Üroteliyal Kanserlerde Tedavi Seçenekleri
ASCO-GU 2026

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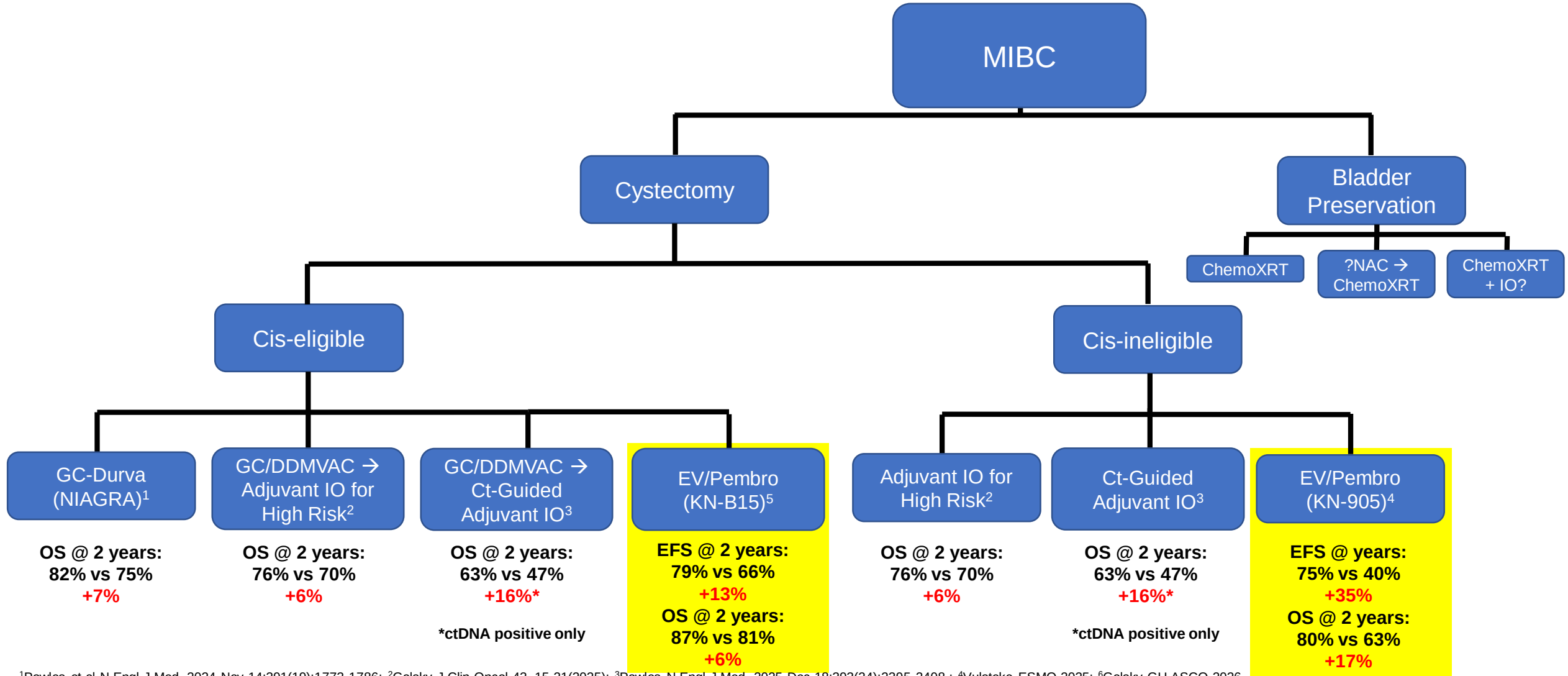
Ders Planı

- **Neoadjuvan tedaviler**
- **Adjuvan Tedaviler**
- **Evre IV birinci basamak**
- **Evre IV birinci basamak sonrası**
- **Yeni tedavi seçenekleri**
- **Erken dönem hastalık evresinde yeni seçenekler**

Üroteliyal Kanserlerde Tedavi Seçenekleri ASCO-GU 2026

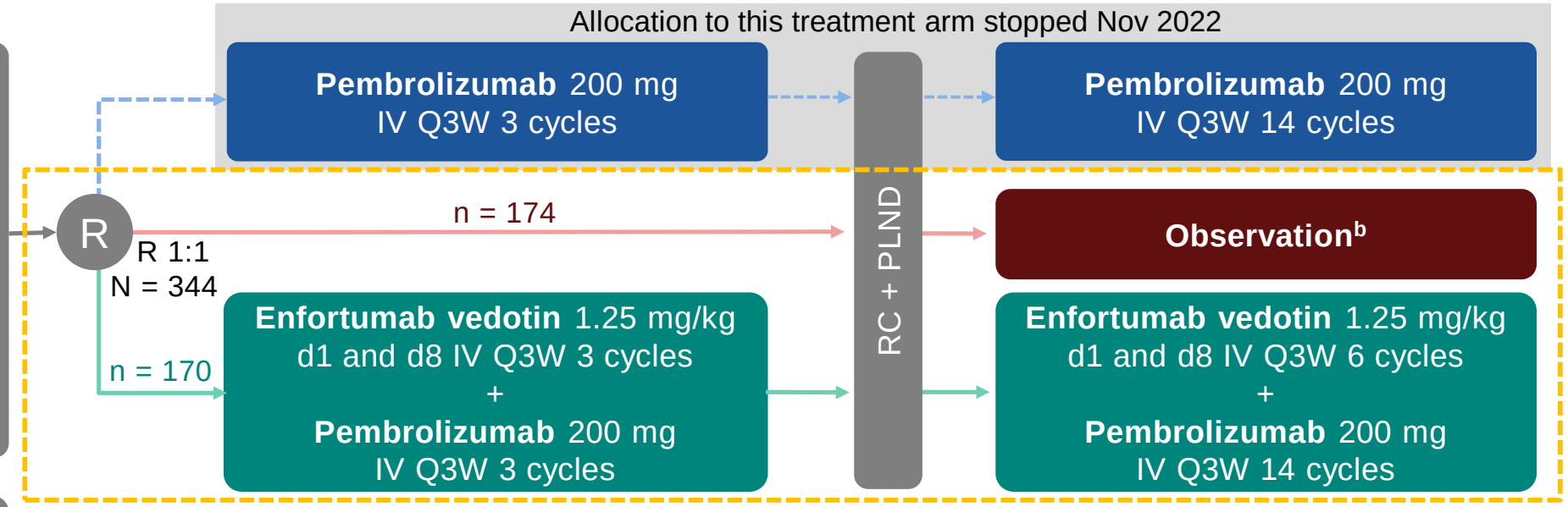
Lokal ileri Neoadjuvan/Adjuvan Dönem Yenilikler

Lokal ileri ürotelyal kanser tedavi seçenekleri



[1]Powles et al N Engl J Med. 2024 Nov 14;391(19):1773-1786; [2]Galsky J Clin Oncol 43, 15-21(2025); [3]Powles N Engl J Med. 2025 Dec 18;393(24):2395-2408.; [4]Vulsteke ESMO 2025; [6]Galsky GU ASCO 2026

KEYNOTE-905/EV-303 Study (NCT03924895)



Key Eligibility Criteria

- Adults with MIBC
- **Clinical stage T2-T4aN0M0 or T1-T4aN1M0 by central assessment**
- **≥50% urothelial histology**
- **Cisplatin ineligible[a] or cisplatin declining**
- ECOG PS score 0-2

Stratification Factors

- Cisplatin ineligibility (ineligible vs eligible but declining)
- Clinical stage (T2N0 vs T3/T4aN0 vs T1-4aN1)
- Region (US vs EU vs most of world)

End points

Primary: EFS by BICR

Key secondary:

- OS
- Pathologic complete response (pCR; absence of viable tumor in tissue from RC + PLND [pT0N0])[c]

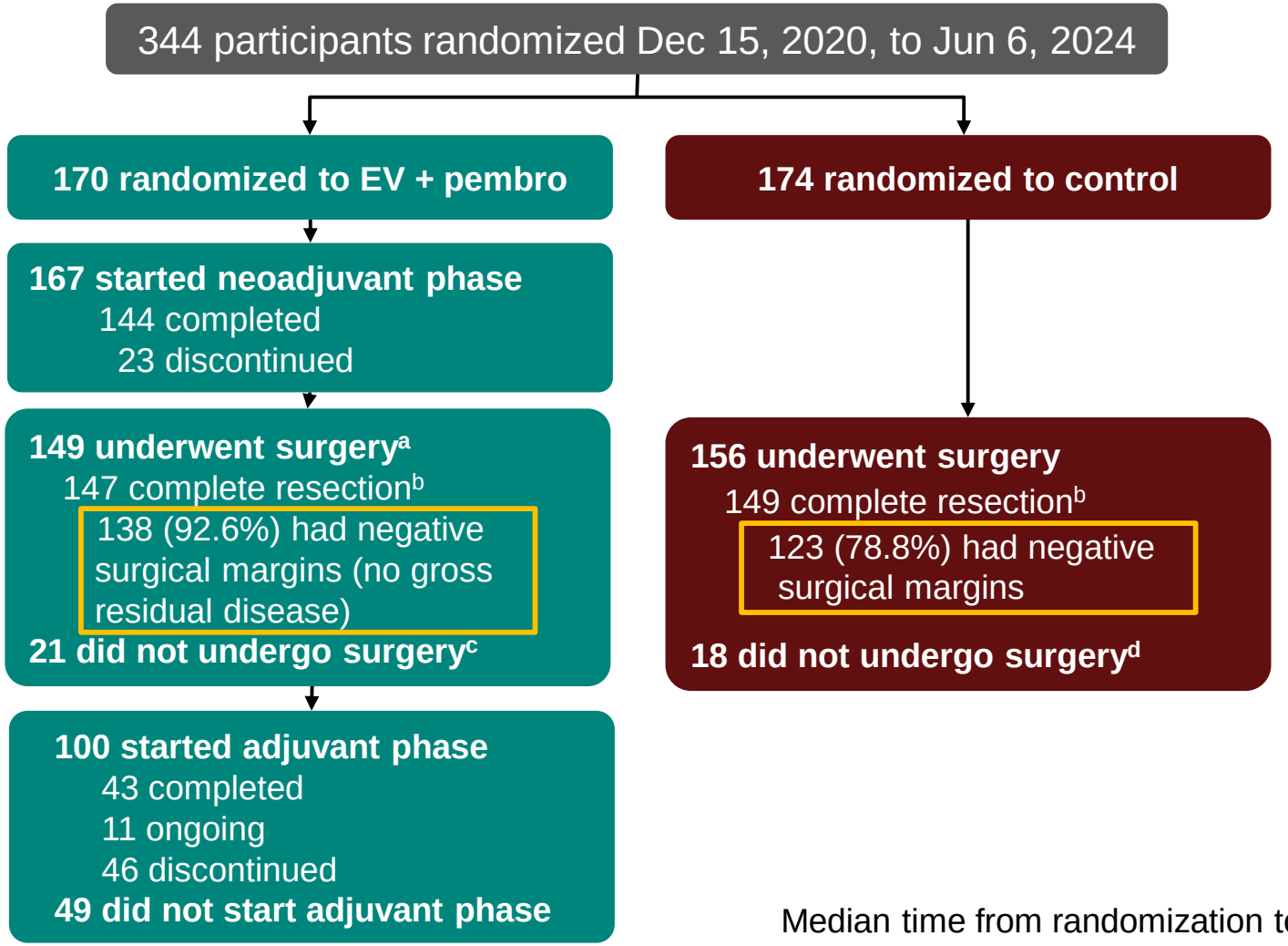
Other secondary:

- Pathologic downstaging (pDS; <pT2 [pT0, pTis, pTa, pT1] and N0 in tissue from RC + PLND)[c]
- Disease-free survival (DFS; time from post-surgery scan to local/distant recurrence or death)[c,d]

BICR, blinded independent central review; d, day; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival; IV, intravenous; MIBC, muscle-invasive bladder cancer; NYHA, New York Heart Association; OS, overall survival; PLND, pelvic lymph node dissection; Q3W, every 3 weeks; R, randomization; RC, radical cystectomy.

[a]Protocol defined as having ≥1 of the following: impaired renal function (creatinine clearance, 30 to 59 mL/min), ECOG PS score 2, CTCAE v4 grade ≥2 audiometric hearing loss, or NYHA Class III heart failure. [b]As of November 2022, adjuvant nivolumab was permitted when clinically indicated and regionally available. [c]Assessed by central pathology or BICR. [d]Participants were considered disease-free after RC + PLND if they had complete resection (no gross residual disease) and no evidence of disease on a post-surgery scan.

Disposition and Demographics

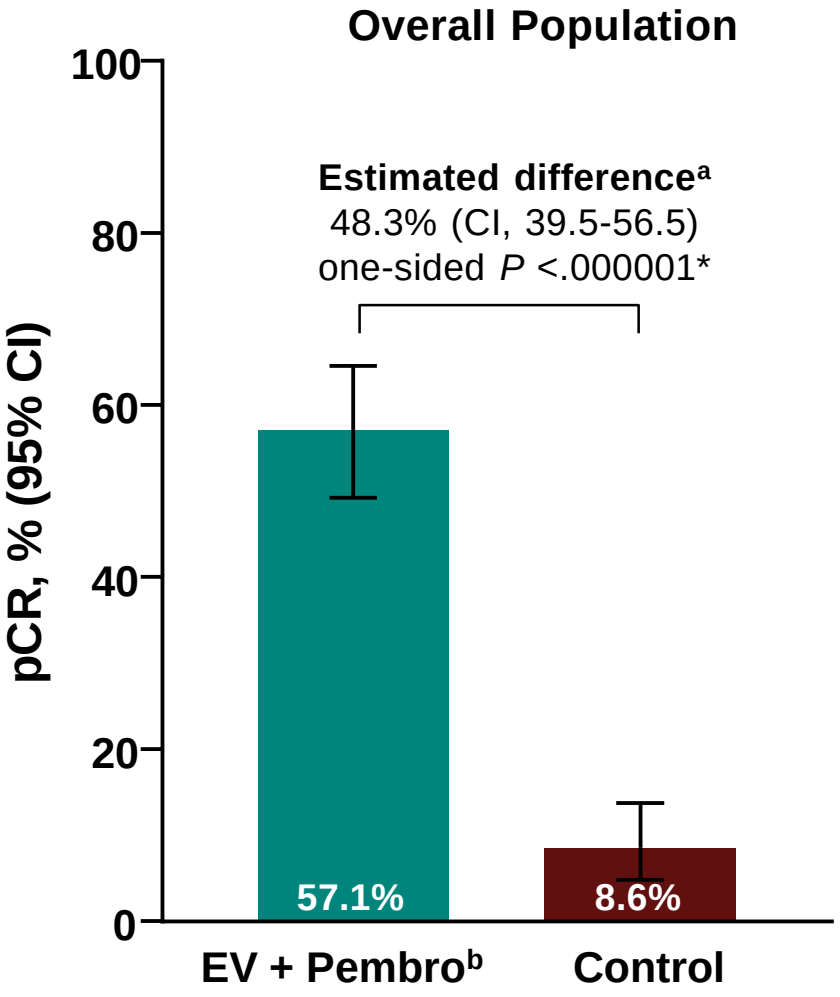


Characteristic, n (%)	EV + Pembro (n = 170)	Control (n = 174)
Median age (range), years	74.0 (47-87)	72.5 (46-87)
Male	137 (80.6)	131 (75.3)
ECOG PS 2	21 (12.4)	26 (14.9)
Cisplatin eligibility status		
Ineligible	142 (83.5)	139 (79.9)
Eligible but declining	28 (16.5)	35 (20.1)
PD-L1 CPS ≥10	80 (47.1)	83 (47.7)
Tumor stage at baseline by central assessment		
T2N0	30 (17.6)	32 (18.4)
T3/T4aN0	133 (78.2)	132 (75.9)
T1-4aN1	7 (4.1)	10 (5.7)
Pure UC histology	152 (89.4)	161 (92.5)

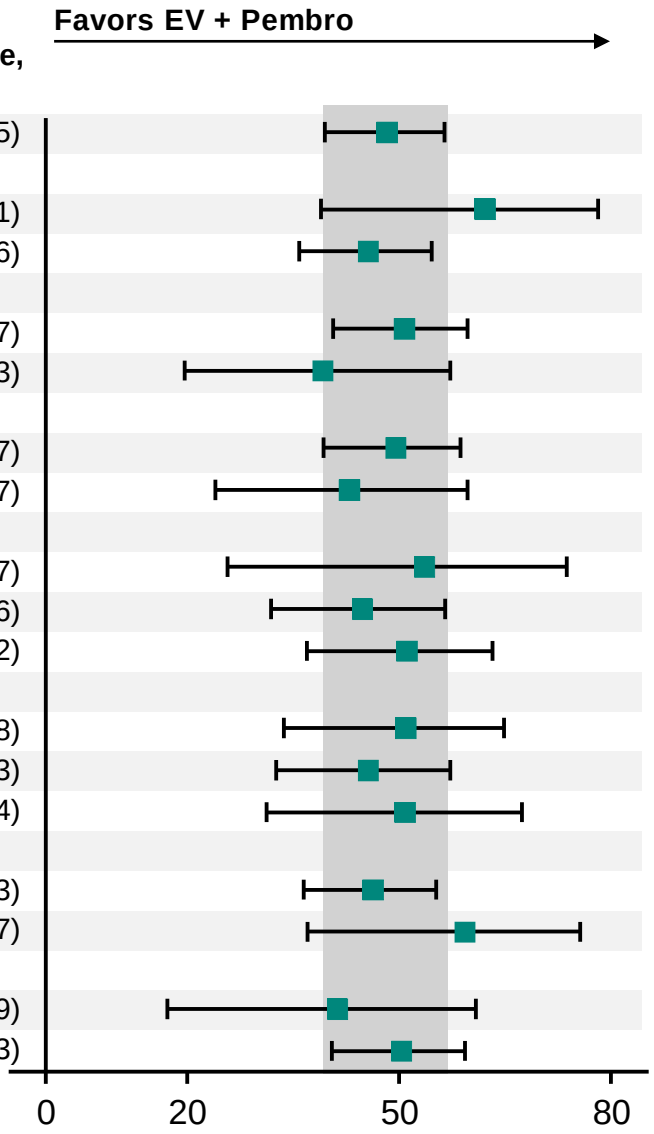
Median time from randomization to data cutoff date: **25.6 months (range, 11.8-53.7)**

CPS, combined positive score; EV, enfortumab verdotin; PD-L1, programmed cell death ligand 1; pembro, pembrolizumab; UC, urothelial carcinoma.
[a]Included 3 participants who received surgery without on-study neoadjuvant therapy. [b]Incomplete resection included: unresectable tumor, newly discovered metastatic disease, or other. [c]10 withdrawal by participant, 7 adverse event, 3 progressive disease, and 1 physician decision. [d]13 withdrawal by participant, 3 adverse event,1 lost to follow-up, and 1 physician decision. Data cutoff date: June 6, 2025.

pCR by BICR in the ITT Population

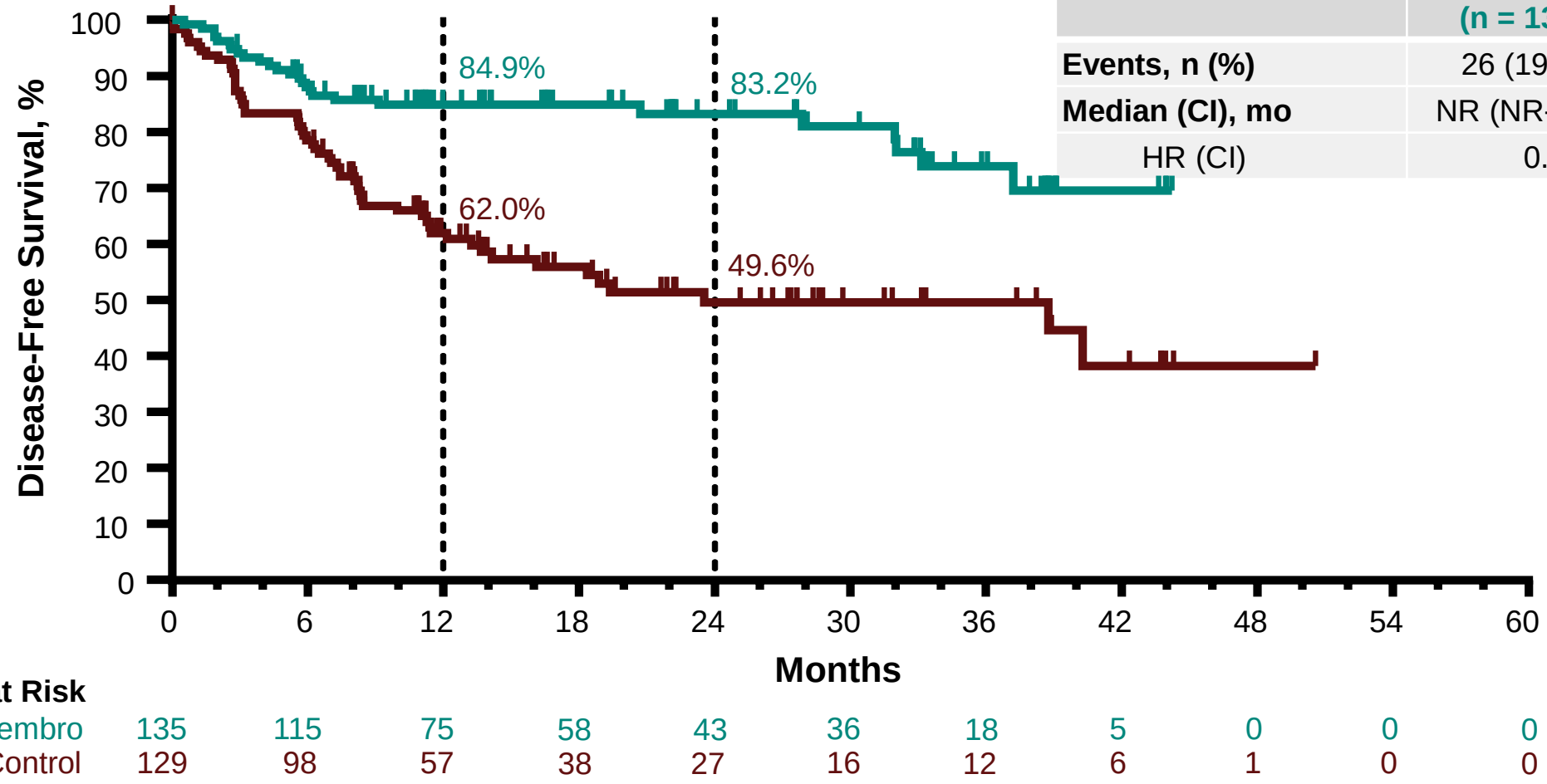


	Number with pCR/N		pCR difference, % (CI)
	EV + Pembro	Control	
Overall	97/170	15/174	48.3 (39.5-56.5)
Age, years			
<65	21/29	3/29	62.1 (38.9-78.1)
≥65	76/141	12/145	45.6 (35.9-54.6)
Sex			
Male	81/137	11/131	50.7 (40.7-59.7)
Female	16/33	4/43	39.2 (19.6-57.3)
Race			
White	78/132	13/136	49.5 (39.3-58.7)
All others	18/37	2/35	42.9 (24.0-59.7)
Geographic region			
US	14/21	3/23	53.6 (25.7-73.7)
EU	40/78	5/77	44.8 (31.9-56.6)
MOW	43/71	7/74	51.1 (37.0-63.2)
Smoking status			
Never	33/55	4/44	50.9 (33.7-64.8)
Former	45/82	8/68	45.6 (32.6-57.3)
Current	19/33	3/44	50.8 (31.3-67.4)
Cisplatin status			
Ineligible	78/142	12/139	46.3 (36.5-55.3)
Declining	19/28	3/35	59.3 (37.1-75.7)
Tumor stage			
T2N0	18/30	6/32	41.3 (17.2-60.9)
T3/T4aN0	76/133	9/132	50.3 (40.5-59.3)



MOW, most of world.
*Denotes statistical significance (one-sided boundary .00025). [a]Based on the stratified Miettinen and Nurminen method.
[b]97 of 149 participants (65.0%) who underwent surgery and received EV + pembro had a pCR. Data cutoff date: June 6, 2025.

Disease-Free Survival by BICR[a]



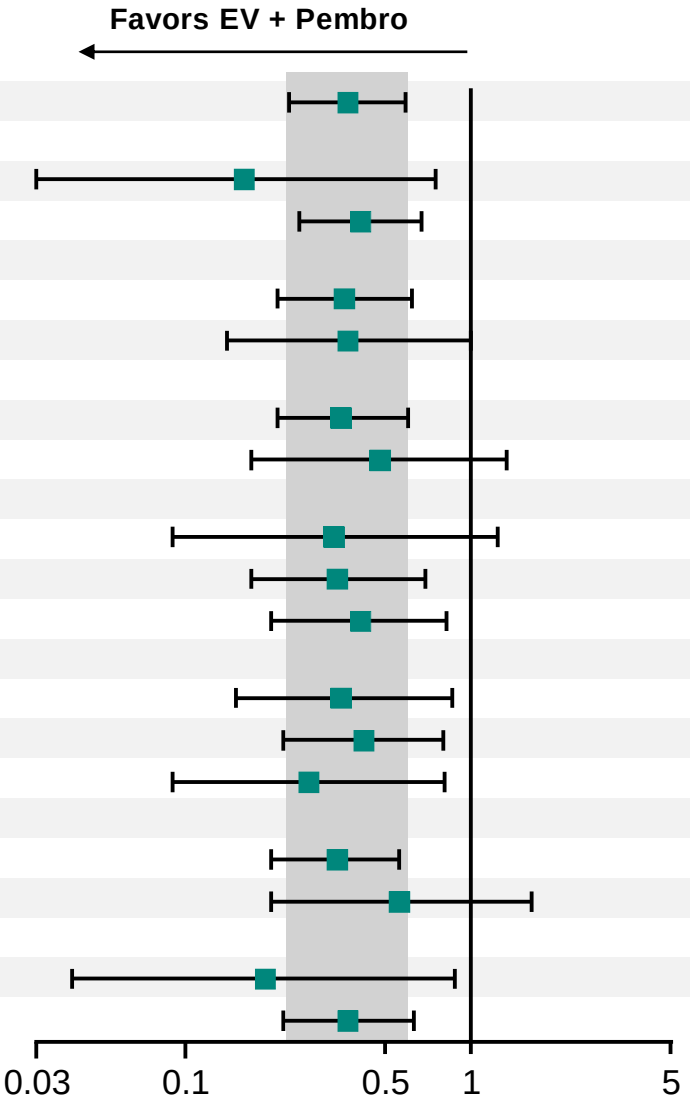
	EV + Pembro (n = 135)	Control (n = 129)
Events, n (%)	26 (19.3)	57 (44.2)
Median (CI), mo	NR (NR-NR)	23.6 (13.7-NR)
HR (CI)	0.37 (0.23-0.59)[b]	

HR, hazard ratio; NR, not reached.

[a]Participants were considered disease-free after RC + PLND for DFS analysis if they had complete resection (no gross residual disease) and no evidence of disease on a post-surgery scan. [b]Based on Cox regression model with the Efron method of tie handling with treatment as a covariate. Data cutoff date: June 6, 2025.

Disease-Free Survival: Subgroups

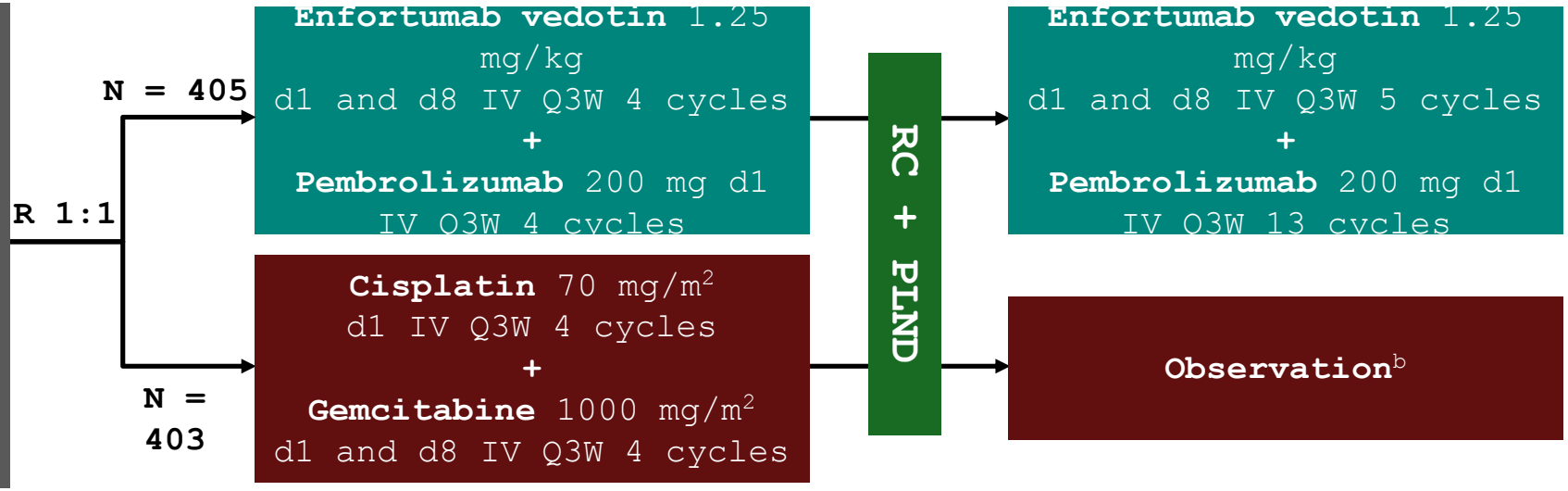
	Events, n/N (%)		HR (CI)
	EV + Pembro	Control	
Overall	26/135 (19.3)	57/129 (44.2)	0.37 (0.23-0.59)
Age, year			
<65	2/28 (7.1)	9/22 (40.9)	0.16 (0.03-0.75)
≥65	24/107 (22.4)	48/107 (44.9)	0.41 (0.25-0.67)
Sex			
Male	20/110 (18.2)	44/99 (44.4)	0.36 (0.21-0.62)
Female	6/25 (24.0)	13/30 (43.3)	0.37 (0.14-1.00)
Race			
White	20/107 (18.7)	46/103 (44.7)	0.35 (0.21-0.60)
All others	6/27 (22.2)	10/24 (41.7)	0.48 (0.17-1.33)
Geographic region			
US	3/18 (16.7)	8/20 (40.0)	0.33 (0.09-1.24)
EU	11/63 (17.5)	26/58 (44.8)	0.34 (0.17-0.69)
MOW	12/54 (22.2)	23/51 (45.1)	0.41 (0.20-0.82)
Smoking status			
Never	8/44 (18.2)	13/29 (44.8)	0.35 (0.15-0.86)
Former	14/66 (21.2)	29/67 (43.3)	0.42 (0.22-0.80)
Current	4/25 (16.0)	15/33 (45.5)	0.27 (0.09-0.81)
Cisplatin status			
Ineligible	21/112 (18.8)	46/98 (46.9)	0.34 (0.20-0.56)
Declining	5/23 (21.7)	11/31 (35.5)	0.56 (0.20-1.63)
Tumor stage			
T2N0	2/24 (8.3)	9/24 (37.5)	0.19 (0.04-0.88)
T3/T4aN0	21/105 (20.0)	46/100 (46.0)	0.37 (0.22-0.63)



Data cutoff date: June 6, 2025.

KEYNOTE-B15/EV-304 Study (NCT04700124)

- Adults with MIBC
- Clinical stage T2-T4aN0M0 or T1-T4aN1M0 by central assessment
- Urothelial histology ≥50%
- Eligible for RC + PLND
- Did not meet any Galsky criteria for cisplatin ineligibility



Stratification Factors

- PD-L1 status (CPS ≥10 vs. <10)[a]
- Clinical stage (T2N0 vs. T3/T4aN0 vs. T1-4aN1)
- Geographic region (US vs. EU vs. Most of World)

Primary endpoint: Event-free survival (EFS) by BICR

Key secondary endpoints: OS and pathological complete response (pCR; pT0N0, i.e. absence of viable tumor in examined tissue from surgery) by central pathologist review

Other secondary endpoints include: Safety

BICR, blinded independent central review; CPS, combined positive score; IV, intravenous; Q3W, every 3 weeks.
[a]Assessed by PD-L1 IHC 22C3 pharmDx (Agilent, Carpinteria, CA); CPS = # PD-L1–staining cells (tumor cells, lymphocytes, and macrophages) ÷ total # viable tumor cells × 100.
[b]As of Feb 2023, adjuvant nivolumab was permitted when clinically indicated and regionally available.

Data cutoff date: 27 October 2025

Baseline Characteristics

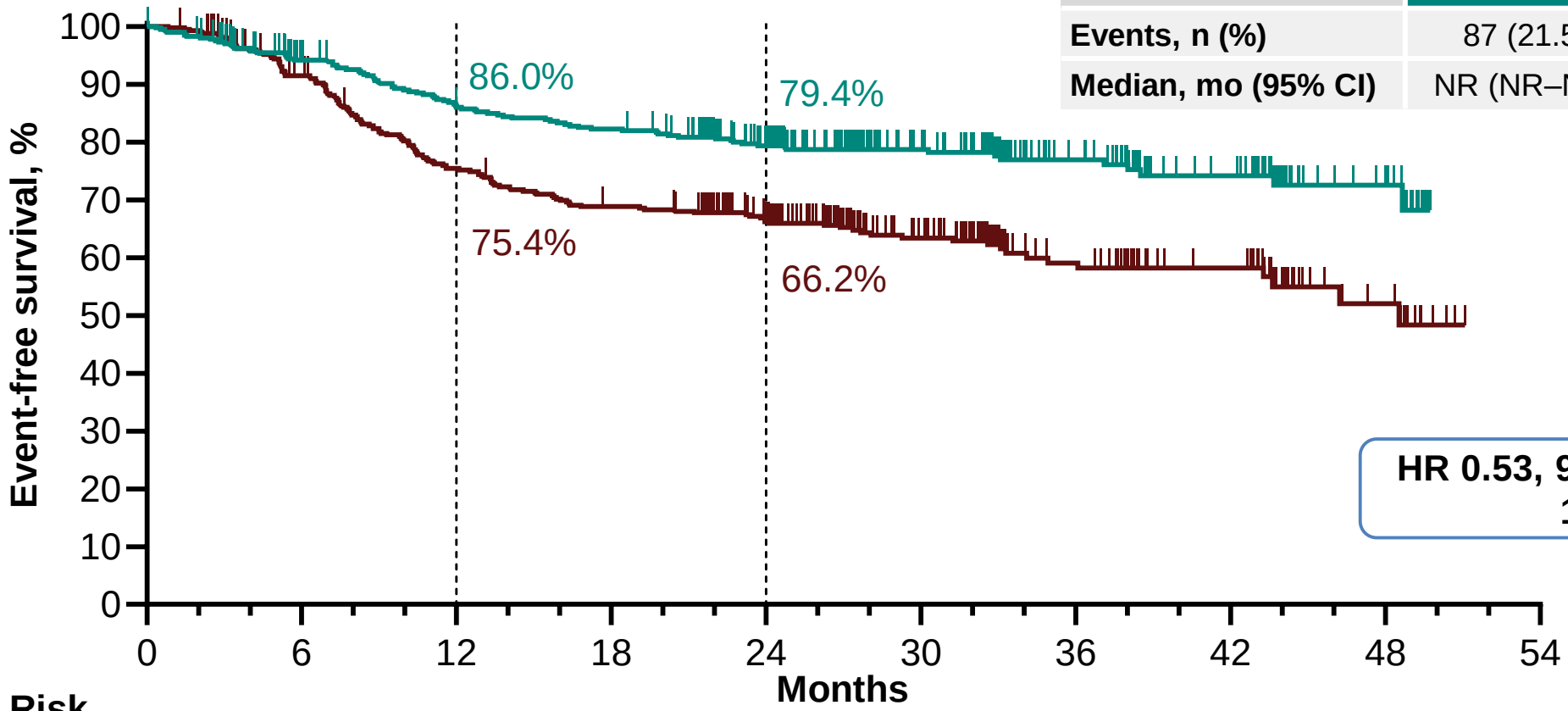
Characteristic, n (%)	EV + pembro N = 405	Cis + gem N = 403
Median age (range), years	66.0 (35−83)	66.0 (37−85)
≥65 years	247 (61.0)	247 (61.3)
Male	327 (80.7)	327 (81.1)
ECOG PS		
0	317 (78.3)	310 (76.9)
1	88 (21.7)	93 (23.1)
Region		
United States	59 (14.6)	59 (14.6)
European Union	206 (50.9)	205 (50.9)
Most of world	140 (34.6)	139 (34.5)
PD-L1 CPS		
≥10	233 (57.5)	230 (57.1)
<10	171 (42.2)	173 (42.9)
Missing	1 (0.2)	0
Tumor stage at baseline (central assessment)[a]		
T2N0	79 (19.5)	77 (19.1)
T3/T4aN0	293 (72.3)	293 (72.7)
T1-4aN1	33 (8.1)	33 (8.2)
Pure urothelial carcinoma histology	370 (91.4)	353 (87.6)
Creatinine clearance		
≥90 mL/min	149 (36.8)	156 (38.7)
≥60 and <90 mL/min	252 (62.2)	245 (60.8)
≥30 and <60 mL/min[b]	4 (1.0)	2 (0.5)

[a]Using both pathology of transurethral resection of bladder tumor specimen and imaging. **By investigator assessment, 287 pts (70.9%) in the EV + pembro arm and 296 pts (73.4%) in the cis + gem arm had T2N0 stage MIBC at baseline.** [b]Protocol deviation.

Data cutoff date: 27 October 2025

Primary Endpoint: EFS by BICR
ITT Population

	EV + pembro N = 405	Cis + gem N = 403
Events, n (%)	87 (21.5)	146 (36.2)
Median, mo (95% CI)	NR (NR–NR)	48.5 (43.3–NR)



HR 0.53, 95% CI 0.41–0.70, 1-sided *P* <.0001*

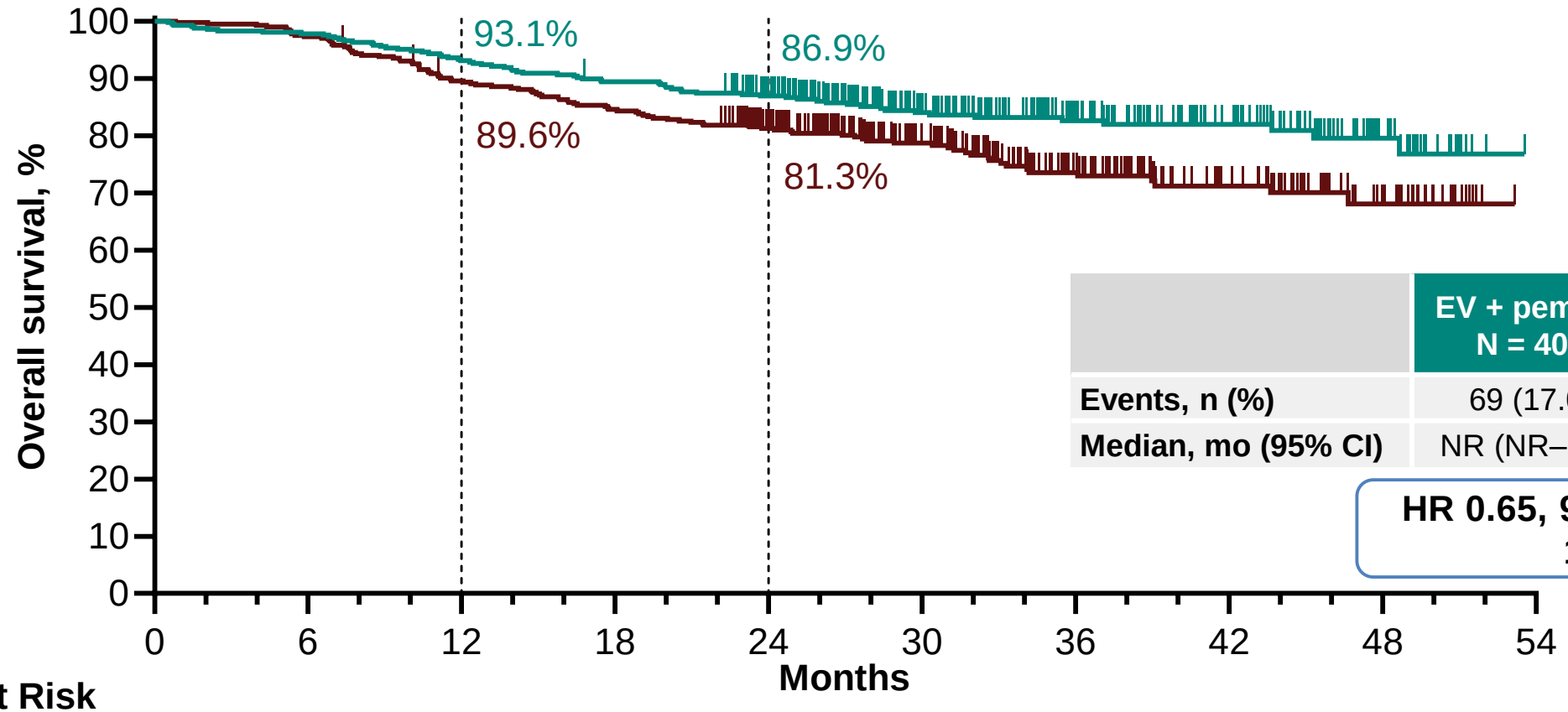
No. at Risk

EV + pembro	405	351	317	303	257	154	100	63	23	0
Cis + gem	403	350	286	259	216	131	70	45	16	0

NR, not reached. * denotes statistical significance (one-sided boundary 0.0082).

Data cutoff date: 27 October 2025

Key Secondary Endpoint: OS
ITT Population



	EV + pembro N = 405	Cis + gem N = 403
Events, n (%)	69 (17.0)	99 (24.6)
Median, mo (95% CI)	NR (NR–NR)	NR (NR–NR)

HR 0.65, 95% CI 0.48–0.89, 1-sided *P* =.0029*

No. at Risk

EV + pembro	405	396	377	361	325	215	142	90	34	0
Cis + gem	403	392	358	338	295	201	119	67	29	0

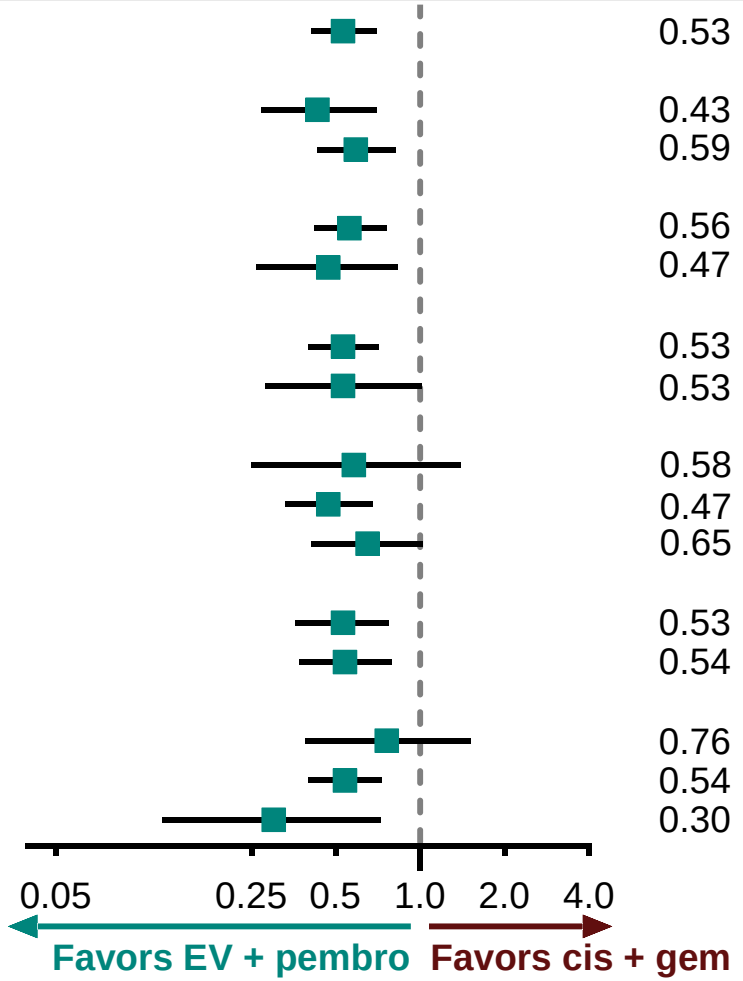
- In total, 44/87 (50.6%) of pts with an EFS event in the EV + pembro arm and 86/146 (58.9%) of pts with an EFS event in the cis + gem arm received any subsequent systemic therapy

NR, not reached. * denotes statistical significance (one-sided boundary 0.0038).

Data cutoff date: 27 October 2025

EFS by BICR in Key Subgroups
ITT Population

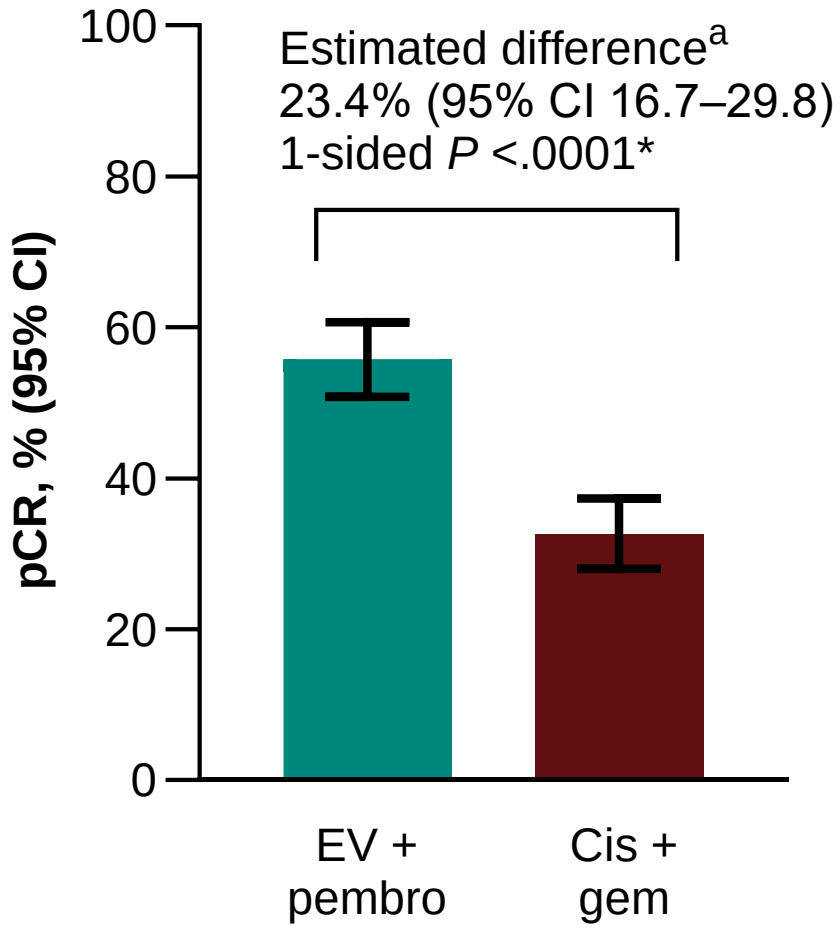
	Events/Participants		HR (95% CI)
	EV + pembro	Cis + gem	
Overall	87/405	146/403	0.53 (0.41-0.70)
Age			
<65 years	24/158	51/156	0.43 (0.27-0.70)
≥65 years	63/247	95/247	0.59 (0.43-0.82)
Sex			
Male	69/327	113/327	0.56 (0.42-0.76)
Female	18/78	33/76	0.47 (0.26-0.83)
Race			
White	73/329	119/314	0.53 (0.40-0.71)
All others	14/76	27/87	0.53 (0.28-1.01)
Region			
United States	8/59	14/59	0.58 (0.25-1.39)
European Union	48/206	86/205	0.47 (0.33-0.68)
Most of world	31/140	46/139	0.65 (0.41-1.02)
PD-L1 CPS			
≥10	43/233	74/230	0.53 (0.36-0.77)
<10	43/171	72/173	0.54 (0.37-0.79)
Tumor stage by BICR			
T2N0	15/79	19/77	0.76 (0.39-1.51)
T3/T4aN0	65/293	110/293	0.54 (0.40-0.73)
T1-4aN1	7/33	17/33	0.30 (0.12-0.72)



Subgroup levels with <10 events across both treatment arms were not included in forest plots.

Data cutoff date: 27 October 2025

Key Secondary Endpoint: pCR by Central Pathology Review
ITT Population



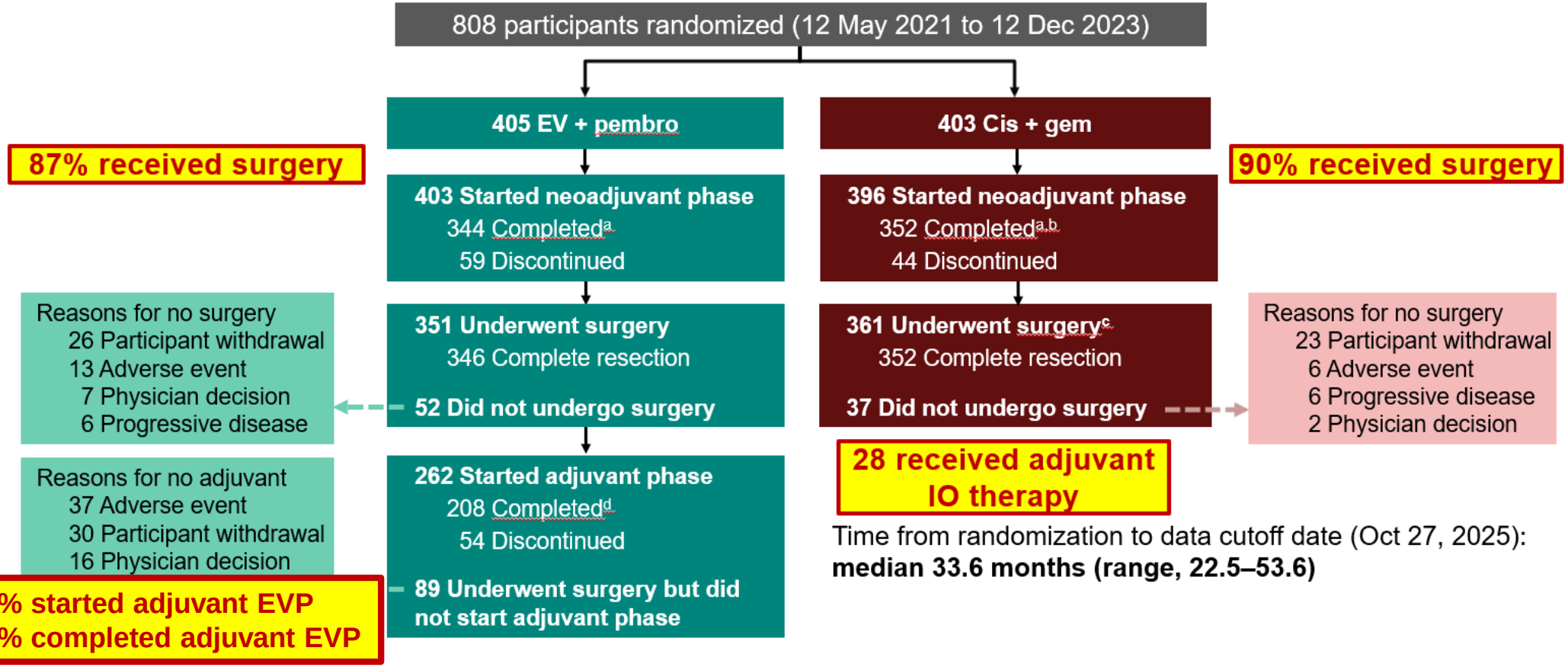
	EV + pembro N = 405	Cis + gem N = 403
pCR, n	226	131
pCR rate, % (95% CI)	**55.8 (50.8–60.7)**	**32.5 (28.0–37.3)**

- **pCR:** defined as absence of viable tumor in examined tissue from RC + PLND (pT0N0)
- Pts who discontinued study therapy prior to definitive surgery were classified as non-responders
- Out of pts who underwent surgery, 226/351 (64.4%) in the EV + pembro arm and 131/361 (36.3%) in the cis + gem arm had pCR

* denotes statistical significance (one-sided boundary 0.001).
[a]Based on stratified Miettinen and Nurminen method.

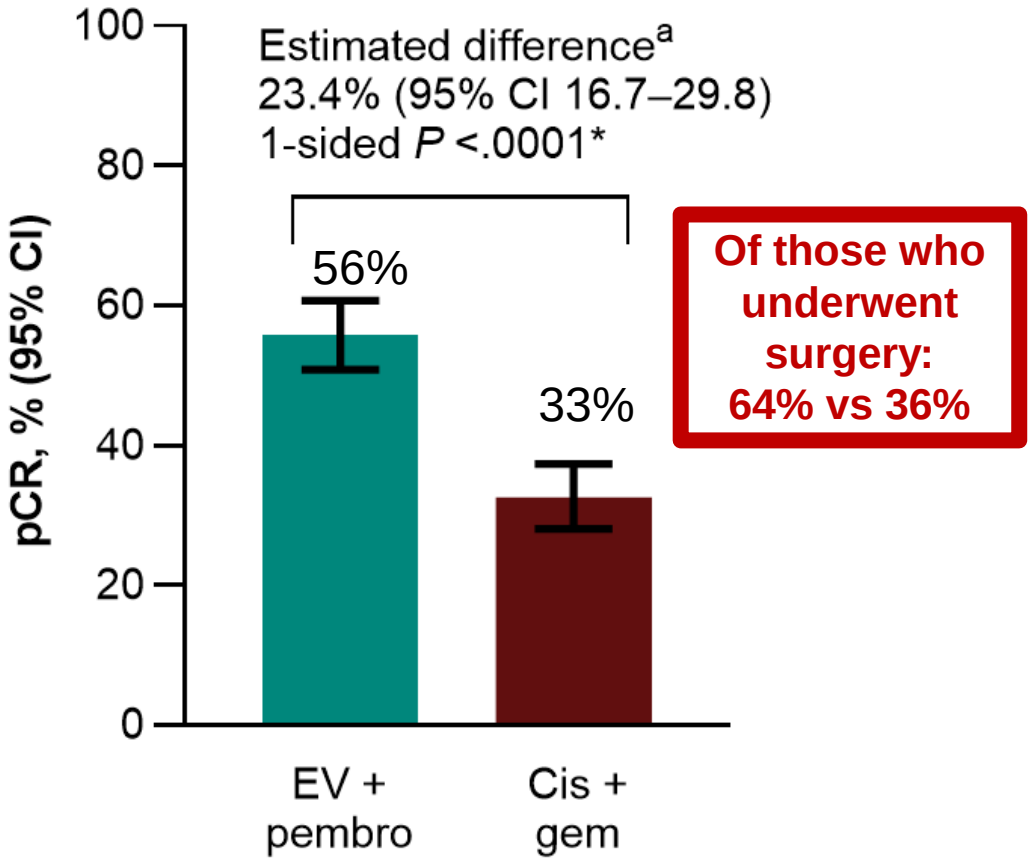
Data cutoff date: 27 October 2025

Patient Disposition

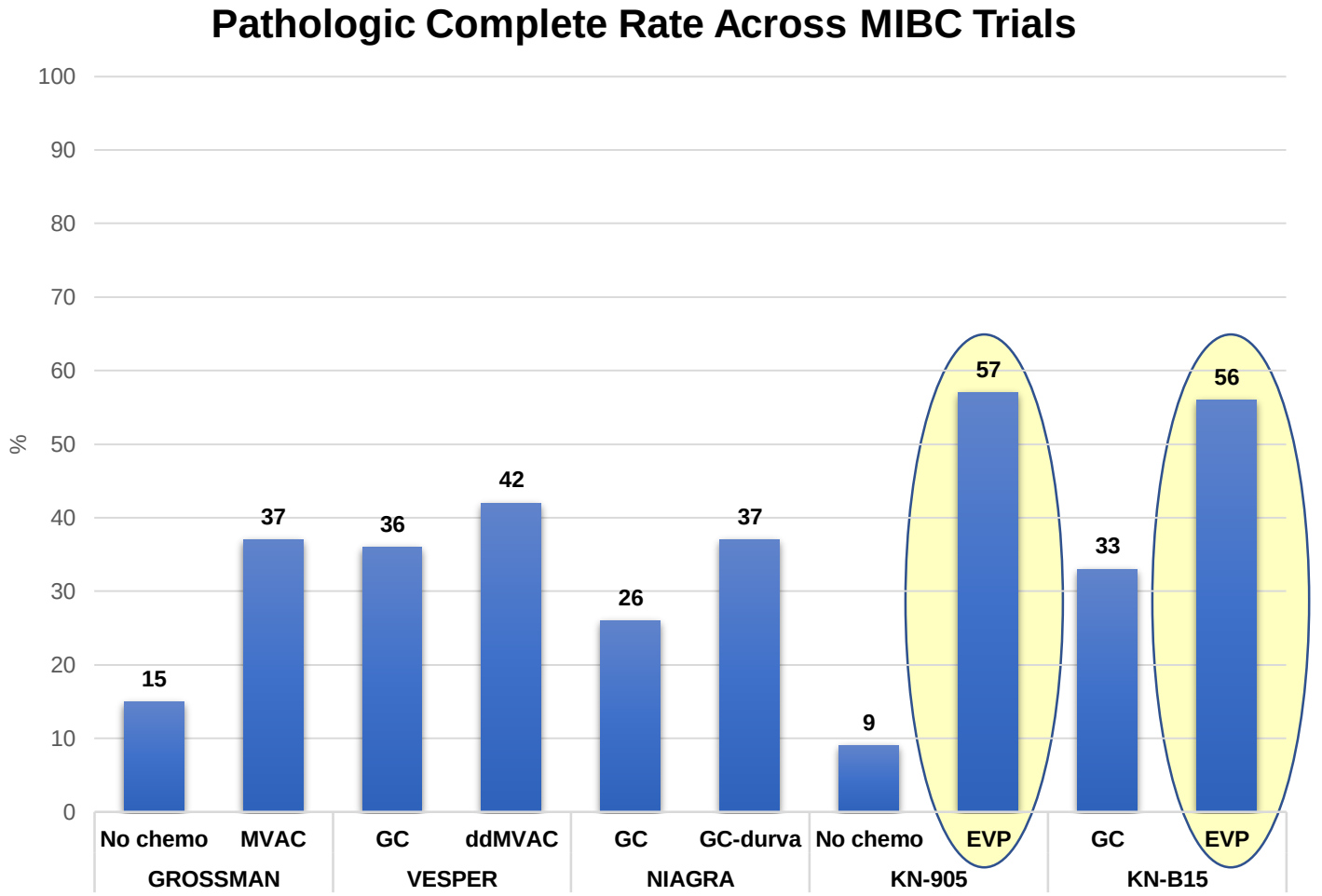


[a]Indicates pt received 4 cycles of at least 1 of the 2 study drugs (EV or pembro or cis or gem). [b]29/396 pts (7.3%) received all cis + gem cycles with split-dose cisplatin.
[c]Two participants underwent surgery but did not start neoadjuvant cis + gem. [d]Completed indicates a pt received 5 adjuvant cycles of EV or 13 adjuvant cycles of pembro.

Complete Pathologic Response Across Trials



Of those who underwent surgery: 64% vs 36%



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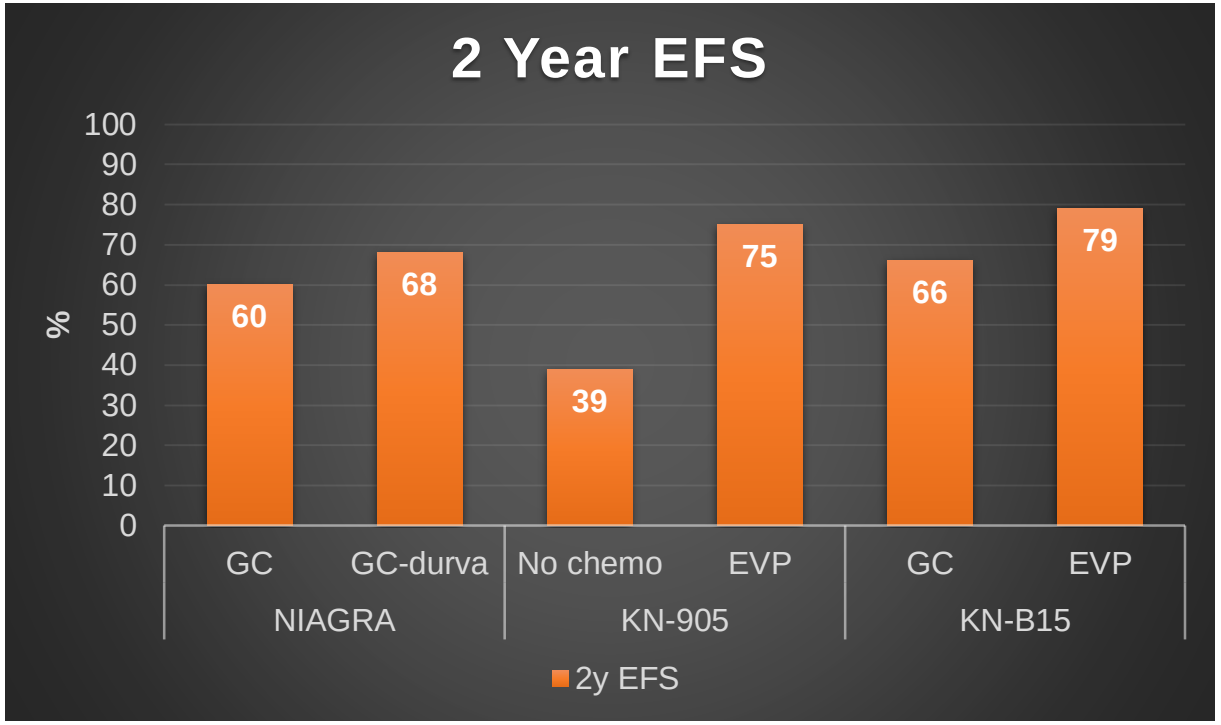
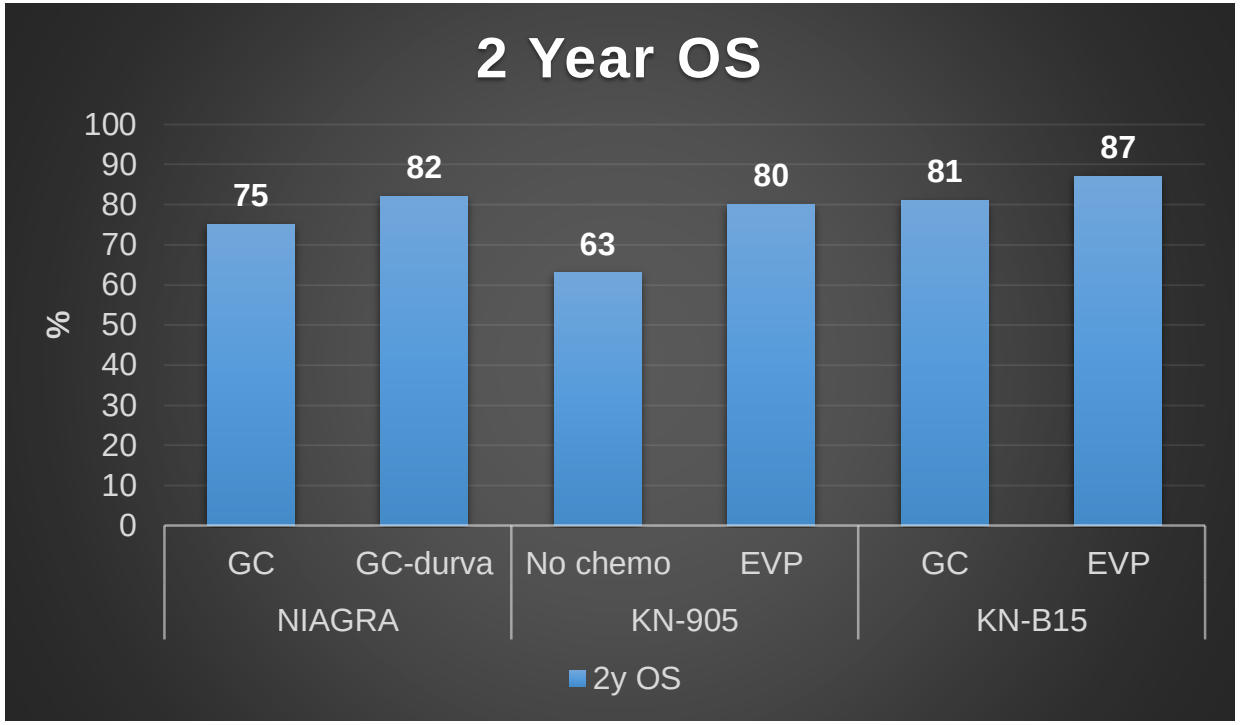
EFS and OS across MIBC Trials





HR 0.68
@ median 42 months

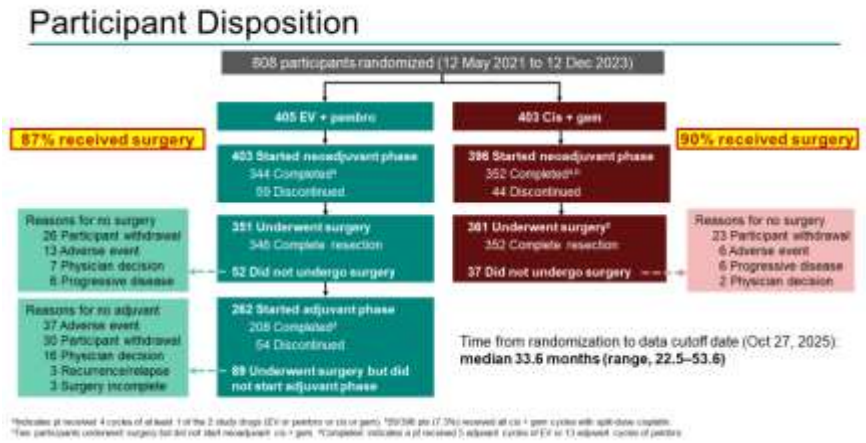
HR 0.53
@ median 33 months

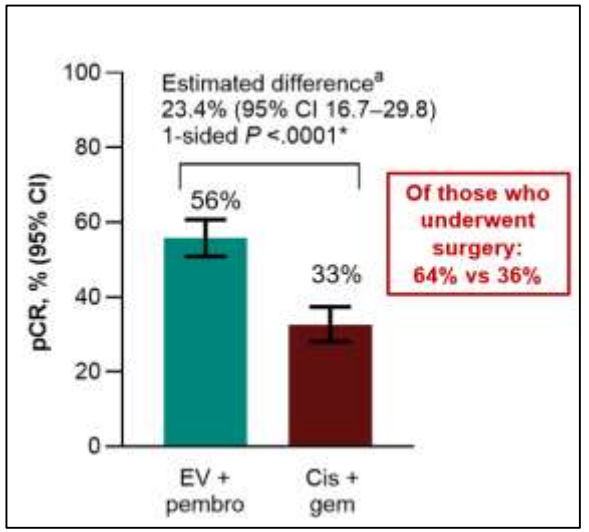
HR 0.75
@ median 46 months

HR 0.65
@ median 33 months

Powles et al N Engl J Med. 2024 Nov 14;391(19):1773-1786; [2]Galsky J Clin Oncol 43, 15-21(2025); [3]N Engl J Med. 2025 Dec 18;393(24):2395-2408.; [4]Vulsteke ESMO 2025; [6]Galsky GU ASCO 2026

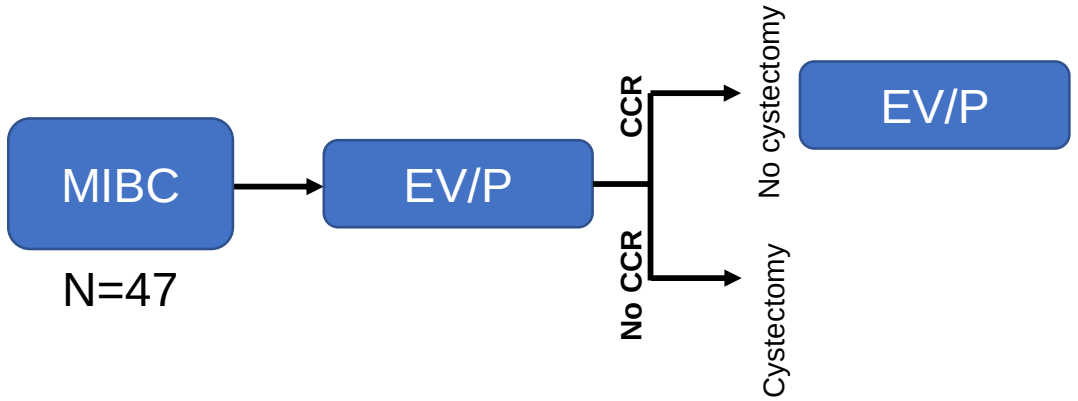
Ongoing Bladder Preservation Trials with EV/P





EV/P Alone

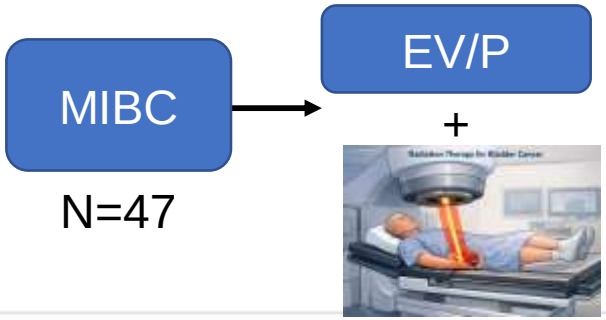
NCT06809140



PI: Matt Galsky

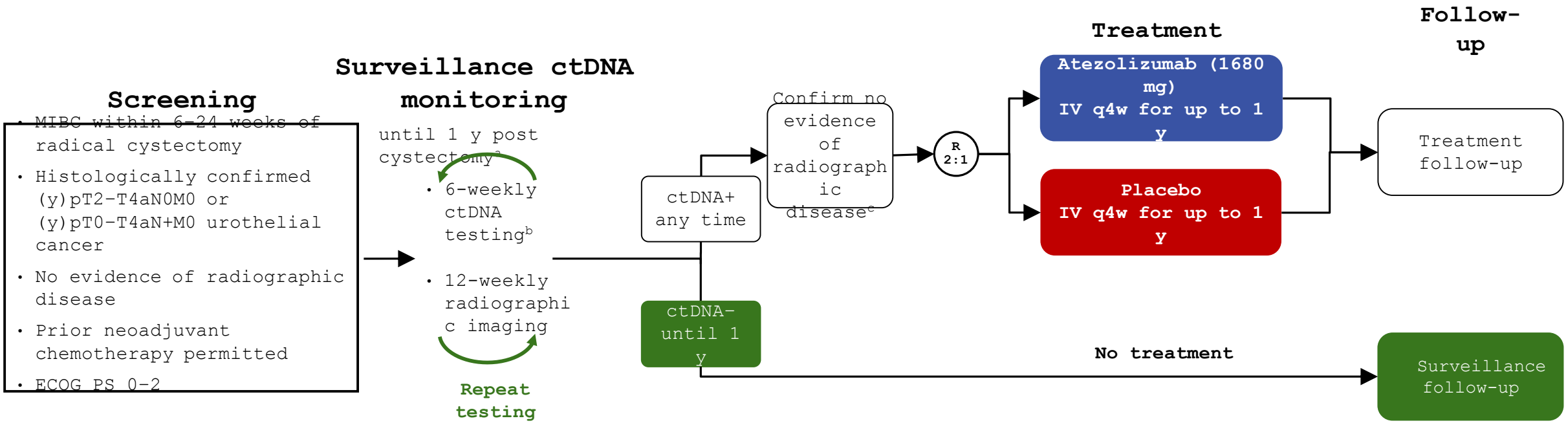
EV/P with Radiation

EV-PRIME (NCT06470282)



PI: Vadim Koshkin

IMvigor011 study design



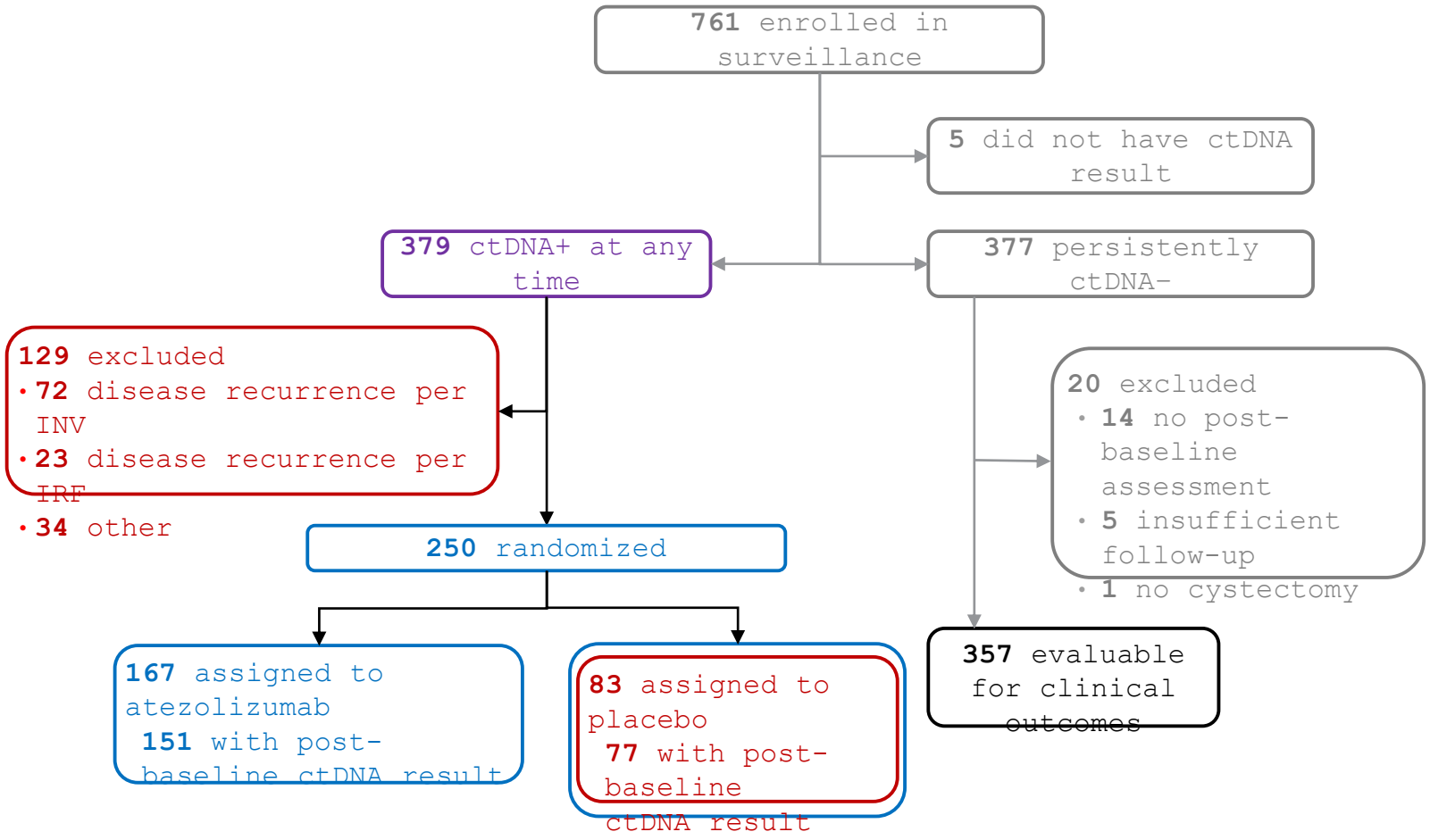
Primary endpoint: INV-assessed DFS

Key secondary endpoint: OS

The global, randomized, Phase III IMvigor011 trial was designed to evaluate ctDNA-guided adjuvant atezolizumab vs placebo in patients with MIBC

ClinicalTrials.gov number, NCT04660344. Stratification factors were nodal status (positive vs negative), tumor stage at cystectomy (≤pT2 vs pT3/pT4), PD-L1 status (IC0/1 [<5%] vs IC2/3 [≥5%] by VENTANA SP142 immunohistochemistry assay) and time from cystectomy to 1st ctDNA+ sample (≤20 vs >20 weeks). [a] Early versions of the protocol included a 21-mo surveillance ctDNA monitoring period. [b] ctDNA status was determined by the Natera Signatera™ MRD test (outside of mainland China) and by the BGI MRD test (in mainland China). [c] By INV and IRF assessment. ctDNA(+/–), circulating tumor DNA(-positive/-negative); DFS, disease-free survival; ECOG PS, Eastern Cooperative Oncology Group performance status; IC, immune cells; INV, investigator; IRF, independent review facility; IV, intravenous; OS, overall survival; PD-L1, programmed death-ligand 1; q4w, every 4 weeks; R, randomized; y, year. Adapted from Powles T, et al. ESMO 2025 (Abstract LBA8) with permission.

Consort diagram and analysis populations



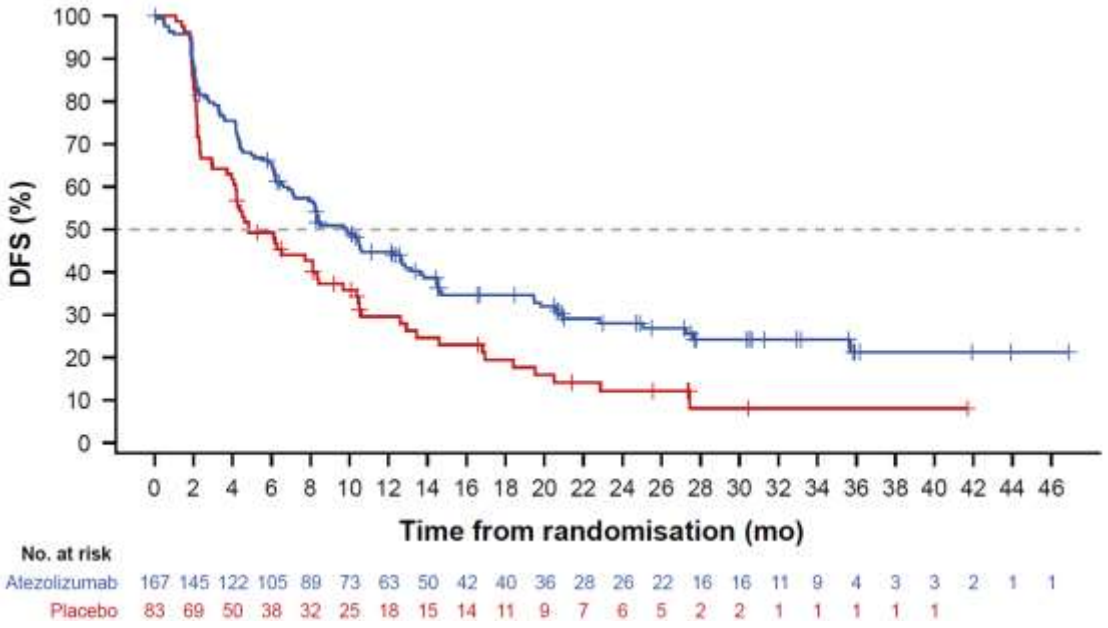
Analysis populations

- All ctDNA+ (n=379)
- ctDNA+ untreated (screen failed or placebo treated; n=212)
- ctDNA+ randomized with ≥1 post-baseline ctDNA result (n=228)
- Persistent ctDNA− (n=357)

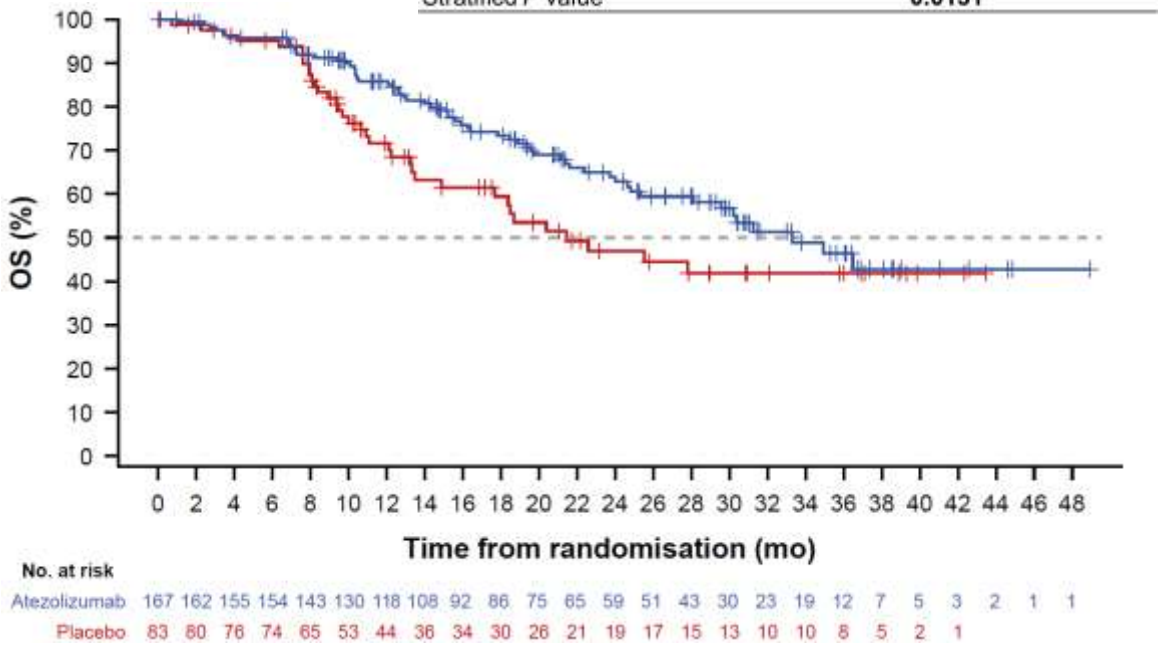
Figure adapted from Powles T, et al. ESMO 2025 (Abstract LBA8) with permission.
Powles T, et al. N Engl J Med 2025;393:2395-408.

IMvigor011 met primary DFS and secondary OS endpoints at the 1st interim analysis

	Atezolizumab (n=167)	Placebo (n=83)
Events, n (%)	112 (67.1)	66 (79.5)
DFS, median (95% CI), mo	9.9 (7.2, 12.7)	4.8 (4.1, 8.3)
Stratified HR (95% CI)	**0.64 (0.47, 0.87)**	
Stratified *P* value	**0.0047**	



	Atezolizumab (n=167)	Placebo (n=83)
Events, n (%)	60 (35.9)	36 (43.4)
OS, median (95% CI), mo	32.8 (27.7, NE)	21.1 (14.7,NE)
Stratified HR (95% CI)	**0.59 (0.39, 0.90)**	
Stratified *P* value	**0.0131**	



CI, confidence interval; HR, hazard ratio; Mo, months; NE, not evaluable.

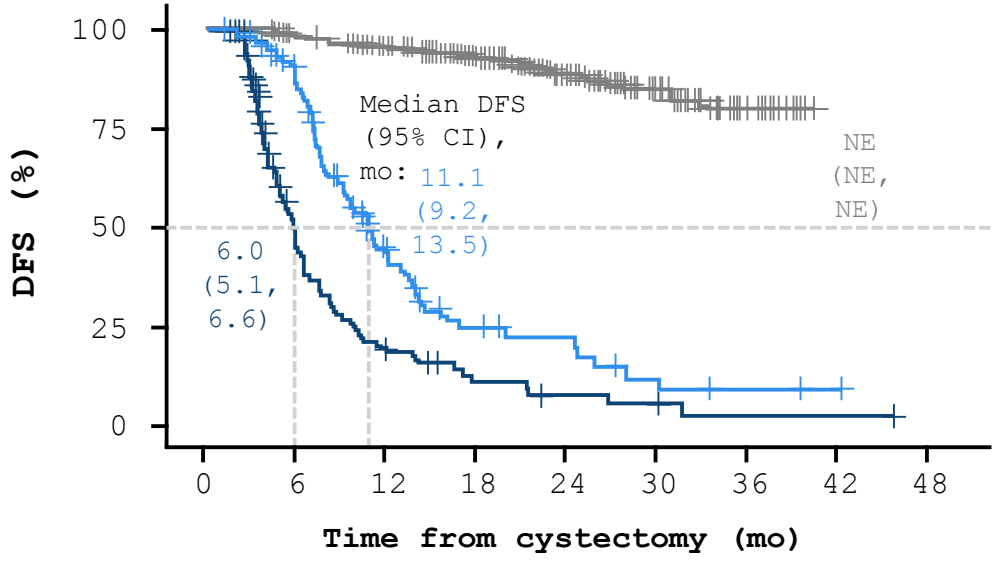
Figures reproduced from Powles T, et al. ESMO 2025 (Abstract LBA8) with permission.
Powles T, et al. N Engl J Med 2025;393:2395-408.

Timing of ctDNA positivity provided prognostic information beyond binary ctDNA status in untreated patients

Early ctDNA positivity was associated with inferior clinical outcomes

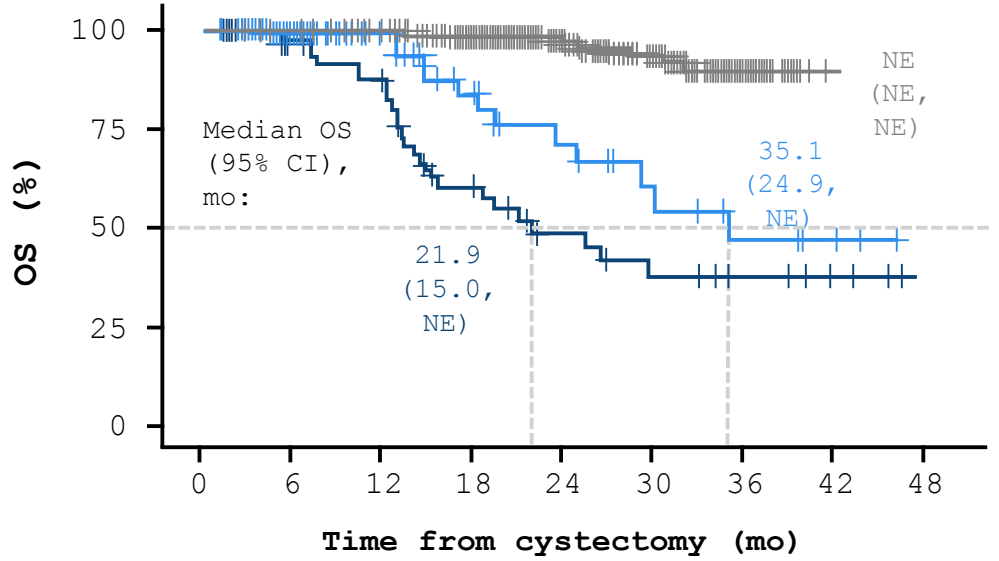
ctDNA+ untreated (n=212)

ctDNA− (n=357)



No. at risk

ctDNA−	357	342	303	233	116	66	20	0	0
ctDNA+ at initial test	126	39	15	7	4	3	1	1	0
ctDNA+ at subsequent test	86	69	28	12	9	4	2	1	0



No. at risk

ctDNA−	357	345	319	250	138	79	26	0	0
ctDNA+ at initial test	126	47	38	22	14	10	7	3	0
ctDNA+ at subsequent test	86	70	42	25	15	10	6	3	0

DFS rate, % (no. at risk)

Mo	ctDNA−	ctDNA+ at initial test	ctDNA+ at subsequent test
6	98.0 (342)	49.9 (39)	89.1 (69)
12	95.4 (303)	19.2 (15)	43.8 (28)
24	88.4 (116)	8.2 (4)	22.3 (9)

OS rate, % (no. at risk)

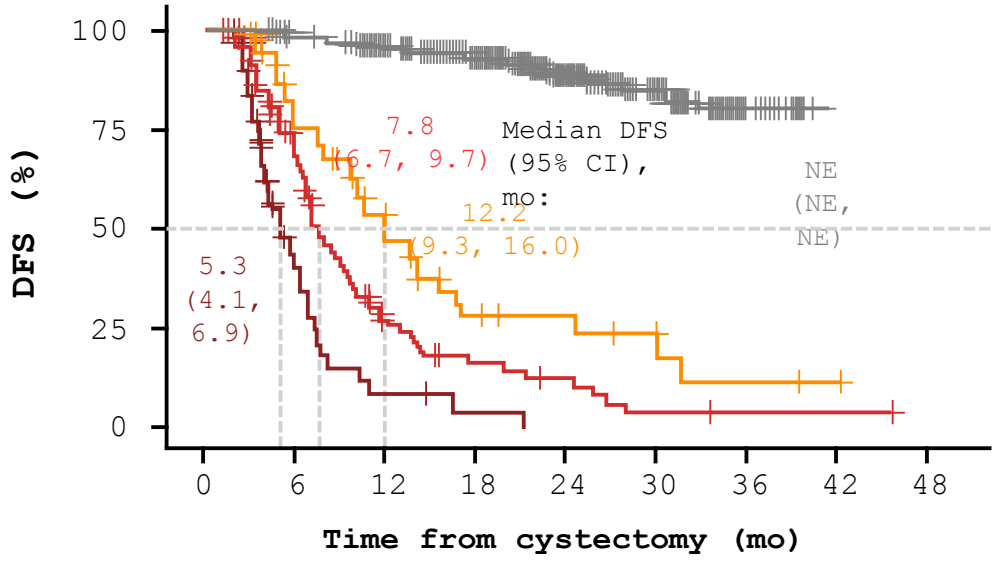
Mo	ctDNA−	ctDNA+ at initial test	ctDNA+ at subsequent test
6	100 (345)	96.4 (47)	98.8 (70)
12	100 (319)	87.4 (38)	98.8 (42)
24	97.1 (138)	48.5 (14)	71.8 (15)

ctDNA concentration provided prognostic information be… binary ctDNA status in untreated patients

High ctDNA concentration was associated with inferior clinical outcomes

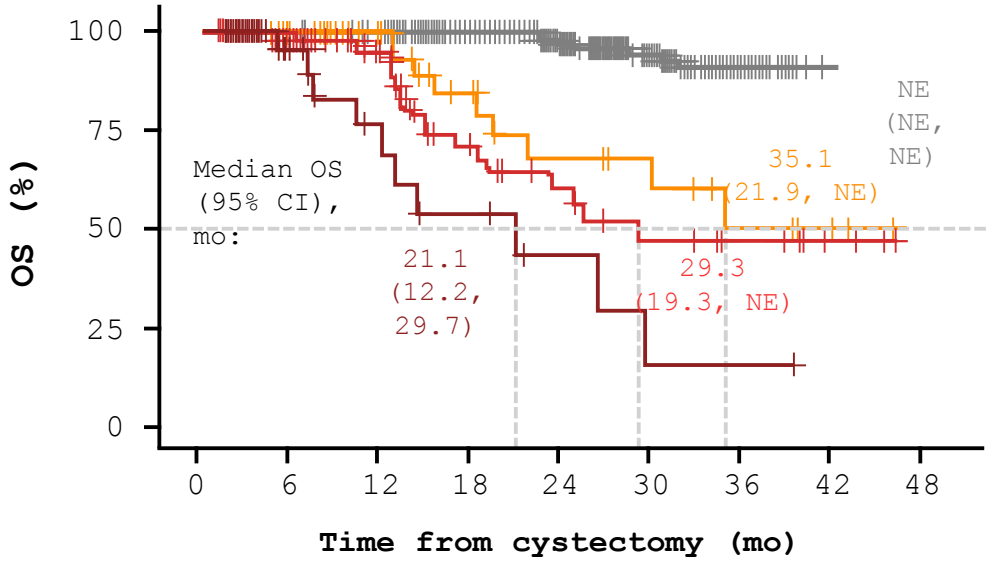
ctDNA+ untreated (n=212)

ctDNA− (n=357)



No. at risk

ctDNA−	357	342	303	233	116	66	20	0	0
≤0.1 MTM/mL	56	39	22	9	7	5	2	1	0
>0.1–≤3 MTM/mL	99	55	18	9	6	2	1	1	0
>3 MTM/mL	57	14	3	1	0	0	0	0	0



No. at risk

ctDNA−	357	345	319	250	138	79	26	0	0
≤0.1 MTM/mL	56	40	30	18	11	9	5	3	0
>0.1–≤3 MTM/mL	99	59	40	23	15	10	7	3	0
>3 MTM/mL	57	18	10	6	3	1	1	0	0

DFS rate, % (no. at risk)

Mo	ctDNA−	≤0.1 MTM/mL	>0.1–≤3 MTM/mL	>3 MTM/mL
6	98.0 (342)	82.1 (39)	71.2 (55)	44.0 (14)
12	95.4 (303)	53.4 (22)	26.6 (18)	9.4 (3)
24	88.4 (116)	28.4 (7)	13.2 (6)	0 (0)

OS rate, % (no. at risk)

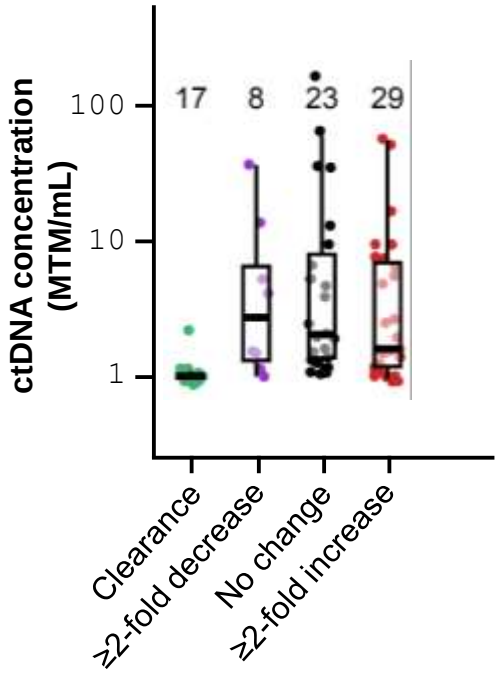
Mo	ctDNA−	≤0.1 MTM/mL	>0.1–≤3 MTM/mL	>3 MTM/mL
6	100 (345)	100 (40)	97.2 (59)	95.2 (18)
12	100 (319)	100 (30)	95.0 (40)	76.0 (10)
24	97.1 (138)	67.4 (11)	60.1 (15)	42.6 (3)

Placebo: ctDNA clearance was associated with improved DFS

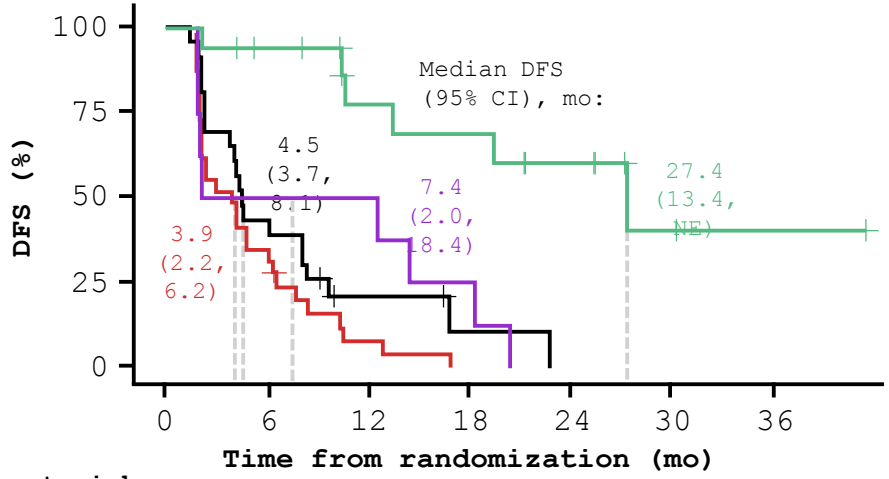
Patients who cleared ctDNA represent a prognostically favorable subgroup with low pre-treatment ctDNA concentration

ctDNA+ randomized (n=228)

Maximum pre-treatment ctDNA concentration



DFS



No. at risk

Clearance	17	14	9	8	6	2	1
≥2-fold decrease	8	4	4	2	0	0	0
No change	23	10	3	1	0	0	0
≥2-fold increase	29	10	2	0	0	0	0

DFS rate, % (no. at risk)

Mo	Clearance	≥2-fold decrease	No change	≥2-fold increase
6	94.1 (14)	50.0 (4)	43.5 (10)	34.5 (10)
12	77.6 (9)	50.0 (4)	20.9 (3)	7.9 (2)
24	60.4 (6)	0	0	0

Pre-treatment ctDNA concentration was defined as the maximum ctDNA concentration measured during surveillance or at C1D1. ctDNA dynamic categories are defined as the maximum observed change from pre-treatment to any single time point during C2–C11 (best ctDNA change). No change was defined as any fluctuation in ctDNA concentration that did not meet criteria for >2-fold increase or >2-fold decrease.

Completed bladder-sparing trials

RETAIN-1

Major Inclusion Criteria:
- **cT2-T3 N0M0**
- **ECOG 0-1**
- **Urothelial Predominant Histology**

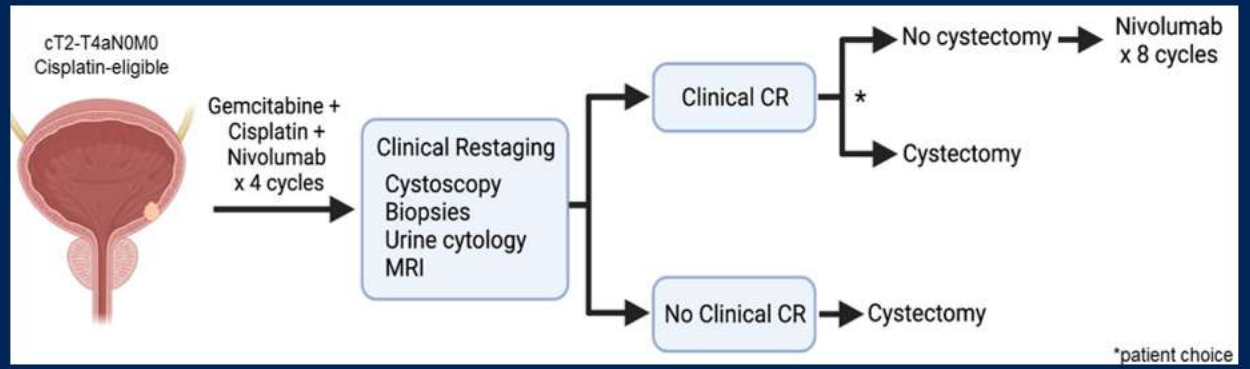
Not a randomized trial

TURBT #1 → AMVAC x 3 → TURBT #2

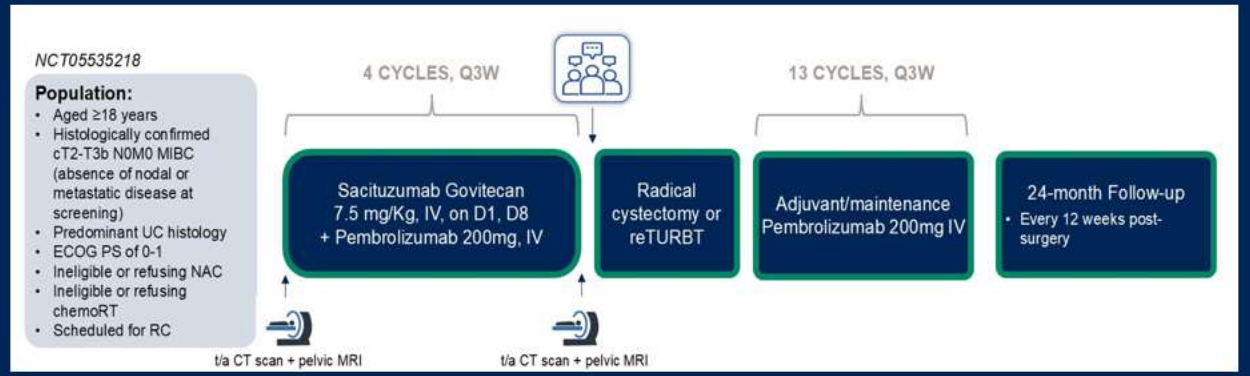
Sequencing (Caris)
Mutation positive defined as any alterations in:
- *ATM*
- *RB1*
- *FANCC*
- *ERCC2*

No residual tumor/cT0 **AND** Mutation Pos (+)		**Active Surveillance**
cTa or cTis or cT1 or Pos (+) cytology **OR** cT0 mutation Neg (-)	Patient & Physician Choose	**Intravesical Tx OR Chemo-RT OR Cystectomy**
cT2	Patient & Physician Choose	**Chemo-RT OR Cystectomy**
≥cT3		**Cystectomy**

HCRN GU16-257



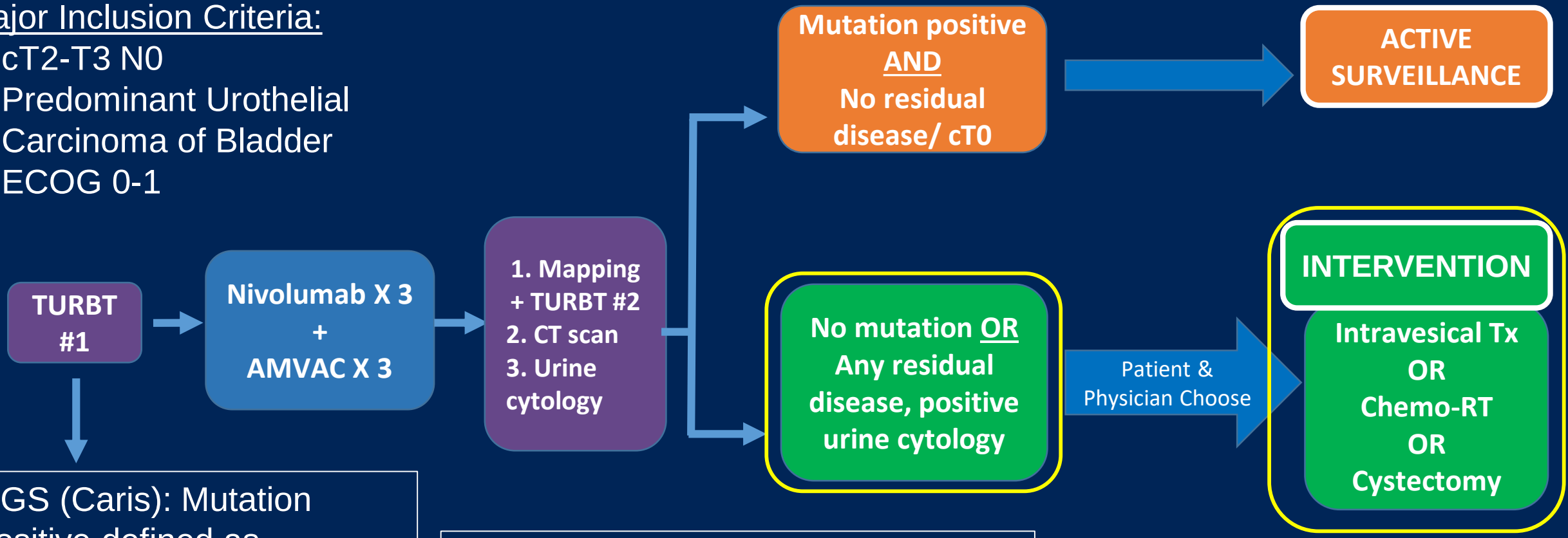
SURE-02



•Geynisman DM, *et al.* **J Clin Oncol.** 2025;43(9):1113–1122; Ghatalia P, *et al.* **J Clin Oncol.** 2025;43(5_suppl):815; Galsky MD, Daneshmand S, Izadmehr S, *et al.* **Nat Med.** 2023;29:2825–2834.
•Necchi A, *et al.* **J Clin Oncol.** 2025;43(16_suppl):4518;

RETAIN-2

Major Inclusion Criteria:
- cT2-T3 N0
- Predominant Urothelial Carcinoma of Bladder
- ECOG 0-1

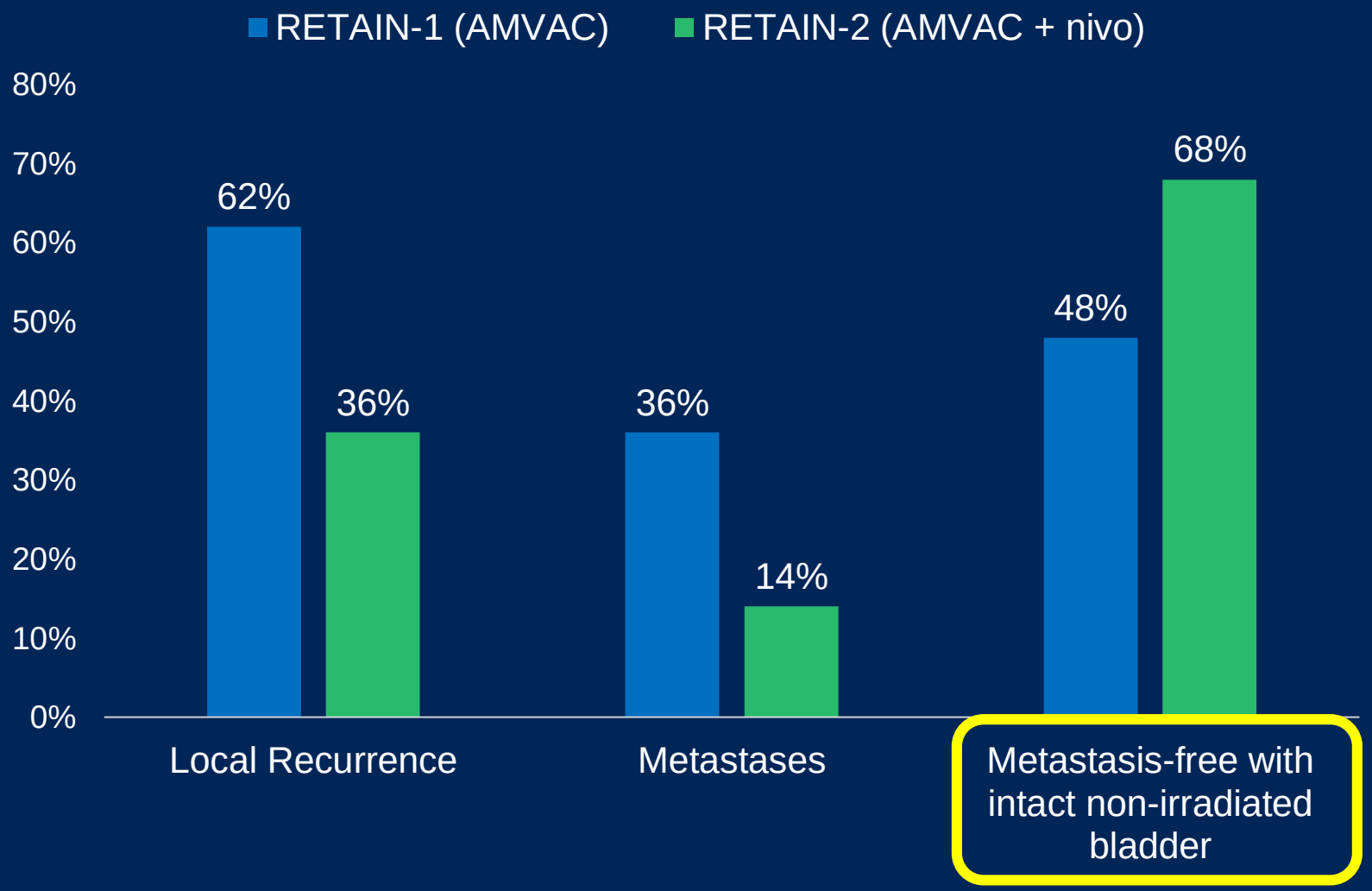


NGS (Caris): Mutation positive defined as alterations in: biomarker *ATM, RB1, ERCC2*

Primary endpoint:
2-yr Metastasis Free Survival
Follow up: 5 years

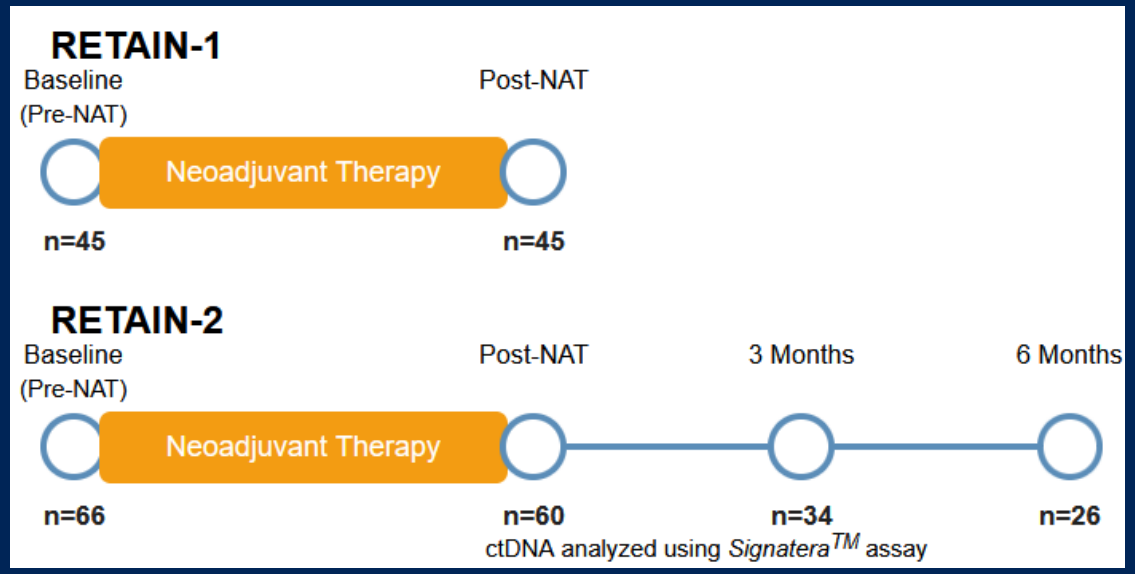
PRESENTED BY: Pooja Ghatalia, MD

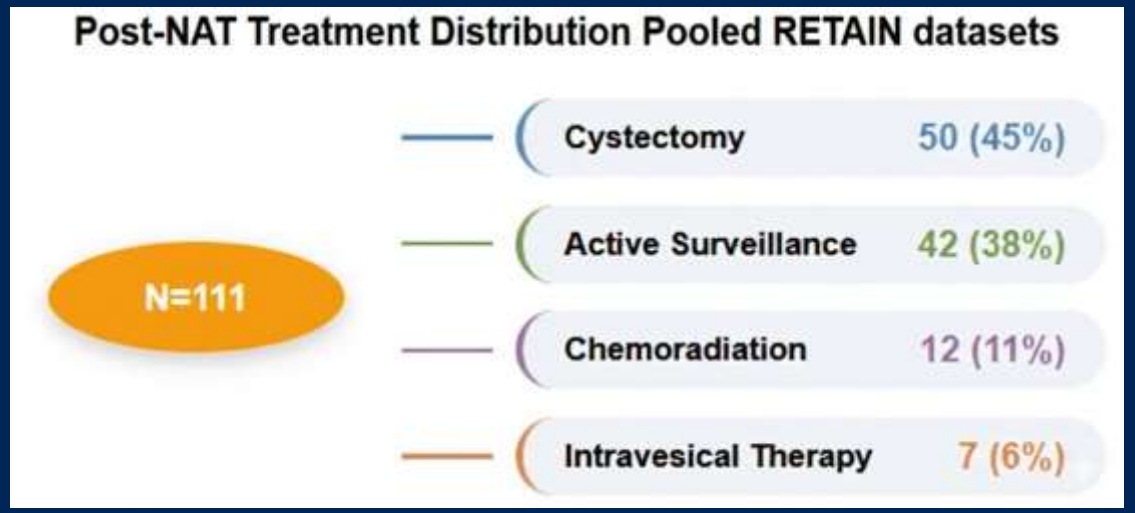
Comparison of RETAIN-1 vs RETAIN-2 Outcomes in Active Surveillance patients

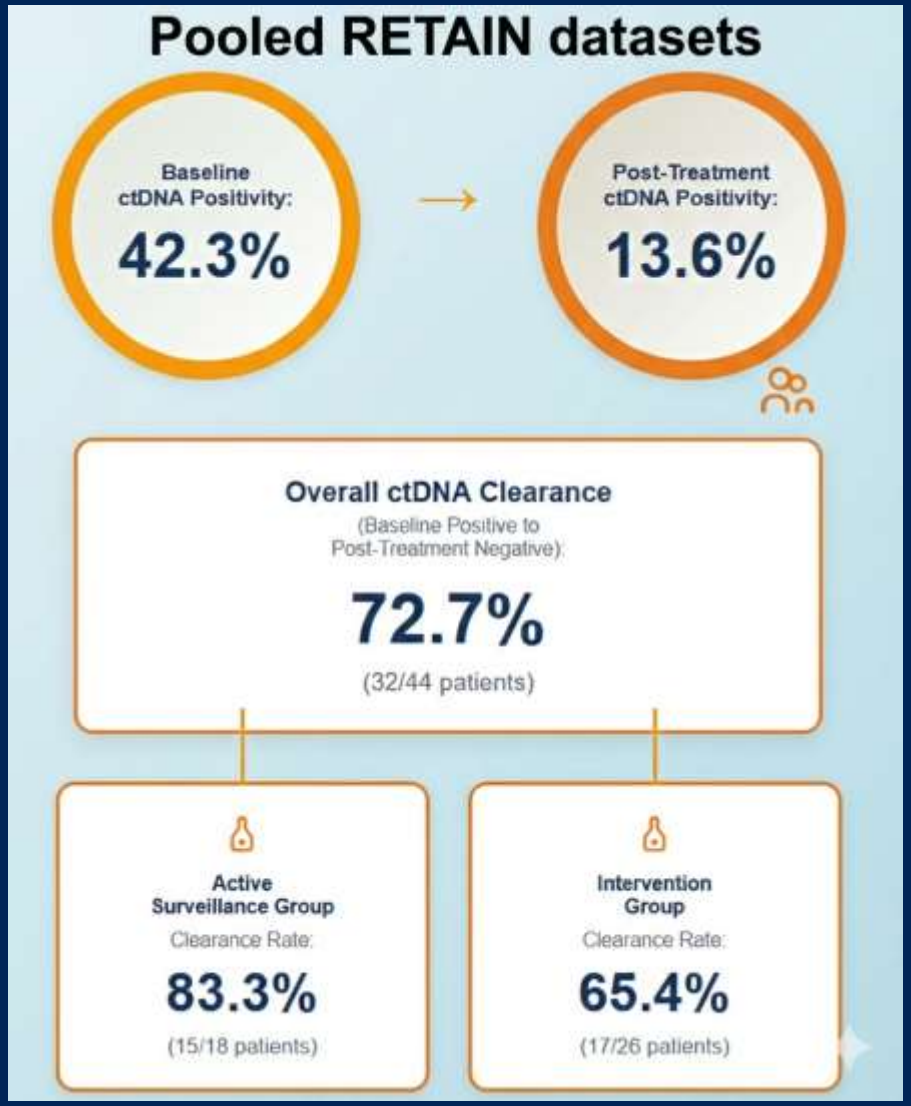


Geynisman DM, *et al.* **J Clin Oncol.** 2025;43(9):1113–1122

ctDNA collection timepoints, detection and clearance rate

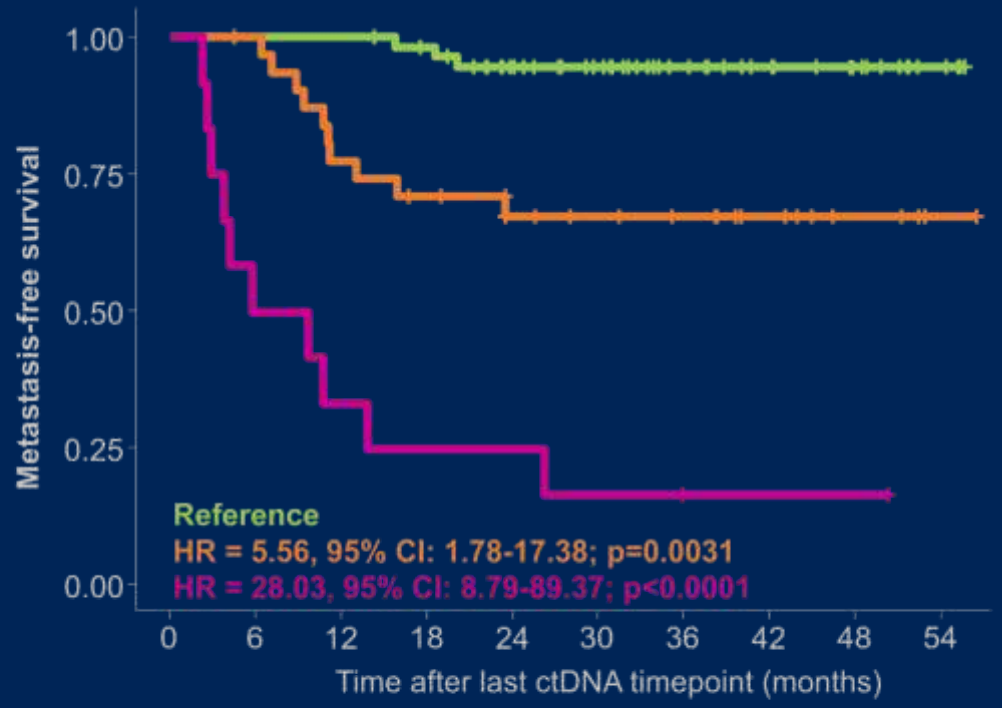






ctDNA dynamics during treatment is prognostic in the overall population

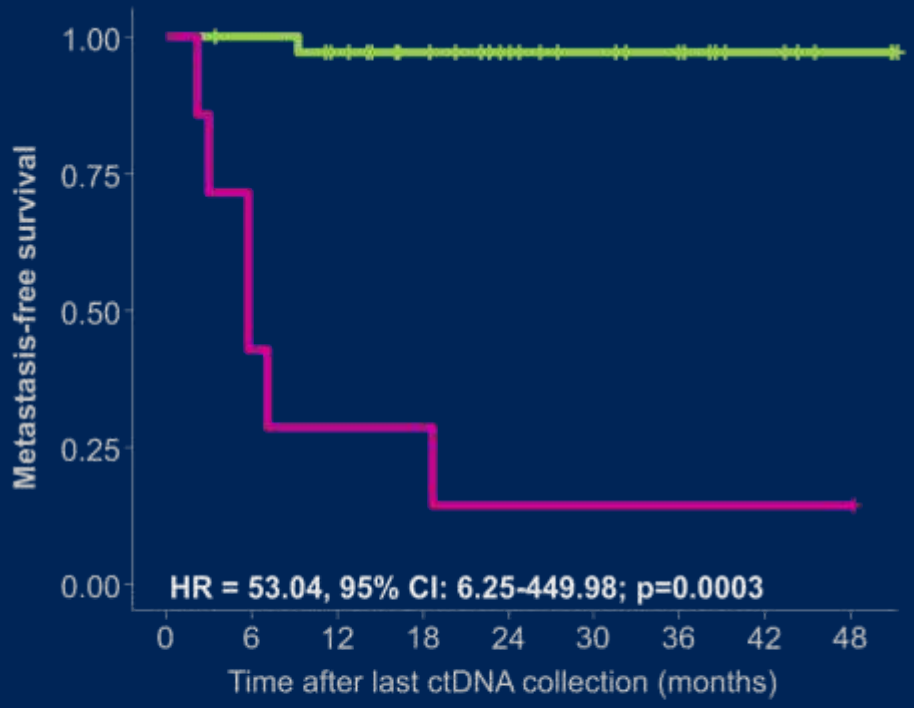
Overall population (RETAIN-1/2), baseline and post-NAT ctDNA



No. at risk

ctDNA-negative	57	57	57	54	45	37	26	19	13	4
ctDNA clearance	32	31	24	21	17	15	13	9	4	1
Persistently ctDNA-positive	12	6	4	3	3	2	1	1	1	0

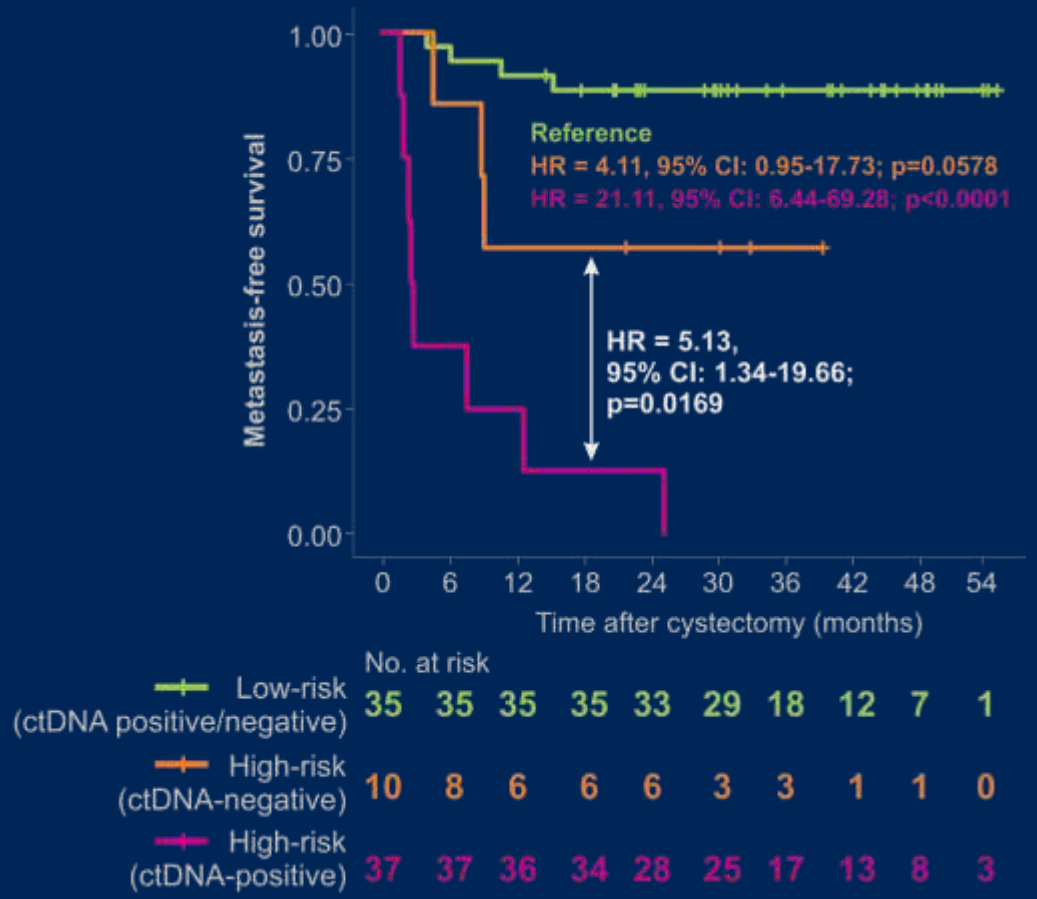
Overall population (RETAIN-2), post-NAT, 3-month, 6-month ctDNA



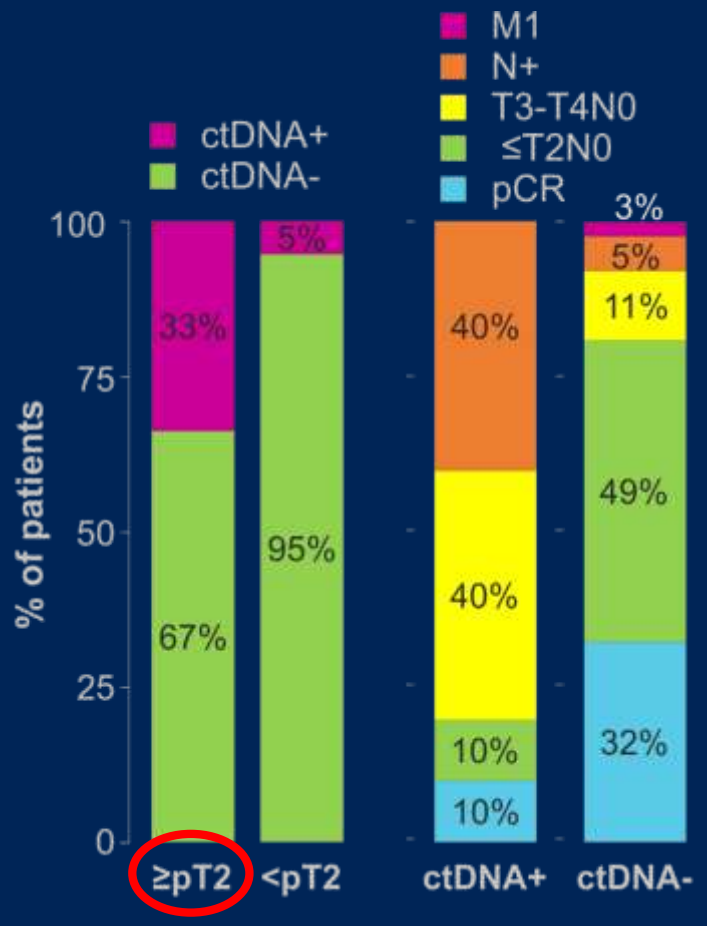
No. at risk

Serially ctDNA-negative	34	33	29	22	17	12	9	5	2
Anytime ctDNA-positive	7	3	2	2	1	1	1	1	1

Post-NAT ctDNA positivity predicted residual disease but ctDNA negativity did not predict ypT0 in cystectomy patients



High pathological risk: pT3-T4N0, N+, and M1
Low pathological risk: ≤pT2 or lower)

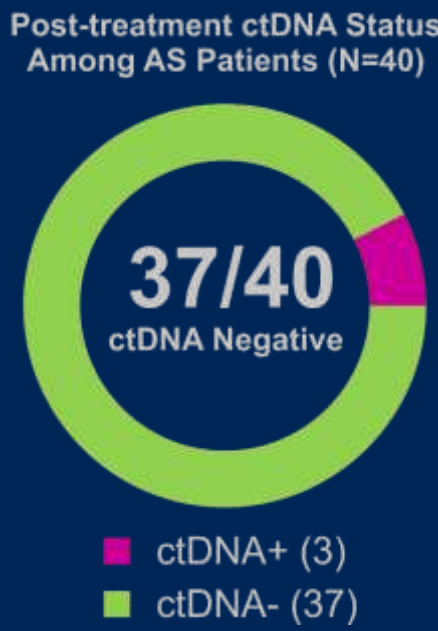


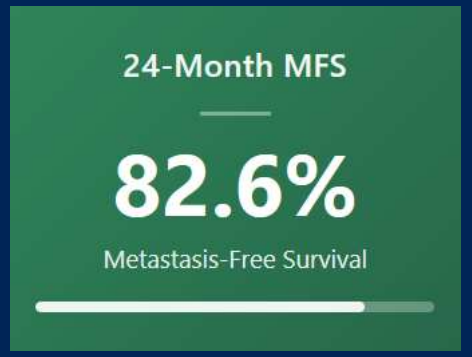
Post-NAT ctDNA and pathological staging from cystectomy (excludes salvage cystectomy)

	>ypT0	ypT0
ctDNA+	9	1
ctDNA-	25	12

PPV: 90% for >ypT0
NPV: 32.4% for ypT0

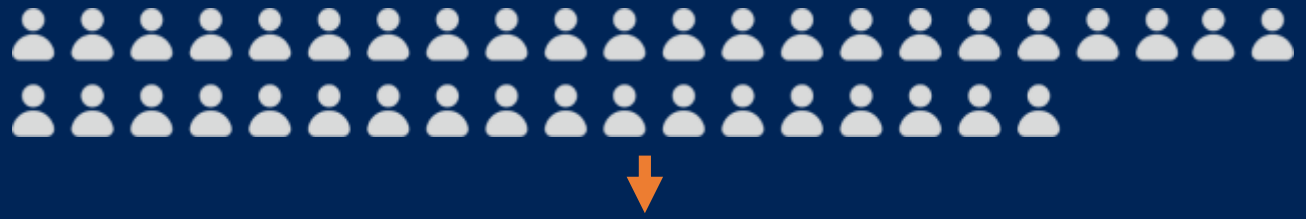
Post-NAT ctDNA status predicts metastatic control but not local control in Active Surveillance patients





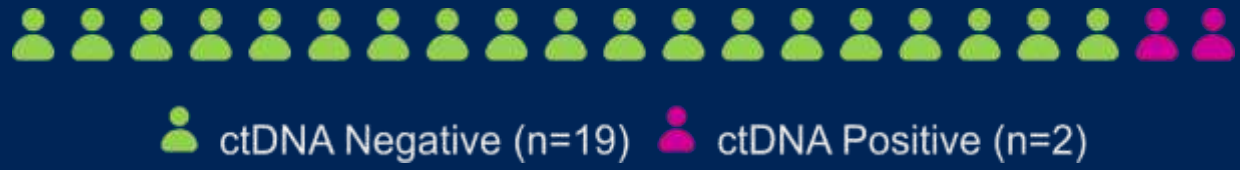
RFS is driven by local recurrence

Patients managed with Active Surveillance: **N=40**



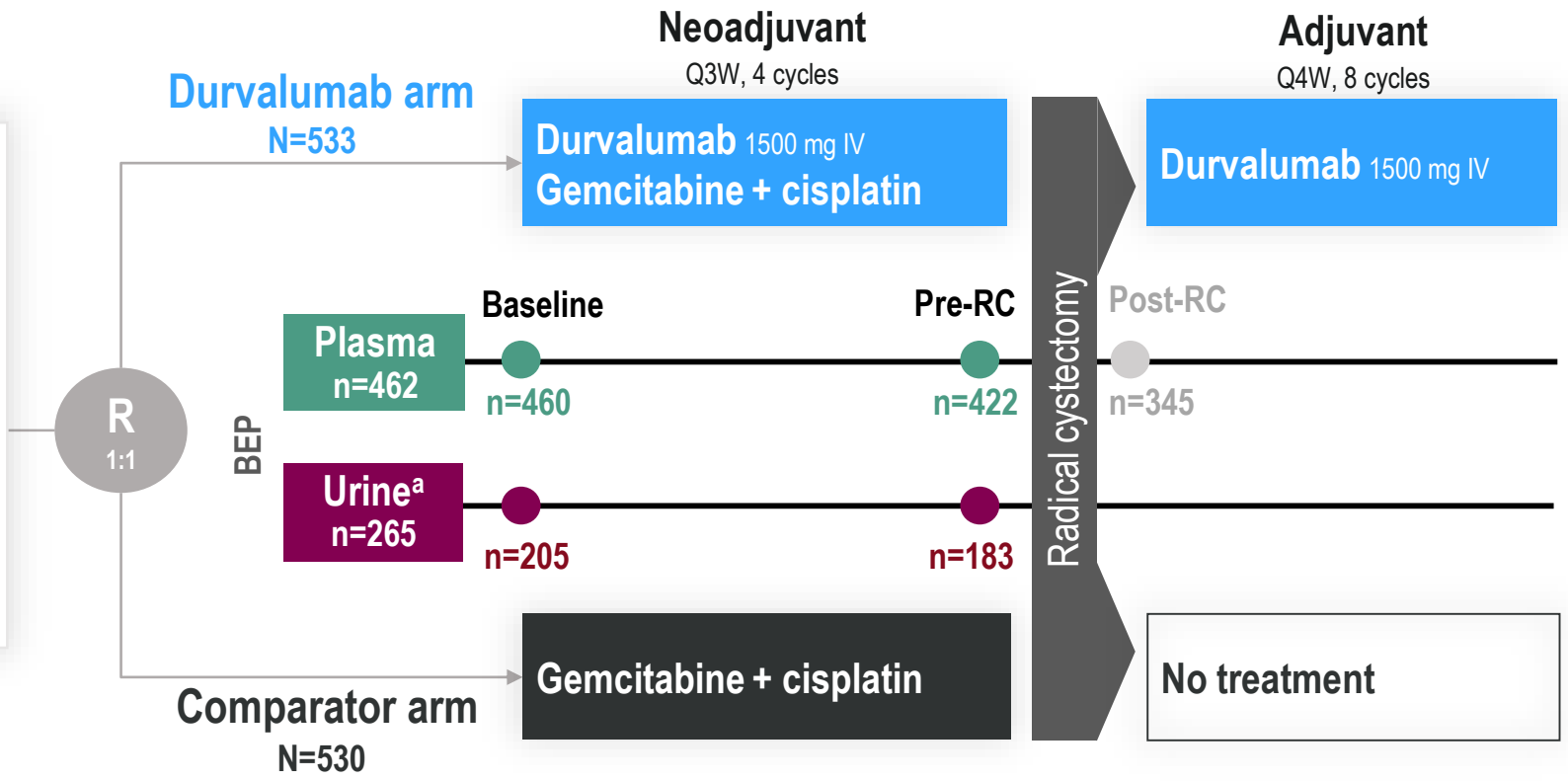
Patients who developed local recurrence: **N=21 (52.5%)**

Of those with local recurrence, ctDNA positive: **Only 2 (9.5%)**



NIAGARA: Study Design and ctDNA/utDNA Analysis

Study population
- Adults
- Cisplatin-eligible MIBC (cT2–T4aN0/1M0)
- UC or UC with divergent differentiation or histologic subtypes
- Evaluated and confirmed for RC
- CrCl of ≥40 mL/min



Primary endpoints
- EFS
- pCR

Key secondary endpoint
- OS

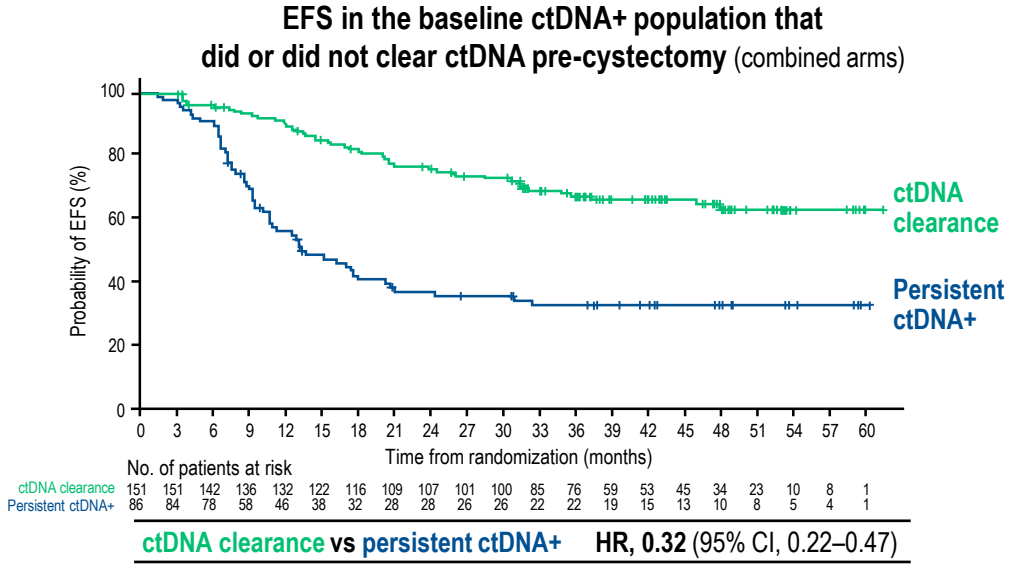
Exploratory analysis
- Association of ctDNA and utDNA with efficacy and clinical parameters

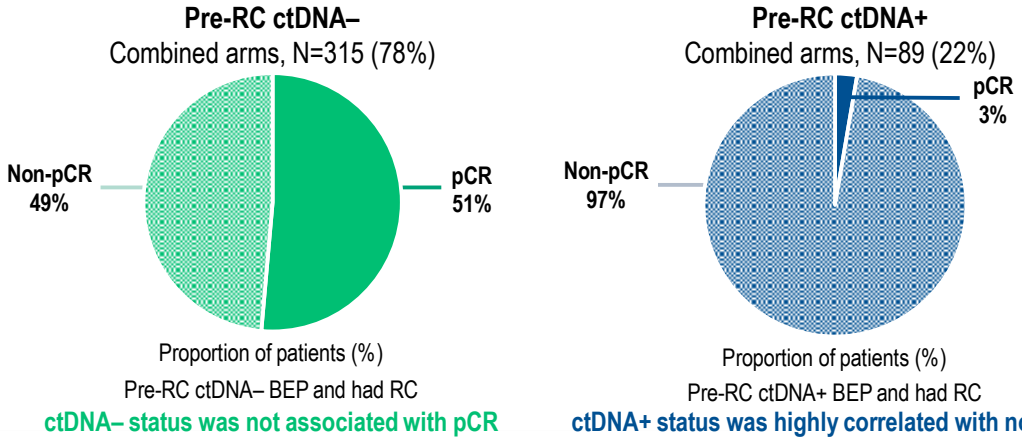
- Baseline characteristics were generally similar between the BEP and ITT populations
- ctDNA/utDNA assessed using Signatera™ assay (Natera, Inc, Austin, TX, USA)

Study design in Powles T, et al. *N Engl J Med*. 2024;391:1773–1786. ClinicalTrials.gov, NCT03732677. Data cutoff Apr 29, 2024. [a]Urine samples collected in ~50% of patients with evaluable ctDNA.
BEP, biomarker-evaluable population; CrCl, creatinine clearance; ctDNA, circulating tumor DNA; EFS, event-free survival; IV, intravenous; MIBC, muscle-invasive bladder cancer; OS, overall survival; pCR, pathological complete response; Q3W, every 3 weeks; Q4W, every 4 weeks; R, randomized; RC, radical cystectomy; UC, urothelial carcinoma; utDNA, urinary tumor DNA.

NIAGARA: Background

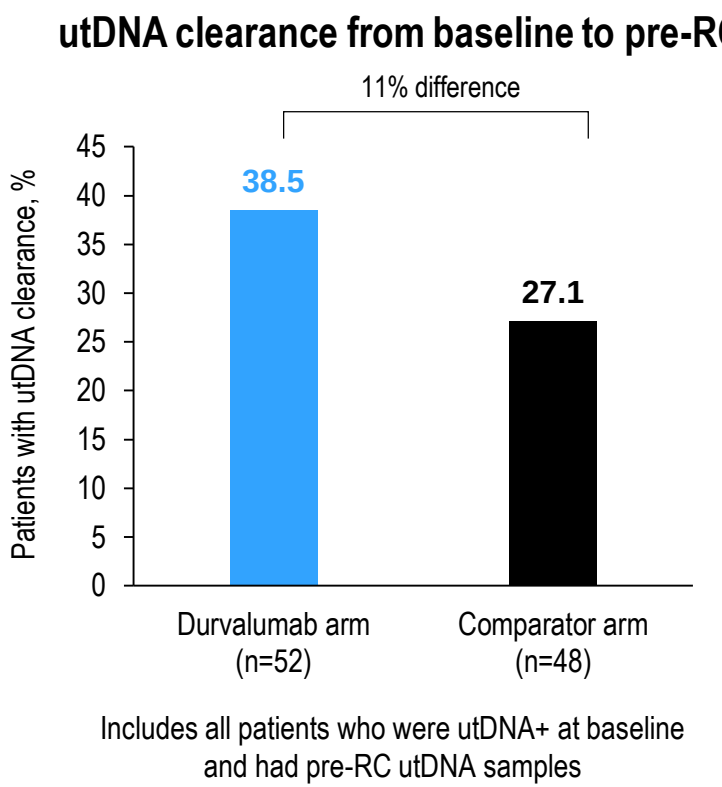
- In NIAGARA, the addition of perioperative durvalumab to NAC demonstrated:
  - Statistically significant improvement in
    - EFS: HR, 0.68 (95% CI, 0.56–0.82), *P*<0.0001
    - OS: HR, 0.75 (95% CI, 0.59–0.93), *P*=0.0106
  - 10% improvement in pCR rate[1]
- In prior exploratory analysis, plasma ctDNA– status after neoadjuvant treatment was not associated with pCR but was prognostic for EFS[2]
- Here, we expanded the analysis to assess potential utility of utDNA testing in MIBC management

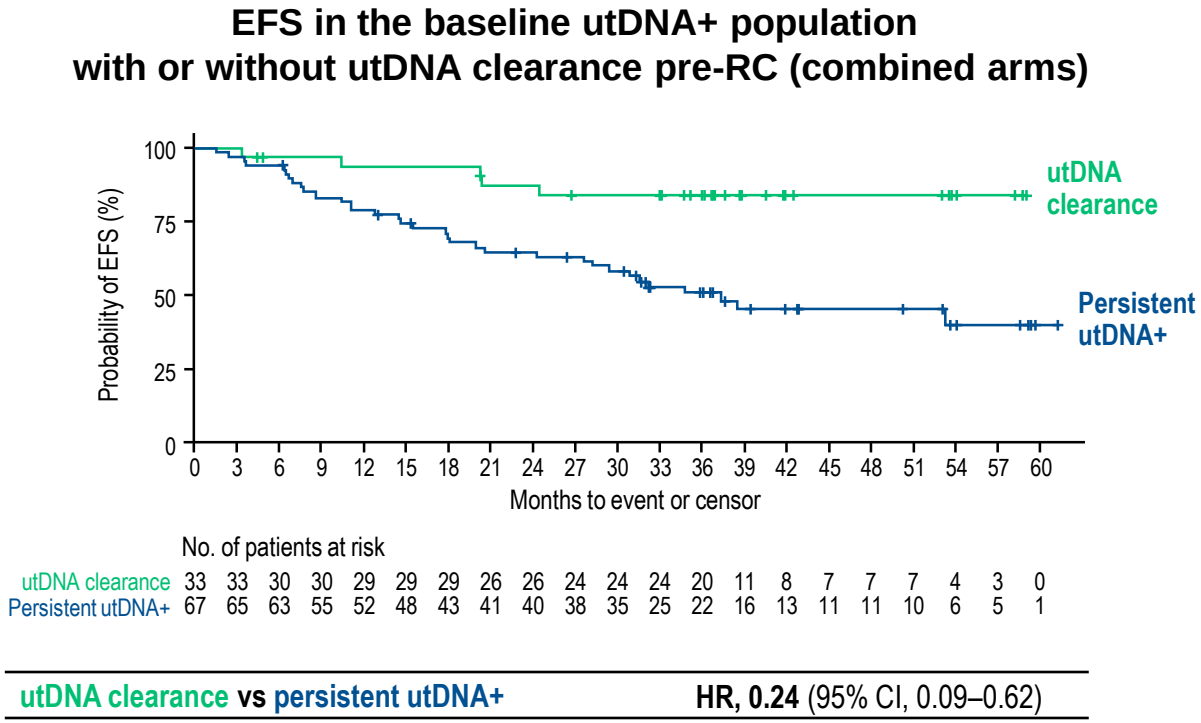




1. Powles T, et al. *N Engl J Med*. 2024;391:1773–1786. 2. Powles T, et al. *J Clin Oncol*. 2025;43:16_suppl:4503. Pre-RC denotes sample collection after neoadjuvant treatment but before RC. BEP, biomarker-evaluable population; CI, confidence interval; ctDNA, circulating tumor DNA; EFS, event-free survival; HR, hazard ratio; MIBC, muscle-invasive bladder cancer; NAC, neoadjuvant chemotherapy; OS, overall survival; pCR, pathological complete response; RC, radical cystectomy; utDNA, urinary tumor DNA.

NIAGARA Neoadjuvant: utDNA Clearance Was 11% Higher in the Durvalumab Arm and Appears to Be Prognostic for EFS

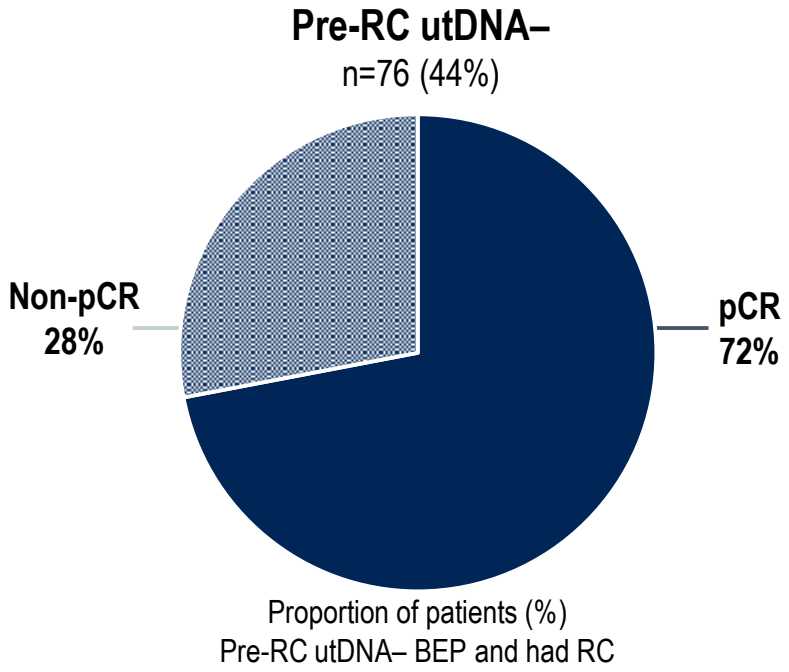




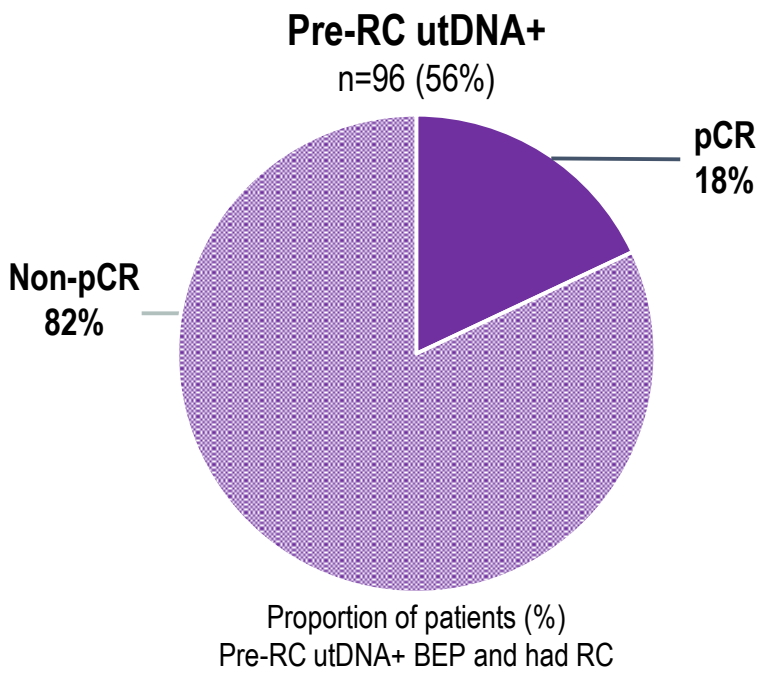
- Similar results were also observed with plasma ctDNA clearance[1]
- 85% of patients were utDNA positive at baseline, which reduced to 55% following neoadjuvant treatment (combined arms)

1. Powles T, et al. *J Clin Oncol.* 2025;43:16_suppl:4503. Pre-RC denotes sample collection after neoadjuvant treatment but before RC. CI, confidence interval; ctDNA, circulating tumor DNA; EFS, event-free survival; HR, hazard ratio; RC, radical cystectomy; utDNA, urinary tumor DNA.

NIAGARA Pre-cystectomy: utDNA– Status Is Associated With pCR



utDNA– status at pre-RC is associated with higher likelihood of pCR



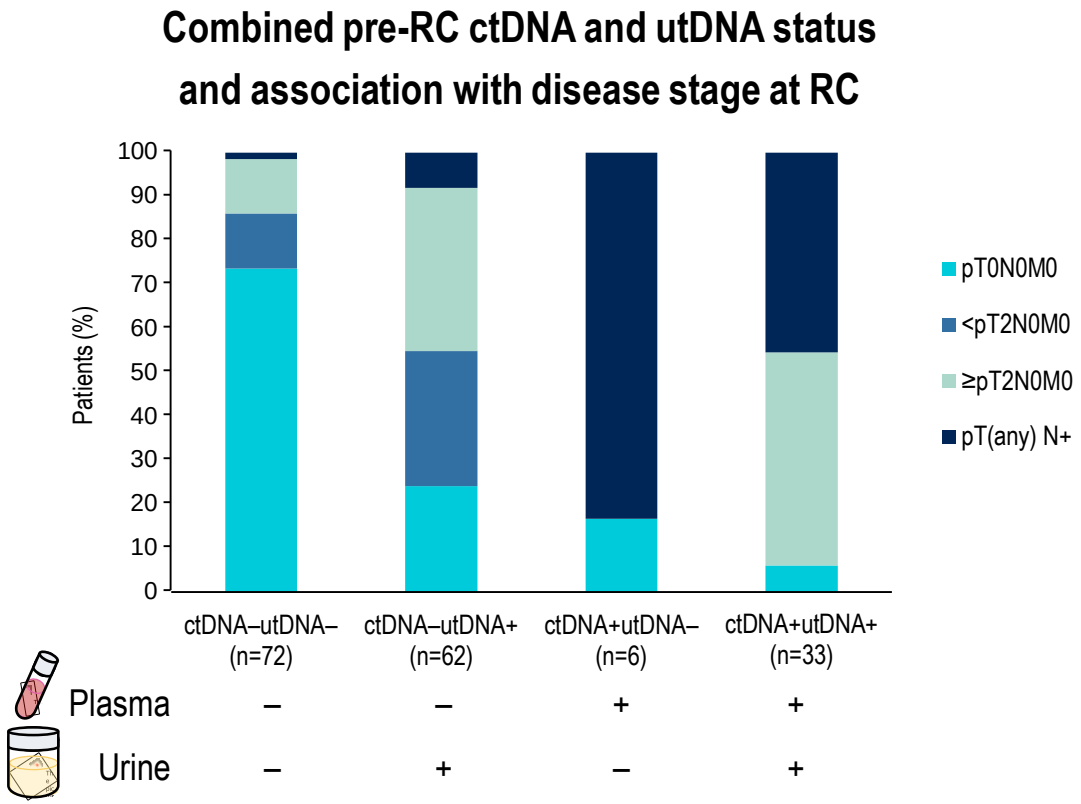
utDNA+ status at pre-RC is associated with higher likelihood of non-pCR

- In contrast, 51% of patients with plasma ctDNA– status after neoadjuvant treatment had pCR[1]

Pre-RC BEP with recorded pCR/non-pCR result, n=172 patients

1. Powles T, et al. *J Clin Oncol.* 2025;43:16_suppl:4503. Pre-RC denotes sample collection after neoadjuvant treatment but before RC. BEP, biomarker-evaluable population; ctDNA, circulating tumor DNA; pCR, pathological complete response; RC, radical cystectomy; utDNA, urinary tumor DNA.

NIAGARA Pre-cystectomy: utDNA and ctDNA Status Is Differentially Associated With Disease Stage at Cystectomy



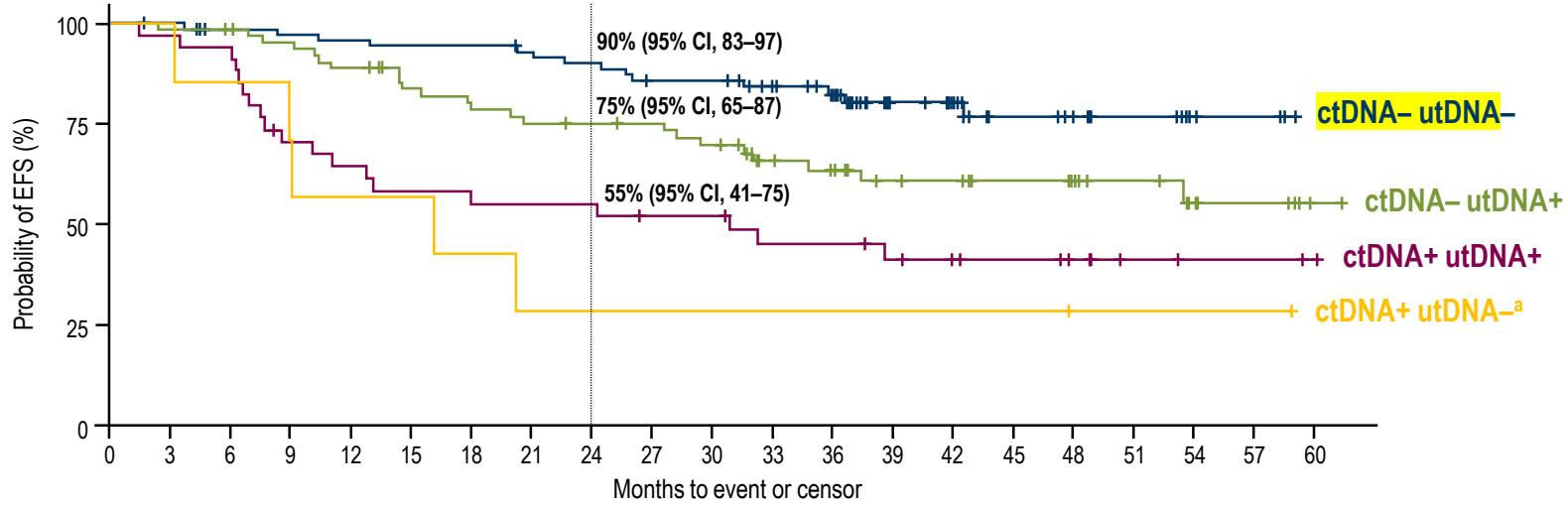
- utDNA+ status is associated with a higher frequency of non–invasive disease (<pT2N0M0), consistent with detection of local residual disease
- ctDNA+ status is associated with a higher frequency of invasive disease (≥pT2N0M0) and nodal involvement (N+), reflecting systemic spread

Pre-RC BEP with ctDNA and utDNA results, n=179[a]

Pre-RC denotes sample collection after neoadjuvant treatment but before RC. [a]Pathological staging was not available for n=6 patients. BEP, biomarker evaluable population; ctDNA, circulating tumor DNA; RC, radical cystectomy; utDNA, urinary tumor DNA.

NIAGARA: 24-Month EFS Was Highest for Patients With Dual-Negative Status at Pre-cystectomy

EFS by combined pre-RC ctDNA/utDNA status (combined arms)



No. of patients at risk

ctDNA– utDNA–	74	73	69	68	67	66	66	64	62	58	58	53	47	30	25	17	13	9	4	3	0
ctDNA– utDNA+	64	63	62	59	55	49	46	44	43	42	39	30	26	21	20	17	15	12	8	6	1
ctDNA+ utDNA–[a]	7	7	6	5	4	4	3	2	2	2	2	2	2	2	2	2	1	1	1	1	0
ctDNA+ utDNA+	34	33	32	23	21	19	18	18	18	16	16	13	13	11	9	8	6	3	2	2	1

ctDNA– utDNA– vs ctDNA– utDNA+	**HR, 0.46** (95% CI, 0.23–0.89)
ctDNA– utDNA– vs ctDNA+ utDNA+	**HR, 0.25** (95% CI, 0.12–0.49)
ctDNA– utDNA+ vs ctDNA+ utDNA+	**HR, 0.51** (95% CI, 0.27–0.93)

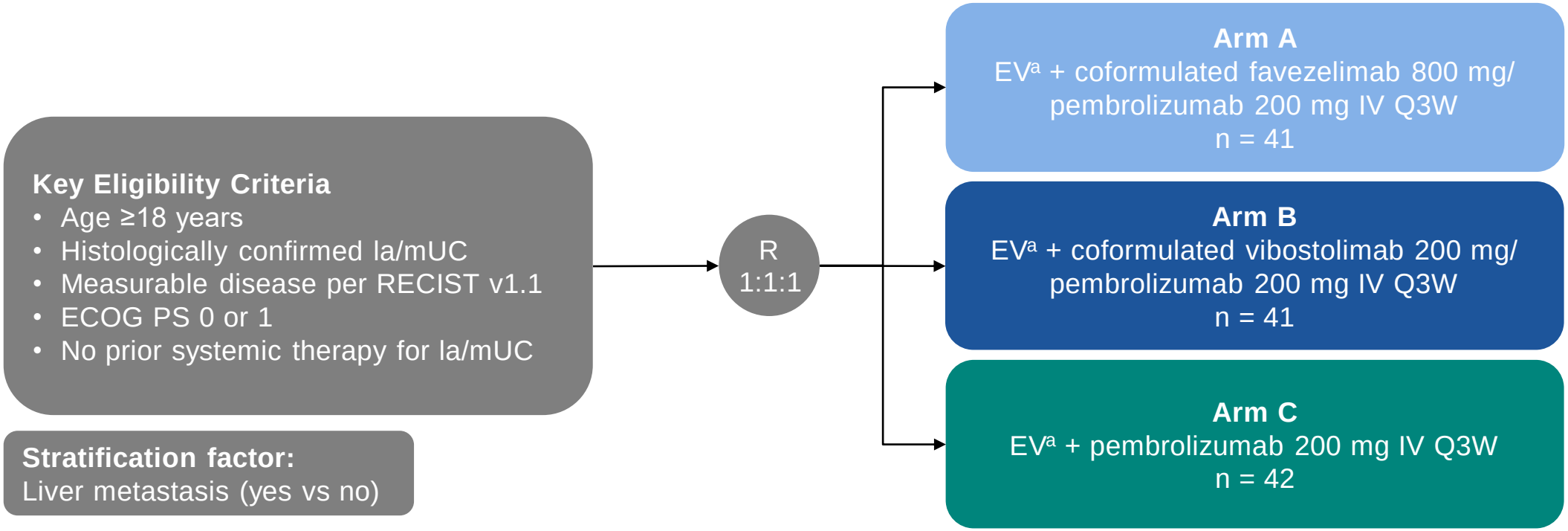
Pre-RC BEP with ctDNA and utDNA results, n=179

Pre-RC denotes sample collection after neoadjuvant treatment but before RC. [a]Note, due to the small sample size for the ctDNA+ and utDNA– group, HRs for group comparisons were not calculated.
BEP, biomarker evaluable population; CI, confidence interval; ctDNA, circulating tumor DNA; EFS, event-free survival; HR, hazard ratio; RC, radical cystectomy; utDNA, urinary tumor DNA.

Üroteliyal Kanserlerde Tedavi Seçenekleri
ASCO-GU 2026

Metastatik Evrede Yenilikler

KEYMAKER-U04 Substudy 04B Study Design (NCT05845814)

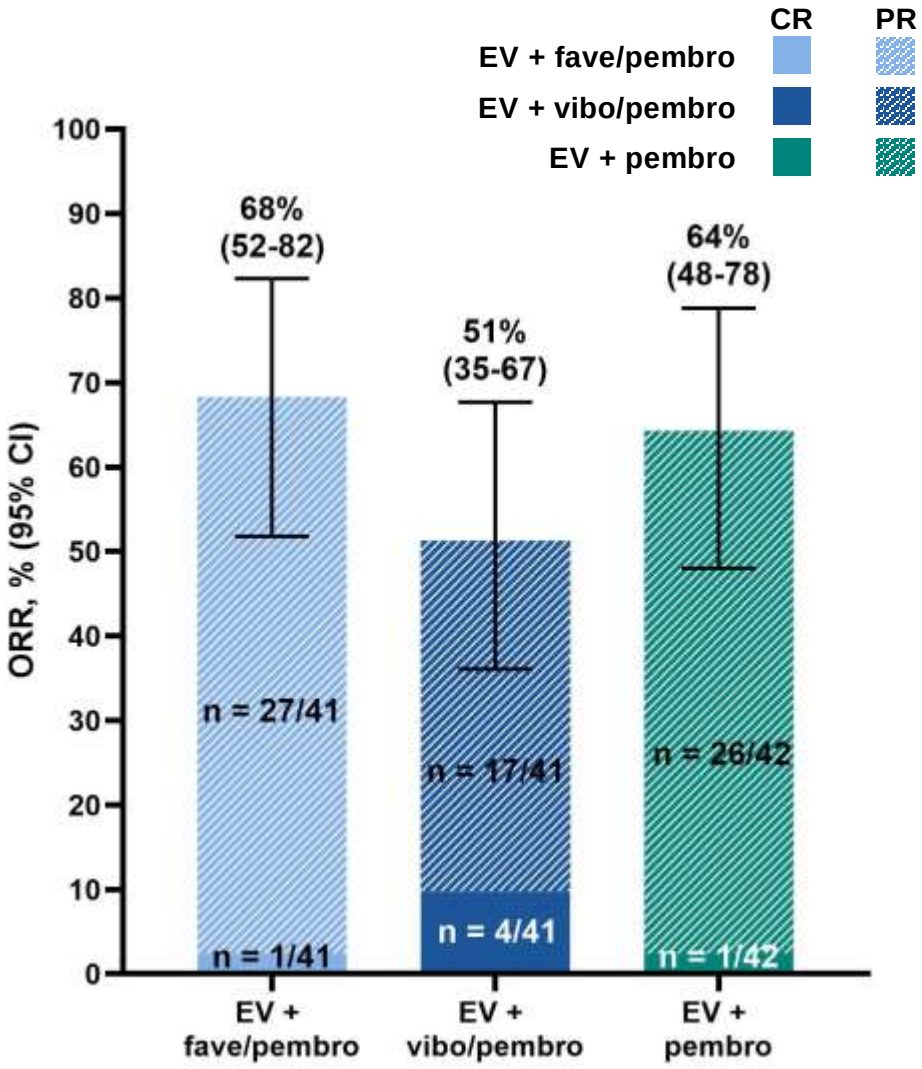


End points
- **Primary:** ORR per RECIST v1.1 by investigator and safety
- **Secondary:** DOR and PFS per RECIST v1.1 by investigator

Median study follow-up[b]:
- **EV + fave/pembro:** 11.9 months (range, 9.7-17.0)
- **EV + vibo/pembro:** 11.7 months (range, 9.7-16.3)
- **EV + pembro:** 11.8 months (range, 9.8-16.8)

DLT, dose-limiting toxicity; EV, enfortumab vedotin; fave/pembro, favezelimab/pembrolizumab; pembro, pembrolizumab; vibo/pembro, vibostolimab/pembrolizumab.
[a]EV 1.25 mg/kg IV (Day 1 and Day 8) Q3W. [b]Time from randomization to data cutoff date.
A safety lead-in phase was performed for the first 10 participants in each of EV + fave/pembro and EV + vibo/pembro arms per modified toxicity probability interval with DLT monitoring in cycle 1 in which DLT was reported for 1 participant on EV + fave/pembro (increased alanine aminotransferase) and no participants on EV + vibo/pembro. Data cutoff date: December 16, 2024.

ORR per RECIST v1.1 by Investigator

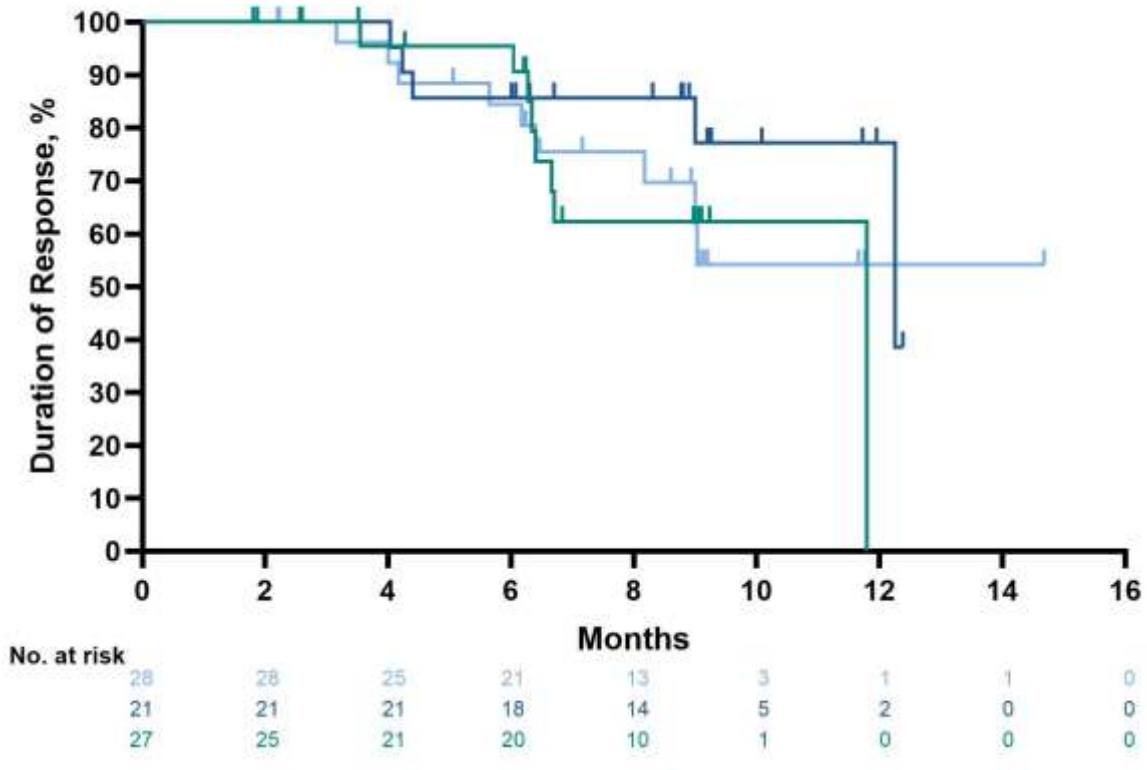


	EV + fave/pembro n = 41	EV + vibo/pembro n = 41	EV + pembro n = 42
Best response, n (%)			
CR	1 (2)	4 (10)	1 (2)
PR	27 (66)	17 (41)	26 (62)
SD	10 (24)	10 (24)	7 (17)
PD	3 (7)	7 (17)	6 (14)
NE/NA	0	3 (7)	2 (5)

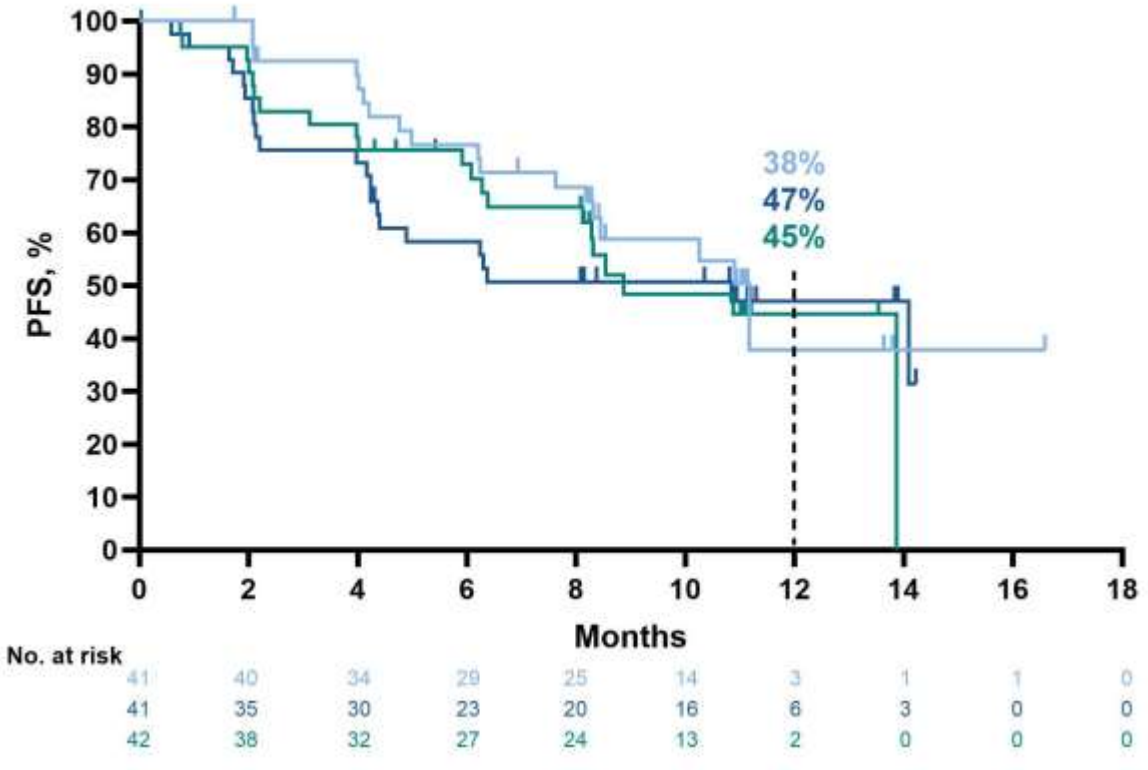
Percentages may not add up to 100% due to rounding. Data cutoff date: December 16, 2024.

DOR and PFS per RECIST v1.1 by Investigator

	EV + fave/pembro n = 41	EV + vibo/pembro n = 41	EV + pembro n = 42
Participants with response, n (%)	28 (68)	21 (51)	27 (64)
Median (range), mo	NR (2.2+ to 14.7+)	12.3 (4.0 to 12.4+)	11.8 (1.8+ to 11.8)



	EV + fave/pembro n = 41	EV + vibo/pembro n = 41	EV + pembro n = 42
Events, n (%)	18 (44)	22 (54)	21 (50)
Median (95% CI), mo	11.2 (8.2-NR)	10.8 (4.2-NR)	8.9 (6.4-NR)



Data cutoff date: December 16, 2024.

ASCO Genitourinary Cancers Symposium

RC48G001: A phase 2 study of disitamab vedotin in HER2-expressing previously treated advanced UC

Thomas Powles[1], Vadim S. Koshkin[2], Jonathan Rosenberg[3], Nobuaki Matsubara[4], Jason R. Brown[5], Alexandra Drakaki[6], Matthew T. Campbell[7], Niara Oliveira[8], Earle Burgess[9], Gopa Iyer[3], Avivit Peer[10], Joachim Chan[11], Hernan Javier Cutuli[12], Bernhard J. Eigl[13], Robert Jones[14], Jeanny B. Aragon-Ching[15], Jessica Schuman,[16] Miao Yang,[16] Kevin Sokolowski,[16] Matthew D. Galsky[17]

[1]Barts Cancer Centre, Queen Mary University of London, London, UK; [2]Helen Diller Family Comprehensive Cancer Center, Division of Hematology/Oncology, Department of Medicine, University of California San Francisco, San Francisco, CA, USA; [3]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [4]National Cancer Center Hospital East, Kashiwa, Japan; [5]University Hospitals Cleveland Medical Center, Case Western Reserve University, Cleveland, OH, USA; [6]David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA, USA; [7]University of Texas MD Anderson Cancer Center, Houston, TX, USA; [8]Mater Hospital Brisbane, Mater Misericordiae Ltd and the School of Clinical Medicine, Mater Clinical Unit, University of Queensland, South Brisbane, QLD, Australia; [9]Atrium Health Wake Forest Baptist Comprehensive Cancer Center, Winston-Salem, NC, USA; [10]Rambam Health Care Campus, Haifa, Israel; [11]The Clatterbridge Cancer Centre NHS Foundation Trust, Wirral, UK; [12]Hospital Sirio Libanés, Buenos Aires, Argentina; [13]British Columbia Cancer – Vancouver Center, Vancouver, BC, Canada; [14]University of Glasgow, Beatson West of Scotland Cancer Centre, Glasgow, UK; [15]Inova Schar Cancer Institute, Fairfax, VA, USA; [16]Pfizer Inc., South San Francisco, CA, USA; [17]Icahn School of Medicine at Mount Sinai, New York, NY, USA

HER2 Biyobelirteci: Yüksek Değer iyi yanıt ve düşük değer daha düşük yanıt ilişkili

Single Agent HER2 ADC in Urothelial Carcinoma

Yan et al Med 2025[1]	
≥2nd Line DV	
ORR (n=19)	
Overall	26%
1+	38%
0	0%

Sheng et al JCO 2024	
2nd Line DV	
ORR	
Overall	51%
3+ or 2+/IHC+	62%
2+/IHC-	40%
mPFS	
Overall	5.9 m
3+ or 2+/IHC+	5.7 m
2+/IHC-	6.2 m

Powles et al GU ASCO 2026	
2nd Line DV	
ORR	
Her2 High	55%
3+	56%
2+/ISH+	52%
Her2 Low	53%
2+/ISH-	59%
1+	35%

Meric-Bernstam, et al JCO 2024	
2nd Line TDxD	
ORR	
*Overall	39%
3+	56%
2+	35%
1+	0% (N=2)
0	0% (N=2)
*Central Her2 assessment	

Her2 biomarker is imprecise, but generally, higher is better.

DV/Tori

Sheng et al NEJM 2025	
1st Line DV/Tori	
ORR	
Overall	76%
2+/3+	79%
1+	66%
mPFS	
Overall	13.1 m
2+/3+	13.1 m
1+	12.3 m
mOS	
Overall	32 m
2+/3+	32 m
1+	26 m

Sheng et al GU ASCO 2025	
DV/Tori Neoadjuvant	
pCR	
Overall	64%
3+	85%
2+	50%
1+	50%

[1]Yan Med. 2025 Jul 11;6(7):100637

RC48G001 Study Design: Cohorts A and B

Cohort A and B are part of an open-label multicohort study in participants with HER2-expressing la/mUC

Eligibility:
- 1-2 prior lines of systemic therapy for la/mUC, including a platinum-containing regimen
- Disease progression during or after most recent line of therapy
- Central laboratory HER2 status[a] IHC ≥1+
- ECOG PS 0 or 1
- No prior MMAE-based ADCs or HER2-directed therapy

→ **Cohort A (HER2-positive):**
IHC 3+ *or* IHC 2+ and ISH-positive
DV 1.5 mg/kg[b] IV Q2W

→ **Cohort B (HER2-low):**
IHC 2+ and ISH-negative/unevaluable *or* IHC 1+
DV 1.5 mg/kg[b] IV Q2W

Treatment until disease progression or intolerable toxicity
Disease assessments Q6W from Cycle 1 Day 1 for 72 weeks, then Q12W until disease progression

Primary endpoint
- Confirmed ORR by BICR per RECIST 1.1

Select secondary endpoints
- DOR, DCR, and PFS by BICR per RECIST 1.1
- OS
- Safety

Data cutoff: September 12, 2025.

BICR, blinded independent central review; BSA, bovine serum albumin; DCR, disease control rate; DOR, duration of response; DISH, dual in situ hybridization; DV, disitamab vedotin; EC, extinction coefficient; ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor 2; IHC, immunohistochemistry; ISH, in-situ hybridization; la/mUC, locally advanced unresectable or metastatic urothelial cancer; MMAE, monomethyl auristatin E; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q2W, once every 2 weeks; Q6W, every 6 weeks, Q12W, every 12 weeks, RECIST, Response Evaluation Criteria in Solid Tumors.

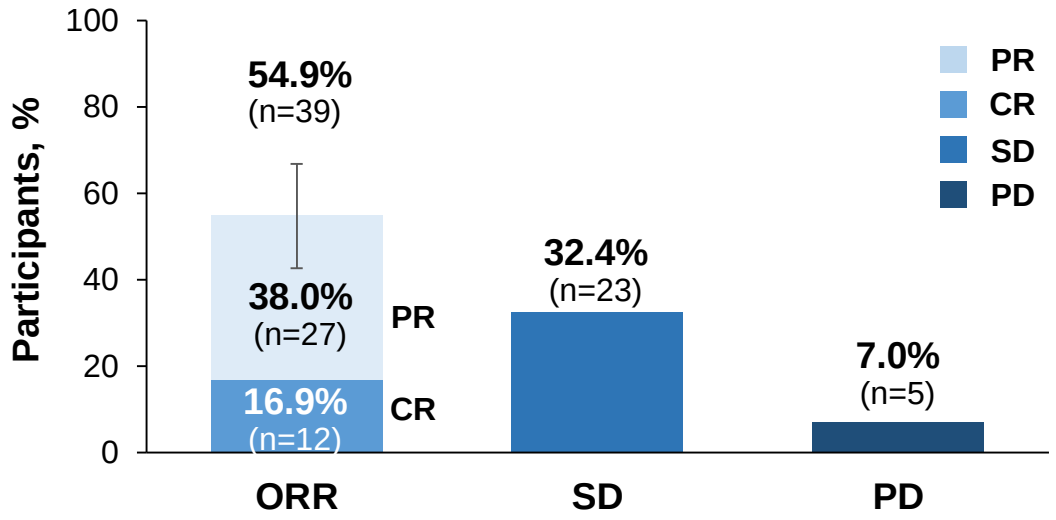
[a]As previously described,[1] HER2 expression was determined by a central laboratory using the VENTANA HER2 IHC and HER2 Dual ISH (DISH) DNA Probe Cocktail assays. Combined IHC and DISH results were scored for HER2 clinical status, according to HER2 guidelines for breast and gastroesophageal cancers (using an algorithm optimized for urothelial cancer), and patients were categorized as HER2-zero (IHC 0), HER2-low (IHC 1+, or IHC 2+/DISH nonamplified or IHC 2+ and DISH unevaluable [following a repeat test, or if a repeat test was not available]), or HER2-positive (IHC 2+/DISH amplified, or IHC 3+). [b]The DV dose of 1.5 mg/kg cited here is based on calculations using DV EC and is equivalent to 2.0 mg/kg based on calculations using BSA-based EC administered in China.

1. Koshkin VS, et al. JCO Precis Oncol. 2025;9:e2400879.

Primary Endpoint: Confirmed ORR by BICR

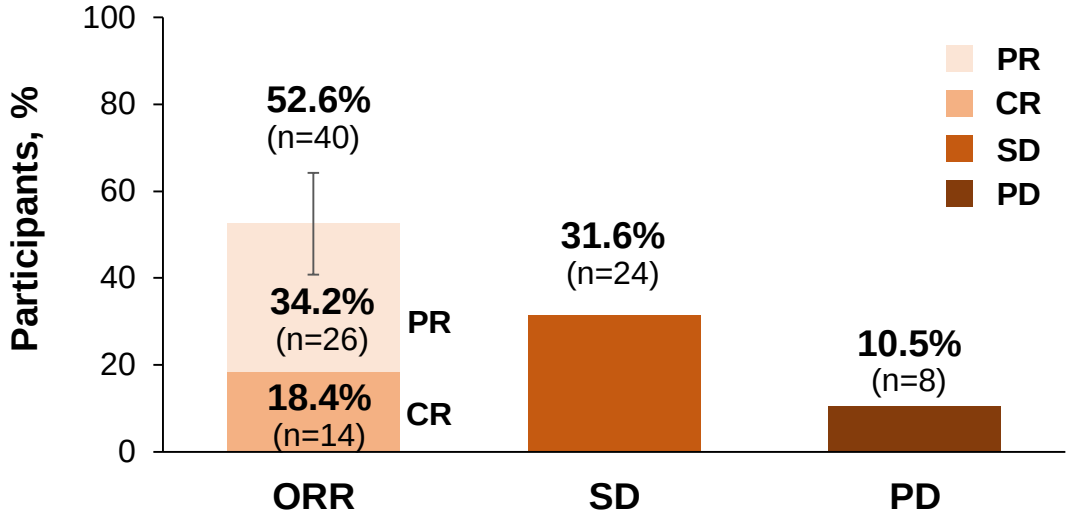
ORR was similar in Cohorts A and B, with a CR rate greater than 16%

Cohort A: HER2-positive (n=71)[a,b]
(IHC 3+ or IHC 2+ and ISH-positive)



Follow-up, median (range), months	11.3 (0-31)
Disease control rate, n (%)[c] [95% CI]	62 (87.3) [77.3-94.0]
DOR, median (95% CI), months	5.8 (4.6-9.4)

Cohort B: HER2-low (n=76)[a,b]
(IHC 2+ and ISH-negative/unevaluable or IHC 1+)



Follow-up, median (range), months	17.1 (1-40)
Disease control rate, n (%)[c] [95% CI]	64 (84.2) [74.0-91.6]
DOR, median (95% CI), months	6.9 (4.7-9.4)

Data cutoff: September 12, 2025.

BICR, blinded independent central review; CI, confidence interval; CR, complete response; DOR, duration of response; HER2, human epidermal growth factor 2; IHC, immunohistochemistry; ISH, in situ hybridization; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

[a]The response-evaluable set included all participants with measurable disease by BICR at baseline, which included 71 of 73 patients in Cohort A, and 76 of 78 patients in Cohort B. [b]Response was not evaluable in 4 participants in each cohort. [c]Defined as the proportion of participants with confirmed CR/PR, or who met SD criteria at least once after treatment initiation at an interval of ≥5 weeks.

Summary of Outcomes in Participants Receiving Subsequent EV-based Therapy

Clinical activity was observed with subsequent EV-based therapy after discontinuation of DV

	Cohort A HER2-positive (n=73)	Cohort B HER2-low (n=78)
Patients receiving EV monotherapy, n (%)	11 (17.2)	8 (11.0)
Best response[a]		
CR	0	0
PR	2 (18.2)	1 (12.5)
SD	2 (18.2)	2 (25.0)
PD	3 (27.3)	4 (50.0)
Participants receiving EV+P, n (%)	4 (6.3)	7 (9.6)
Best response[b]		
CR	0	0
PR	0	0
SD	2 (50.0)	2 (28.6)
PD	0	3 (42.9)

- Of participants who received subsequent EV monotherapy, 2 of 11 in Cohort A and 1 of 8 in Cohort B achieved PR
- Of participants who received subsequent EV+P, 2 of 4 in Cohort A and 2 of 7 in Cohort B achieved SD

Data cutoff: September 12, 2025.

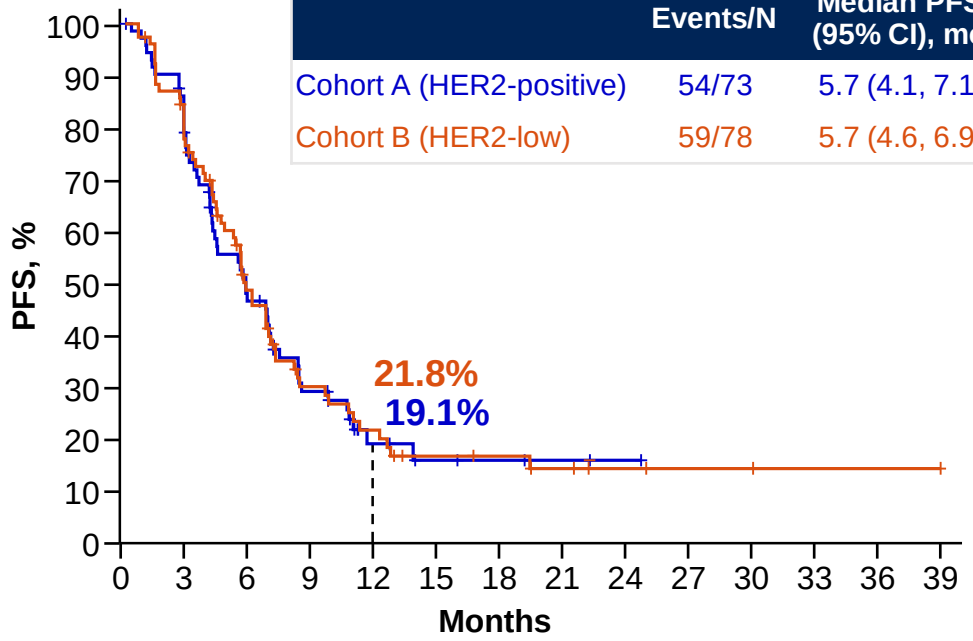
CR, complete response; DV, disitamab vedotin; EV, enfortumab vedotin; HER2, human epidermal growth factor 2; P, pembrolizumab; PD, progressive disease; PR, partial response; SD, stable disease.

[a]The denominator is the number of participants who received EV monotherapy; best response was unknown for 4 participants in Cohort A and 1 participant in Cohort B. [b]The denominator is the number of participants who received EV+P; best response was unknown for 2 participants in Cohort A and 2 participants in Cohort B.

Progression-Free Survival and Overall Survival

PFS and OS were similar between cohorts

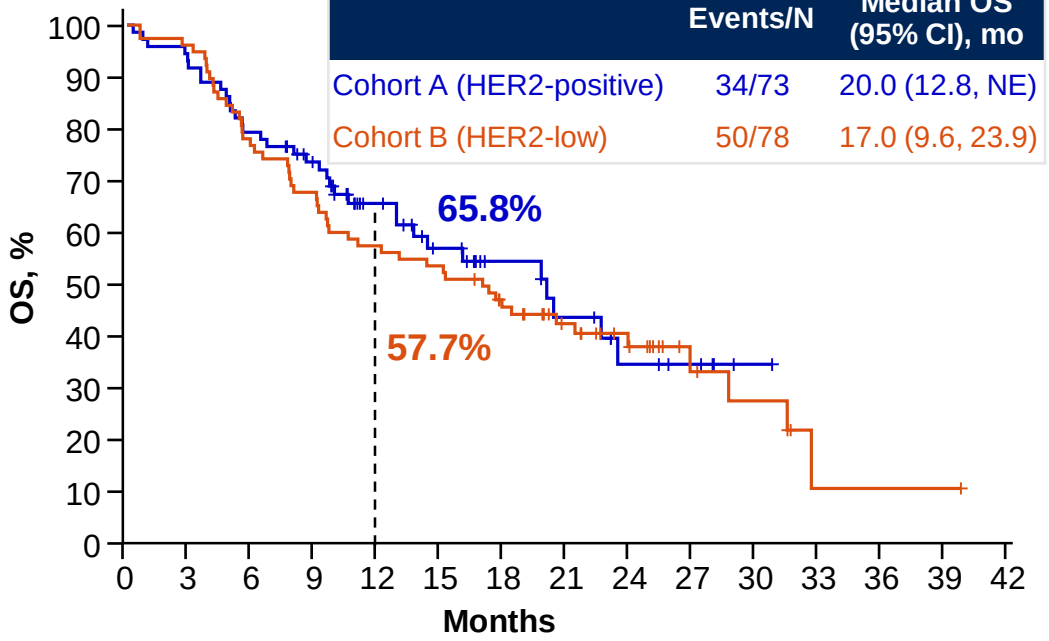
	Events/N	Median PFS (95% CI), mo
Cohort A (HER2-positive)	54/73	5.7 (4.1, 7.1)
Cohort B (HER2-low)	59/78	5.7 (4.6, 6.9)



No. at risk

Cohort A	73	52	31	18	7	4	3	2	1	0	0	0	0	0
Cohort B	78	58	33	18	13	8	7	5	3	2	1	1	1	0

	Events/N	Median OS (95% CI), mo
Cohort A (HER2-positive)	34/73	20.0 (12.8, NE)
Cohort B (HER2-low)	50/78	17.0 (9.6, 23.9)



No. at risk

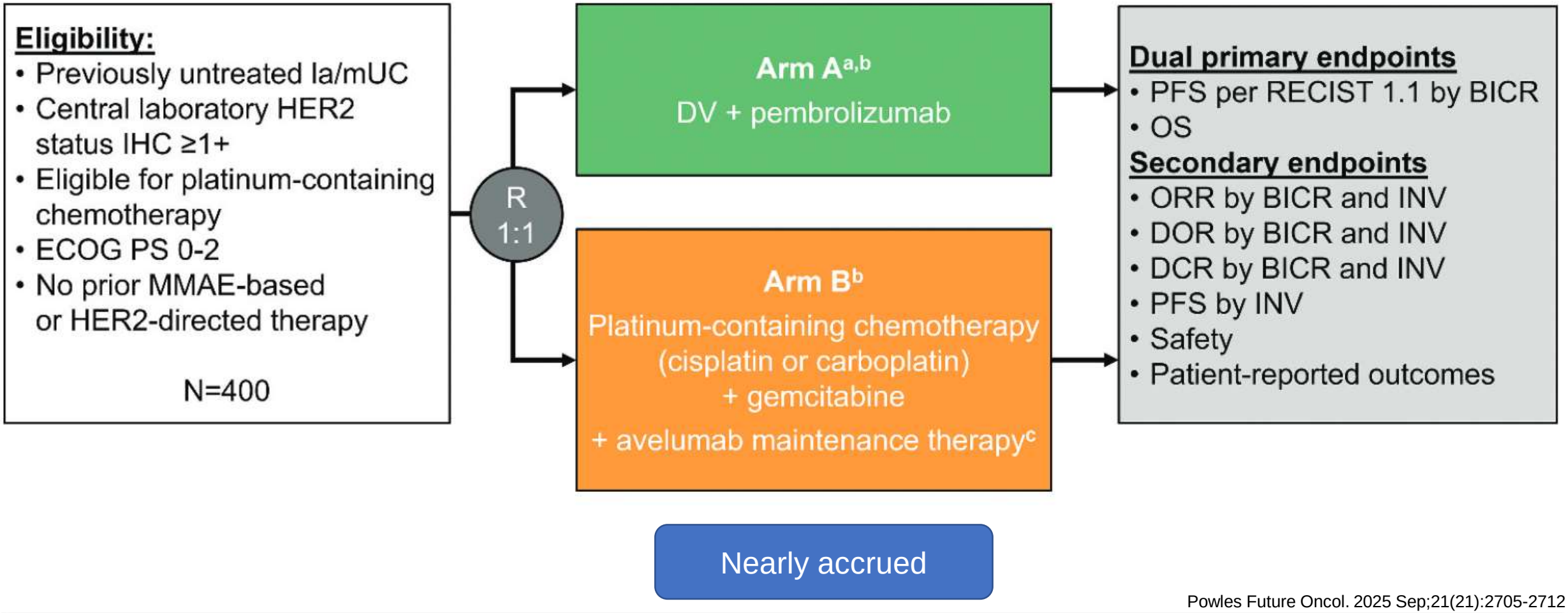
Cohort A	73	67	58	48	33	24	16	12	7	5	1	0	0	0	0
Cohort B	78	75	60	53	45	42	33	23	14	7	5	1	1	1	0

- The median PFS and OS were consistent across HER2 expression levels
- OS was favorable in this 2L/3L therapeutic setting for la/mUC

Data cutoff: September 12, 2025. Median follow-up was 11.3 months for Cohort A and 17.1 months for Cohort B.

2L, second line; 3L, third line; HER2, human epidermal growth factor 2; la/mUC, locally advanced unresectable or metastatic urothelial cancer; NE, not evaluable; PFS, progression-free survival; OS, overall survival.

SGNDV-001: Phase 3, DV/P vs Gem-Platinum-Ave



Nearly accrued

Powles Future Oncol. 2025 Sep;21(21):2705-2712

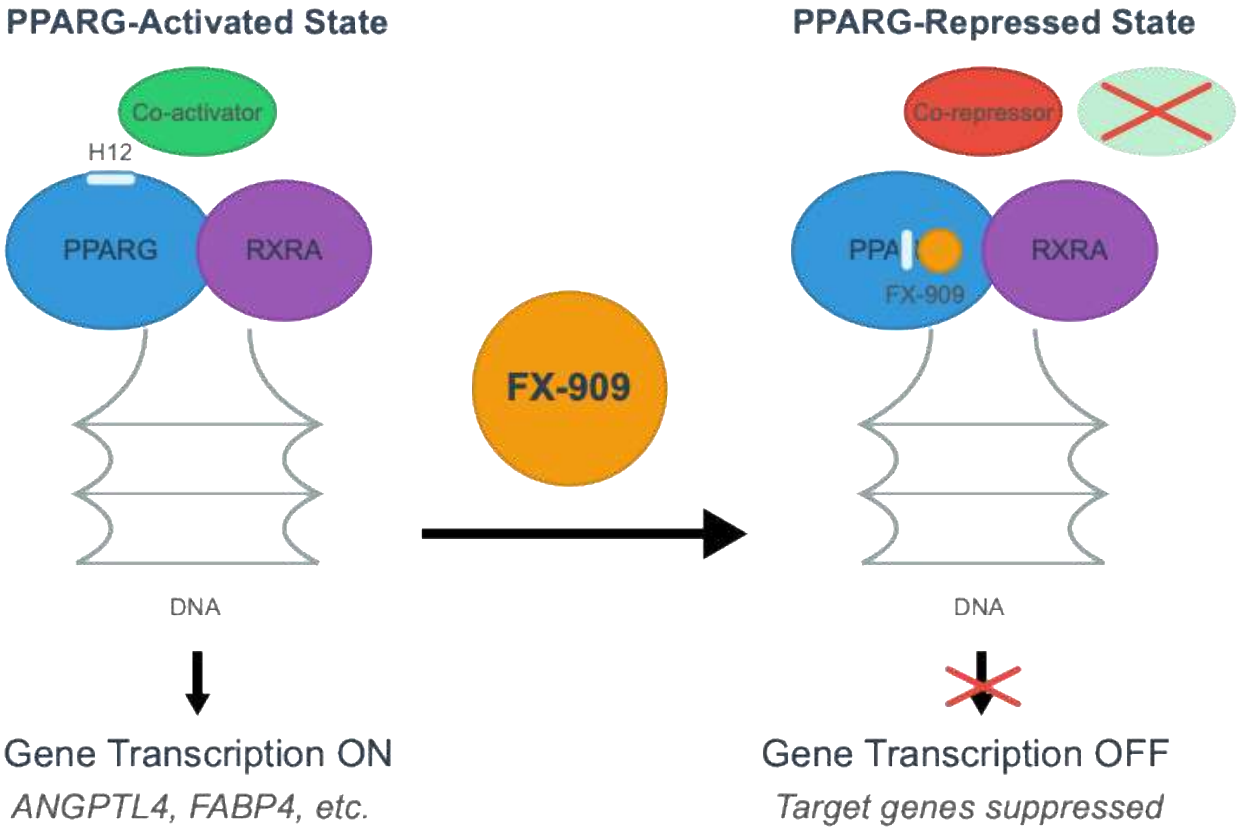
Üroteliyal Kanserlerde Tedavi Seçenekleri
ASCO-GU 2026

Metastatik Evrede Yeni Seçenekler

Background

- The transcription factor PPARG is the master regulator of the luminal lineage in advanced urothelial cancer[1,2]
  - The luminal subtype comprises 65% of urothelial cancers[3,4]
- Genomic evidence for PPARG activation in UC includes recurrent focal amplifications, activating mutations, and hotspot mutations in *RXRA* (S427F/Y), the obligate heterodimeric partner of PPARG[3,4]
- FX-909 is a novel **first-in-class**, orally bioavailable potent and selective **PPARG inverse agonist** that stably enforces a conformationally 'repressive' state that elicits durable tumor regressions in xenograft models[5]

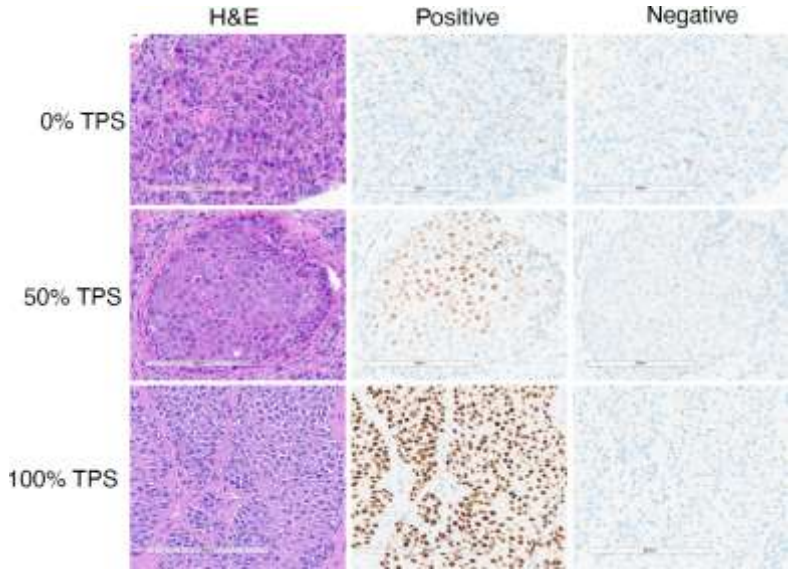
PPARG Inverse Agonist Mechanism of Action



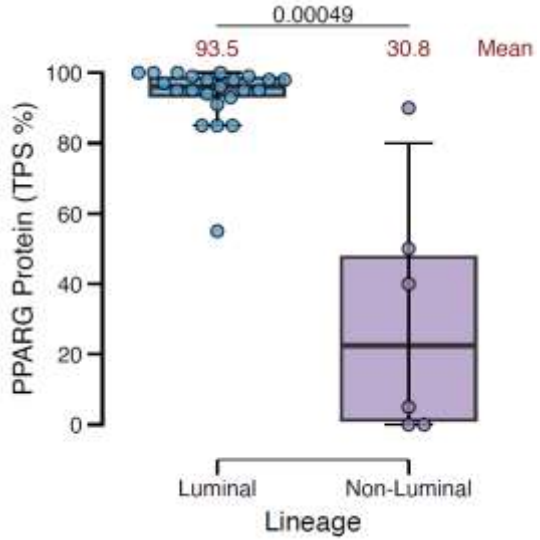
1 Rochel et al. *Nature Comm* (2019); 2 Tate et al. *Nature Comm* (2021); 3 Robertson et al. *Cell* (2017); 4 Motley et al. *Euro J. Caner* (2022); 5 Sims et al. Proc.. AACR, *Cancer Res* (2023)

High Protein Expression of PPARG is Associated with Luminal Lineage

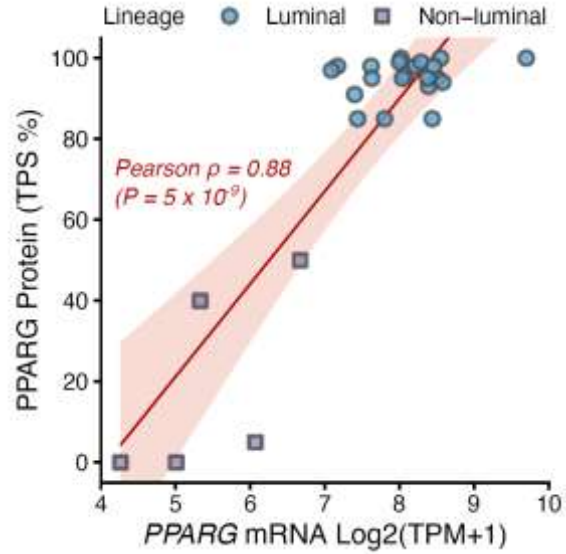
Nuclear tumor staining of PPARG by immunohistochemistry (SP-500)



PPARG protein expression is significantly enriched in luminal tumors



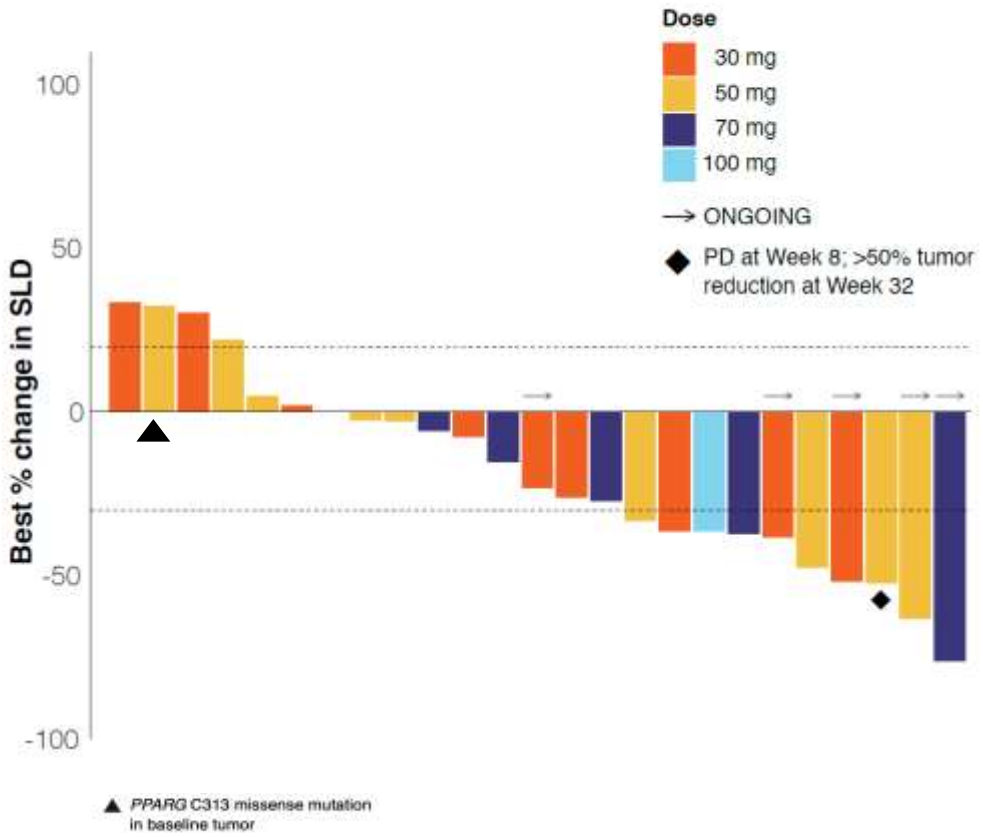
Correlation between PPARG mRNA and protein expression (%TPS)

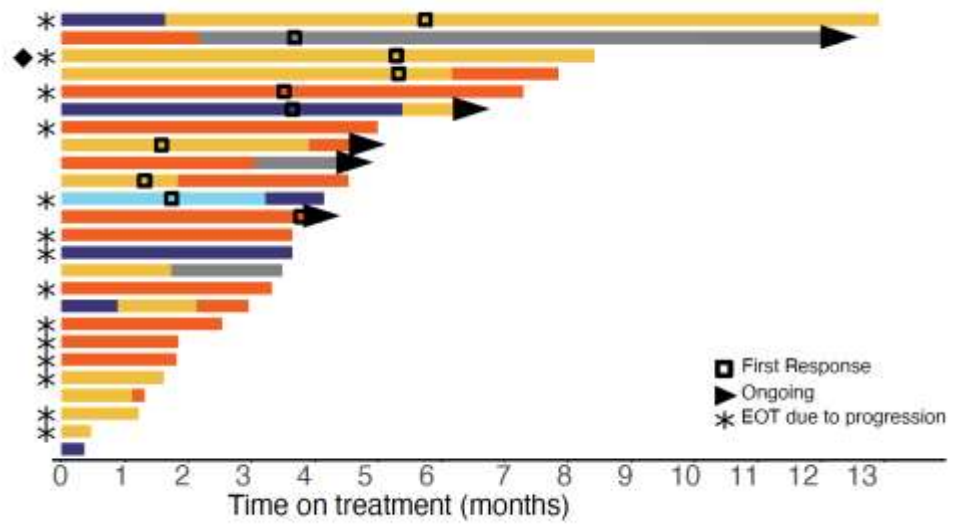


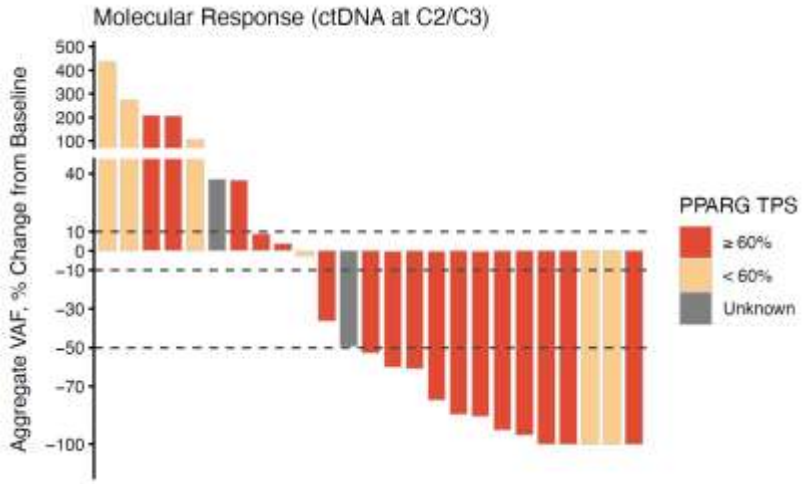
Provisional cutoff of **TPS ≥60%** was determined from integrative biostatistical modeling leveraging the Tempus xT RWD, patients with expression at this threshold are defined as PPARG^{high}

Antitumor Activity in Patients with PPARG^{high} Advanced UC

N=25







Üroteliyal Kanserlerde Tedavi Seçenekleri ASCO-GU 2026

Erken Evrede Yeni Seçenekler

SunRISe-2 Study: Randomized, Controlled Superiority Design

NCT04658862

Population:
- Aged ≥18 years
- Histologically confirmed cT2-T4a, N0, M0 MIBC
- ECOG PS of 0-2
- Declined/ineligible for RC
- Adequate organ function

- Screening re-TURBT: tumor ≤3 cm; no diffuse CIS

Stratification:
- Screening re-TURBT: visibly complete vs incomplete
- Tumor stage at screening re-TURBT: T0 vs Ta/T1/Tis vs T2-T4a

R 1:1

Gem-iDRS + IV cetrelimab *Arm 1*
Gem-iDRS Q3W (21-day indwelling) for 18 weeks, followed by Q12W from Week 24 until Week 144
+ cetrelimab IV Q3W until Week 78

Concurrent CRT *Arm 2*
Investigator's choice of cisplatin (QW for 4-6 weeks) **or gemcitabine** (twice weekly for 4-6 weeks) **+ RT**[a]

Primary end point
- BI-EFS[b]

Secondary end points
- ORR at Week 18[c]
- MFS
- OS
- Safety

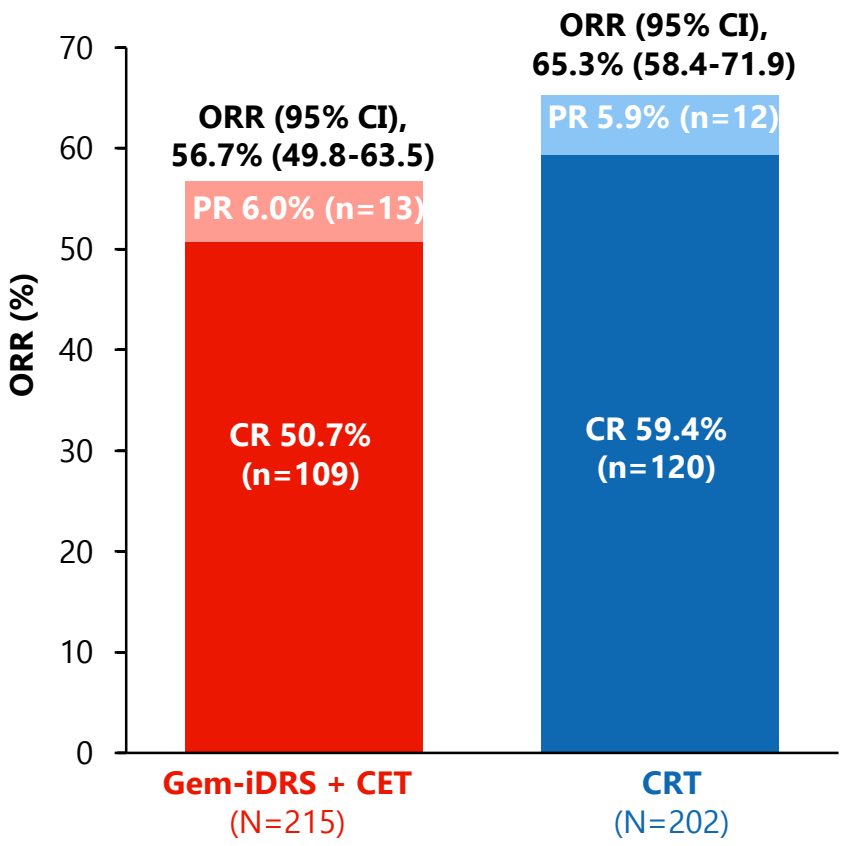
- Median follow-up: 11.3 (range, 0.03-43.2) months
- The study was designed assuming a 12% absolute improvement in the 2-year BI-EFS rate, providing 90% power to detect an HR of 0.65 between treatment vs control arms using a 2-sided alpha of 0.05[d]

[a]RT was either conventional (64 Gy, bladder only) for up to 6.5 weeks or hypofractionated (55 Gy, bladder only) for up to 4 weeks. [b]Defined as any of the following: histologically proven presence of MIBC, clinical evidence of nodal or metastatic disease, RC, or death due to any cause. [c]A futility analysis based on ORR was conducted after 300 patients completed the Week 18 disease assessment. [d]Assumes a 34-month accrual, 24 months of additional follow-up, and a 5% annual dropout rate.
BI-EFS, bladder-intact event-free survival; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; MFS, metastasis-free survival; ORR, overall response rate; OS, overall survival; QW, every week; Q3W, every 3 weeks; Q12W, every 12 weeks; R, randomization; RT, radiation therapy; TURBT, transurethral resection of bladder tumor.

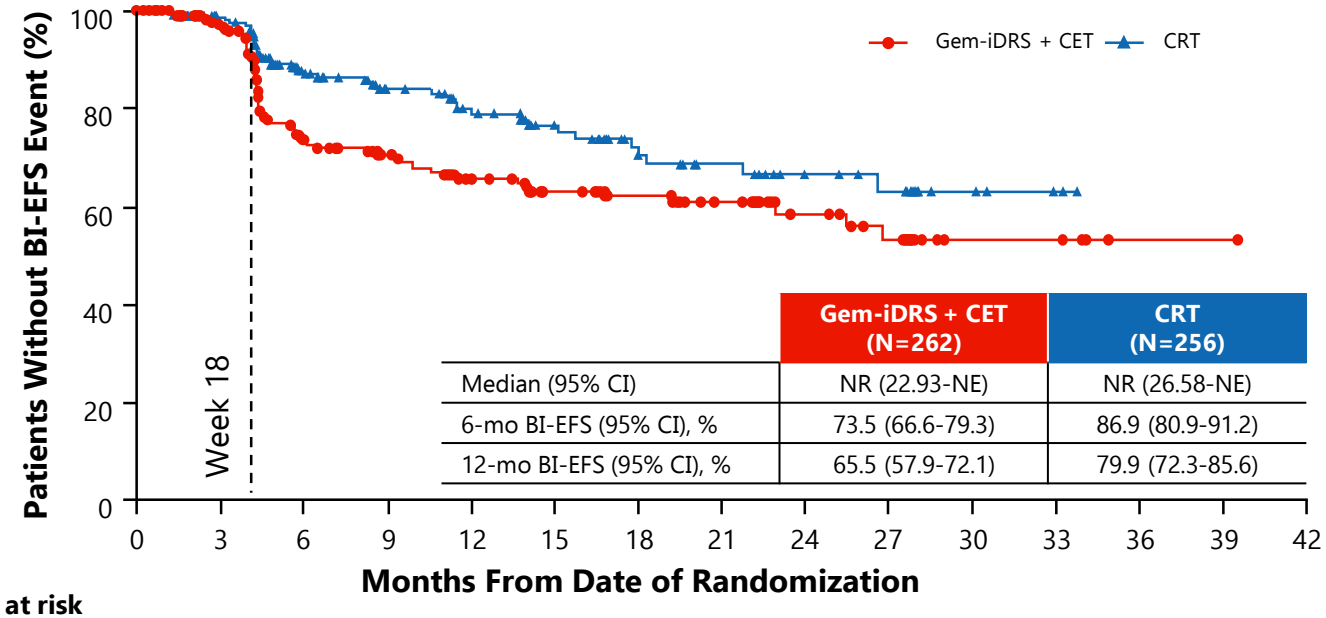
Presented by A Necchi at the ASCO Genitourinary Cancers Symposium; February 26-28, 2026; San Francisco, CA, USA

Majority of Patients in Both Arms Achieved CR at Week 18;
Gem-iDRS + Cetrelimab Did Not Show Superior BI-EFS

ORR at Week 18[a]



BI-EFS



	Gem-iDRS + CET (N=262)	CRT (N=256)
Median (95% CI)	NR (22.93-NE)	NR (26.58-NE)
6-mo BI-EFS (95% CI), %	73.5 (66.6-79.3)	86.9 (80.9-91.2)
12-mo BI-EFS (95% CI), %	65.5 (57.9-72.1)	79.9 (72.3-85.6)

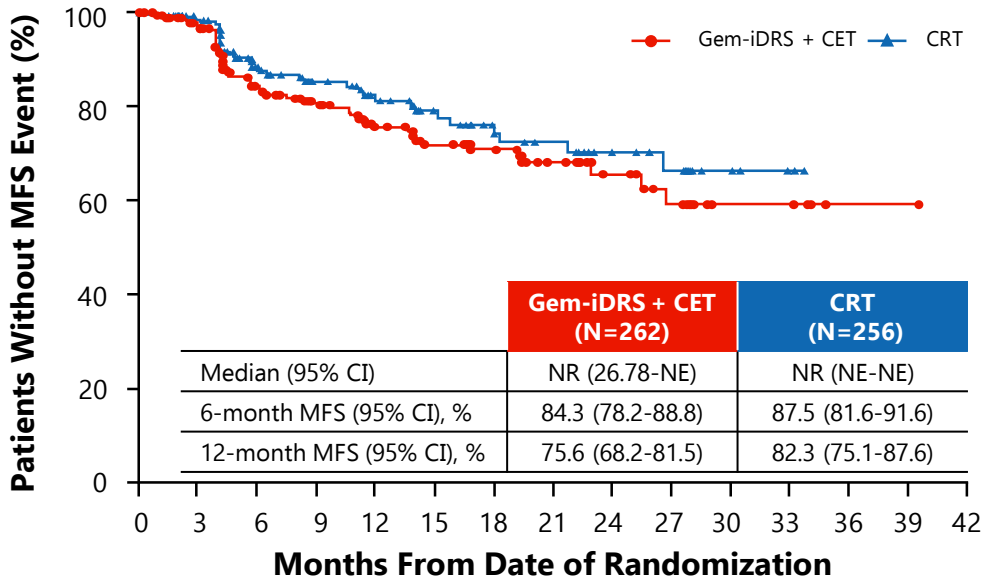
Patients at risk

Gem-iDRS + CET	262	198	122	104	82	67	55	41	24	18	8	8	1	1	0
CRT	256	183	123	92	75	55	42	34	20	17	6	2	0	0	0

Clinical cutoff date July 7, 2025. [a]ORR was for the evaluable analysis set that consisted of all patients who had at least 1 Week 18 efficacy assessment, had disease progression prior to or in Week 18, or discontinued the study without the Week 18 assessment. Nonresponse was reported in 93 (43.3%) patients in the gem-iDRS + CET arm and 70 (34.7%) patients in the CRT arm. NE, not estimable; NR, not reached; PR, partial response; RECIST, Response Evaluation Criteria In Solid Tumors.

Gem-iDRS + Cetrelimab Did Not Show Superior MFS or OS, Compared With CRT

Metastasis-free survival

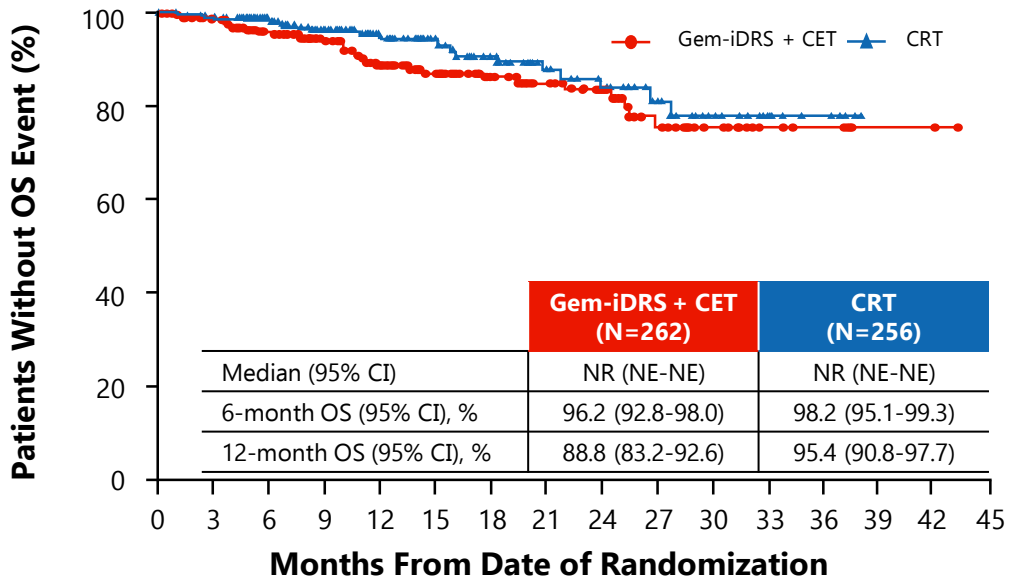


	Gem-iDRS + CET (N=262)	CRT (N=256)
Median (95% CI)	NR (26.78-NE)	NR (NE-NE)
6-month MFS (95% CI), %	84.3 (78.2-88.8)	87.5 (81.6-91.6)
12-month MFS (95% CI), %	75.6 (68.2-81.5)	82.3 (75.1-87.6)

Patients at risk

Gem-iDRS + CET	262	200	136	112	86	70	58	41	24	18	8	8	1	1	0
CRT	256	186	125	93	75	55	42	34	20	17	6	2	0	0	0

Overall survival



	Gem-iDRS + CET (N=262)	CRT (N=256)
Median (95% CI)	NR (NE-NE)	NR (NE-NE)
6-month OS (95% CI), %	96.2 (92.8-98.0)	98.2 (95.1-99.3)
12-month OS (95% CI), %	88.8 (83.2-92.6)	95.4 (90.8-97.7)

Patients at risk

Gem-iDRS + CET	262	239	193	156	126	106	82	67	49	33	20	11	9	2	1	0
CRT	256	236	167	127	105	82	67	51	40	28	18	10	5	0	0	0

Clinical cutoff date July 7, 2025.

MFS is defined as the time from randomization to first radiologic (as assessed by RECIST 1.1 criteria) evidence of metastatic disease or death due to any cause. Evidence of metastatic disease was determined by imaging results showing progression. Patients known to be alive and free of metastatic disease were censored at the date of last assessment.

OS is defined as the time from randomization to death from any cause. Patients who did not have an OS event were censored at the date when they were last known to be alive.

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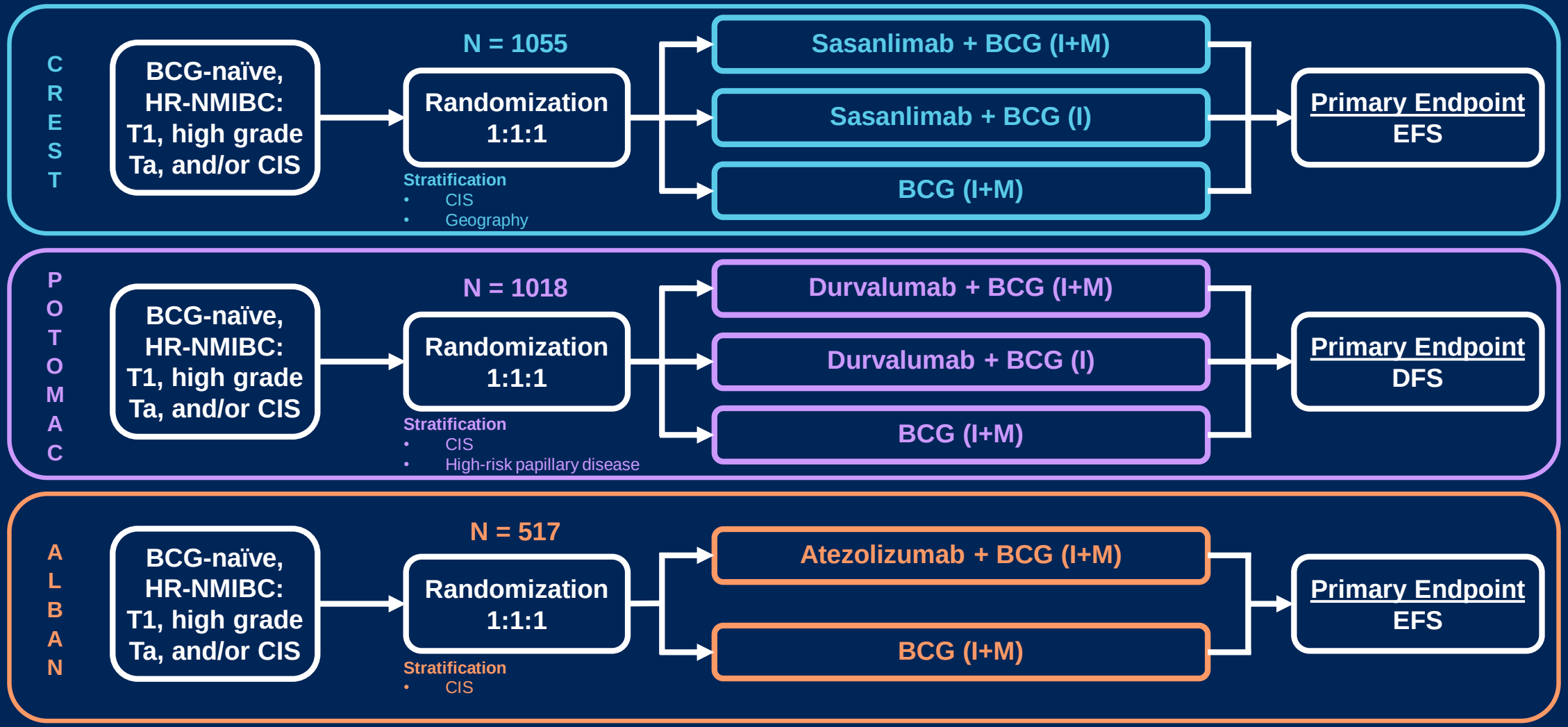
Recurrence after BCG… FDA approvals (CIS)

2020	FDA approves pembrolizumab for BCG-unresponsive, high-risk non-muscle invasive bladder cancer	CRR 41%
2022	FDA D.I.S.C.O. Burst Edition: FDA approval of Adstiladrin (nadofaragene firadenovec-vncg) for patients with high-risk Bacillus Calmette-Guérin unresponsive non-muscle invasive bladder cancer with carcinoma in situ with or without papillary tumors	CRR 53.4%
2024	FDA approves nogapendekin alfa inbakicept-pmln for BCG-unresponsive non-muscle invasive bladder cancer	CRR 71%
2025	FDA approves gemcitabine intravesical system for non-muscle invasive bladder cancer	CRR 82.4%

www.fda.gov

The Evidence

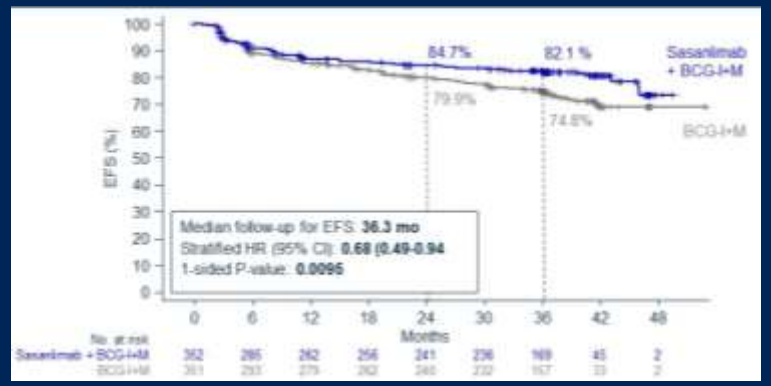


Shore NS et al, AUA 2025 / Nat Med 2025;31:2806-14 / De Santis M et al, ESMO 2025 / Lancet 2025;406(10516):2221-2234 / Roupret M et al, ESMO 2025 / Ann Oncol 2026;37(1):44-52

HR-NMIBC = High-risk Non-muscle invasive bladder cancer; I = Induction; M = Maintenance; EFS = Event-free survival; DFS = Disease-free survival

The Evidence

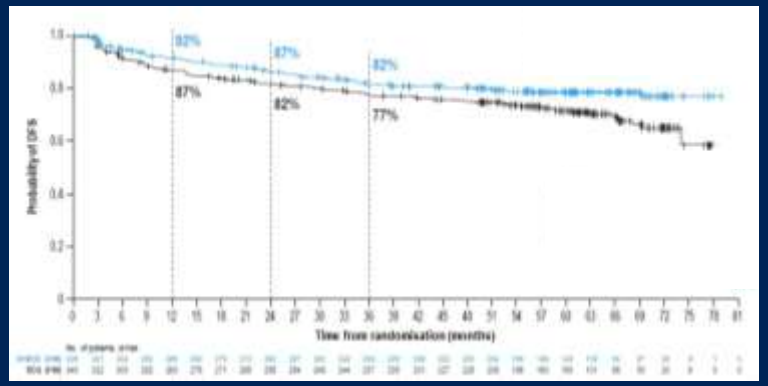
CREST



EFS HR 0.68 (0.49-0.94) p=0.0095

- 7.3% absolute 3-yr EFS improvement
- S + BCG (I+M) Gr 3-4 irAE TRAE = 15.7%
- 2 yrs Sasanlimab tx
- 2 yrs BCG tx

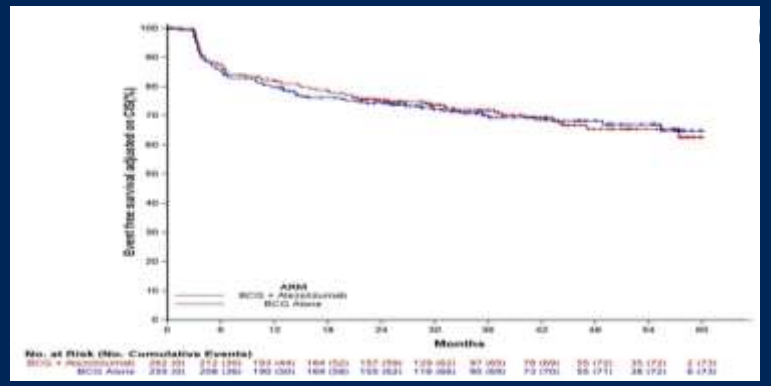
POTOMAC



DFS HR 0.68 (0.50-0.93) p=0.0154

- 4.4% absolute 3-yr DFS improvement
- D + BCG (I+M) Gr 3-4 irAE TRAE = 8.0%
- 1 yr Durvalumab tx
- 2 yrs BCG tx

ALBAN



EFS HR 0.98 (0.71-1.36) p=0.91

- 0% absolute 3-yr EFS improvement
- A + BCG (I+M) Gr 3-4 irAE TRAE = 5.5%
- 1 yr Atezolizumab tx
- 1 yr BCG tx

Shore NS et al, AUA 2025 / Nat Med 2025;31:2806-14 / De Santis M et al, ESMO 2025 / Lancet 2025;406(10516):2221-2234 / Roupret M et al, ESMO 2025 / Ann Oncol 2026;37(1):44-52

EFS = Event-free survival; DFS = Disease-free survival; S = Sasanlimab; D = Durvalumab; A = Atezolizumab; I = Induction; M = Maintenance

Sonuç

- Enfortumab vedotin+Pembrolizumab Sisplatin uygun ve olmayanlarda standart
- Patolojik tam yanıt elde edilen ctDNA ve utDNA negatif adjuvan tedavi gerekmiyor görünüyor
- Patolojik tam yanıt elde edilen ctDNA ve utDNA negatif cerrahi isteksiz hastayı operasyona zorlamam ve radyoterapi için zorlamam
- Neoadjuvan/adjuvan Durvalumab ve ctDNA +Adjuvan Atezolizumab sadece bilimsel bir veri klinik uygulamada yeri kalmadı
- Her-2 +≥1pozitif yeni marker metastatik ve neoadjuvan disitamab vedotin+pembrolizumab sonuçları bekleniyor ve pCR %60 ve üstü olursa yeni bir seçenek olabilir