylaxis was defined as G-CSF use on or after cycle 1 day 1 and prior to the onset of the first occurrence of neutropenia or no event of neutropenia
- Secondary prophylaxis was defined as G-CSF use after resolution of grade ≥ 2 neutropenia (to grade ≤ 1) or after occurrence of grade 1 neutropenia; and prior to any subsequent grade ≥ 2 neutropenia or no occurrence of subsequent grade ≥ 2
- G-CSF use was considered therapeutic if administered during grade ≥ 2 neutropenia

Patients Receiving SG, n (%)	With Primary Prophylactic G-CSF n = 74	Without Primary Prophylactic G-CSF n = 275
AESI neutropenia[a]	32 (43)	162 (59)
AESI neutropenia grade ≥ 3[a]	24 (32)	131 (48)
Febrile neutropenia	7 (9)	33 (12)
AESI serious infections secondary to neutropenia after the first AESI neutropenia[b]	1 (1)	22 (8)
Fatal infection secondary to neutropenia	2 (3)[c,d]	14 (5)

- **G-CSF primary prophylactic use was 21% and 22% with SG and TPC, respectively, in this population at high risk for febrile neutropenia**
- **Incidence of grade ≥ 3 neutropenia with or without primary prophylactic G-CSF was 32% and 48%, respectively**

[a]AESI neutropenia includes preferred terms: neutropenia, neutrophil count decreased, febrile neutropenia. [b]AESI serious infections secondary to neutropenia includes an AE with a preferred term from System Organ Class Infections and Infestations that was assessed as serious by the investigator and started on or within 11 days after start date of AESI neutropenia. [c]1 patient had a preexisting open wound/ulceration, underwent an invasive procedure without adequate (per protocol) healing before next SG, and did not receive prophylactic G-CSF with their last SG dose; the patient died of sepsis. Another patient had rapid tumor progression with kidney damage resulting on the placement of a nephrostomy tube without adequate healing before next SG (per protocol); the patient died of septic shock. [d]Includes 1 patient with serious infection occurring on 15 days after neutropenia, therefore outside the window of AESIs of serious infection secondary to neutropenia.
AE, adverse event; **AESI**, adverse event of special interest; **G-CSF**, granulocyte colony stimulating factor; **SG**, sacituzumab govitecan; **TPC**, treatment of physician's choice.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

ORIGINAL ARTICLE

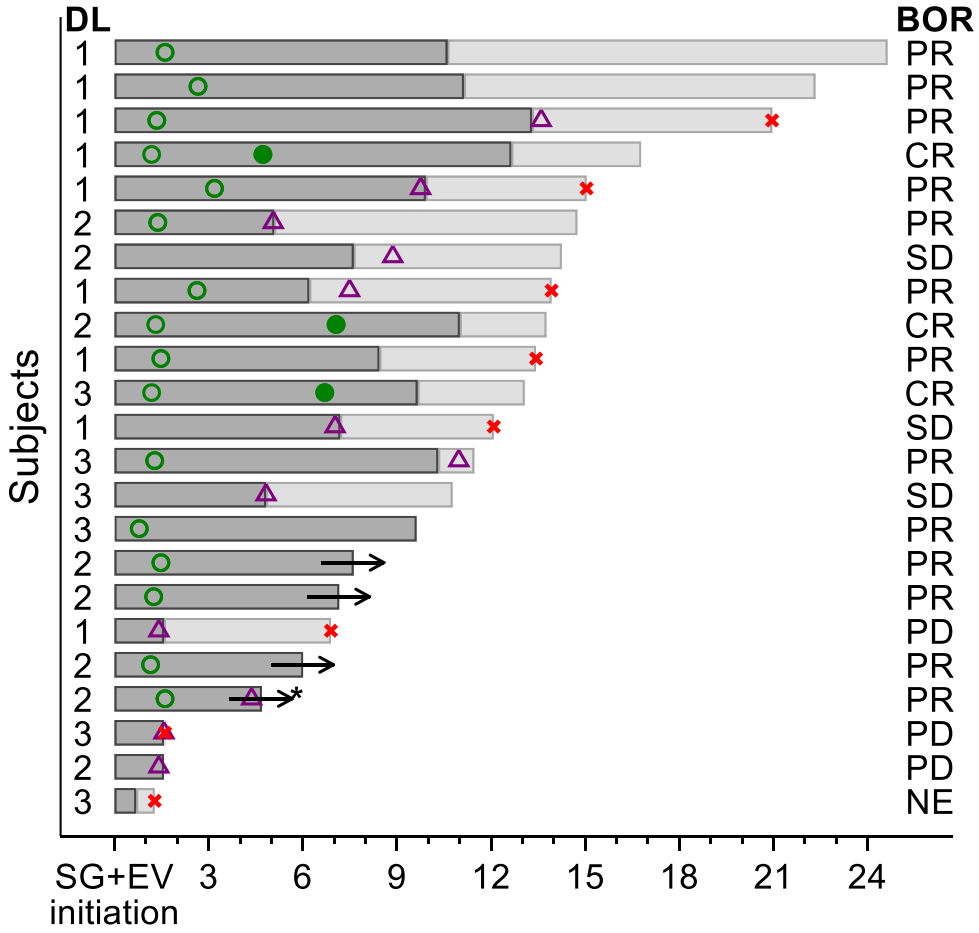
The Double Antibody Drug Conjugate (DAD) phase I trial: sacituzumab govitecan plus enfortumab vedotin for metastatic urothelial carcinoma☆

B. A. McGregor[1*†], G. P. Sonpavde[1,2†], L. Kwak[1], M. M. Regan[1], X. Gao[3], H. Hvidsten[1], C. M. Mantia[1], X. X. Wei[1], J. E. Berchuck[1], S. A. Berg[1], P. K. Ravi[1], M. D. Michaelson[3], T. K. Choueiri[1] & J. Bellmunt[1*]

[1]Dana Farber Cancer Institute, Harvard Medical School, Boston; [2]Advent Health Cancer Institute and the University of Central Florida, Orlando; [3]Massachusetts General Hospital, Harvard Medical School, Boston, USA

Available online 21 October 2023

	Overall (N=23)	DL1 (N=9)	DL2 (N=8)	DL3 (N=6)
Objective Response Rate, % (95% CI)	70 (47-87)	78 (40-97)	75 (35-97)	50 (12-88)
Best Overall Response				
CR	3	1	1	1
PR	13	6	5	2
SD	3	1	1	1
PD	3	1	1	1
NE	1	0	0	1
Total	23	9	8	6



* Despite disease progression, this patient continues treatment based on clinical benefit per her study MD.

Three patients who initially met the criteria for PR achieved CR later.

Abstract # 603
Poster Bd # G9

Datopotamab deruxtecan in advanced/ metastatic urothelial cancer: Results from the phase 1 TROPION-PanTumor01 study

Aaron Lisberg,[1a] Alexandra Drakaki,[1ab] Funda Meric-Bernstam,[2] Omar Alhalabi,[3] Takahiro Kojima,[4] Manabu Kato,[4] Alexander Spira,[5] Mohamad A. Salkeni,[5] Rebecca Heist,[6] Xin Gao,[6] Manali Bhave,[7] Gunnar Klauss,[8] Hayato Sakaki,[9] Yasuyuki Kakurai,[10] Takahiro Kogawa[11]

[a]Indicates co-first authors. [b]Indicates presenting author.

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Objective

- To assess the safety, tolerability, and antitumor activity of Dato-DXd 6 mg/kg in patients with advanced/metastatic urothelial cancer treated with ≥1 prior line of therapy (including a checkpoint inhibitor) in the advanced setting

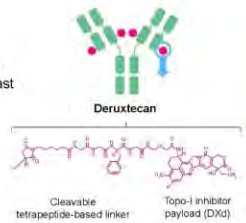
Conclusions

- In this interim analysis of the ongoing Phase 1 TROPION-PanTumor01 study, Dato-DXd demonstrated encouraging antitumor activity and a manageable safety profile in patients with pretreated advanced/metastatic urothelial cancer
  - Confirmed ORR was 19.2% ([95% CI, 6.6–39.4]1 CR and 4 PR) in all response-evaluable patients regardless of follow-up time and 22.7% (95% CI 7.8–45.4) in patients with at least 2 post-baseline tumor assessments
  - Tumor burden reduction was observed in 82% of evaluable patients
- TEAEs were primarily grade 1 or 2; stomatitis, nausea, and fatigue were the most frequently reported
- Enrollment in this cohort is now complete, and updated efficacy and safety data will be presented at a future meeting
- Dato-DXd is being further evaluated as a monotherapy and in combination in patients with urothelial cancer in the phase 1/2 TROPION-PanTumor02 (NCT05460273) and the phase 2 TROPION-PanTumor03 (NCT05489211) studies[7,8]

Introduction

- Dato-DXd is an ADC composed of a TROP2-directed IgG1 monoclonal antibody covalently linked to a highly potent cytotoxic topoisomerase I inhibitor payload via a plasma-stable, tumor-selective, tetrapeptide-based cleavable linker[1]
- In the Phase 1 TROPION-PanTumor01 study, Dato-DXd has previously shown encouraging antitumor activity and a manageable safety profile in patients with HR+/HER2- breast cancer, triple-negative breast cancer, and advanced/ metastatic NSCLC[2–4]
- Dato-DXd demonstrated significant improvements in PFS vs SOC in two Phase 3 trials:
  - TROPION-Lung01 (NCT04656652) met the primary endpoint of PFS, showing significant improvement vs docetaxel in patients with previously-treated advanced NSCLC[5]
  - TROPION-Breast01 (NCT05104866) met the primary endpoint of PFS, showing significant improvement vs investigator's choice of chemotherapy in patients with previously treated metastatic HR+/HER2- breast cancer[6]
- Here, we present the first interim results from patients with advanced/metastatic urothelial cancer in this actively enrolling cohort of TROPION-PanTumor01

Dato-DXd: Humanized anti-TROP2 IgG1 mAb



Plain language summary

Please scan this quick response (QR) code with your smartphone camera or app to obtain a copy of the plain language summary. Alternatively, please click on the link below.

Poster presented at ASCO GU, January 25–27, 2024, San Francisco, USA

Corresponding author email address: ADrakaki@mednet.ucla.edu

Methods

Study design

- TROPION-PanTumor01 (NCT03401385) is an ongoing phase 1, multicenter, open-label, 2-part dose-escalation and -expansion study evaluating Dato-DXd in patients with previously treated advanced solid tumors, including urothelial cancer (renal pelvis, ureters, urinary bladder, and urethra)
- The study design for this patient cohort is shown in **Figure 1**
- The response evaluable population in this ongoing study included patients who received at least one dose of Dato-DXd and had tumor assessments at both baseline and post-baseline; patients who discontinued Dato-DXd and had baseline tumor assessment but lacked post-baseline assessment were also included

Figure 1. TROPION-PanTumor01 study design

Results

Patients

Table 1. Baseline characteristics and prior treatments

Characteristic	All patients (N=33)
Age, median (range), years	67 (46–83)
Female, n (%)	7 (21)
ECOG PS, n (%)	
0	18 (55)
1	15 (46)
Site, n (%)	
USA	21 (64)
Japan	12 (36)
Number of prior lines of therapy, n (%)[a]	
1	1 (3)
2	6 (18)
≥3	25 (76)
Prior systemic treatment, n (%)	32[a] (97)
Immune checkpoint inhibitors	31 (94)
Platinum-based chemotherapy	27 (82)
Taxanes	5 (15)
Enfortumab vedotin	26 (79)
History of brain metastasis, n (%)	
Yes	1 (3)
No	31 (94)

[a]Data for one patient was missing at DCO. The maximum number of prior therapies was 6.

- At data cut-off (DCO, September 14, 2023), thirty-three patients were enrolled and treated with Dato-DXd 6 mg/kg Q3W (**Table 1**)
- Sixteen (49%) patients had treatment ongoing, and 17 (52%) patients had discontinued, primarily due to disease progression
- The median study duration was 9.0 (range, 0–21) months and the median treatment duration was 2.8 (range, 0.7–12.8) months

Efficacy

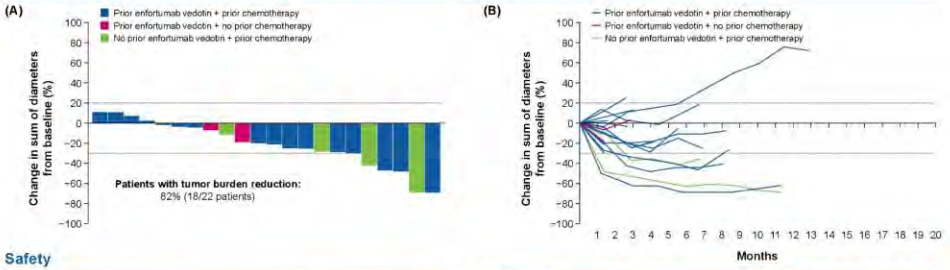
Table 2. Tumor response by BICR

Response, n (%)	All response-evaluable patients (N=26)[a]	Patients with 2 post-baseline scans (N=22)[b]
ORR (confirmed)	5 (19.2)	5 (22.7)
(95% CI)	(6.6, 39.4)	(7.8, 45.4)
CR	1 (3.8)	1 (4.5)
PR	4 (15.4)	4 (18.2)
Non-CR/non-PD	1 (3.8)	1 (4.5)
SD	15 (57.7)	11 (50.0)
DCR	21 (80.8)	17(77.3)
(95% CI)	(60.6, 93.4)	(54.6, 92.2)
PD	3 (11.5)	3 (13.6)
NE	2 (7.7)[c]	2 (9.1)[c]

[a]7 patients without tumor assessment at baseline and/or a post-baseline were excluded from the response-evaluable population. [b]Patients who discontinued study treatment before 2 scans were also included. [c]NE due to no adequate post-baseline tumor assessment.

- The abstract (ASCO GU 2024, abstract #603), presented efficacy from 18 patients who were enrolled and response-evaluable at the May 18, 2023, DCO. Confirmed ORR was 27.8% (95% CI, 9.7–53.5; 5/18 patients)
- At the September 14, 2023, DCO presented in this poster, among 26 response-evaluable patients (regardless of follow-up time), the confirmed ORR was 19.2% (95% CI, 6.6–39.4; **Table 2**)
  - Duration of response ranged from 2.6 to 10.1+ months (+ indicates ongoing treatment at DCO)
  - In total, 80% (95% CI, 20–97) of responders had ongoing responses for ≥6 months per Kaplan-Meier estimate
- Among 22 patients with at least 2 post-baseline tumor assessments, ORR was 22.7% (95% CI, 7.8–45.4)
- Tumor burden reduction was observed in 82% of evaluable patients (**Figure 2A**)

Figure 2. Change in tumor burden from baseline per BICR (A) Best change (N=22) and (B) Change over time (N=22)



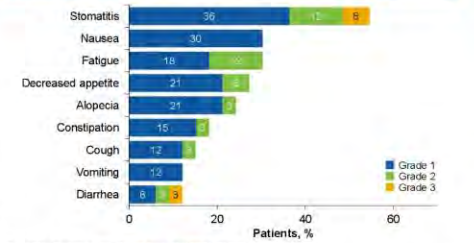
Safety

Table 3. Safety summary

TEAE, n (%)	All patients (N=33)
TEAEs	
Any grade	30 (91)
Grade ≥3	11 (33)
Drug-related	29 (88)
Grade ≥3	3 (9)
Serious TEAEs	
Any grade	7 (21)
Grade ≥3	6 (18)
Drug-related	0
Dose adjustments due to TEAEs	
Dose reduction	5 (15)
Dose interruption	9 (27)
Treatment discontinuation	2 (6)
TEAEs associated with death	0

- Any grade and grade ≥3 TEAEs were observed in 30 (91%) and 11 (33%) patients, respectively (**Table 3**)
  - No TEAEs associated with death were observed
- Drug-related TEAEs of any grade and grade ≥3 occurred in 29 (88%) and 3 (9%) patients
  - No drug-related serious TEAEs were reported
  - Nine (27%) patients had a TEAE associated with dose interruption and 5 (15%) patients had a TEAE associated with dose reduction

Figure 3. All-cause TEAEs occurring in ≥10% of patients[a]



[a]Owing to rounding, summed rates may not reflect total percentage of TEAEs.

- The most common TEAEs were stomatitis (55%), nausea (30%), and fatigue (30%) (**Figure 3**)
  - The most common grade ≥3 TEAEs were stomatitis (6%) and diarrhea (3%)
- The majority of TEAEs were grade 1–2; no grade 4 or 5 TEAEs were reported
- 61% of patients experienced an AESI, the majority of which were grade 1–2 (**Table 4**)

Table 4. AESIs[a]

	AESIs				AESIs leading to:		
n (%)	Any grade	Grade 1	Grade 2	Grade 3[b]	Dose reduction	Dose interruption	Treatment discontinuation
Oral mucositis/stomatitis[a]	18 (55)	12 (36)	4 (12)	2 (6)	1 (3)	1 (3)	0
Ocular surface events[b]	5 (15)	3 (9)	2 (6)	0	1 (3)	2 (6)	0
IRR	2 (6)	1 (3)	1 (3)	0	0	1 (3)	0
Adjudicated drug-related ILD[c]	1 (3)	0	1 (3)	0	0	1[c] (3)	0

[a]Events included the selected PTs oral mucositis/stomatitis, oropharyngeal pain, mouth ulceration, odynophagia, dysphagia, oral pain, glossitis, pharyngeal inflammation, aphthous ulcer, and oral mucosa erosion. [b]Ocular surface events included selected PTs from the corneal disorder SMQ and selected relevant PTs from the eye disorder SOC. [c]ILD includes events that were adjudicated as ILD and related to use of Dato-DXd (includes cases of potential ILD/pneumonitis based on MedDRA v26.0 for the narrow ILD SMQ, selected terms from the broad ILD SMQ, and PTs of respiratory failure and acute respiratory failure).

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1. Okajima D, et al. Mol Cancer Ther. 2021;20:2329–40. 2. Shimizu T, et al. J Clin Oncol. 2023;41:4670–87. 3. Meric-Bernstam F, et al. Presented at SABCS 2022, December 6–10, 2022; 4. Barda A, et al. Presented at SABCS 2022, December 6–10, 2022; 5. Ahn M, et al. Presented at ESMO 2023, October 20–24, 2023; 6. Barda A, et al. Presented at ESMO 2023, October 20–24, 2023; 7. ClinicalTrials.gov. Available at: https://clinicaltrials.gov/study/NCT05460273. Accessed November 8, 2023; 8. ClinicalTrials.gov. Available at: https://clinicaltrials.gov/study/NCT05489211. Accessed November 8, 2023.

Abbreviations

ADC, antibody-drug conjugate; AESI, adverse event of special interest; BICR, blinded independent central review; CI, confidence interval; CR, complete response; Dato-DXd, datopotamab deruxtecan; DCO, data cut-off; DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IgG1, immunoglobulin G1; ILD, interstitial lung disease; IRR, infusion-related reaction; mAb, monoclonal antibody; NE, non-evaluable; NSCLC, non-small cell lung cancer; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; PT, preferred terms; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; SMQ, standardized MedDRA queries; TEAE, treatment-emergent adverse event; Topo-I, topoisomerase I; TROP2, trophoblast cell-surface antigen 2.

Funding

This study is sponsored by Daiichi Sankyo, Inc. In July 2020, Daiichi Sankyo entered into a global development and commercialization collaboration agreement with AstraZeneca for datopotamab deruxtecan (Dato-DXd).

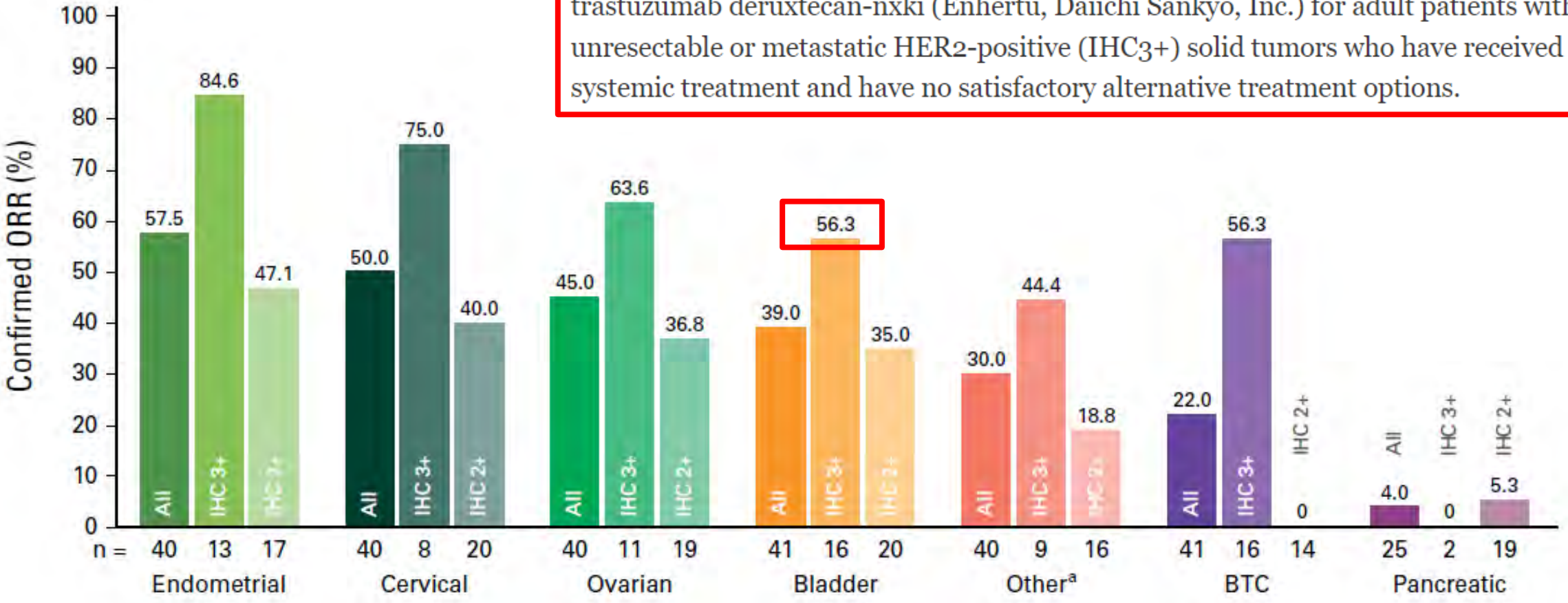
Acknowledgments

The authors would like to thank the patients, their families, and their caregivers for their participation, and the investigators and study staff for their contributions. We would also like to thank members of the Daiichi Sankyo study team for their valuable contributions to study conduct and analyses. Medical writing support, under direction of the authors, was provided by Jennie Pollard and editorial support was provided by Tina Allen and Isobel Markham, all of Core Medica, London, and funded by Daiichi Sankyo, Inc. in accordance with Good Publication Practice (GPP 2022) guidelines.

Trastuzumab-Deruxtecan (T-Dxd) approved by FDA for Her2 IHC 3+ tumors

HER2 binding ADC with Topo1 inhibitor payload

On April 5, 2024, the Food and Drug Administration granted accelerated approval to fam-trastuzumab deruxtecan-nxki (Enhertu, Daiichi Sankyo, Inc.) for adult patients with unresectable or metastatic HER2-positive (IHC3+) solid tumors who have received prior systemic treatment and have no satisfactory alternative treatment options.



Merc-Bernstam F, et al. J Clin Oncol 2023; 42:47-58

Toxicities of Trastuzumab Deruxtecan

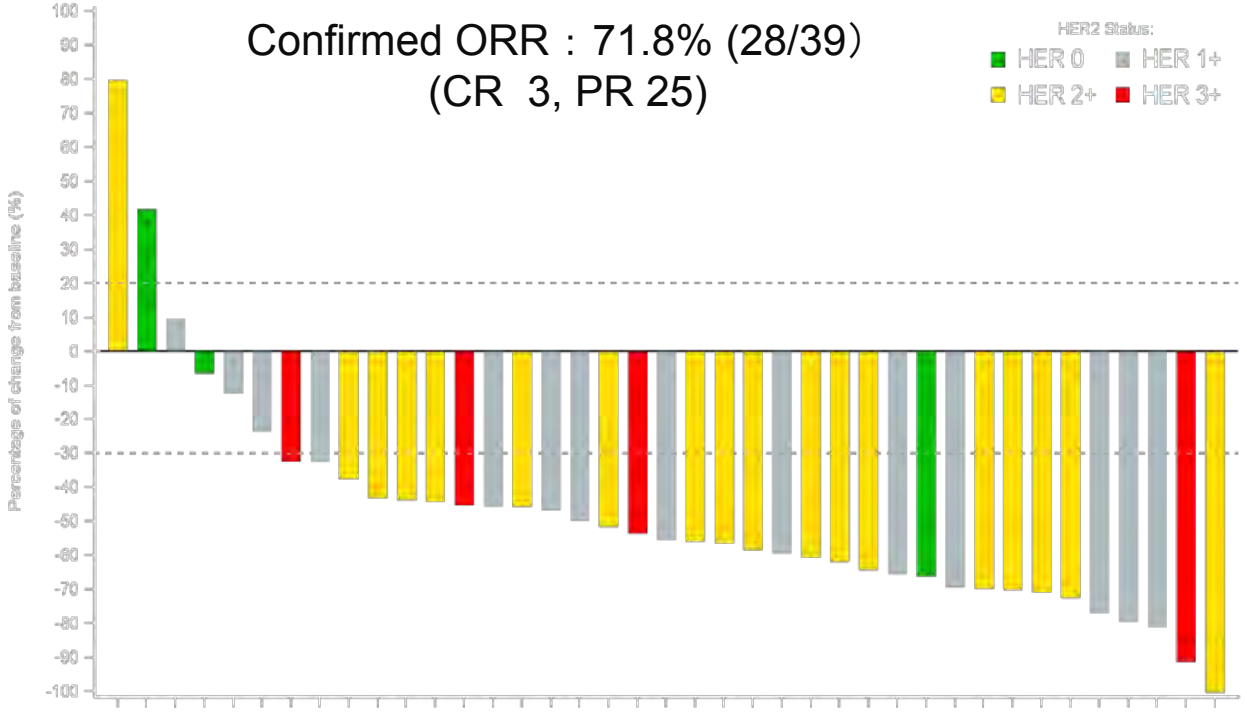
Adverse Event	Endometrial Cancer (n = 40)	Cervical Cancer (n = 40)	Ovarian Cancer (n = 40)	Bladder Cancer (n = 41)	Other Tumors (n = 40)	Biliary Tract Cancer (n = 41)	Pancreatic Cancer (n = 25)
Drug-related adverse events, No. (%)	36 (90.0)	36 (90.0)	34 (85.0)	38 (92.7)	34 (85.0)	33 (80.5)	15 (60.0)
Grade ≥3	14 (35.0)	19 (47.5)	21 (52.5)	17 (41.5)	15 (37.5)	16 (39.0)	7 (28.0)
Serious adverse events	4 (10.0)	3 (7.5)	11 (27.5)	4 (9.8)	6 (15.0)	5 (12.2)	3 (12.0)
Leading to discontinuation	3 (7.5)	3 (7.5)	1 (2.5)	4 (9.8)	6 (15.0)	5 (12.2)	1 (4.0)
Leading to dose modification[a]	13 (32.5)	13 (32.5)	18 (45.0)	15 (36.6)	13 (32.5)	13 (31.7)	0
Associated with death	2 (5.0)	0	0	1 (2.4)	1 (2.5)	0	0
Most common drug-related adverse events (>10% of total patients), No. (%)							
Nausea	29 (72.5)	26 (65.0)	22 (55.0)	21 (51.2)	23 (57.5)	19 (46.3)	7 (28.0)
Anemia	7 (17.5)	15 (37.5)	15 (37.5)	12 (29.3)	11 (27.5)	10 (24.4)	4 (16.0)
Diarrhea	16 (40.0)	15 (37.5)	8 (20.0)	13 (31.7)	6 (15.0)	8 (19.5)	3 (12.0)
Fatigue	10 (25.0)	9 (22.5)	11 (27.5)	11 (26.8)	12 (30.0)	9 (22.0)	4 (16.0)
Vomiting	16 (40.0)	10 (25.0)	7 (17.5)	6 (14.6)	15 (37.5)	9 (22.0)	3 (12.0)
Neutropenia	4 (10.0)	8 (20.0)	5 (12.5)	11 (26.8)	9 (22.5)	9 (22.0)	4 (16.0)
Decreased appetite	8 (20.0)	7 (17.5)	8 (20.0)	8 (19.5)	7 (17.5)	7 (17.1)	2 (8.0)
Asthenia	11 (27.5)	9 (22.5)	6 (15.0)	3 (7.3)	8 (20.0)	6 (14.6)	3 (12.0)
Alopecia	9 (22.5)	8 (20.0)	5 (12.5)	5 (12.2)	7 (17.5)	9 (22.0)	2 (8.0)
Thrombocytopenia	2 (5.0)	2 (5.0)	5 (12.5)	6 (14.6)	7 (17.5)	5 (12.2)	3 (12.0)

[a]Dose modification includes adverse events with action taken of dose reduced or drug interrupted. Adverse events associated with death included pneumonia (n = 1), organizing pneumonia (n = 1), pneumonitis (n = 1), and neutropenic sepsis (n = 1).

Merc-Bernstam F, et al. J Clin Oncol 2023; 42:47-58

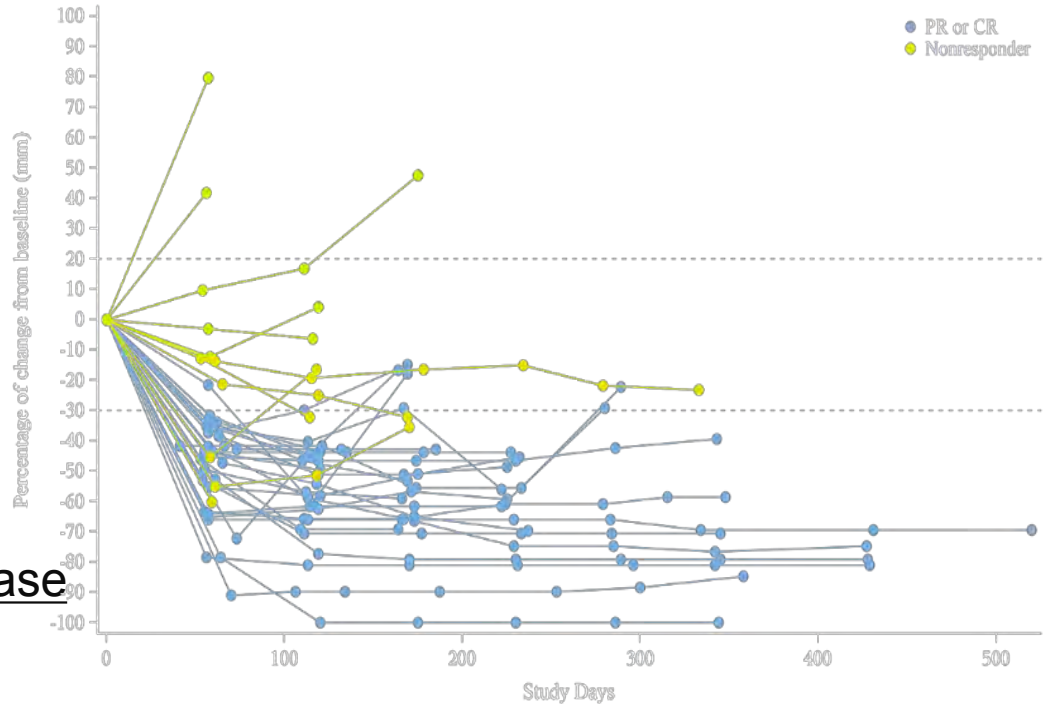
Disitamab Vedotin (Her2 targeting ADC with MMAE toxin & cleavable linker) + Toripalimab (PD1 inhibitor) is active in mUC

Confirmed ORR：71.8% (28/39)
(CR 3, PR 25)



Prior systemic treatment (n,%)

0 Line	25 (60.98%)
≥1 Lines	16 (39.02%)



ORR appeared higher in those with HER2 2-3+ (~86%) disease

Sheng et al. ASCO 2022, abstract 4518

BL-B01D1, an EGFR x HER3 Bispecific Antibody-drug Conjugate (ADC), in Patients with Locally Advanced or Metastatic Urothelial Carcinoma (UC)

Dingwei Ye[1]

Xiaojie Bian[1], Tiejun Yang[2], Shusuan Jiang[3], Manming Cao[4], Sa Xiao[5], Hongwei Wang[6], Hai Zhu[6], Yi Zhu[7]

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[4]Breast Oncology Dept., Zhujiang Hospital of Southern Medical University, Guangzhou, China;
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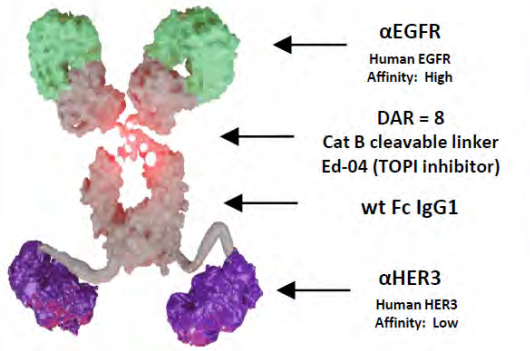
Shanghai, China 9/13/2024

Background

BL-B01D1 (EGFRxHER3 ADC)



wt: wild type; Cat B: cathepsin B; TOPI: Topoisomerase I
*: Chow NH, Chan SH, Tzai TS, Ho CL, Liu HS. *Clin Cancer Res.* 2001 Jul;7(7):1957-62.

- EGFR and HER3 are highly expressed in urothelial carcinoma* Targeting EGFR and HER3 could provide a promising therapeutic option for urothelial carcinoma.
- BL-B01D1 is a potential first-in-class (FIC) ADC consisting of an EGFRxHER3 bispecific antibody bound to a novel topoisomerase I inhibitor payload via a cleavable linker.
- Results for safety, tolerability and preliminary efficacy in previously treated patients with locally advanced or metastatic urothelial carcinoma (UC) in phase II study (BL-B01D1-201) are presented.

Preliminary Efficacy in UC

	2.2 mg/kg D1D8Q3W	
	Total (N = 27)[1]	1 Prior line of chemo (PBC or ADC) (N=12)[2]
Prior line of therapy, median (range)	2 (1-7)	1 (1-2)
Best Overall Response (BOR), n		
PR	11	9
Confirmed PR	9	9
SD	15	3
PD	0	0
NE	1	0
ORR, % (95%CI)	40.7 (22.4, 61.2)	75.0 (42.8, 94.5)
cORR, % (95%CI)	33.3 (16.5, 54.0)	75.0 (42.8, 94.5)
DCR, % (95%CI)	96.3 (81.0, 99.9)	100 (73.5, 100.0)
Median DOR (months) (95% CI)	NR (NR, NR)	NR (NR, NR)
6-month DOR rate, %, (95% CI)	100 (100.0, 100.0)	100 (100.0, 100.0)
Median PFS (months) (95% CI)	NR (4.2, NR)	NR (NR, NR)
6-month PFS rate, %, (95% CI)	62.4 (32.2, 82.2)	100 (100.0, 100.0)

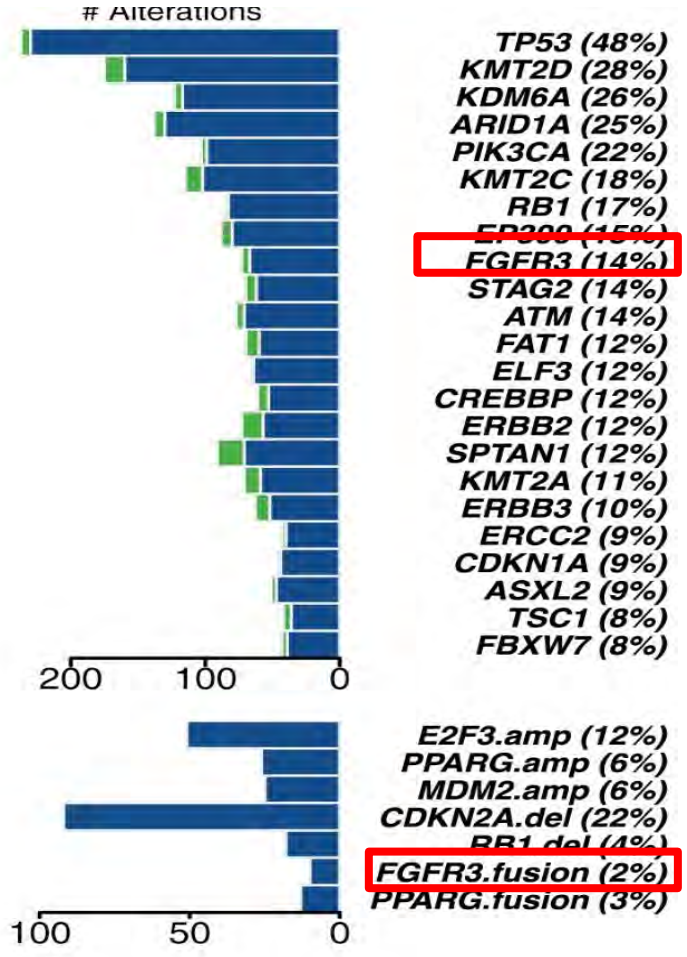
[1] Among of the 27 patients, 24 patients had received anti-PD-(L)1, 24 patients had received PBC, and 14 patients had received 1-2 prior lines of ADCs.
[2] Among of the 12 patients, 11 patients had received anti-PD-(L)1, 9 patients had received PBC, 2 patients had received ADCs, and 1 patient had received anti-PD-(L)1 + gemcitabine.
ORR was calculated based on response evaluable population defined as at least 1 post-baseline scan; CI: confidence interval; cORR: confirmed objective response rate; NE: not evaluable; NR: not reached; PD: progressive disease; PR: partial response; SD: stable disease.

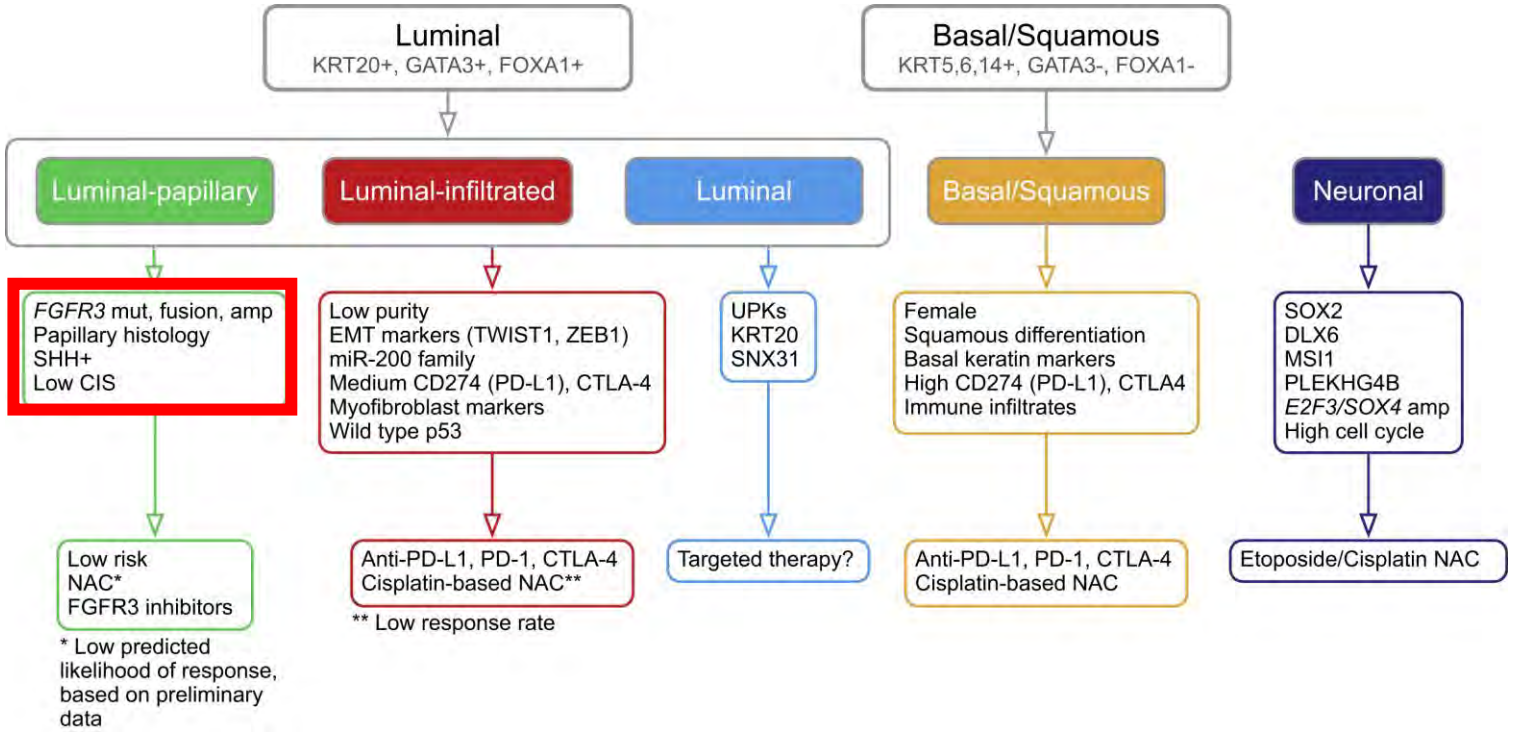
Data cutoff: June 30, 2024

Conclusions

- BL-B01D1 showed encouraging preliminary efficacy and favorable safety profile at 2.2 mg/kg D1D8 Q3W in previously treated urothelial carcinoma, especially at second line.
- Biomarker analysis demonstrated that clinical activity was seen across various levels of EGFR and HER3 expression.
- The most common TRAEs were hematological toxicities, which were manageable.
- The incidence and severity of toxicities related to EGFR and HER3 targeting were relatively low, and no new safety signals were observed.
- Given the promising results, plans are underway for registrational studies.

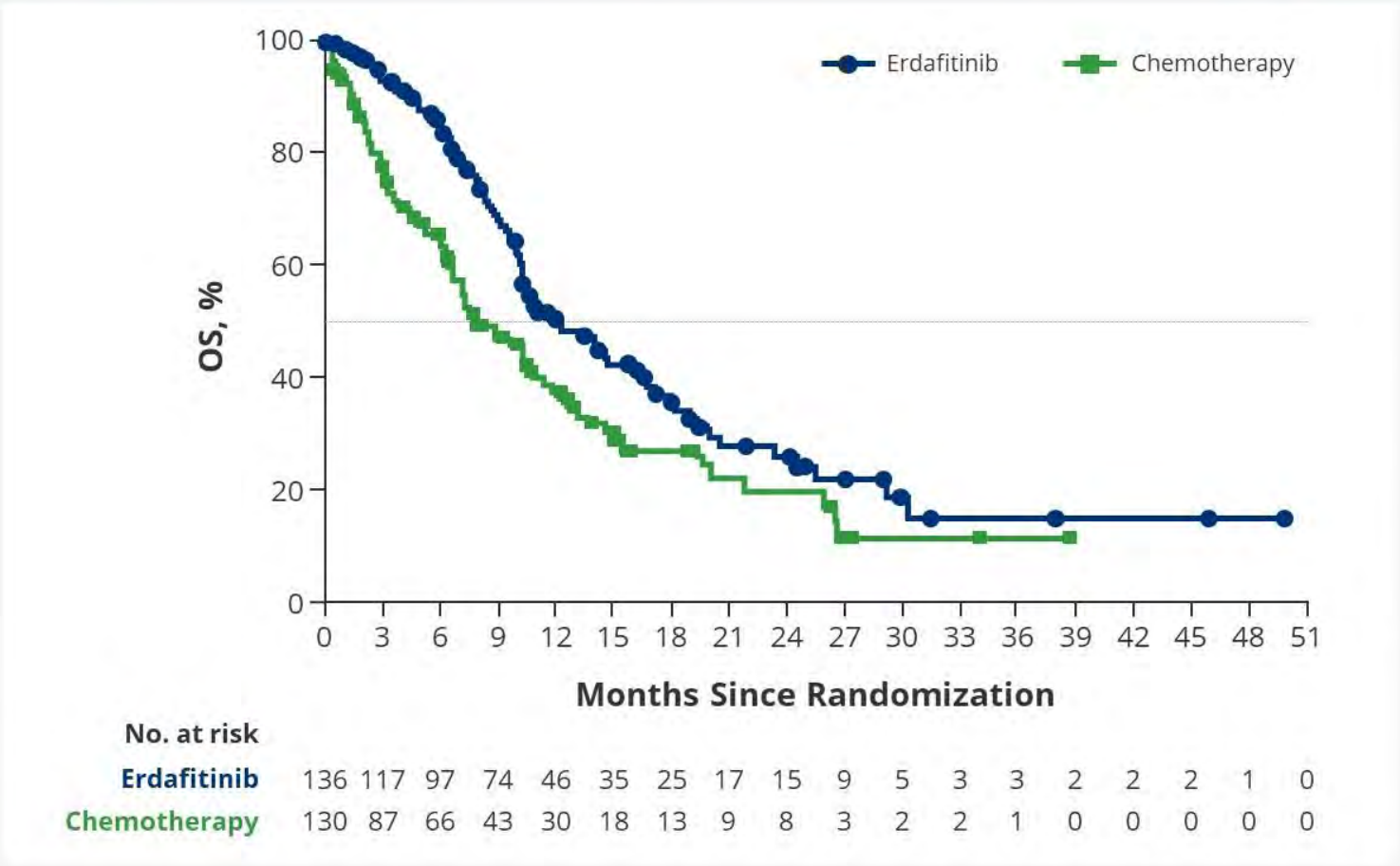
FGFR3 mutations and fusions are important therapeutic targets





Robertson AG, et al. **Comprehensive Molecular Characterization of Muscle-Invasive Bladder Cancer.** Cell. 2017 Oct 19;171(3):540-556.

Overall Survival for Erdafitinib Was Superior to Investigator's Choice of Chemotherapy

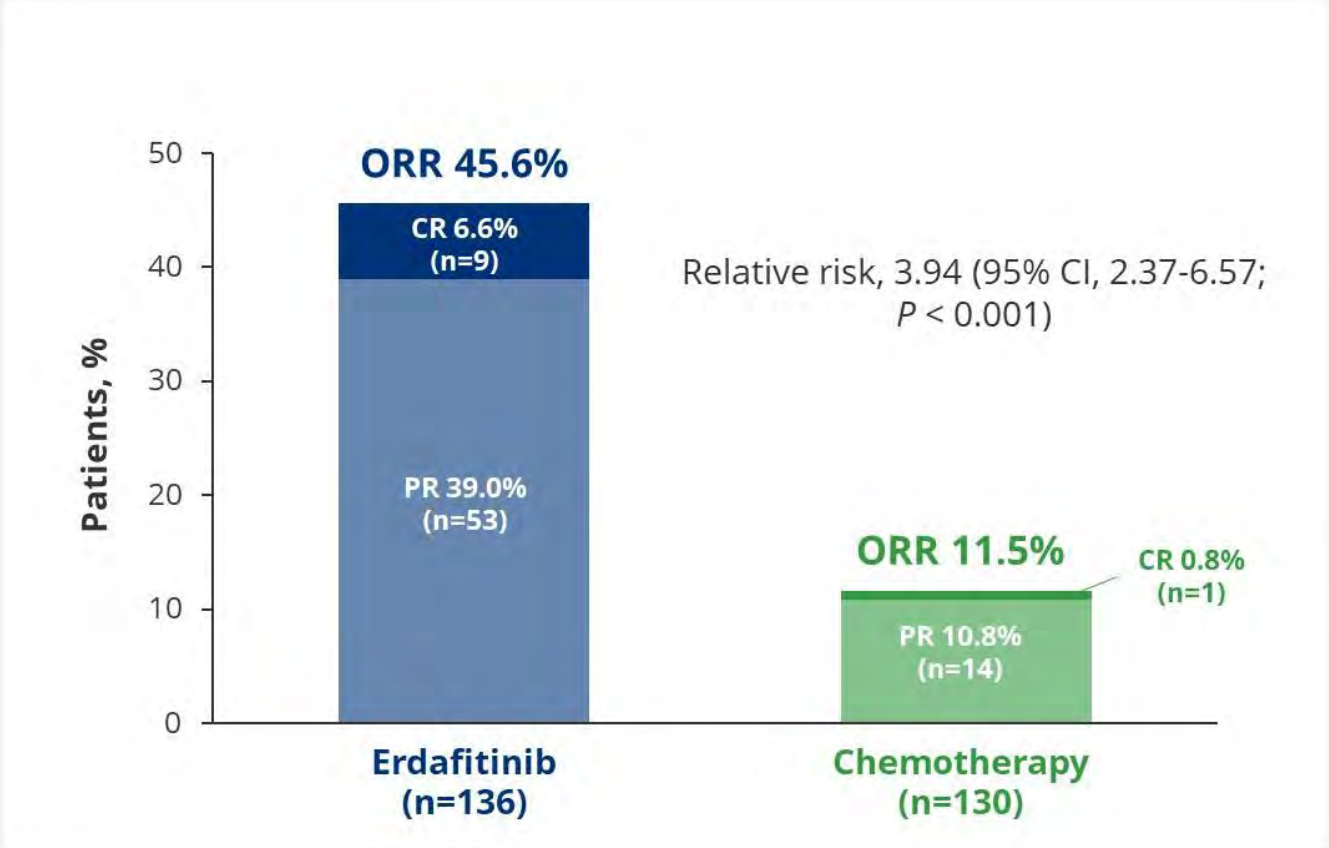


- Median follow-up was 15.9 months
- Median OS was 12.1 months for erdafitinib versus 7.8 months for chemotherapy
- Erdafitinib reduced the risk of death by 36% versus chemotherapy
  - HR, 0.64 (95% CI, 0.47-0.88; *P* = 0.005)[a]
- Based on these interim analysis results, the IDMC recommended to stop the study, unblind data, and cross over patients from chemotherapy to erdafitinib

CI, confidence interval; HR, hazard ratio; IDMC, independent data monitoring committee; OS, overall survival.
[a]The significance level for stopping for efficacy was p=0.019, corresponding to a HR of 0.69.

THOR trial. Loriot Y, et al. ASCO 2023, NEJM 2023.

Objective Response Rate Was Significantly Higher for Erdafitinib Versus Chemotherapy[a]



CI, confidence interval; CR, complete response; ORR, objective response rate; PR, partial response.
[a]Responses were best overall response per investigator assessment.

THOR trial. Loriot Y, et al. ASCO 2023, NEJM 2023

Toxicities of Erdafitinib: THOR trial

Event	Erdafitinib (N=135)				Chemotherapy (N=112)			
	Any Grade	Grade 1	Grade 2	Grade ≥3	Any Grade	Grade 1	Grade 2	Grade ≥3
	number (percent)							
Hyperphosphatemia	108 (80.0)	70 (51.9)	31 (23.0)	7 (5.2)	0	0	0	0
Diarrhea	84 (62.2)	49 (36.3)	31 (23.0)	4 (3.0)	19 (17.0)	7 (6.2)	9 (8.0)	3 (2.7)
Stomatitis	65 (48.1)	22 (16.3)	32 (23.7)	11 (8.1)	14 (12.5)	4 (3.6)	8 (7.1)	2 (1.8)
Dry mouth	53 (39.3)	45 (33.3)	8 (5.9)	0	4 (3.6)	4 (3.6)	0	0
Palmar–plantar erythrodysesthesia syndrome	41 (30.4)	6 (4.4)	22 (16.3)	13 (9.6)	1 (0.9)	0	1 (0.9)	0
Dysgeusia	37 (27.4)	28 (20.7)	8 (5.9)	1 (0.7)	8 (7.1)	5 (4.5)	3 (2.7)	0
Alanine aminotransferase increased	37 (27.4)	24 (17.8)	9 (6.7)	4 (3.0)	4 (3.6)	2 (1.8)	1 (0.9)	1 (0.9)
Constipation	36 (26.7)	24 (17.8)	12 (8.9)	0	31 (27.7)	13 (11.6)	16 (14.3)	2 (1.8)
Decreased appetite	36 (26.7)	18 (13.3)	14 (10.4)	4 (3.0)	23 (20.5)	10 (8.9)	10 (8.9)	3 (2.7)
Anemia	35 (25.9)	10 (7.4)	15 (11.1)	10 (7.4)	36 (32.1)	8 (7.1)	19 (17.0)	9 (8.0)
Alopecia	34 (25.2)	29 (21.5)	4 (3.0)	1 (0.7)	27 (24.1)	16 (14.3)	11 (9.8)	0
Dry skin	31 (23.0)	23 (17.0)	6 (4.4)	2 (1.5)	5 (4.5)	4 (3.6)	1 (0.9)	0
Onycholysis	31 (23.0)	9 (6.7)	14 (10.4)	8 (5.9)	1 (0.9)	0	1 (0.9)	0
Weight decreased	30 (22.2)	12 (8.9)	15 (11.1)	3 (2.2)	3 (2.7)	3 (2.7)	0	0
Aspartate aminotransferase increased	29 (21.5)	21 (15.6)	5 (3.7)	3 (2.2)	3 (2.7)	2 (1.8)	1 (0.9)	0
Onychomadesis	28 (20.7)	9 (6.7)	17 (12.6)	2 (1.5)	2 (1.8)	1 (0.9)	1 (0.9)	0
Nail discoloration	24 (17.8)	16 (11.9)	7 (5.2)	1 (0.7)	2 (1.8)	1 (0.9)	1 (0.9)	0
Dry eye	23 (17.0)	20 (14.8)	3 (2.2)	0	2 (1.8)	1 (0.9)	1 (0.9)	0
Asthenia	20 (14.8)	6 (4.4)	12 (8.9)	2 (1.5)	28 (25.0)	9 (8.0)	15 (13.4)	4 (3.6)
Nausea	20 (14.8)	10 (7.4)	8 (5.9)	2 (1.5)	27 (24.1)	15 (13.4)	10 (8.9)	2 (1.8)
Neutropenia	0	0	0	0	22 (19.6)	1 (0.9)	5 (4.5)	16 (14.3)
Fatigue	20 (14.8)	12 (8.9)	8 (5.9)	0	21 (18.8)	13 (11.6)	4 (3.6)	4 (3.6)

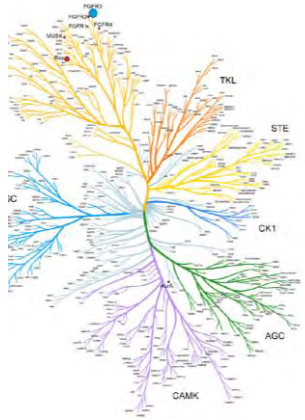
Novel FGFR3-specific agents

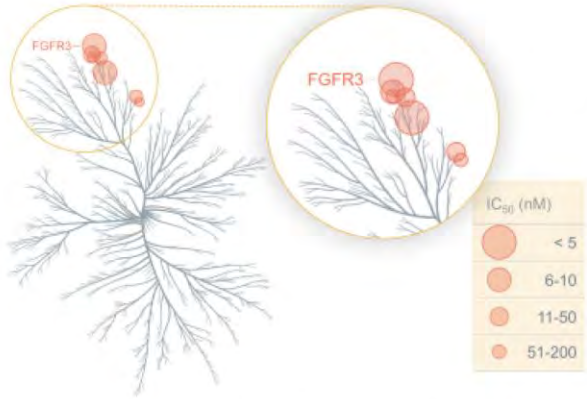
(FGFR1 and FGFR2 sparing)

Preclinical characterization of LOXO-435 (LOX-24350), a potent and highly isoform-selective FGFR3 inhibitor

Presented at: AACR-NCI-EORTC VIRTUAL INTERNATIONAL CONFERENCE ON MOLECULAR TARGETS AND CANCER THERAPEUTICS

Date: October 7, 2021





	TYRA-300	FGFR3 selectivity
FGFR3	1.6	1.0x
FLT4	2.1	1.3x
FGFR2	6.5	4.0x
FGFR4	11.0	6.9x
JAK2	35.5	22x
LTK	65.1	41x
FGFR1	108	68x
FLT1	201	126x
JAK3	206	129x

TYRA-300 was highly selective for FGFR3 over other protein kinases

	Enzyme Inhibition				Fold Selectivity	
	FGFR1 IC_{50} (nM)	FGFR2 IC_{50} (nM)	FGFR3 IC_{50} (nM)	FGFR3 V555M IC_{50} (nM)	FGFR3 over FGFR1	FGFR3 over FGFR2
Erdafitinib	0.3	0.6	0.2	1218.0	1.5x	2.0x
Pemigatinib	0.5	0.3	1.0	752.0	0.5x	0.3x
Infigratinib	0.4	0.7	0.3	579.8	1.3x	0.6x
Futibatinib	0.7	0.4	0.4	14.4	1.8x	1.8x
LOXO-435	108.2	19.7	0.3	1.1	361x	66x

Enzymatic IC_{50} (nM) of TYRA-300 and other approved or late-stage clinical compounds

Kinase Domain	Alteration	erdafitinib	futibatinib	pemigatinib	infigratinib	TYRA-300
FGFR3 WT		0.6	2.3	1.3	2.0	1.6
FGFR3 [K650E]	A-loop Activator	1.0	3.7	3.9		2.8
FGFR3 [K650M]	A-loop Activator	1.4	5.9	9.6		2.3
FGFR3 [V555L]	Gatekeeper	19.7	175	206		1.5
FGFR3 [V555M]	Gatekeeper	90.6	1509	530	662	2.0

Ratios of Resistance Mutations Compared to Unmutated (Fold Difference in IC50)

FGFR3 [K650E]	A-loop Activator	1.7x	1.6x	3.0x		1.8x
FGFR3 [K650M]	A-loop Activator	2.3x	2.6x	7.4x		1.4x
FGFR3 [V555L]	Gatekeeper	33x	76x	159x		0.9x
FGFR3 [V555M]	Gatekeeper	151x	656.0x	408x	331x	1.3x

All assays run at Km of ATP for individual enzymes

Ongoing First-Line Phase III Trials in Advanced UC

Trial	Strategy	Experimental Arm(s)	Standard Arm	Endpoint
CM-901	PD-1 + CTLA-4	Nivo + Ipi*	Gem-Platinum	OS in cis-inelig
NILE	PD-L1 +/- CTLA-4 (+ Chemo)	Durvalumab + Gem-Plat OR Durva + Treme + Gem-Plat	Gem-Platinum	PFS, OS
NCT05302284 (Her2+)	Her2 ADC + PD1	Disitamab Vedotin + Pembro	Gem-Platinum	PFS, OS
DURAVELO	Nectin4 BTC + PD1	BT8009 + Pembro	Gem-Platinum	
MAIN-CAV* Maintenance	PD-L1+VEGF	Avelumab + Cabozantinib	Avelumab	OS

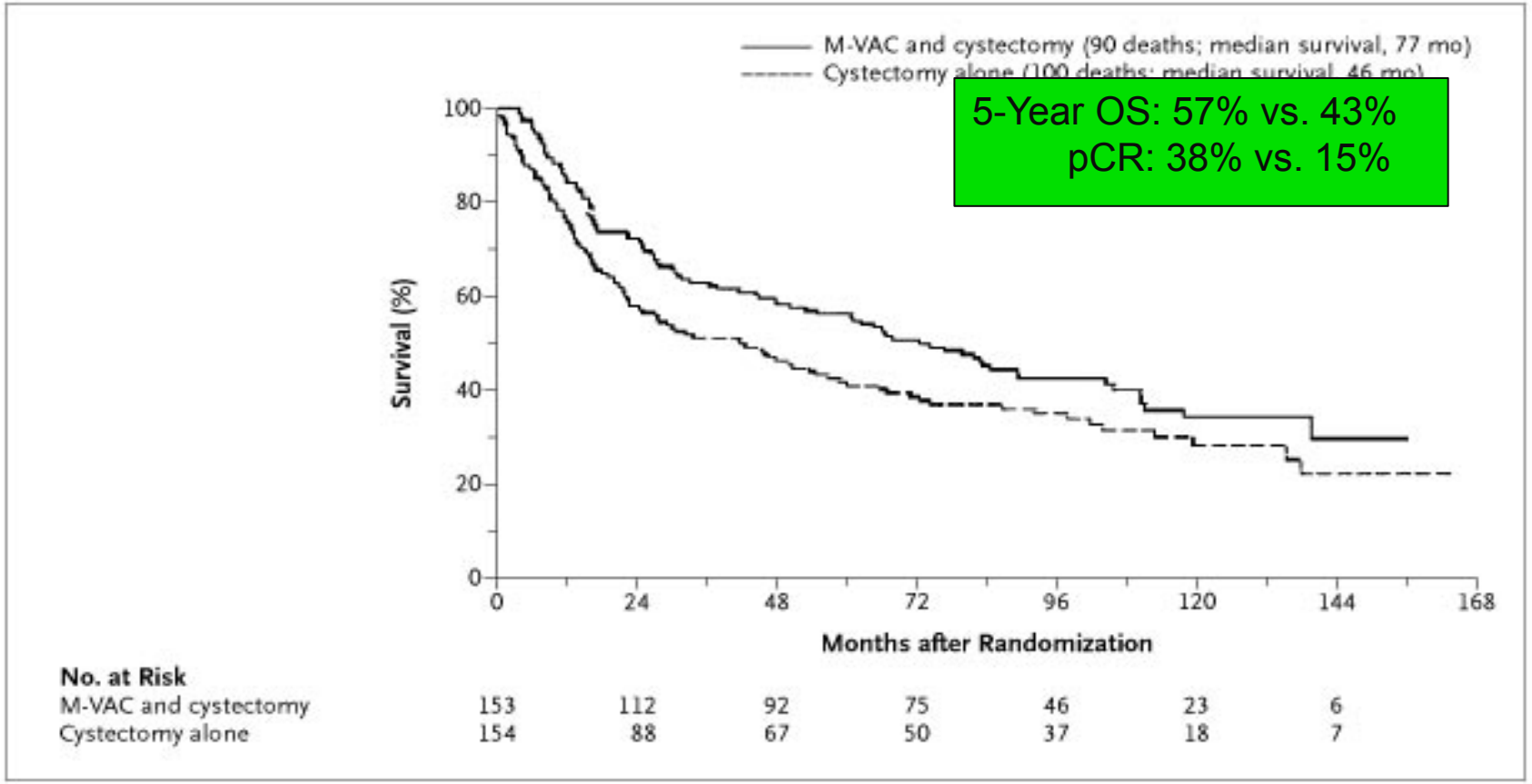
*Stopped early for poor accrual

Emerging agents to treat mUC

- Antibody drug conjugates (ADCs)
- Bispecific T-cell engagers (BITE)
- Radioligand Therapeutics (RLT)
- Neoantigen immunotherapy (peptides, mRNA)
- Targeted agents (HER2, PIK3CA, EZH2)
- T-cell therapy: CAR-T, TIL
- NK-cell therapy
- Combinations

Neoadjuvant MVAC Improves Survival in Resectable muscle-invasive bladder cancer (MIBC): SWOG-8710

Early distant dissemination of cancer cells in common



M-VAC, methotrexate, vinblastine, doxorubicin and cisplatin; OS, overall survival; pCR, pathologic complete response.

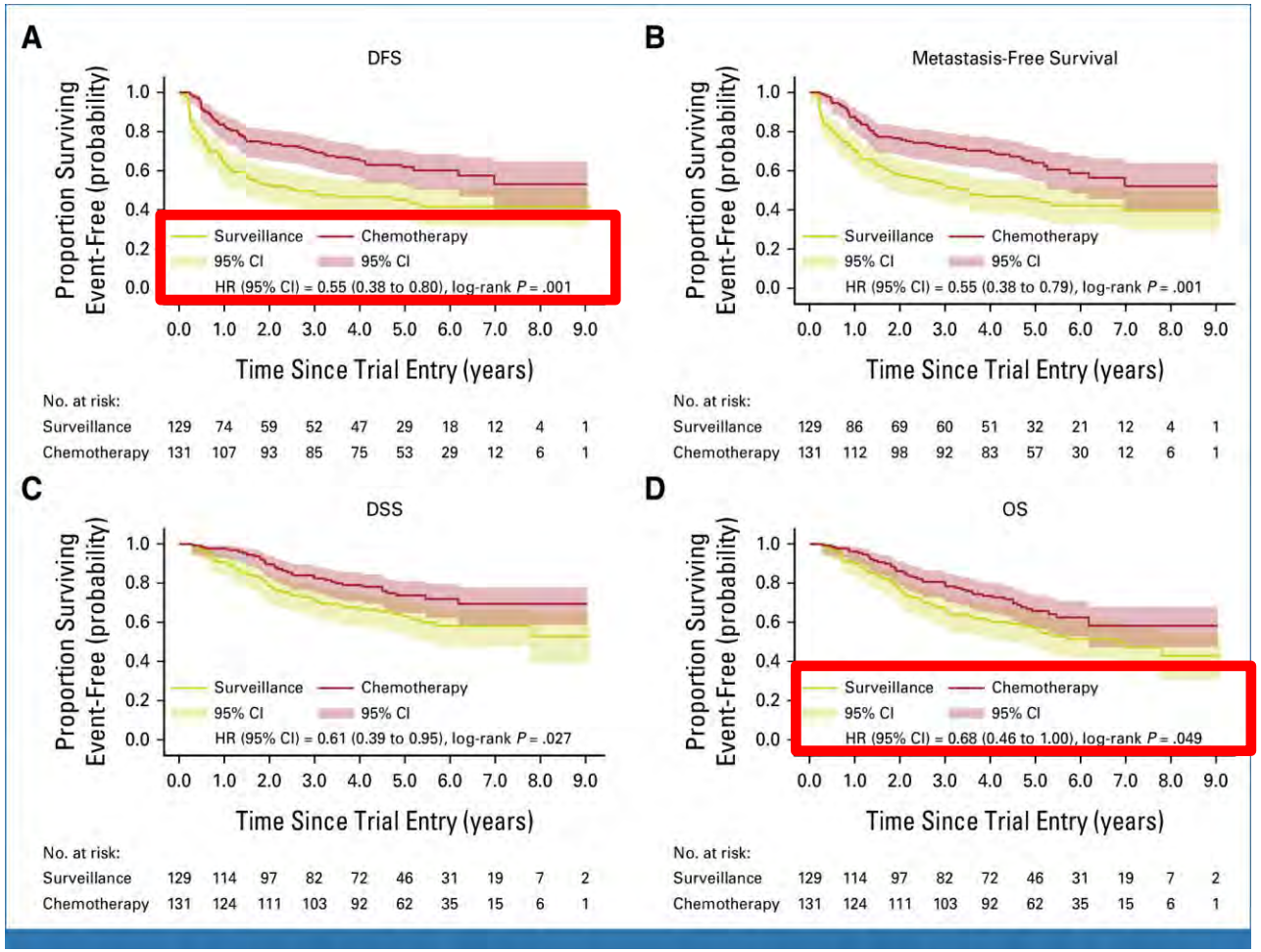
Grossman HB, NEJM 2003

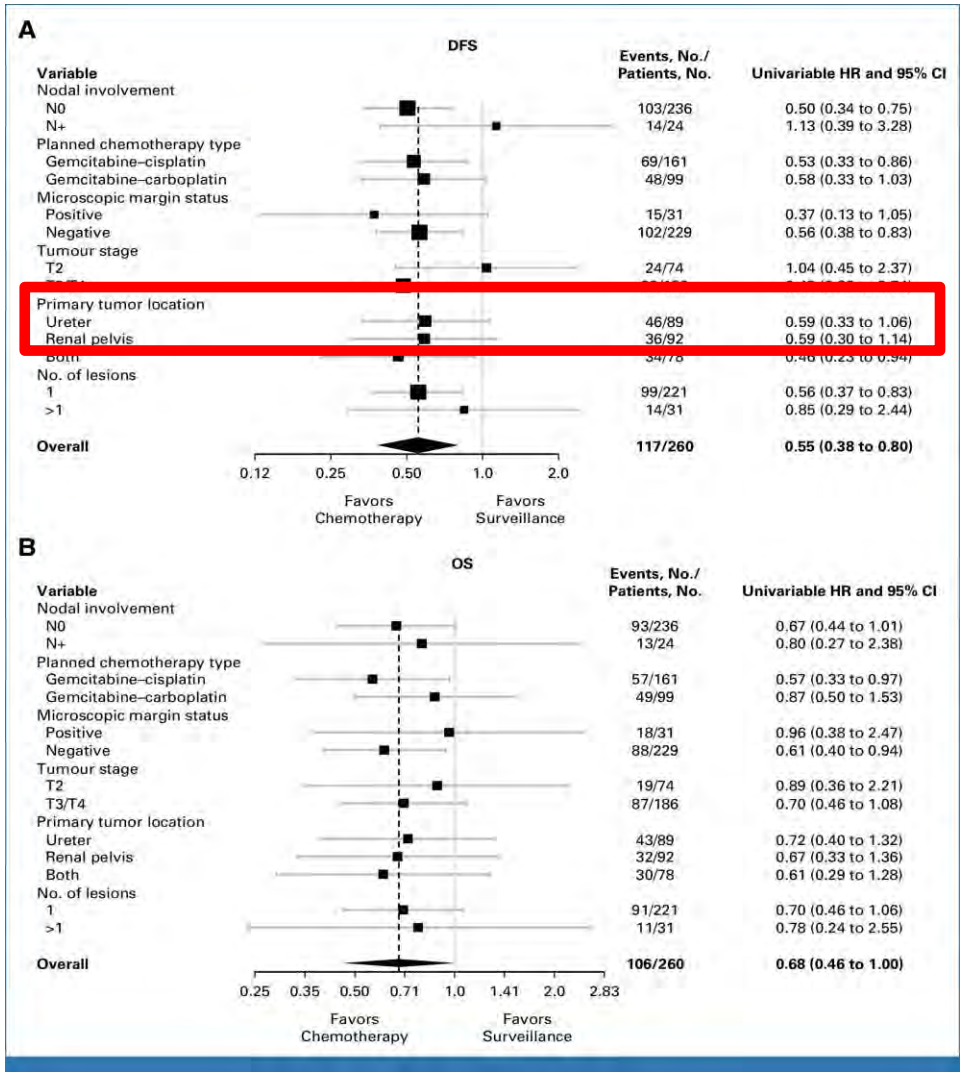
ICR The Institute of Cancer Research

POUT

CANCER RESEARCH UK

Results of POUT - A phase III randomised trial of peri-operative chemotherapy versus surveillance in upper tract urothelial cancer (UTUC)





- 5-year DFS was 62% versus 45%, HR = 0.55 (*P* = .001).
- 5-year OS was 66% versus 57%, HR = 0.68 (*P* = .049)

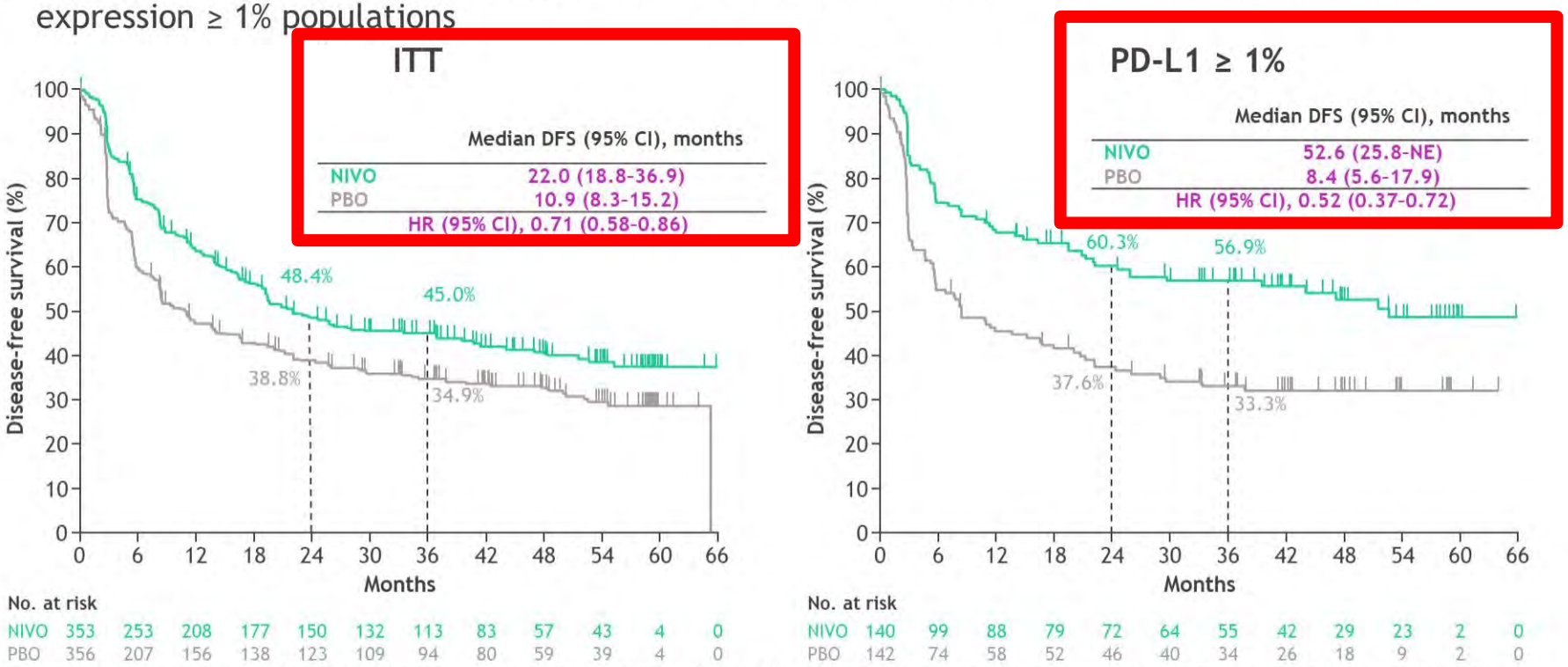
Birtle AJ, et al. 2018 ASCO GU. Abstract 407; J Clin Oncol 2024

CHECKMATE274: Adjuvant nivolumab for high-risk muscle-invasive urothelial carcinoma

CheckMate 274

Disease-free survival (primary endpoint)

- Continued DFS benefit was observed with NIVO versus PBO both in the ITT and tumor PD-L1 expression ≥ 1% populations



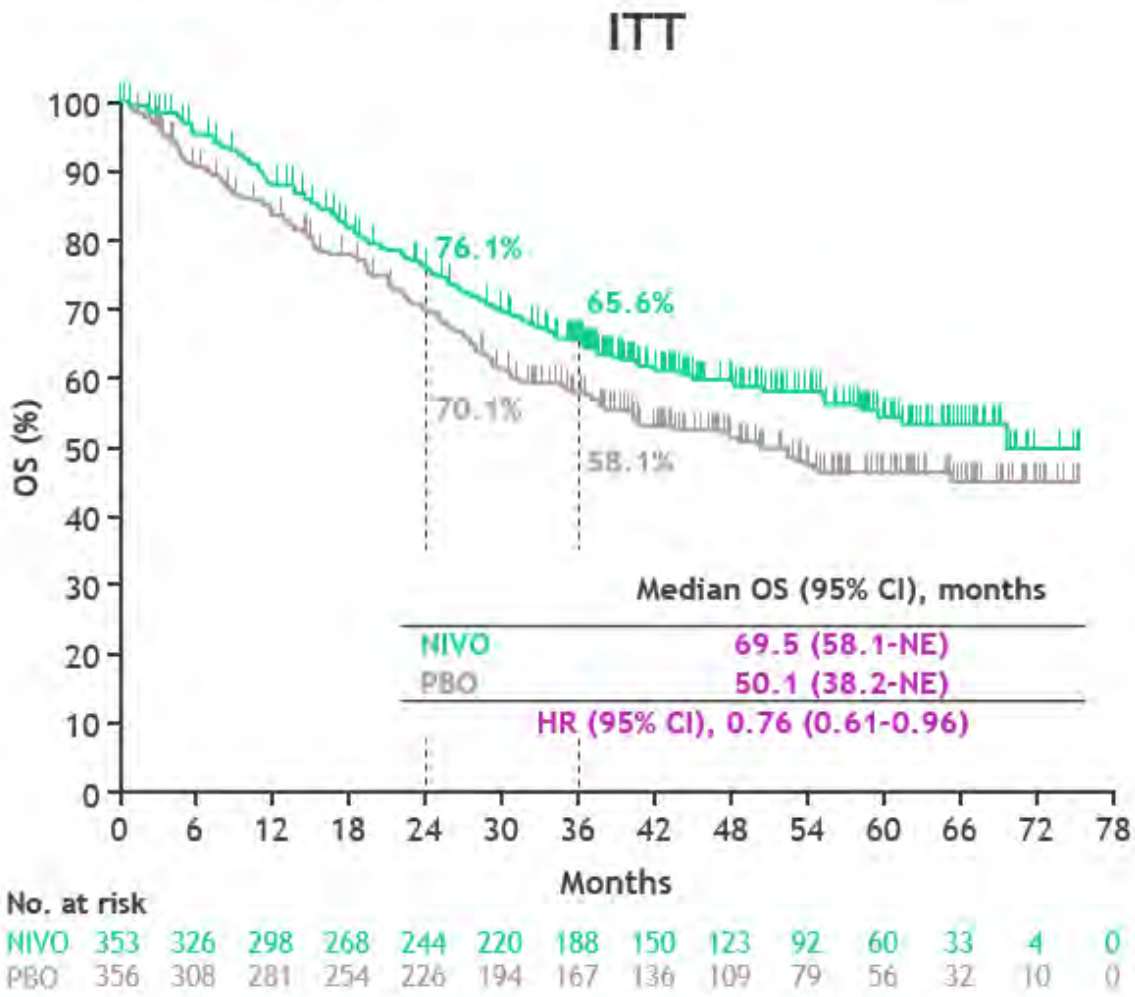
Minimum follow-up in the ITT population, 31.6 months. DFS was defined as the time between the date of randomization and the date of first recurrence (local urothelial tract, local non-urothelial tract or distant) or death.
NE, not estimable.

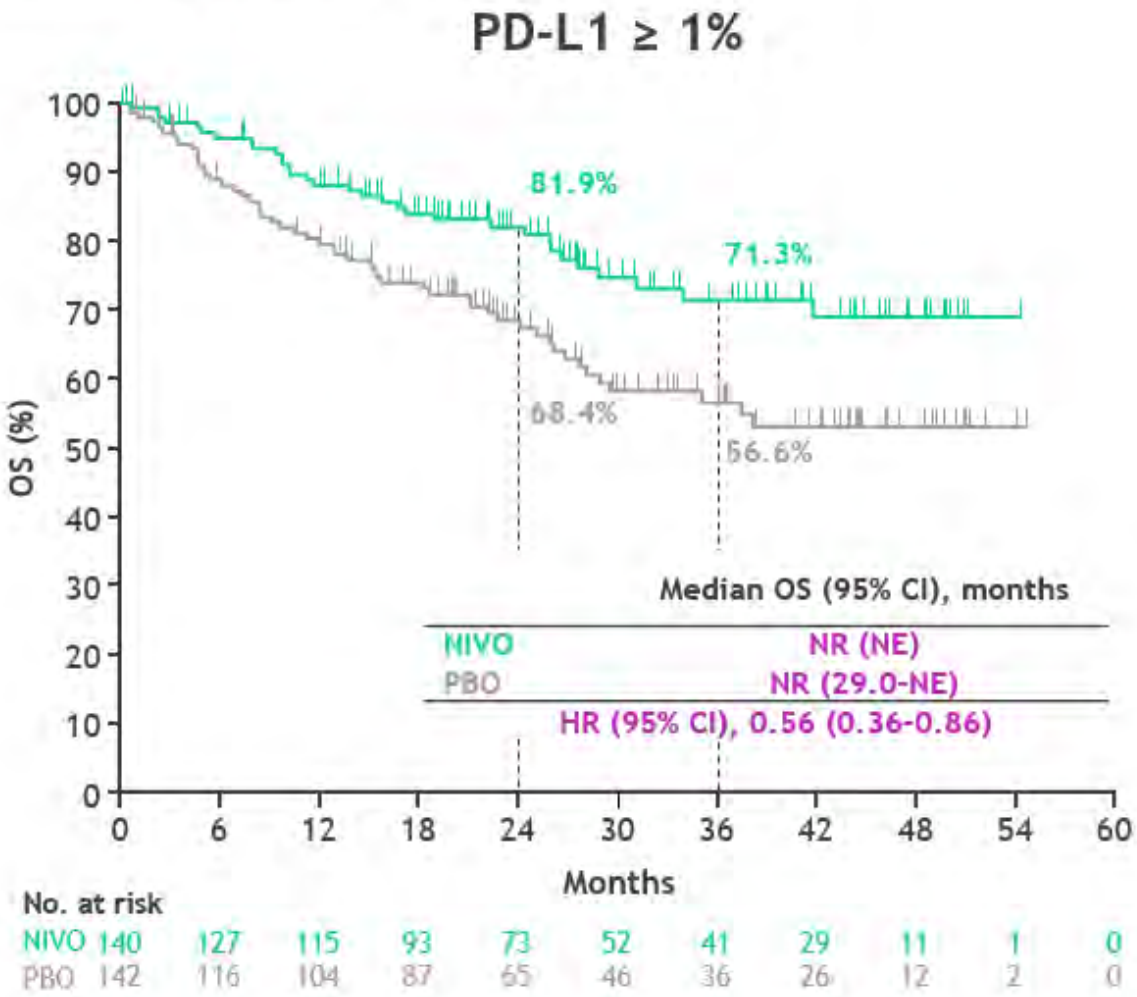
Approved in USA for all-comers, but in EU for PD-L1+ only

Bajorin D, et al. GU ASCO Feb 2021, NEJM Jun 2021, Galsky M, et al, GU-ASCO 2023

CHECKMATE274: Trend for improved survival with adjuvant nivolumab

- Interim OS data favored NIVO versus PBO in the ITT and tumor PD-L1 ≥ 1% populations





OS follow-up is ongoing, as the prespecified statistical boundary for significance was not met at the time of these analyses. Median (minimum) follow-up in the ITT population, 36.1 (31.6) months; median (minimum) follow-up in PD-L1 ≥ 1% population, 23.4 (11.4) months. OS was defined as time from date of randomization to date of death (from any cause).

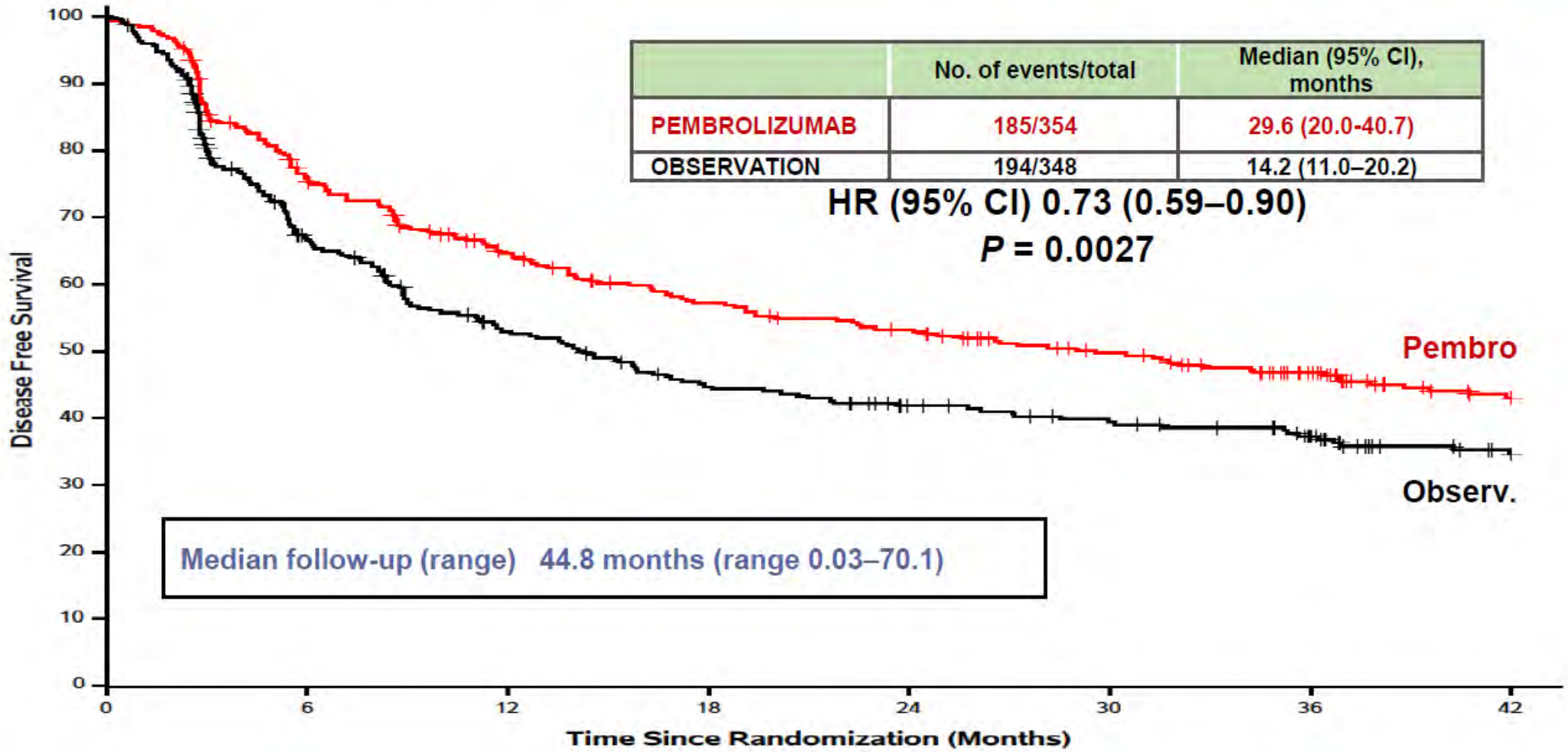
Galsky M, et al. EAU 2024

A031501 AMBASSADOR: Disease-Free Survival (ITT)

	No. of events/total	Median (95% CI), months
PEMBROLIZUMAB	185/354	29.6 (20.0-40.7)
OBSERVATION	194/348	14.2 (11.0–20.2)

HR (95% CI) 0.73 (0.59–0.90)

***P* = 0.0027**



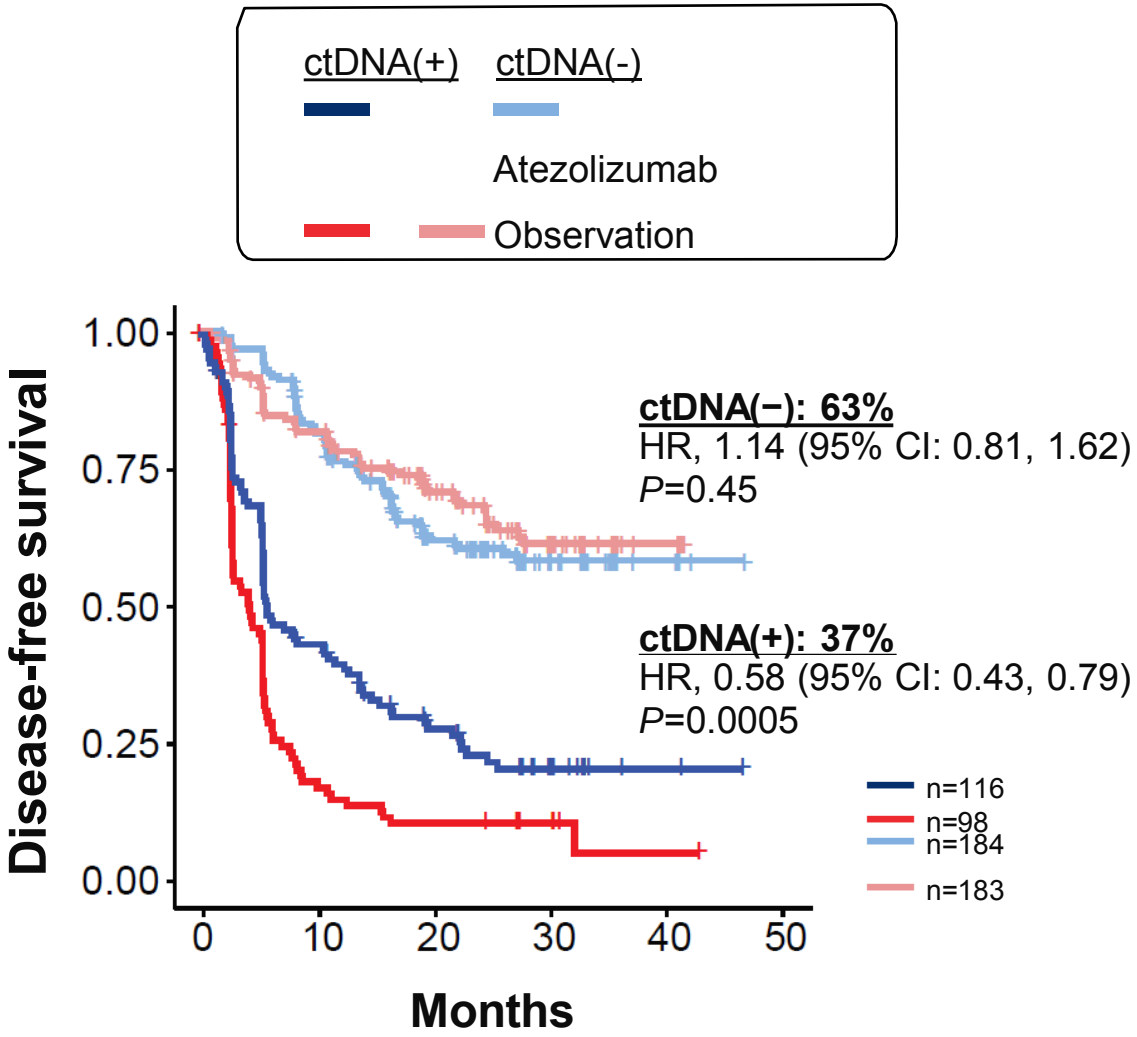
Andrea B. Apolo, MD @apolo_andrea

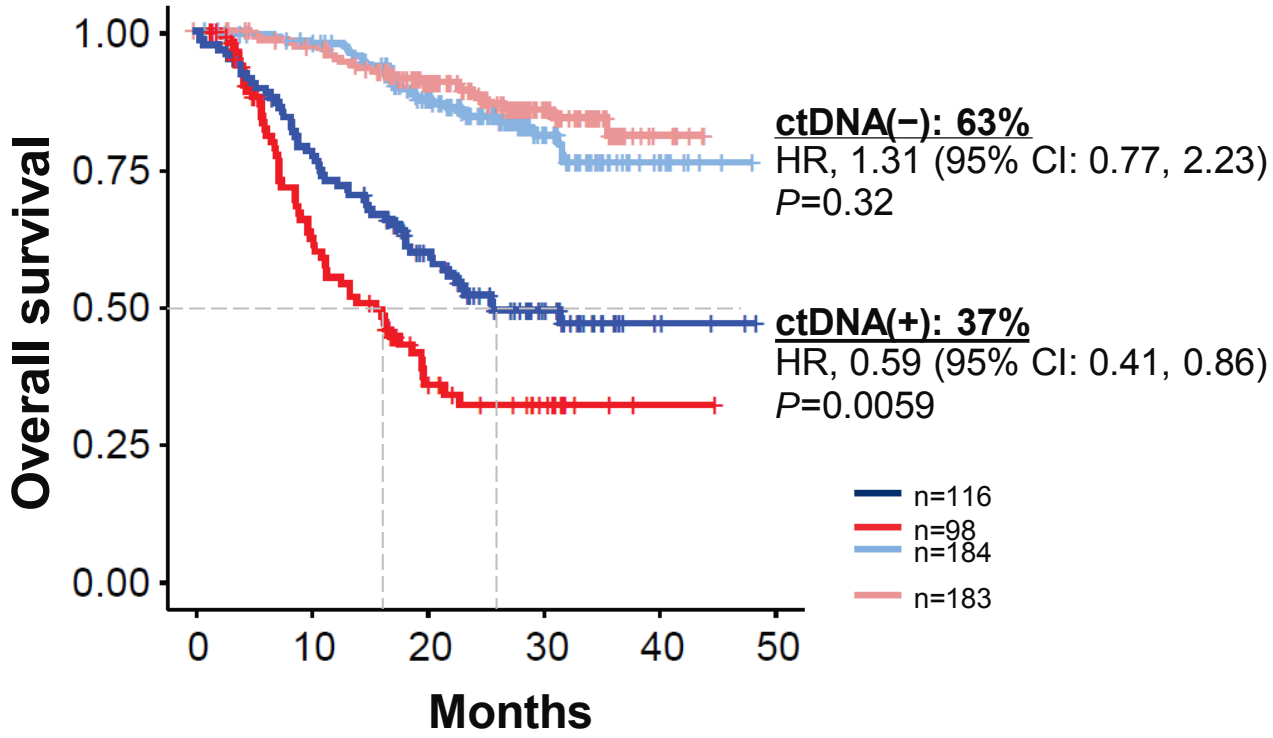
Apolo A, Ballman K, Sonpavde G, et al. ESMO Congress September 2024; N Engl J Med September 2024

Minimal residual disease using post-op ctDNA to select for adjuvant atezolizumab:

retrospective IMvigor010 analysis- ctDNA(+) patients had improved DFS and OS with atezo

	ctDNA(+) patients	
	Atezolizumab	Observation
Median DFS (95% CI), mo	5.9 (5.6, 11.2)	4.4 (2.9, 5.6)
Median OS (95% CI), mo	25.8 (20.5, NR)	15.8 (10.5, 19.7)

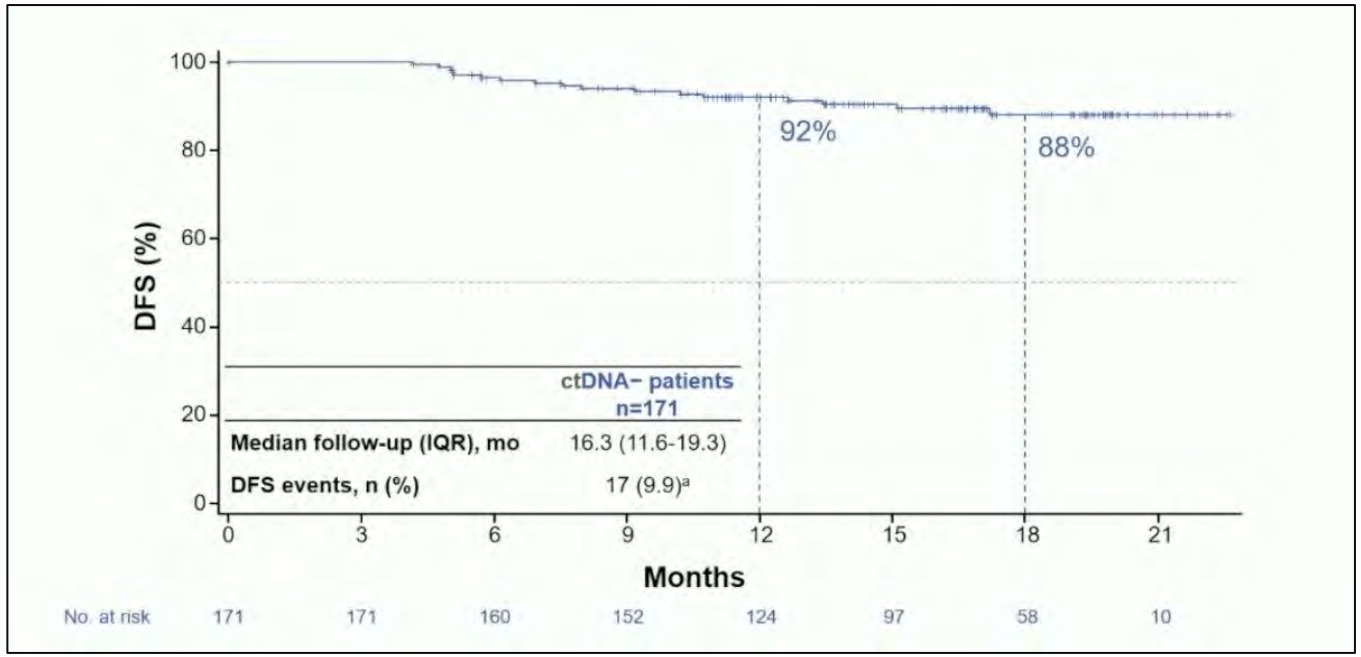




NR, not reached.

Powles T, ESMO IO 12/2020

IMvigor-011: Preliminary data from ctDNA-negative group



- Continuously ctDNA- population (n=171)
- Median follow-up of 16.3 months
- 17 recurrence events (9.9%) that did not appear to be related to pathologic stage or PD-L1 status
- 12-month DFS rate was 92% and 18-month DFS rate 88%

Powles T, et al. EAU April 2024

BARCELONA 2024 ESMO congress

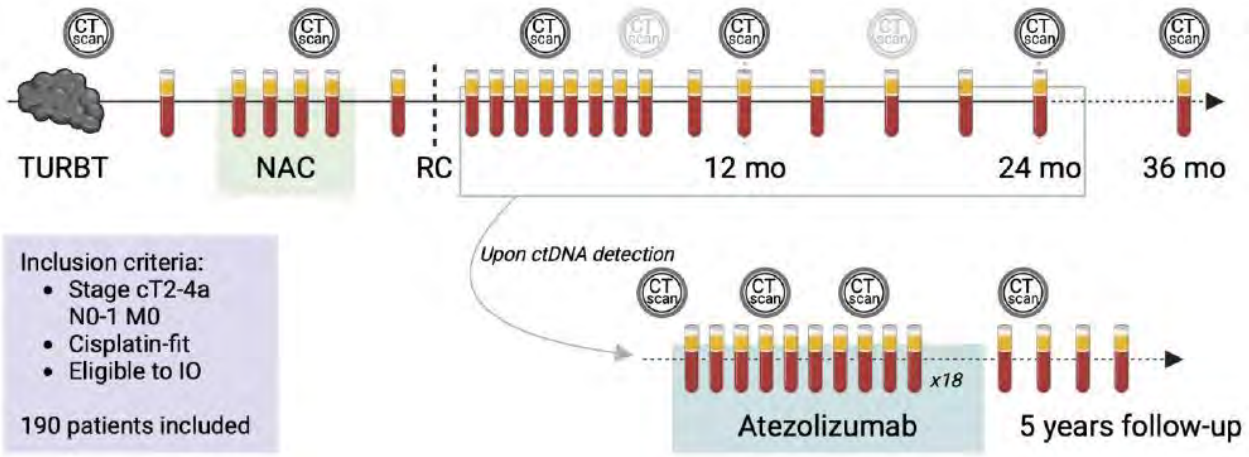
Specific identification of bladder cancer patients that could benefit from early post-cystectomy immunotherapy based on serial circulating tumour DNA (ctDNA) testing

Preliminary results from the TOMBOLA trial

Jørgen Bjerggaard Jensen, Karin Birkenkamp-Demtröder, Iver Nordentoft, Rikke Vilsbøll Milling, Stefanie Korsgaard Körner, Simone Burchardt Brandt, Michael Knudsen, Gitte Lam, Line Hammer Dohn, Knud Fabrin, Andreas Carus, Astrid Petersen, Ulla Joensen, Helle Pappot, Per Søndergaard Holt, Niels Viggo Jensen, Mads Agerbæk, Lars Dyrskjøt

TOMBOLA

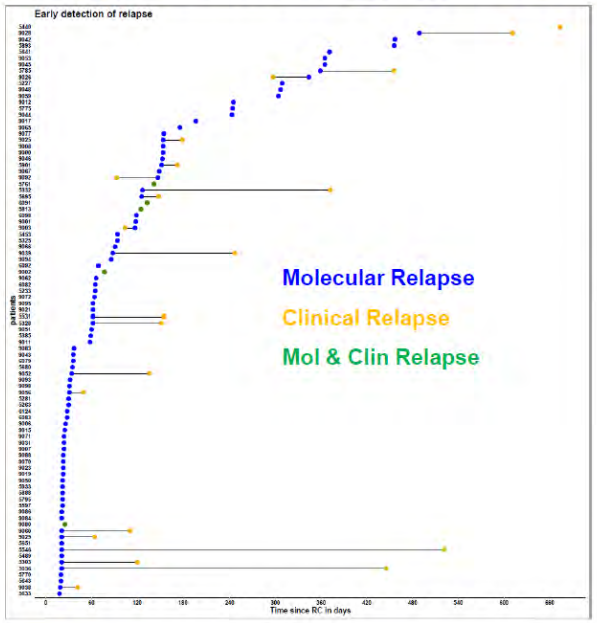
A national, non-randomized, ctDNA based intervention study



Inclusion criteria:
- Stage cT2-4a N0-1 M0
- Cisplatin-fit
- Eligible to IO

190 patients included

Relapse following cystectomy

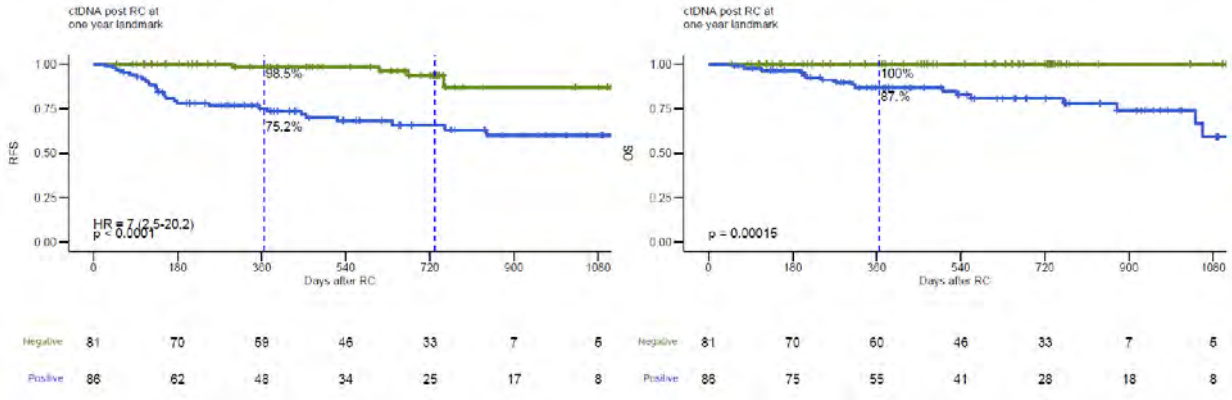


56% were ctDNA+ post-RC

75% were detected < 4 months post RC

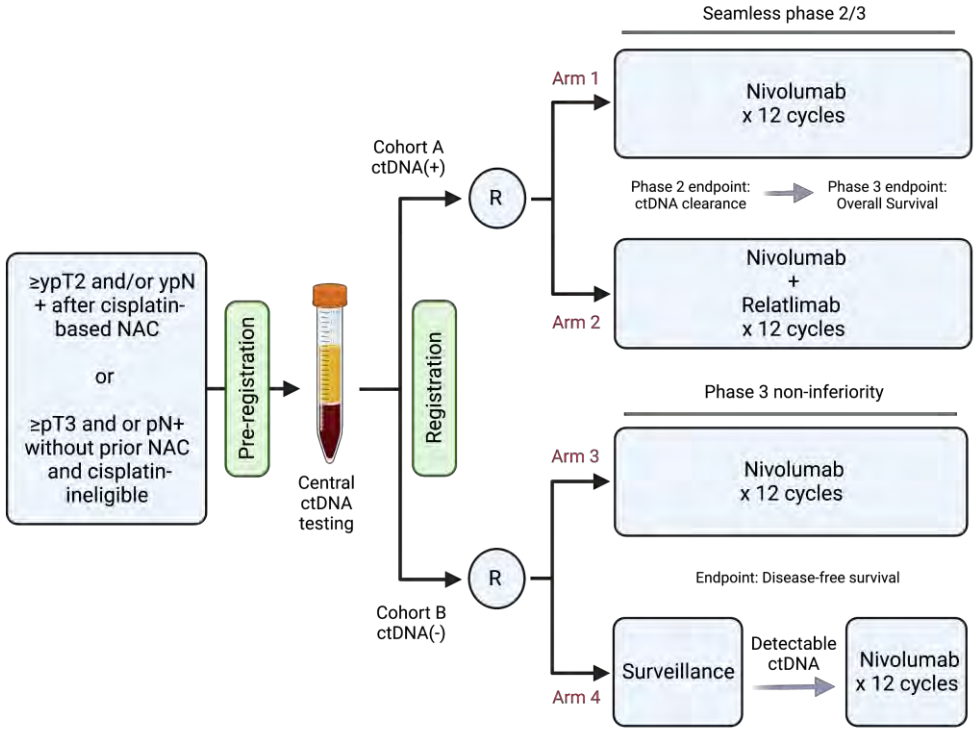
Of the ctDNA- patients, only 2 (3%) developed metastases on CT-scan during follow-up

Oncological outcome – immunotherapy at the time of molecular relapse



Ongoing trials of adjuvant therapy

A032103 (MODERN)



Interpath-005

Pembrolizumab + V940 (individualized mRNA therapy encoding up to 34 neoantigens) as adjuvant therapy for high-risk muscle-invasive urothelial carcinoma: V940-005 randomized Phase II trial

Eligibility
- Muscle-invasive urothelial carcinoma
- h/o radical cystectomy or nephroureterectomy
- pT2-4aNany or pTanyN+ post-neoadjuvant cisplatin -based chemotherapy
  OR
  pT3-4Nany or pN+ post surgery with no neoadjuvant chemotherapy (cisplatin-ineligible or declined adjuvant cisplatin-based chemo)
- ECOG-PS 0-2
- Predominant urothelial carcinoma
- Tissue adequate for NGS and V940 production
- Blood sample for V940 manufacture process and tumor-informed ctDNA assay

RANDOMIZE

N=200

Pembrolizumab q6W IV x 9 + Placebo q3W IM x 9

Pembrolizumab q6W IV x 9 + V940 q3W IM x 9

V940 may begin as soon as Cycle 1 Day 22

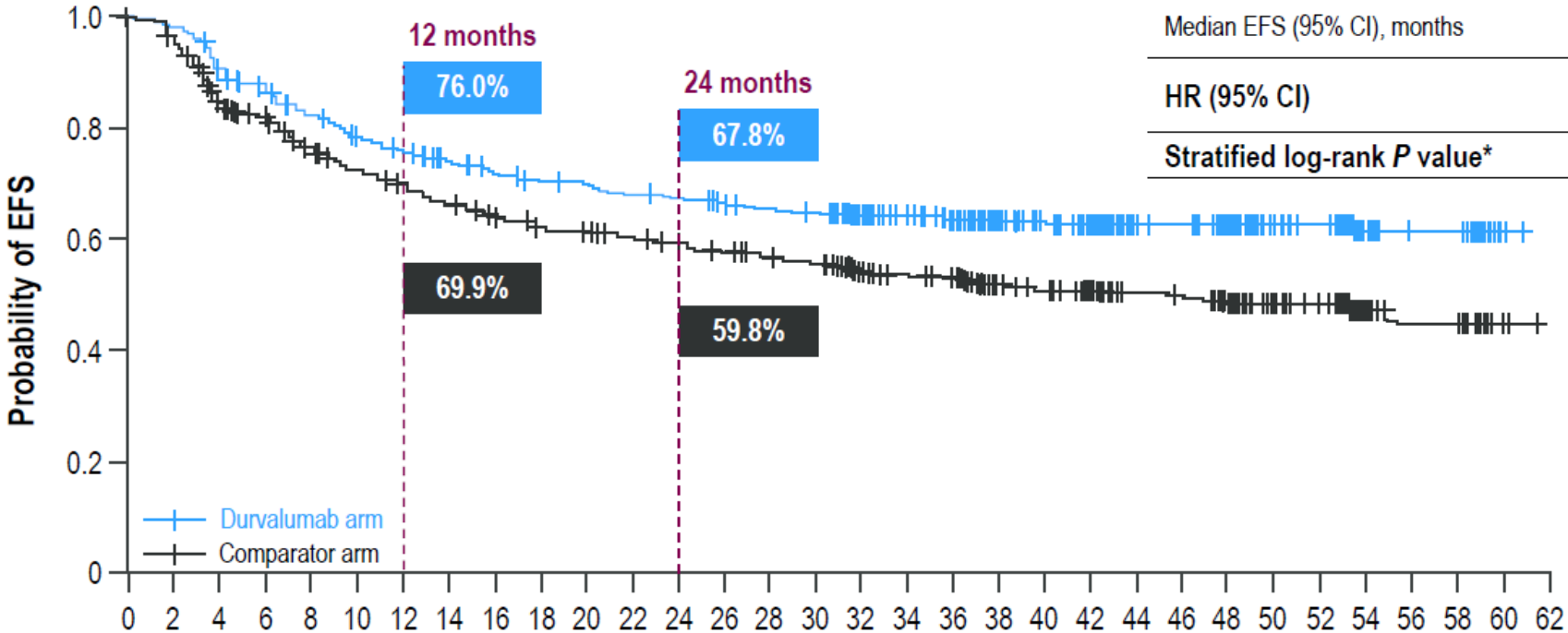
Primary endpoint
DFS (Investigator assessed)

Secondary endpoints
OS
DMFS
Safety

NCT06305767

NIAGARA: Event-free Survival by Blinded Independent Central Review (ITT)

	Durvalumab arm N=533	Comparator arm N=530
Number of events, n (%)	187 (35.1)	246 (46.4)
Median EFS (95% CI), months	NR (NR–NR)	46.1 (32.2–NR)
HR (95% CI)	0.68 (0.56–0.82)	
Stratified log-rank *P* value*	<0.0001	



Median follow-up in censored patients: 42.3 months (range, 0.03–61.3)

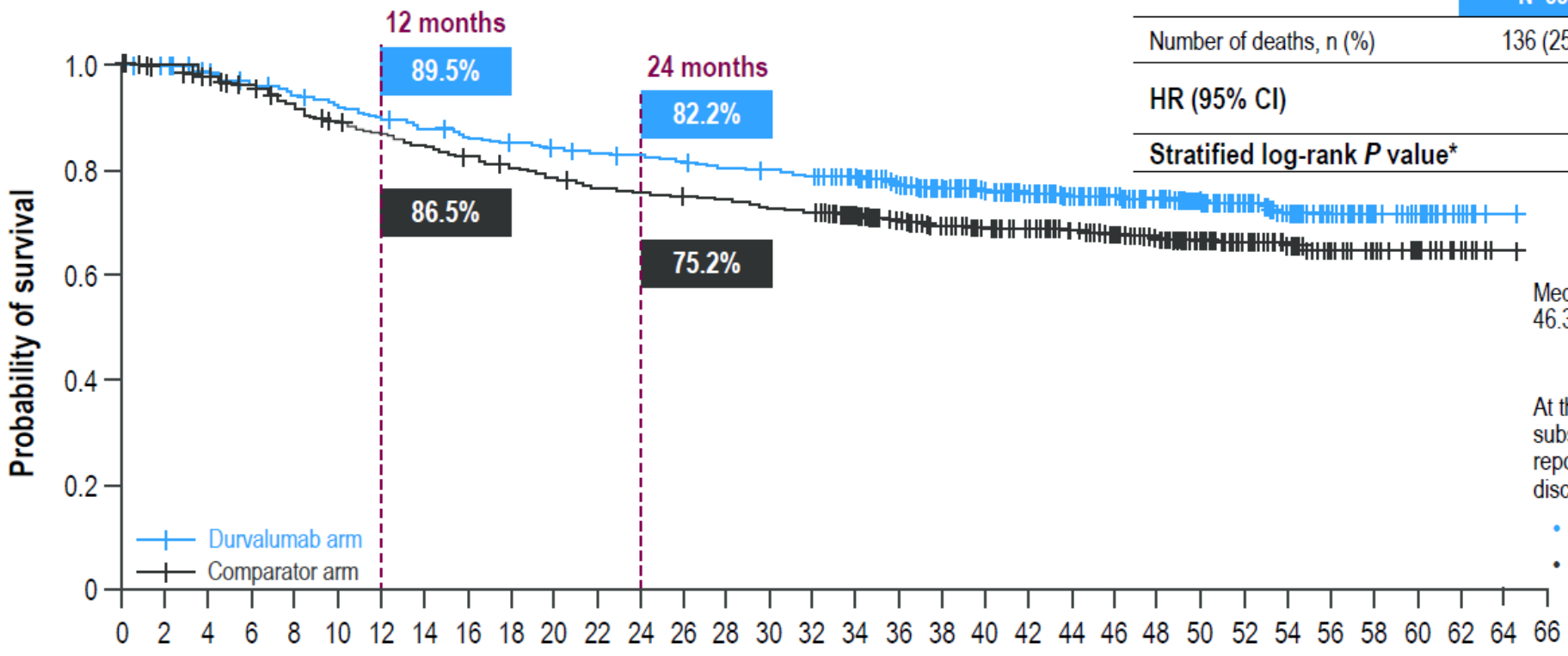
No. of patients at risk

Durvalumab arm	533	519	475	454	424	401	386	370	356	348	344	335	330	321	315	312	282	269	255	214	202	180	141	140	115	86	81	32	20	20	1	0
Comparator arm	530	498	437	416	381	358	343	328	313	300	296	288	281	273	264	259	228	219	214	177	172	159	132	129	94	69	62	24	18	16	2	0

EFS was assessed using RECIST v1.1. EFS is defined as the time from randomisation to the first: 1) progressive disease that precluded RC; 2) recurrence after RC; 3) date of expected surgery in patients who did not undergo RC; 4) death from any cause.
*The threshold to declare statistical significance was based on a Lan-DeMets alpha spending function with O'Brien-Fleming boundary – with the observed number of events, the boundary for declaring statistical significance was 0.04123 for a 4.9% overall 2-sided alpha.
Data cutoff 29 Apr 2024. CI, confidence interval; EFS, event-free survival; HR, hazard ratio; ITT, intent-to-treat population; NR, not reached; RC, radical cystectomy; RECIST, Response Evaluation Criteria In Solid Tumors.

Powles T, et al. NEJM 2024

NIAGARA: Overall Survival (ITT)



	Durvalumab arm N=533	Comparator arm N=530
Number of deaths, n (%)	136 (25.5)	169 (31.9)
HR (95% CI)	0.75 (0.59–0.93)	
Stratified log-rank *P* value*	0.0106	

Median follow-up in censored patients: 46.3 months (range, 0.03–64.7)

At the time of this analysis, at least 1 subsequent anti-cancer therapy was reported after treatment discontinuation for:

- 53 patients in the durvalumab arm
- 93 patients in the comparator arm

No. of patients at risk

Durvalumab arm	533	528	517	505	492	478	468	457	446	440	434	428	423	418	410	408	400	375	349	321	295	271	238	207	182	152	125	96	68	34	21	7	1	0
Comparator arm	530	516	507	490	467	450	438	425	413	402	392	383	378	373	368	363	358	334	311	281	259	239	215	194	174	141	113	90	60	38	21	10	2	0

OS is the time from the date of randomisation until death due to any cause regardless of whether the patient withdraws from randomised therapy or receives another anti-cancer therapy. *The threshold for statistical significance was based on a Lan-DeMets alpha spending function with O'Brien-Fleming boundary – with the observed number of events, the boundary for declaring statistical significance was 0.01543 for a 4.9% overall 2-sided alpha.
Data cutoff 29 Apr 2024. CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat population; OS, overall survival.

Powles T, et al. NEJM 2024

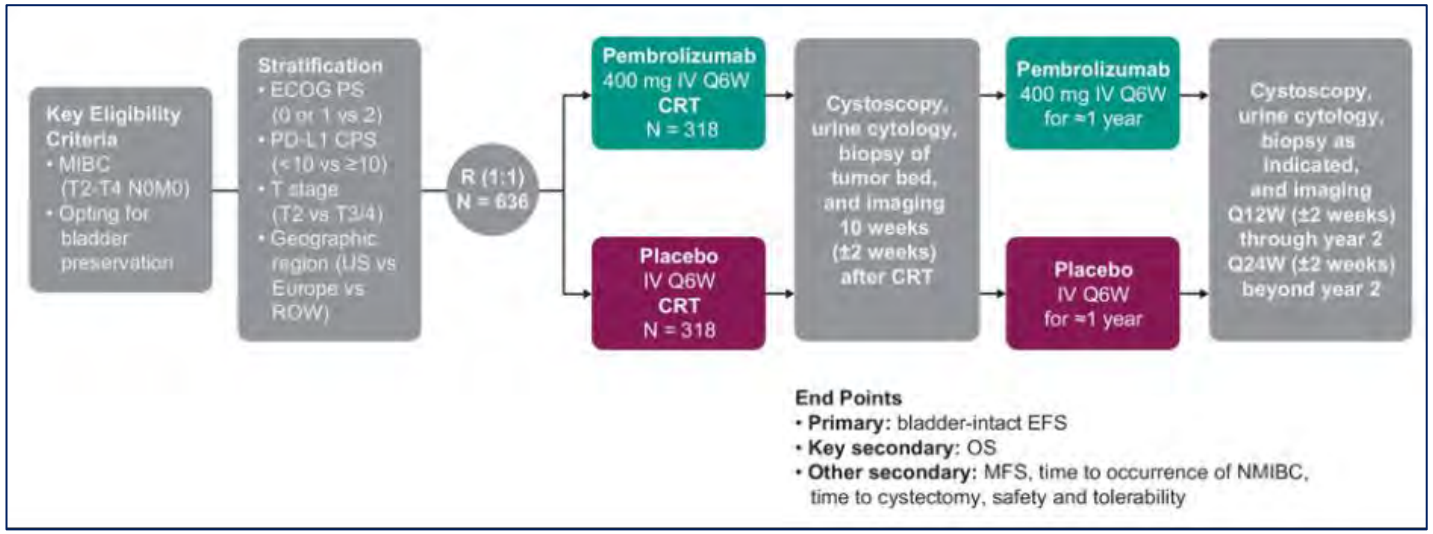
Neoadjuvant Phase III Trials in muscle-invasive urothelial carcinoma are likely to impact subsequent therapy (adjuvant/metastatic)

Trial ID	Sponsor	Primary endpoint (s)	Control arm	Experimental arm
CISPLATIN-ELIGIBLE				
NCT03661320	BMS	pCR, EFS	GC / Split Dose-GC	Control + Nivolumab + Placebo
NCT03732677	Astrazeneca	pCR, EFS	GC / Split Dose-GC	Control + Durvalumab
NCT03924856	Merck	pCR (all, PD-L1+) EFS (all, PD-L1+)	GC + Placebo	Control + Pembrolizumab
NCT04700124	Merck, Seagen	pCR EFS	GC	EV + Pembrolizumab
CISPLATIN-INELIGIBLE				
2018-002676-40	BMS	pCR, EFS	-	Nivolumab
NCT03924895	Merck	pCR (all, PD-L1+) EFS (all, PD-L1+)	-	Pembrolizumab Pembrolizumab + EV
NCT04960709	Astrazeneca	pCR EFS	-	Durvalumab + EV Durvalumab + Tremelimumab + EV

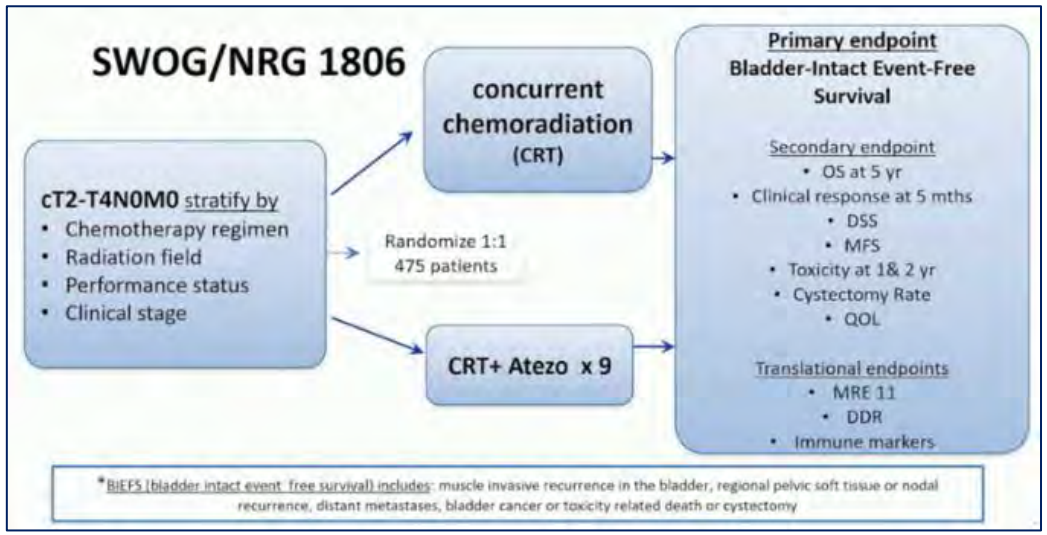
Bladder-preserving chemoradiation +/- PD1/L1 inhibitor

Ongoing Phase III trials

KEYNOTE-992

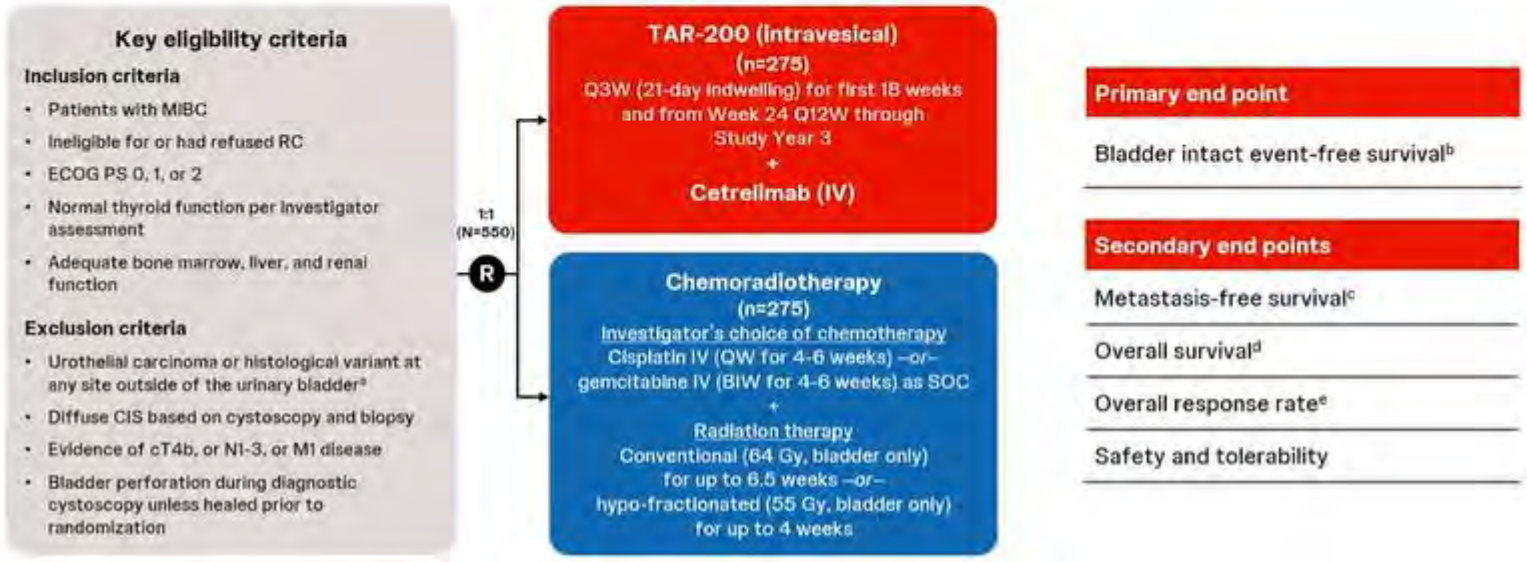


SWOG-1806



SunRISe-2 Trial: TAR-200 and Cetrelimab vs. Chemoradiotherapy for Muscle-Invasive Bladder Cancer - Stephen Williams

SunRISe-2 (NCT04658862) Is a Phase 3, Open-Label, Multicenter, Randomized Study



The SunRISe-2 study in patients with muscle-invasive bladder cancer (MIBC) who are not receiving radical cystectomy was a bold approach to disrupt the established standard of care in chemoradiation in this difficult-to-treat population. Following an Independent Data Monitoring Committee recommendation and pre-specified interim analysis, SunRISe-2 was discontinued for not showing superiority versus chemoradiation.

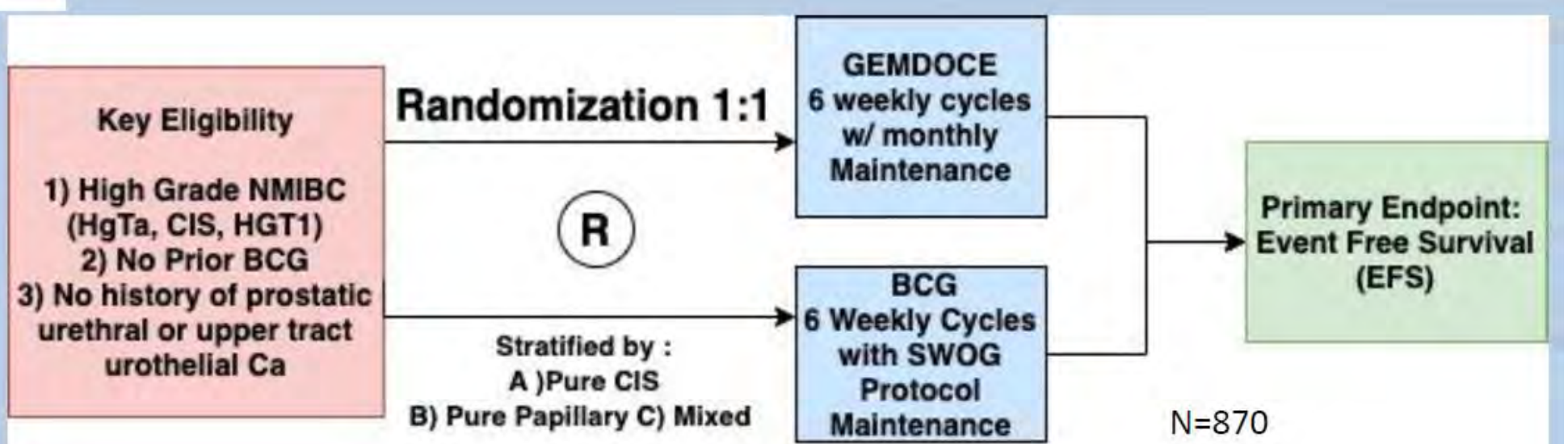
Johnson & Johnson Statement on the SunRISe-2 Study

October 7, 2024

EA8212 BRIDGE

Objective: To assess whether EFS is non-inferior for Gem/Doce vs. standard BCG for patients with BCG naïve high grade NMIBC

Max Kates – Study Chair
Angie Smith –PRO Co-Chair
Eugene Pietzak –TM Co-Chair
Noah Hahn—ECOG Bladder Chair
Claire Chu–Study Statistician



Gemcitabine 2g in sodium chloride 0.9 % 102.6 mL
Docetaxel 40g in sodium chloride 0.9 % 54 mL
BCG 50 mg in sodium chloride 0.9 % 50 ml

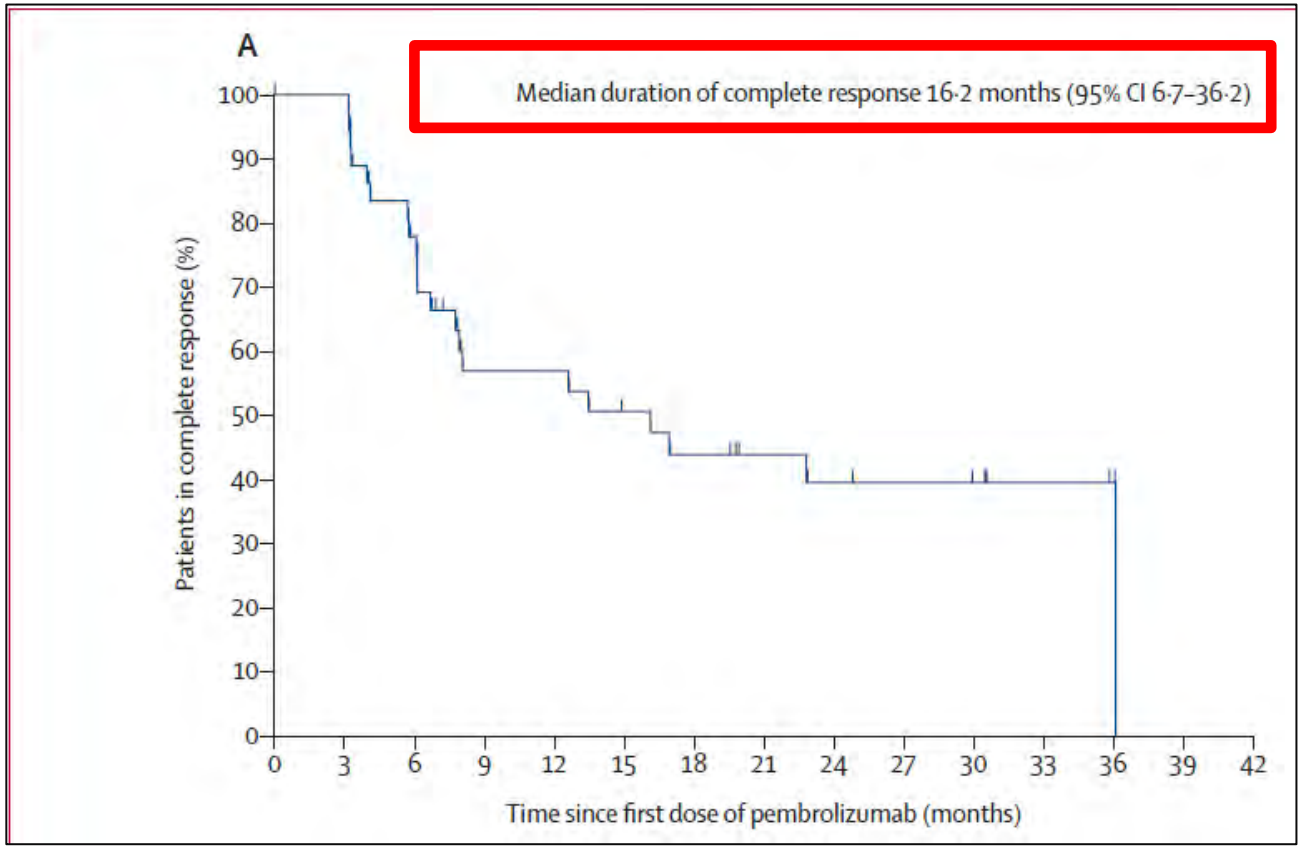
SWOG Protocol BCG Maintenance: 3 weekly instillations 3,6,12,18,24,30,36 months after initial induction course

EFS: Defined as the time from randomization to high grade recurrence in the bladder (CIS, HgTa, HGT1 or HGT2), progression of disease, or death, whichever occurs first.

BRIDGE Slide courtesy of:
Max Kates – Study Chair

Pembrolizumab for BCG-refractory Non-Muscle Invasive Bladder Cancer (NMIBC)

	Cohort A efficacy population (n=96)*
Complete response	39 (41%, 30·7–51·1)
Non-complete response	56 (58%, 47·8–68·3)
Persistent disease†‡	40 (42%, 31·7–52·2)
Recurrent disease	6 (6%, 2·3–13·1)
Non-muscle-invasive bladder cancer stage progression§	9 (9%, 4·4–17·1)
Non-bladder malignancy¶	1 (1%, 0·0–5·7)
Progression to muscle-invasive disease (T2)	0 (NA–NA)
Non-evaluable‖	1 (1%, 0·0–5·7)



Balar et al, ASCO 2019, abstract 350, Lancet Oncol 2021; 2021 Jul;22(7):919-930.

Phase III trials evaluating first-line BCG + PD1/L1 inhibitor for NMIBC

Pfizer's Sasanlimab in Combination with BCG Improves Event-Free Survival in Patients with BCG-Naïve, High-Risk Non-Muscle Invasive Bladder Cancer

Friday, January 10, 2025 - 06:45am

- *Clinically meaningful and statistically significant results are the first pivotal Phase 3 data for sasanlimab, a subcutaneously administered PD-1 inhibitor*
- *If approved, sasanlimab would be the first PD-1 inhibitor, in combination with BCG, to significantly prolong event-free survival in this patient population*
- *Treatment naïve high-risk NMIBC is an area of significant unmet need, where therapeutic options have largely remained unchanged for over three decades*

Intravesical Nadofaragene firadenovec for BCG-unresponsive NMIBC

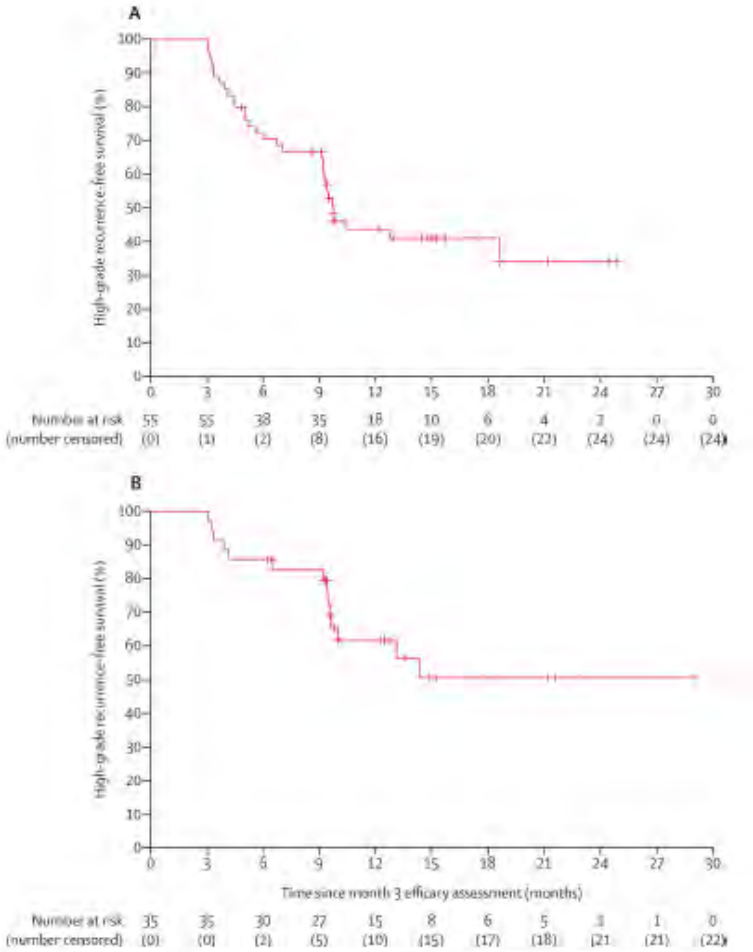


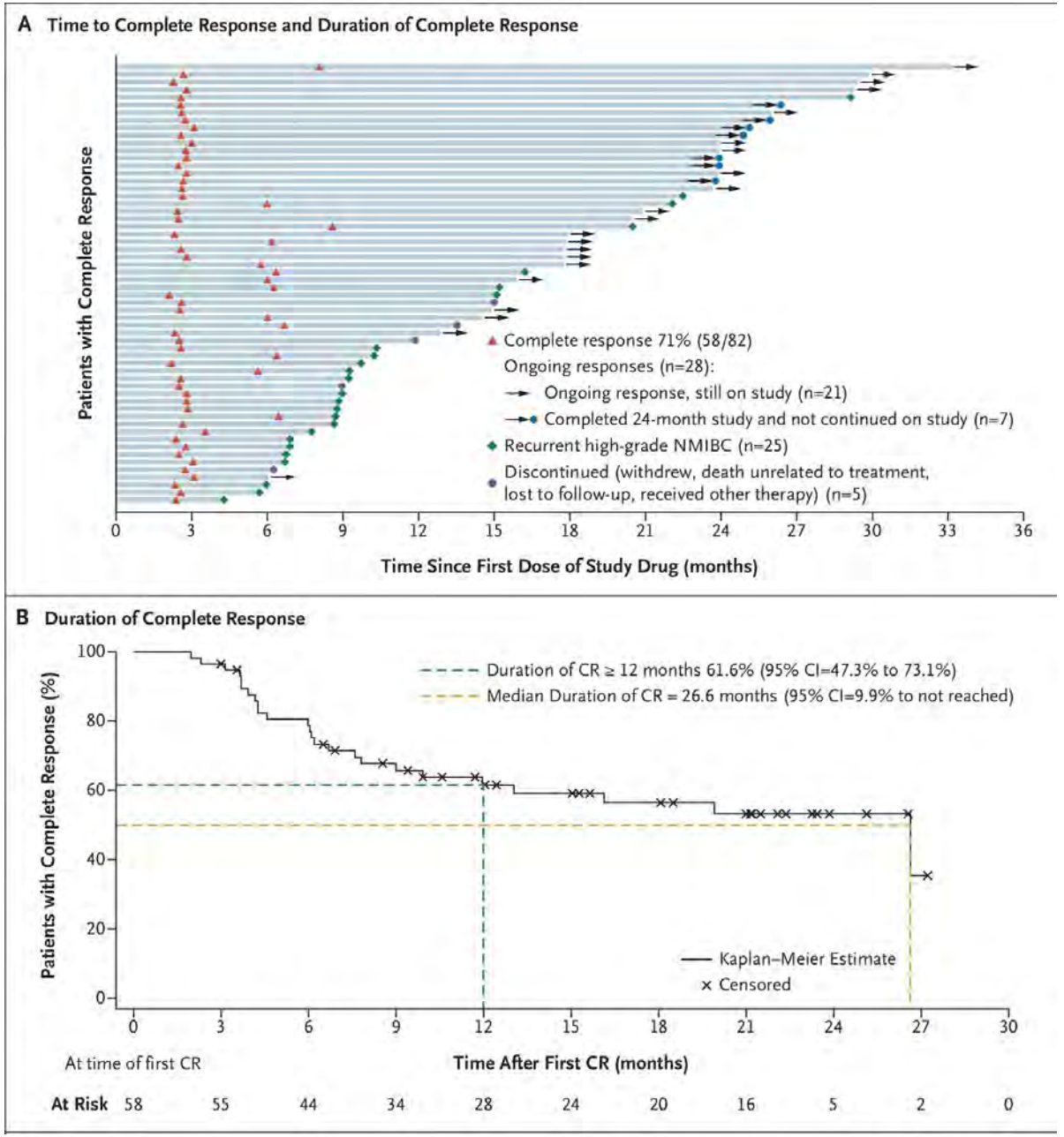
Figure 2: High-grade recurrence-free survival in patients with non-muscle-invasive bladder cancer given nadofaragene firadenovec, in patients who had a complete response at 3 months
(A) Patients with carcinoma in situ, with or without Ta or T1. (B) Patients with high-grade Ta or T1.

- Replication-deficient recombinant adenovirus that delivers human interferon alfa-2b gene into the bladder epithelium
- Phase 3, multicenter, open-label, BCG-unresponsive NMIBC patients received a single intravesical 75 mL dose of nadofaragene firadenovec (3×10^{11} viral particles per mL).
- Repeat dosing at months 3, 6, and 9 in the absence of high-grade recurrence.
- 55 (53·4%) of 103 patients with CIS (+/1 high-grade Ta or T1 tumor) had a CR within 3 months that was maintained in 25 (45·5%) of 55 patients at 12 months.
- Micturition urgency was the most common grade 3–4 study drug-related adverse event (1%), and there were no treatment-related deaths.
- US FDA approved December 2022.

Boorjian S, et al. Lancet Oncol 2021 January ; 22(1): 107–117.

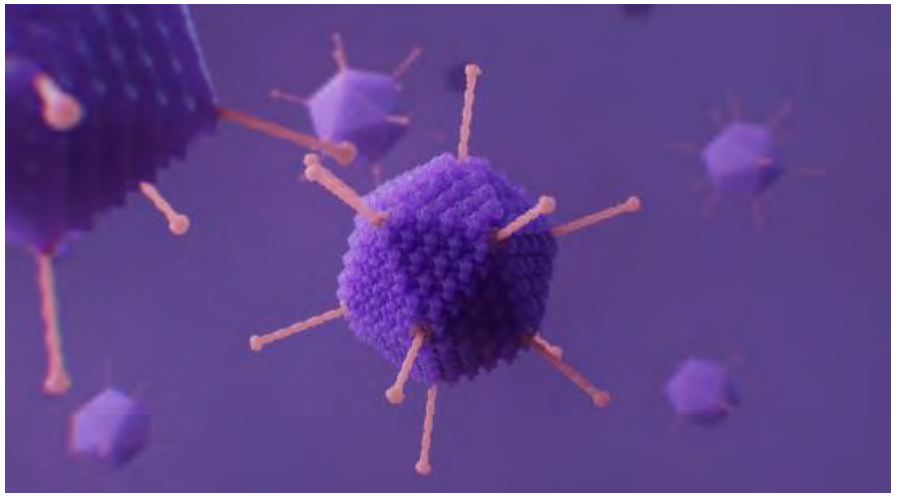
NAI (N803) + BCG

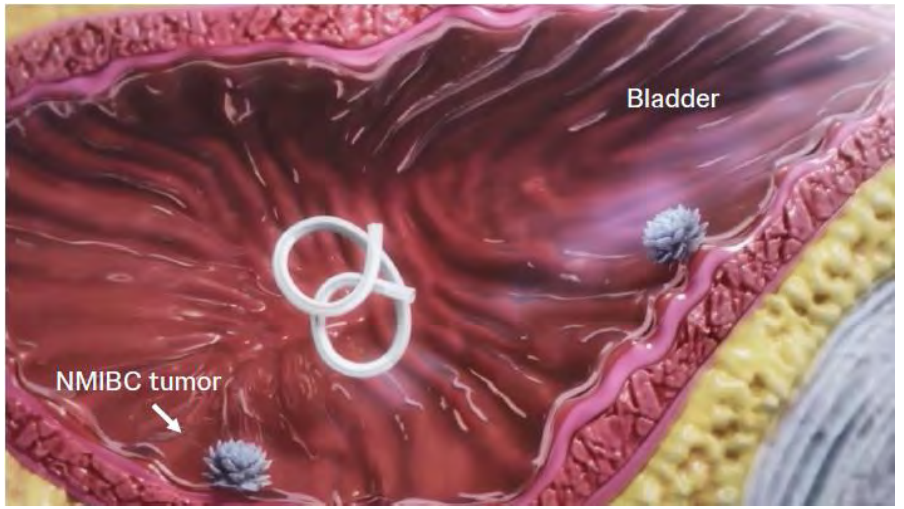
- Nogapendekin alfa-inbakicept (NAI) is an IL-15 superagonist.
- Cohort A: BCG-unresponsive CIS +/- Ta/T1 papillary disease- CR was achieved in 58 (71%) of 82 patients with a median duration of 26.6 months; At 24 months in patients with CR, the probability of avoiding cystectomy was 89.2%.
- Cohort B: BCG-unresponsive high-grade Ta/T1 papillary NMIBC- DFS rate was 55.4% at 12 months, with median DFS of 19.3 months
- Most treatment-emergent adverse events were grade 1 to 2 (86%); three grade 3 immune-related treatment emergent adverse events occurred.
- US FDA approved April 2024
- ImmunityBio entered into partnership with Serum Institute of India to manufacture BCG



Emerging intravesical agents

- **Cretostimogene Grenadenorepvec (CG0070):** cancer-selective oncolytic adenovirus with insertion of E2F Promoter + GM-CSF transgene that preferentially replicates in RB-deficient tumors
- **TAR200**: Intravesical release of gemcitabine over 3 weeks relying on osmotic system for sustained release from pretzel shaped device
- **TAR210**: Intravesical release of erdafitinib (FGFR inhibitor) for sustained release over 3 months from pretzel shaped device





Therapy for bladder cancer: Take home message

- EV-pembrolizumab is the preferred firstline therapy for mUC, but GC-nivolumab, gem-platinum→avelumab and pembrolizumab monotherapy can retain roles in selected patients.
- Durvalumab added to neoadjuvant cisplatin-gemcitabine chemotherapy followed by adjuvant durvalumab improved both EFS and OS in the NIAGARA Phase III trial, which is expected to be practice-changing (data from other neoadjuvant chemo-IO combinations and EV+pembrolizumab are expected in the near future).
- Adjuvant pembrolizumab improved DFS following surgery for muscle-invasive urothelial carcinoma and might be an additional option if approved by regulatory authorities (adjuvant nivolumab is already approved).
- Incorporation of PD1/L1 inhibitors with chemoradiation for MIBC is undergoing Phase III investigation.
- Impact of prior peri-op PD1/L1 inhibition on first-line mUC therapy needs more study.
- Erdafitinib is an option for those with somatic FGFR3 mutations/fusions and following previous PD1/L1 inhibitors (more specific FGFR3 inhibitors are undergoing early development)
- T-Dxd is an option for HER2 IHC3+ mUC following prior therapy (Sacituzumab Govitecan indication withdrawn)
- Other promising ADCs emerging and further development is expected: 1) BL-B01-D1- dual EGFR + HER3 binding ADC with a Topo1i payload and 2) Datopotamab Deruxtecan (Trop2 targeting with Topo1i payload)
- Intravesical delivery of sustained-release gemcitabine (TAR-200) and erdafitnib (TAR210) promising (definitive data are awaited; other recent advances in NMIBC include IV pembro, intravesical BCG+NAI IL-15 superagonist and Nadofaragene Firadenovec; CG0070 [oncolytic virus] and TAR-210 [sustained erfaditinib intravesical release using pretzel-sheped device] emerging)
- Data supporting the use of tumor-informed ctDNA to identify MRD and inform systemic therapy continues to grow (await confirmatory data from IMvigor-011 Phase III trial)
- Trials evaluating new therapies should be preferred since current therapies do not cure most patients.