Consensus or Controversy? Clinical Investigators Provide Perspectives on the Current and Future Clinical Care of Patients with Urothelial Bladder Cancer

Saturday, May 31, 2025
6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)

Faculty

Andrea Necchi, MD
Thomas Powles, MBBS, MRCP, MD

Moderator

Matthew D Galsky, MD

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Data and Safety Monitoring Boards/Committees	Bicycle Therapeutics

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Data and Safety Monitoring Boards/Committees	Bristol Myers Squibb, Strata Oncology

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Dr Love — Disclosures

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Friday May 30	**Immunotherapy and Antibody–Drug Conjugates in Lung Cancer** 11:15 AM – 12:45 PM CT (12:15 PM – 1:45 PM ET)
	Colorectal Cancer 6:30 PM – 8:30 PM CT (7:30 PM – 9:30 PM ET)
	EGFR Mutation–Positive Non–Small Cell Lung Cancer 6:30 PM – 8:30 PM CT (7:30 PM – 9:30 PM ET)
Saturday May 31	**Urothelial Bladder Cancer** 6:45 AM – 7:45 AM CT (7:45 AM – 8:45 AM ET)
	Non–Hodgkin Lymphoma 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
	Prostate Cancer 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
Sunday June 1	**Chronic Lymphocytic Leukemia (Webinar)** 7:00 AM – 8:00 AM CT (8:00 AM – 9:00 AM ET)
	HER2–Positive Gastrointestinal Cancers 7:00 PM – 8:30 PM CT (8:00 PM – 9:30 PM ET)
	Ovarian and Endometrial Cancer 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
Monday June 2	**Renal Cell Carcinoma (Webinar)** 7:00 AM – 8:00 AM CT (8:00 AM – 9:00 AM ET)
	Multiple Myeloma (Webinar) 6:00 PM – 7:00 PM CT (7:00 PM – 8:00 PM ET)
	Metastatic Breast Cancer 7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)
Tuesday June 3	**Soft Tissue Sarcoma and Other Connective Tissue Neoplasms (Webinar)** 7:00 AM – 8:00 AM CT (8:00 AM – 9:00 AM ET)

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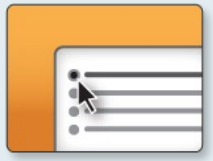
Clinicians in the Meeting Room

Networked iPads are available.

Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.



Answer Survey Questions: Complete the pre- and postmeeting surveys.

Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

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Clinicians Attending via Zoom

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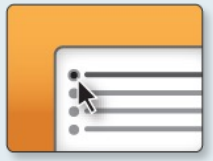

Answer Survey Questions: Complete the pre- and postmeeting surveys.

Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.

Get CME Credit: A CME credit link will be provided in the chat room at the conclusion of the program.

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About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based program. An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

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Matthew D Galsky, MD

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Agenda

MODULE 1: Current and Future Management of Muscle-Invasive Bladder Cancer — Prof Powles

MODULE 2: Novel Intravesical Therapies Under Evaluation for Nonmetastatic Urothelial Bladder Cancer (UBC) — Prof Necchi

MODULE 3: Selection and Sequencing of Therapy for Metastatic UBC — Dr Galsky

Agenda

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MODULE 2: Novel Intravesical Therapies Under Evaluation for Nonmetastatic Urothelial Bladder Cancer (UBC) — Prof Necchi

MODULE 3: Selection and Sequencing of Therapy for Metastatic UBC — Dr Galsky

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Current and future management of MIBC treatment

Thomas Powles

Director of Barts Cancer Center
Professor of Urology Cancer, Barts Cancer Institute

Monotherapy PD(L)1 trials in bladder cancer in chronological order

Setting	Study Name	Study drug	PD-L1 biomarker Endpoint	MOA	Achieved primary endpoint	OS +ve
Advanced disease	KN45	Pembrolizumab	ITT	PD1	Yes	Yes
Advanced disease	IM211	Atezolizumab	PD-L1 +ve	PD-L1	No	No
Advanced disease	DANUBE	Durvalumab	PD-L1 +ve	PD-L1	No	No
Advanced disease	DANUBE	Durva/Treme	ITT	PD-L1/CTLA4	No	No
Advanced disease	KN361	Pembrolizumab	PD-L1 +ve	PD-1	No	No
Advanced disease	IM130	Atezolizumab	PD-L1 +ve	PD-L1	No	No
Advanced disease	Javelin	Avelumab	ITT	PD-L1	Yes	Yes
Advanced disease	CM901	Ipi/nivo (press release)	PD-L1/ITT	PD-1/CTLA4	No	No
Adjuvant	CM274	Nivolumab	ITT	PD-1	Yes	No
Adjuvant	IM010	Atezolizumab	ITT	PD-L1	No	No
Adjuvant	Ambassador	Pembrolizumab	ITT	PD-1	Yes	No
Perioperative	Niagara	Durvalumab	ITT	PD-L1	Yes	Yes
NMIBC	CREST	Sasanlimab	ITT	PD-1	Yes	No
NMIBC	Potomac	Durvalumab	ITT (press release)	PD-L1	Yes	No

CheckMate 274 is a phase 3, randomized, double-blind, multicenter study of adjuvant nivolumab versus placebo in patients with high-risk MIUC[a]

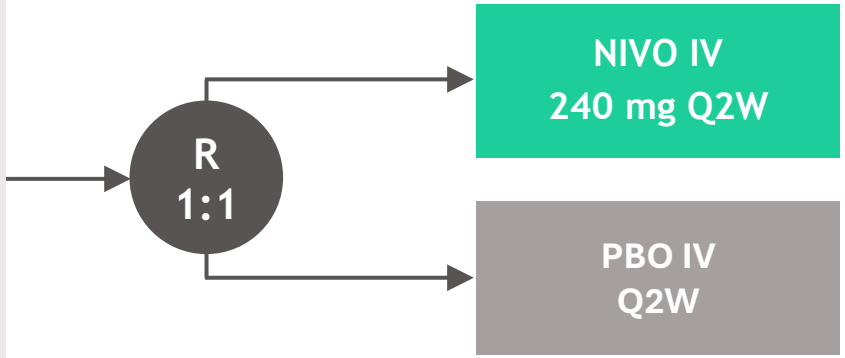
N = 709

Key eligibility criteria

- Patients with ypT2-ypT4a or ypN+ MIUC who had neoadjuvant cisplatin chemotherapy
- Patients with pT3-pT4a or pN+ MIUC without prior neoadjuvant cisplatin chemotherapy and not eligible/refuse adjuvant cisplatin chemotherapy
- Radical surgery within the past 120 days
- Disease-free status within 4 weeks of randomization

Stratification factors

- Tumor PD-L1 status (≥ 1% vs < 1% or indeterminate)[b]
- Prior neoadjuvant cisplatin-based chemotherapy
- Nodal status



Treat for up to 1 year of adjuvant therapy

Primary endpoints: DFS in all randomized patients (ITT population) and DFS in all randomized patients with tumor PD-L1 ≥ 1%
Secondary endpoints: NUTRFS, DSS, and OS[c]
Exploratory endpoints included: DMFS, PFS2, safety, HRQoL

Milowsky M et al. ASCO GI 2025;Abstract 658.

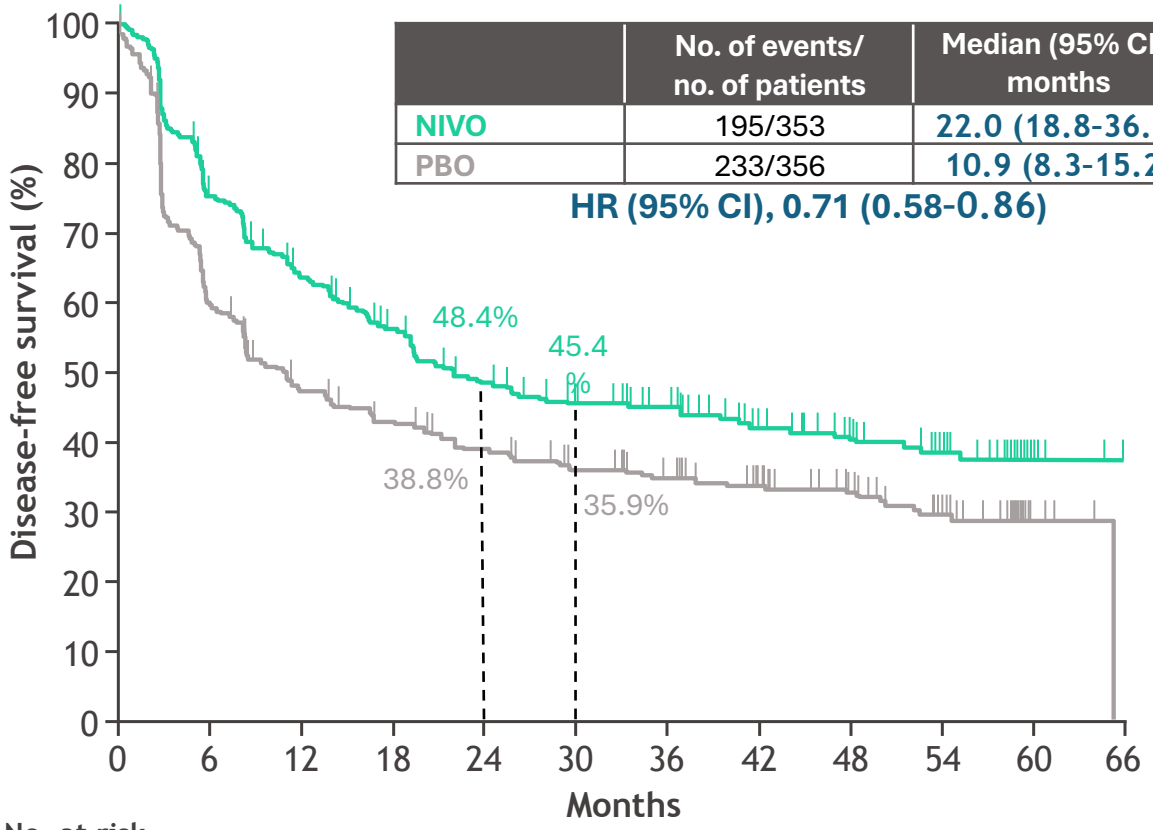
Disease-free survival

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

ITT

	No. of events/ no. of patients	Median (95% CI), months
NIVO	195/353	22.0 (18.8-36.9)
PBO	233/356	10.9 (8.3-15.2)

HR (95% CI), 0.71 (0.58-0.86)



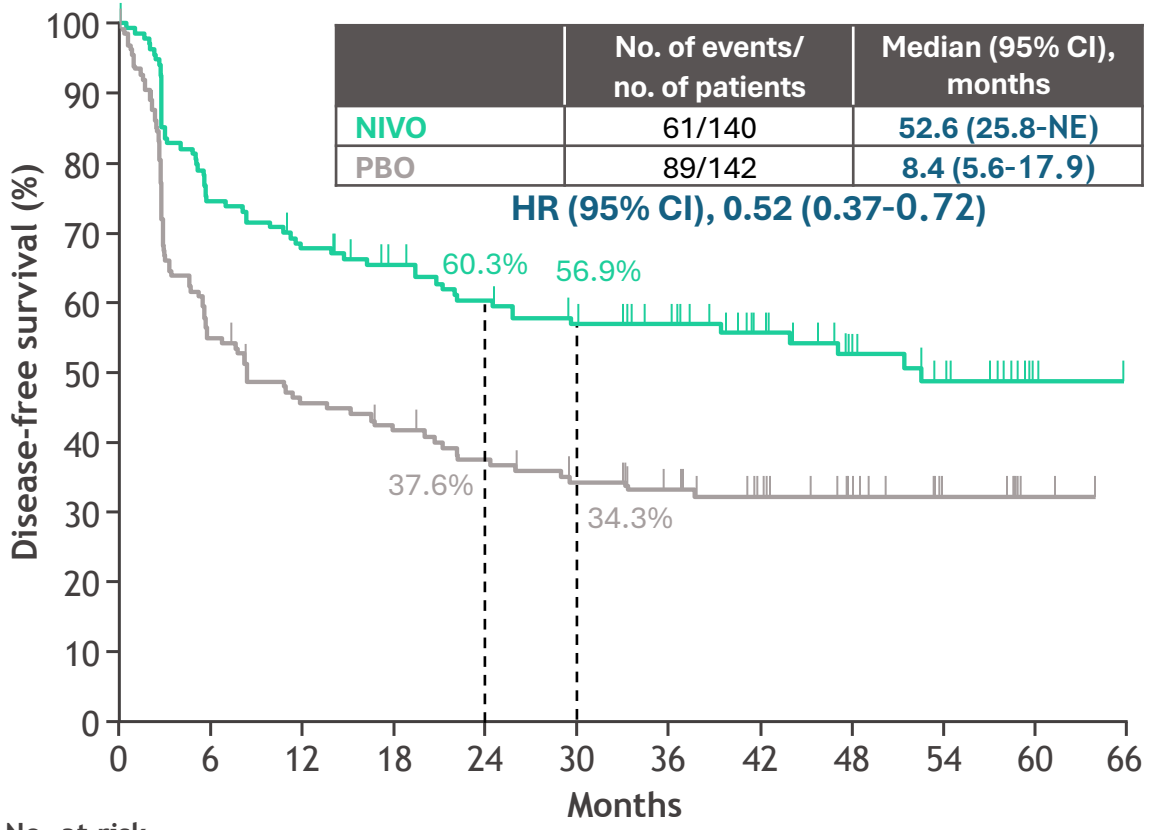
No. at risk

NIVO	353	253	208	177	150	132	113	83	57	43	4	0
PBO	356	207	156	138	123	109	94	80	59	39	4	0

PD-L1 ≥ 1%

	No. of events/ no. of patients	Median (95% CI), months
NIVO	61/140	52.6 (25.8-NE)
PBO	89/142	8.4 (5.6-17.9)

HR (95% CI), 0.52 (0.37-0.72)



No. at risk

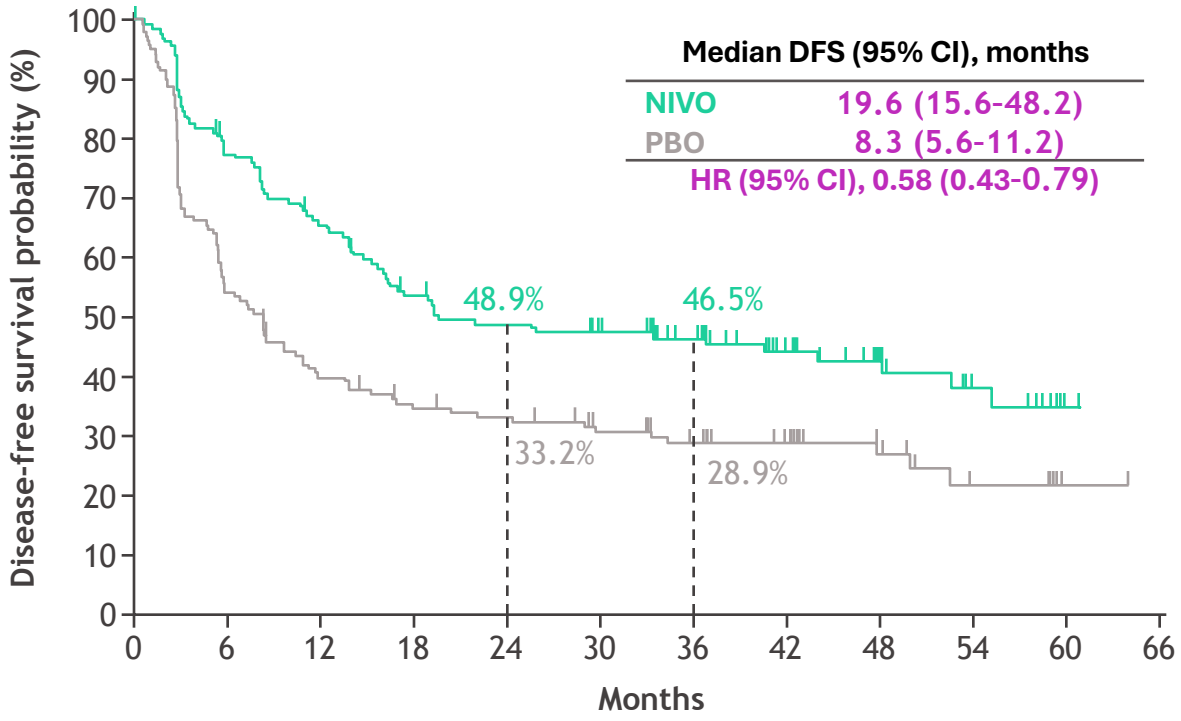
NIVO	140	99	88	79	72	64	55	42	29	23	2	0
PBO	142	74	58	52	46	40	34	26	18	9	2	0

Minimum follow-up, 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.

Milowsky M et al. ASCO GI 2025;Abstract 658.

DFS: patients with MIBC according to prior NAC

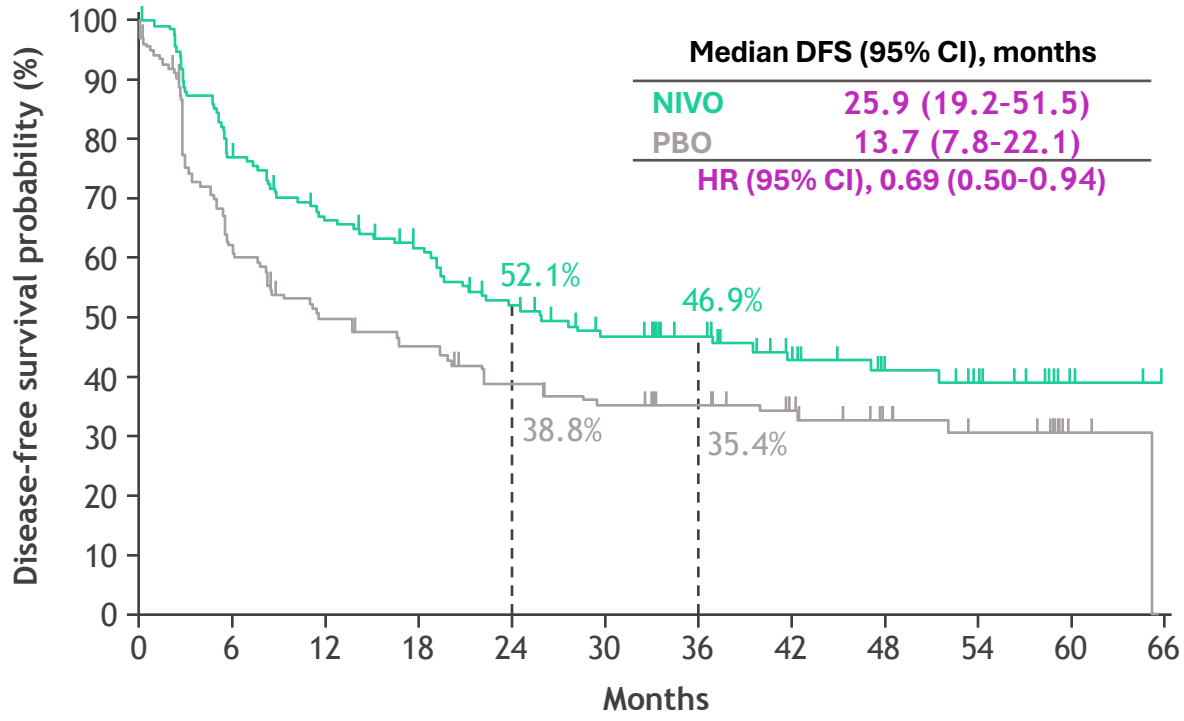
Patients with MIBC with prior NAC



No. at risk

NIVO	142	105	88	70	63	58	48	34	20	12	1	0
PBO	142	77	55	46	43	36	29	24	15	7	1	0

Patients with MIBC without prior NAC[a]

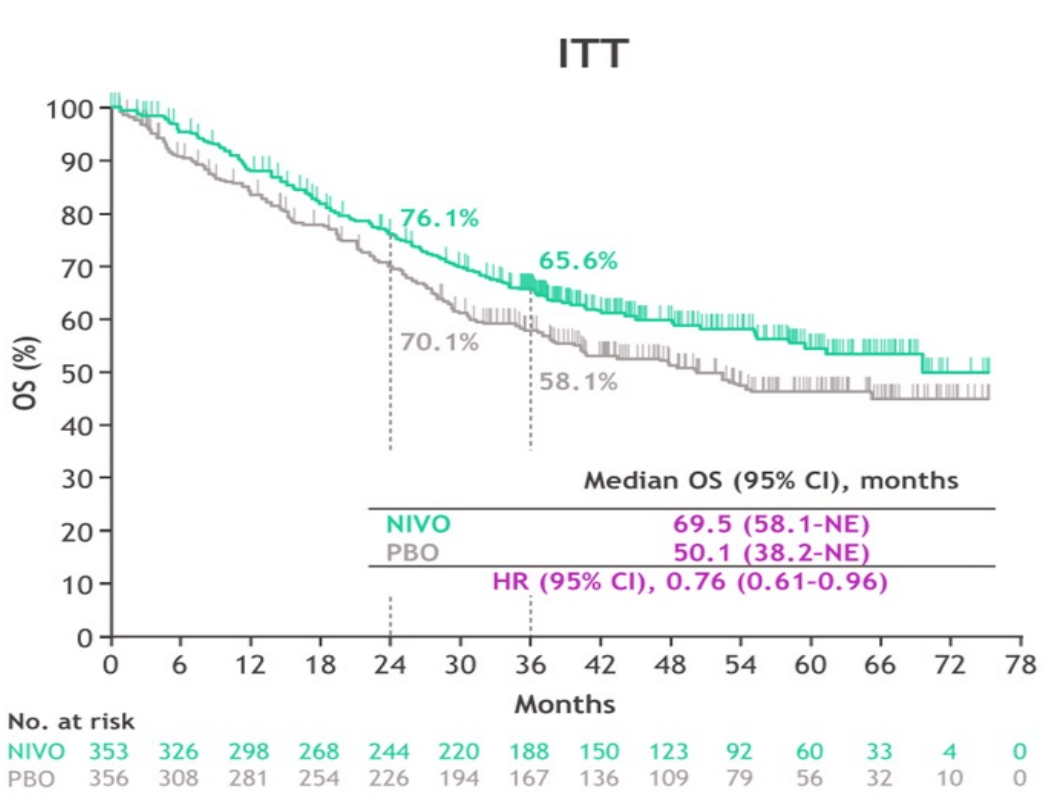


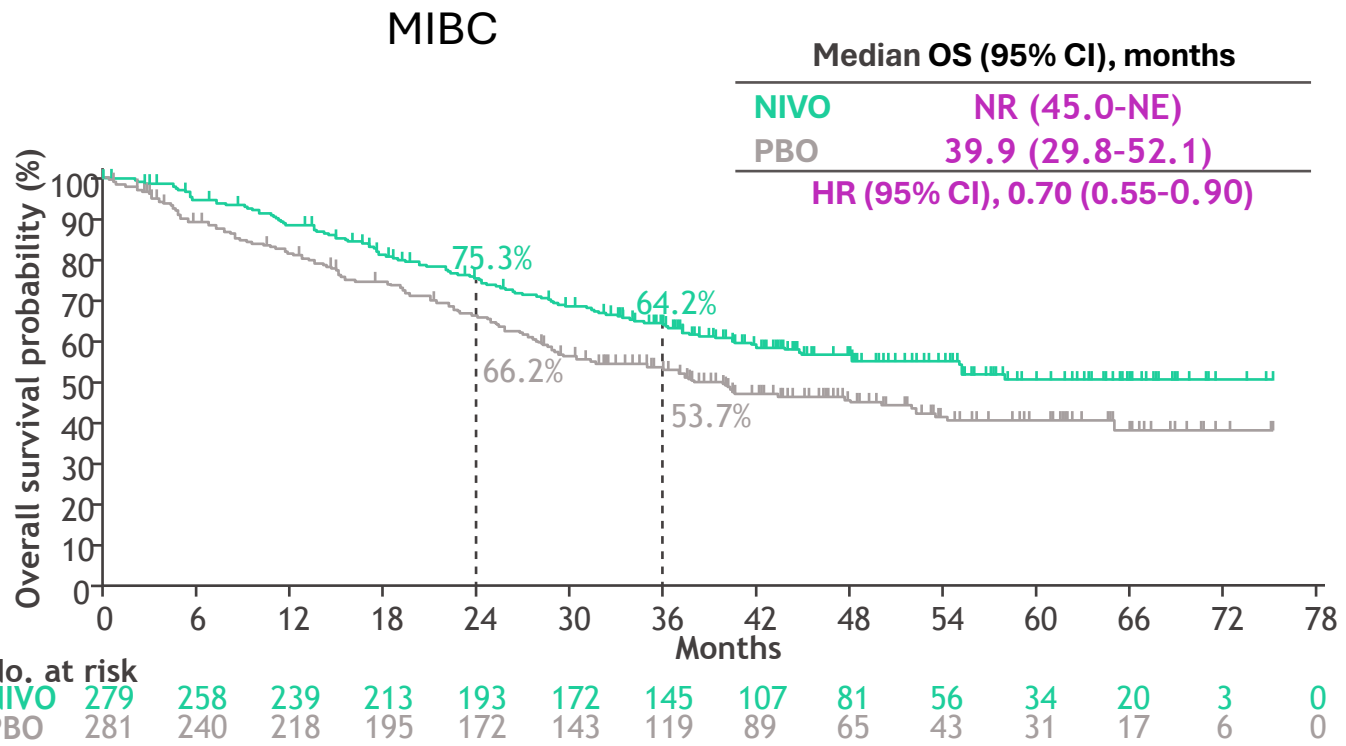
No. at risk

NIVO	137	103	87	77	63	52	44	30	21	16	3	0
PBO	139	82	64	57	47	42	35	28	19	12	2	0

Median follow-up of 36.1 months in the ITT population and 34.5 months in the MIBC population.
[a]This includes patients who had not received neo-adjuvant cisplatin chemotherapy and are not eligible for or refuse adjuvant cisplatin chemotherapy.

OS[a]: all randomized patients with ITT and MIBC





[a]Interim OS analysis.
Median follow-up of 36.1 months in the ITT population and 34.5 months in the MIBC population.
Galsky MD, et al. *J Clin Oncol* 2025;43:15-21.

Milowsky M et al. ASCO GI 2025;Abstract 658.

Summary of perioperative immune therapy trials in UC

neoadjuvant	cT2 %	pCR	24 mnth EFS	G3+ TRAE
Atezo (95)	74%	28%	68%	7%
Pembro (114)	48%	37%	71%	5%
TAR200+PD1 (53) vs PD1 (31)	80%	42%/23%	NA	11%/5%
MVAC(153)	40%	48/153 (31%)		>33%
CMV (150)	34%	RC+RT	46%	
DDMVAC (218)	95%	84/218 (39%)	~75%	>55%
GemCis nivo	66%	35%	73%	~40%
EV	68%/66%	36%		
SG (21)	52%	38 (11-45%)	NA <85%	36%
DV+Toripalimab (31)	46%	61%		
NIAGARA -D Niagara- contro	40%	37% 27%	74% 68%	

The T stage is radiological and not accurate

The definition of pCR varies across trials

Baseline procedures vary

Surgery is not universally performed

Cross trial comparison is very unwise here

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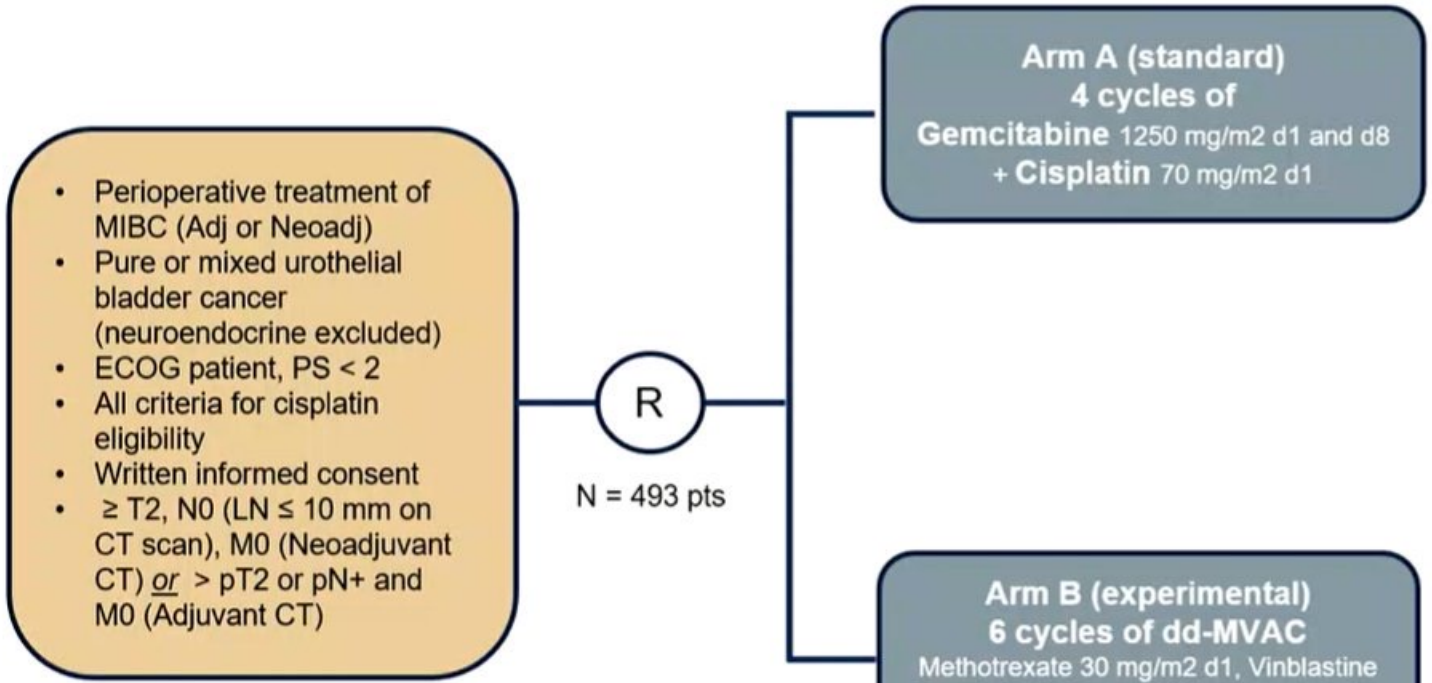
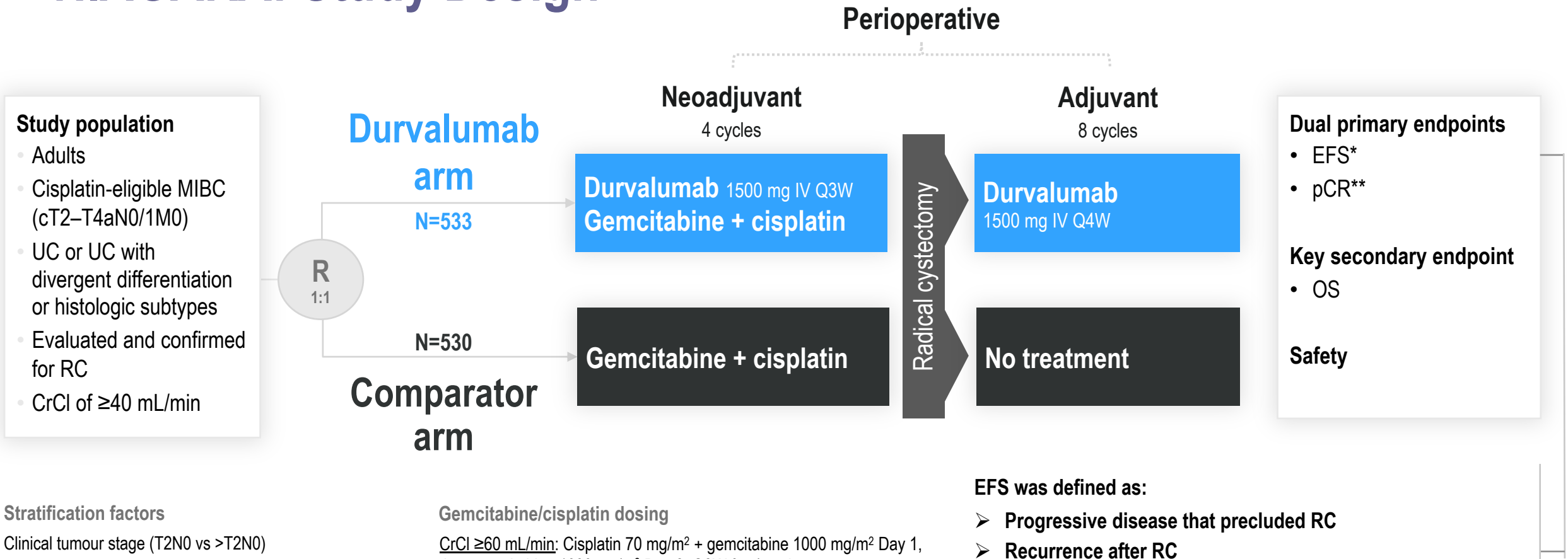


- **Primary endpoint: PFS at 3 years**
- **median follow-up 40 months**

A randomized phase II study of coexpression extrapolation (COXEN) with neoadjuvant chemotherapy for bladder cancer (SWOG S1314; NCT02177695)

NIAGARA: Study Design



Stratification factors

Clinical tumour stage (T2N0 vs >T2N0)

Renal function (CrCl ≥60 mL/min vs ≥40–<60 mL/min)

PD-L1 status (high vs low/negative expression)

Gemcitabine/cisplatin dosing

CrCl ≥60 mL/min: Cisplatin 70 mg/m^2 + gemcitabine 1000 mg/m^2 Day 1, then gemcitabine 1000 mg/m^2 Day 8, Q3W for 4 cycles

CrCl ≥40–<60 mL/min: Split-dose cisplatin 35 mg/m^2 + gemcitabine 1000 mg/m^2 Days 1 and 8, Q3W for 4 cycles

EFS was defined as:

- **Progressive disease that precluded RC**
- **Recurrence after RC**
- **Date of expected surgery in patients who did not undergo RC**
- **Death from any cause**

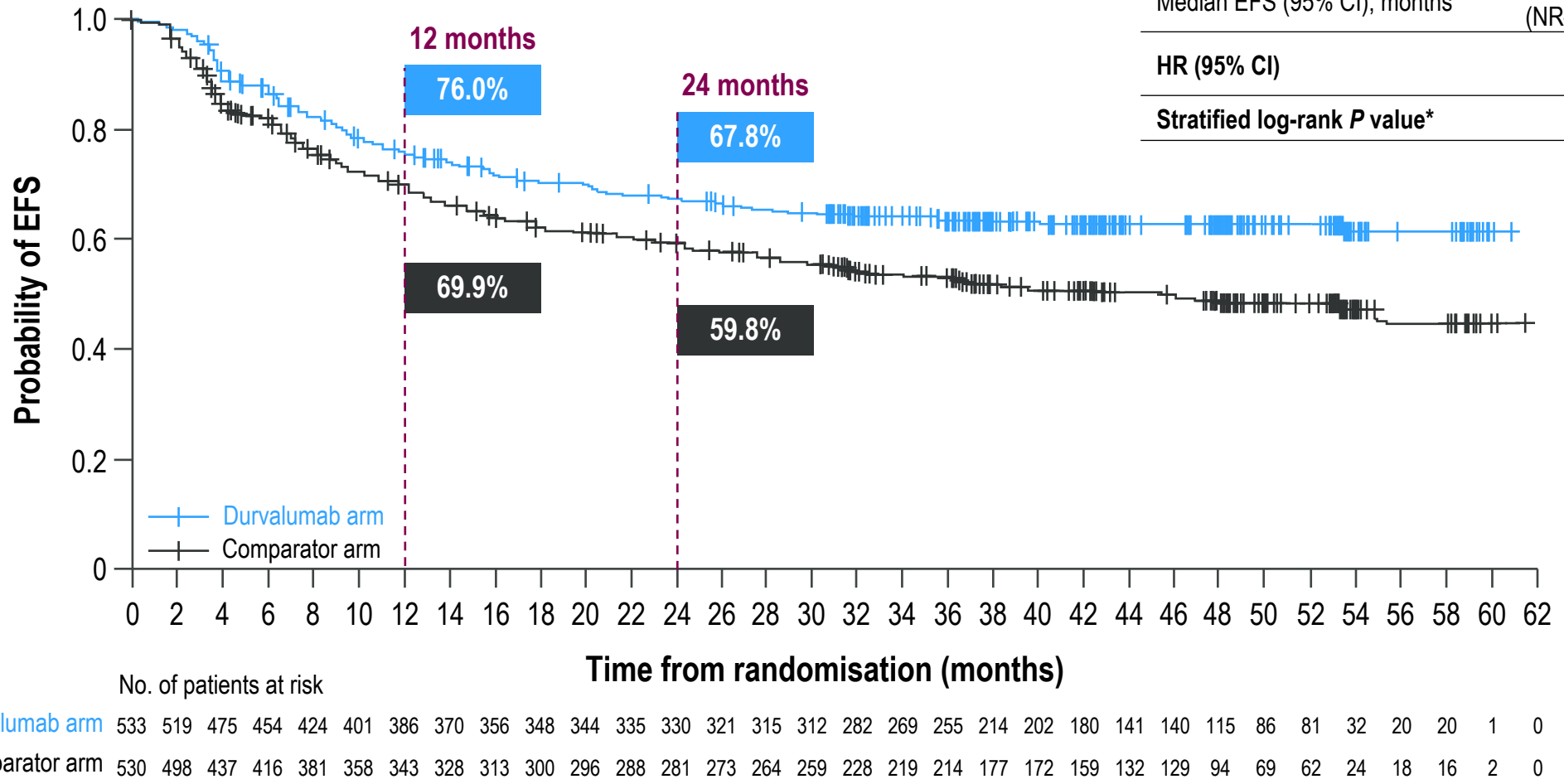
Other endpoints (not reported here): DFS, DSS, MFS, HRQoL, 5-year OS

*Evaluated by blinded independent central review or central pathology review (if a biopsy was required for a suspected new lesion). **Evaluated by blinded central pathology review.
ClinicalTrials.gov, NCT03732677; EudraCT number, 2018-001811-59. CrCl, creatinine clearance; DFS, disease-free survival; DSS, disease-specific survival; EFS, event-free survival; HRQoL, health-related quality of life; IV, intravenous; MFS, metastasis-free survival; MIBC, muscle-invasive bladder cancer; OS, overall survival; pCR, pathologic complete response; PD-L1, programmed cell death ligand-1; Q3W, every 3 weeks; Q4W, every 4 weeks; R, randomised; RC, radical cystectomy; UC, urothelial carcinoma..

1. Powles T, et al. Presented at: ESMO Congress; September 13-17, 2024; Barcelona, Spain. Abs LBA5. 2. Powles T, et al. *N Engl J Med.* 2024 Nov 14;391(19):1773-1786.

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**	



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

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

EFS is defined as the time from randomisation to the first:

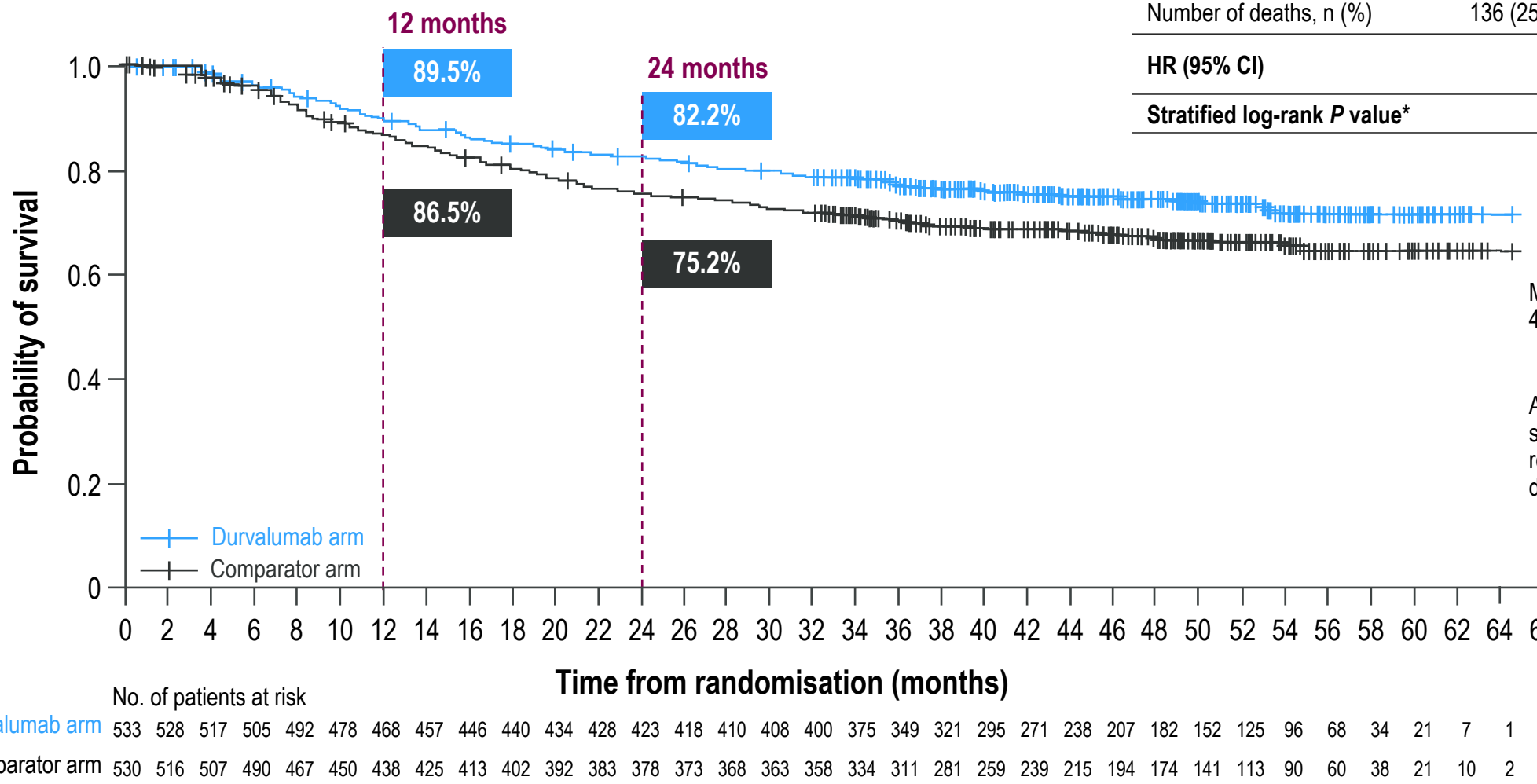
- Recurrence of disease after RC;
- Progressive disease that precluded RC;
- Date of expected surgery in patients who failed to undergo RC;
- Death from any cause.

EFS was assessed using RECIST v1.1. *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. BICR, blinded independent central review; 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.

1. Powles T, et al. Presented at: ESMO Congress; September 13-17, 2024; Barcelona, Spain. Abs LBA5. 2. Powles T, et al. *N Engl J Med.* 2024 Nov 14;391(19):1773-1786.

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**	



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

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:

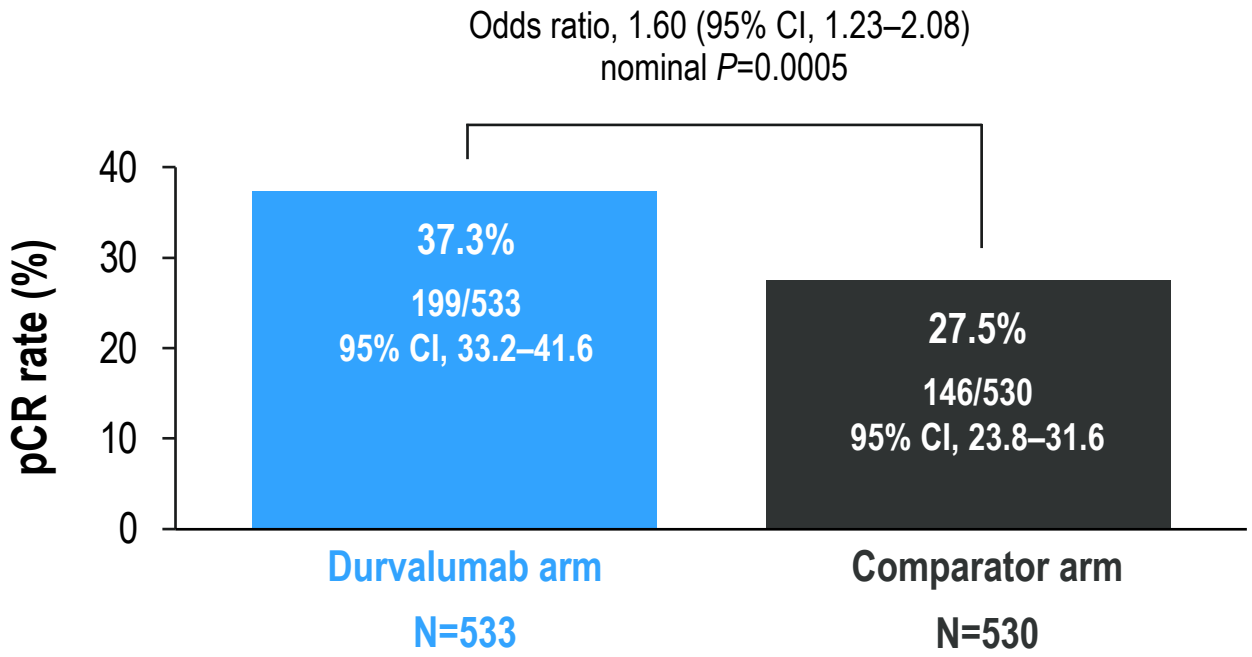
- 53 patients in the durvalumab arm
- 93 patients in the comparator arm

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.

1. Powles T, et al. Presented at: ESMO Congress; September 13-17, 2024; Barcelona, Spain. Abs LBA5. 2. Powles T, et al. *N Engl J Med.* 2024 Nov 14;391(19):1773-1786.

NIAGARA: Pathological Complete Response (ITT)

10% improvement in pathological complete response rate in favor of the durvalumab arm

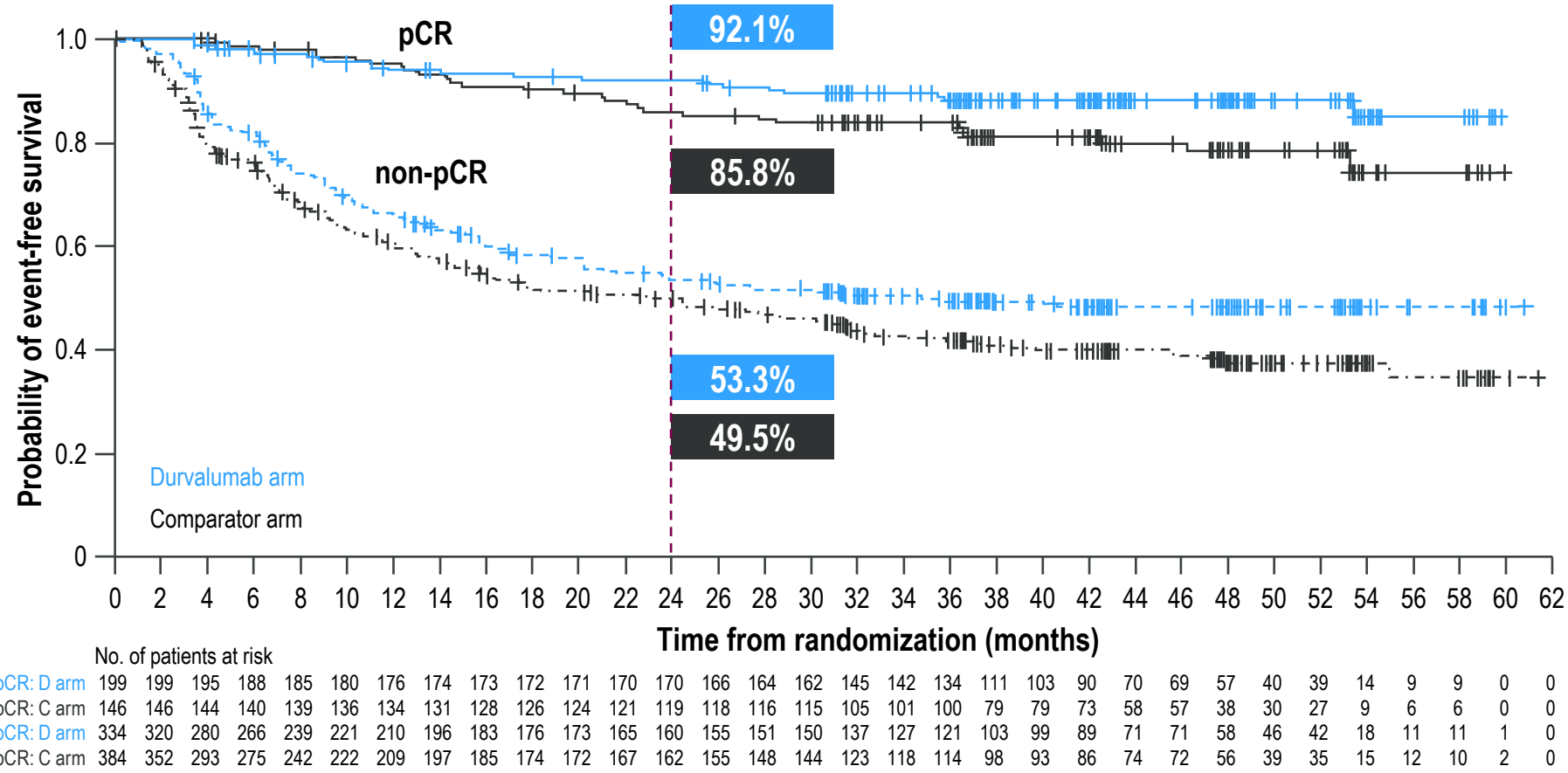


pCR was statistically tested as the final analysis in Jan 2022 (formal analysis). The results of 59 evaluable samples were omitted due to applying the DCO to the date of central review, rather than date of surgery. The re-analysis is a descriptive analysis of pCR rate and associated ORs that includes all samples from the formal pCR analysis and applies the DCO to the date of surgery for all samples. Alpha spend for the multiple testing procedure is associated with the formal pCR analysis only. pCR statistical significance was set at a threshold of 0.001. 95% CIs for the pCR rate are calculated using the Clopper-Pearson method. OR, corresponding CI, and P value are obtained using logistic regression adjusted for the stratification factors (renal function, tumour stage, and PD-L1 status). Pathological staging of samples taken during RC was performed centrally; pCR was the proportion of patients with stage T0N0M0 at RC (American Joint Committee on Cancer 8th edition classification). CI, confidence interval; ITT, intent-to-treat population; pCR, pathological complete response; RC, radical cystectomy.
Further details are available in Powles T, et al. N Engl J Med. 2024;391:1773–1786.
Data cutoff Apr 29, 2024.

1. Powles T, et al. Presented at: ESMO Congress; September 13-17, 2024; Barcelona, Spain. Abs LBA5. 2. Powles T, et al. *N Engl J Med.* 2024 Nov 14;391(19):1773-1786. 3. Galsky MD, et al. Presented at ASCO-GU Cancers Symposium; February 13-15, 2025; San Francisco, CA. Abs 659

NIAGARA: Event-free Survival (pCR and Non-pCR Groups)

Perioperative D + NAC improved EFS in both groups



No. of patients at risk

pCR: D arm	199	199	195	188	185	180	176	174	173	172	171	170	170	166	164	162	145	142	134	111	103	90	70	69	57	40	39	14	9	9	0	0
pCR: C arm	146	146	144	140	139	136	134	131	128	126	124	121	119	118	116	115	105	101	100	79	79	73	58	57	38	30	27	9	6	6	0	0
non-pCR: D arm	334	320	280	266	239	221	210	196	183	176	173	165	160	155	151	150	137	127	121	103	99	89	71	71	58	46	42	18	11	11	1	0
non-pCR: C arm	384	352	293	275	242	222	209	197	185	174	172	167	162	155	148	144	123	118	114	98	93	86	74	72	56	39	35	15	12	10	2	0

pCR

	Durvalumab N=199	Comparator N=146
No. events, n (%)	23 (12)	29 (20)
Median EFS (95% CI), months	NR (NR–NR)	NR (NR–NR)
EFS HR (95% CI)	**0.58** (0.332–0.999)	

non-pCR

	Durvalumab N=334	Comparator N=384
No. events, n (%)	164 (49)	217 (57)
Median EFS (95% CI), months	34.7 (20.5–NR)	22.8 (15.5–30.6)
EFS HR (95% CI)	**0.77** (0.631–0.948)	

ITT

EFS HR (95% CI)	**0.68** (0.56–0.82)

Data cutoff Apr 29, 2024. Exploratory post-hoc analysis. Event-free survival by blinded independent central review or by central pathology review. Tick marks indicate patients with censored data. C, comparator; D, durvalumab; EFS, event-free survival; HR, hazard ratio; ITT, intent-to treat population; NAC, neoadjuvant chemotherapy; pCR, pathological complete response.

Galsky MD, et al. Presented at ASCO-GU Cancers Symposium; February 13-15, 2025; San Francisco, CA. Abs 659.

NIAGARA: AE Summary (Safety Population)

Overall study period (unless otherwise stated)	Durvalumab arm N=530	Comparator arm N=526
AEs of any cause, n (%)	**527 (99)**	**525 (100)**
Grade 3 or 4	**368 (69)**	**355 (68)**
Serious AEs	326 (62)	287 (55)
Outcome of death	**27 (5)**	**29 (6)**
Leading to discontinuation of study treatment	112 (21)	80 (15)
Leading to discontinuation of neoadjuvant durvalumab	50 (9)	---
Leading to discontinuation of NAC	72 (14)	80 (15)
Leading to patient not undergoing RC	6 (1)	7 (1)
Leading to delay in surgery*	9 (2)	6 (1)
Leading to discontinuation of adjuvant durvalumab	30/383† (8)	---
AEs possibly related to any treatment, n (%)‡	502 (95)	487 (93)
Grade 3 or 4 (treatment related)	215 (41)	215 (41)
Outcome of death (treatment related)	**3 (0.6)**	**3 (0.6)**
Any-grade immune-mediated AEs	111 (21)	16 (3)

The safety population includes all patients who received treatment. *Recommended timeframe for RC was within 56 days after the last dose of NAC. †In patients who started adjuvant durvalumab. ‡Investigator-assessed causality.
The overall study period includes AEs that occurred between the first dose of study treatment, and whichever occurred first: 1) 90 days after the last dose of treatment, surgery, or last adjuvant visit; 2) date of first dose of subsequent anti-cancer therapy; or 3) data cutoff date.
Data cutoff 29 Apr 2024. AE, adverse event; NAC, neoadjuvant chemotherapy; RC, radical cystectomy.

1. Powles T, et al. Presented at: ESMO Congress; September 13-17, 2024; Barcelona, Spain. Abs LBA5. 2. Powles T, et al. *N Engl J Med.* 2024 Nov 14;391(19):1773-1786.

Circulating Tumor DNA (ctDNA) in Patients with Muscle-Invasive Bladder Cancer (MIBC) Who Received Perioperative Durvalumab (D) in NIAGARA

Powles T et al.
ASCO 2025;Abstract 4503.

June 1, 2025
Hall D2| 10:45 AM CT

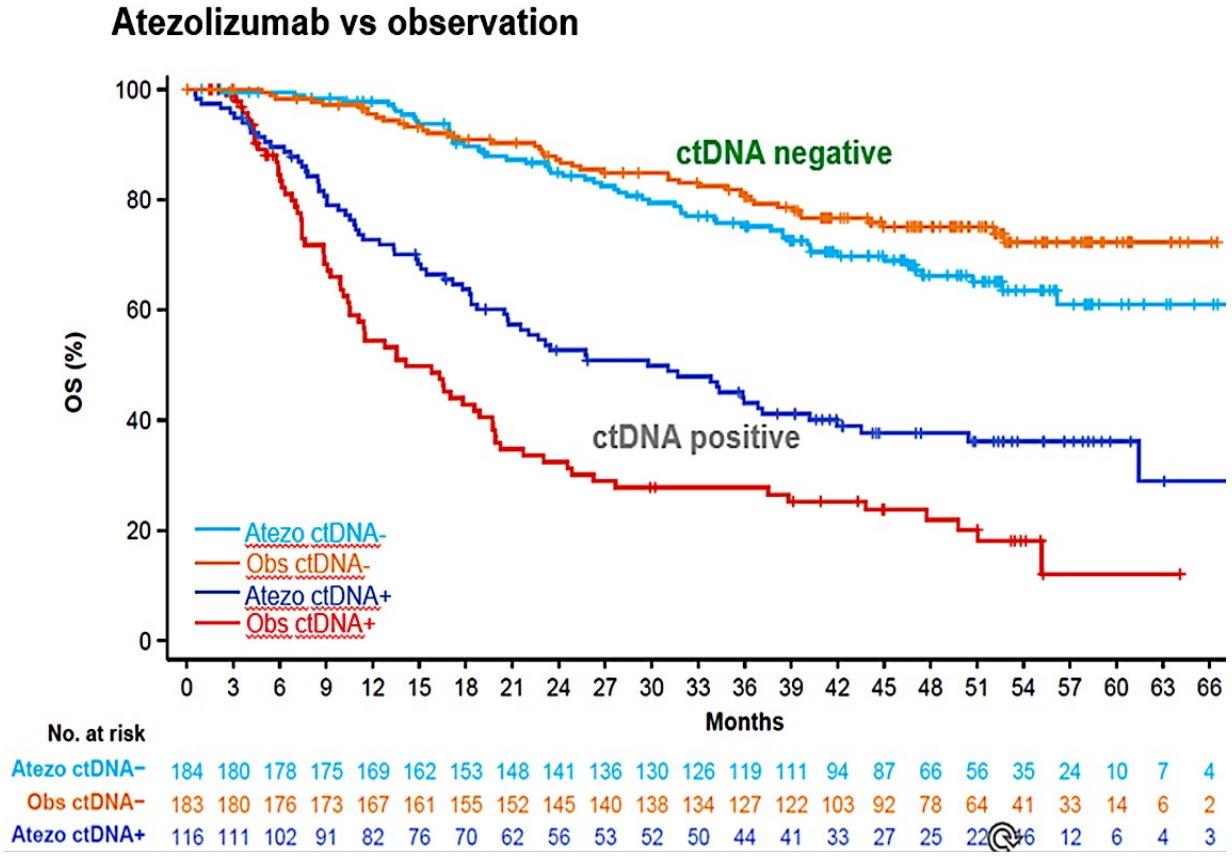
	EFS				DFS			
	Baseline ctDNA+		Baseline ctDNA-		Post-RC ctDNA+		Post-RC ctDNA-	
	D	C	D	C	D	C	D	C
n	137	123	99	101	9	8	129	126
Median (95% CI), months	NR (NR–NR)	32.3 (24.3–NR)	NR (NR–NR)	NR (NR–NR)	9.5 (2.8–NR)	6.2 (2.9–NR)	NR (NR–NR)	NR (NR–NR)
Hazard ratio (95% CI)	0.73 (0.51–1.06)		0.45 (0.25–0.84)		NC*		0.49 (0.28–0.84)	

CI, confidence interval; NC, not calculable; NR, not reached.

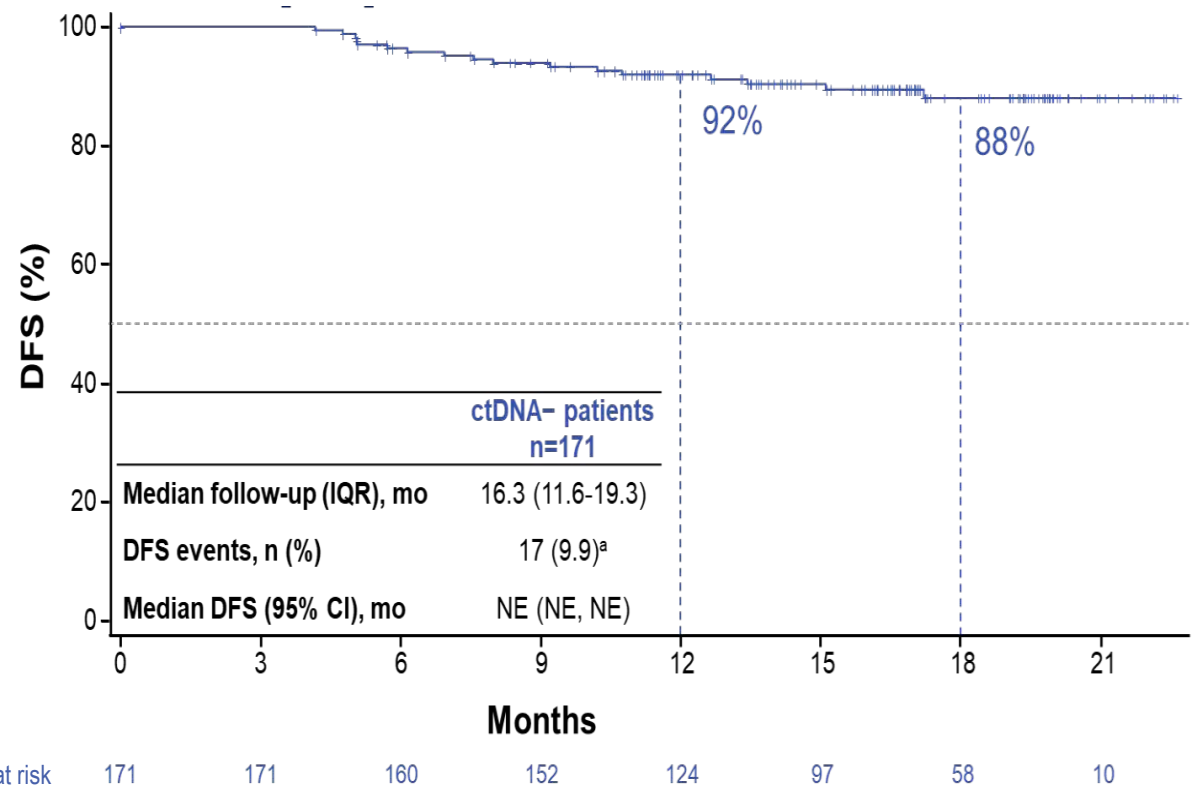
*NC due to <20 events between arms.

Powles T et al. ASCO 2025;Abstract 4503.

ctDNA identifies a high risk population which benefits from adjuvant atezolizumab.

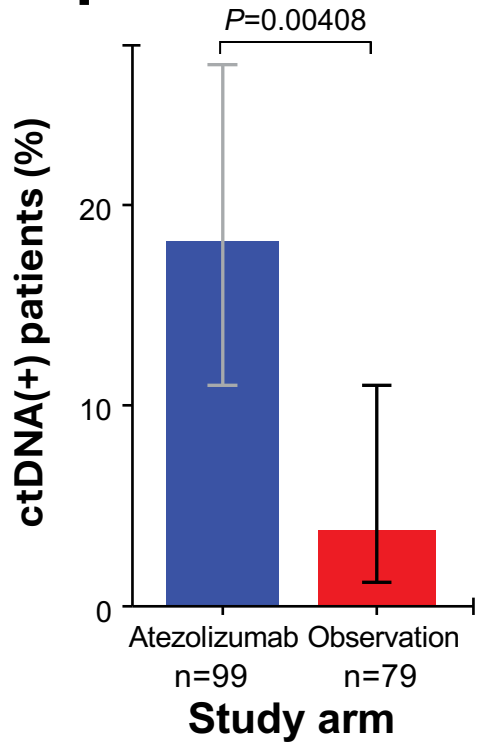


Relapse in the persistently ctDNA-ve surveillance population from IM011



IMVIGOR011 tests atezolizumab vs placebo in ctDNA positive patients within 1st year of surgery (enrolment complete)
MODERN Trial tests nivolumab + LAG3 vs nivolumab alone in ctDNA+ve and nivolumab vs placebo in ctDNA -ves

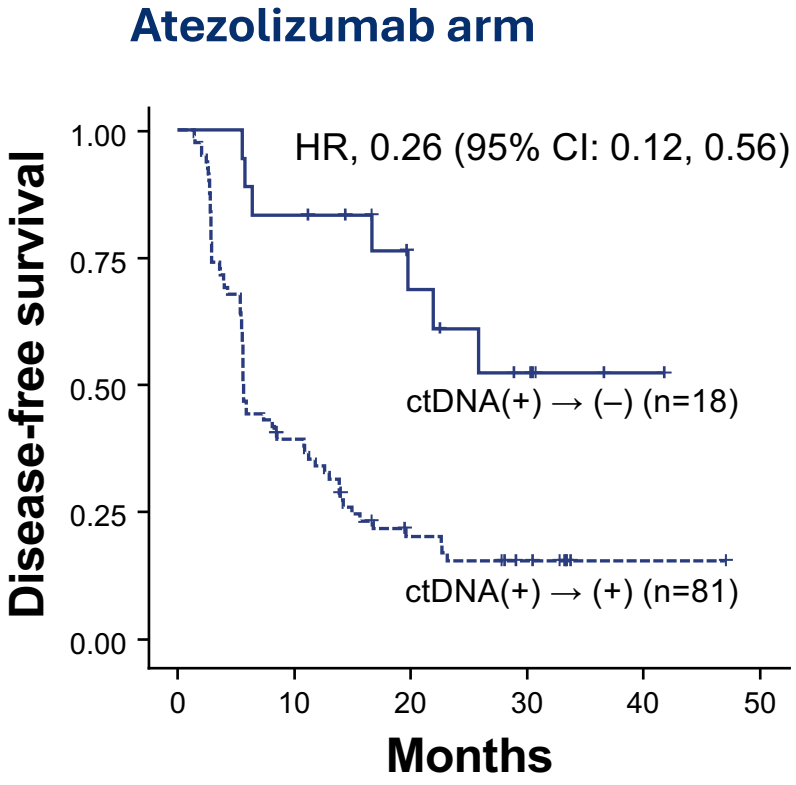
ctDNA clearance was associated with improved outcomes in the atezolizumab arm

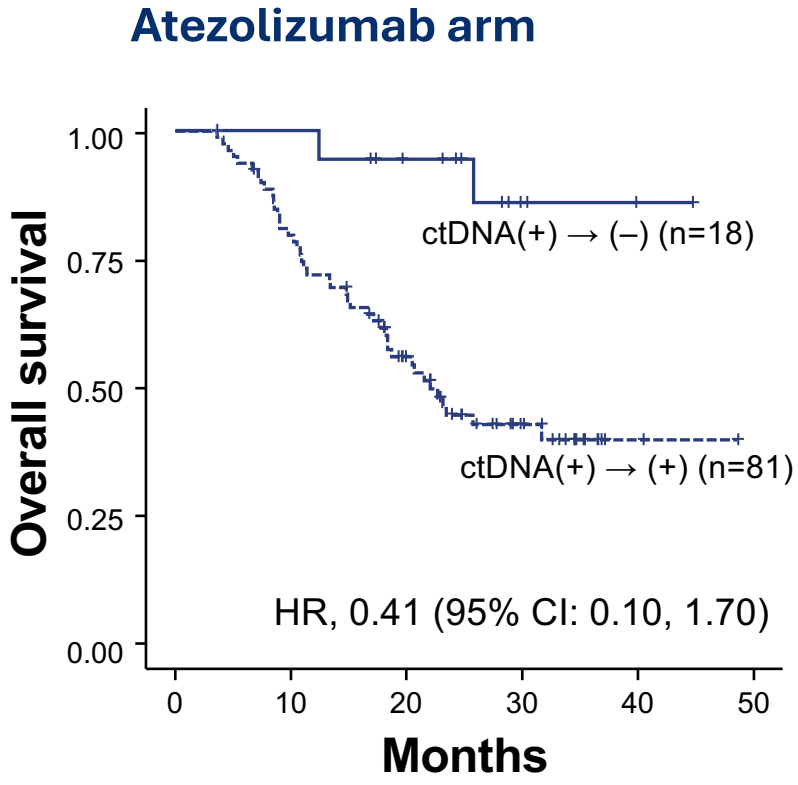


ctDNA(+) → (–)	18 (18.8%)	3 (3.8%)
ctDNA(+) → (+)	81 (81.82%)	76 (96.2%)

- ctDNA clearance occurs at a higher rate in the atezolizumab vs observation arm (C1 → C3)

Assessed using Fisher exact test.

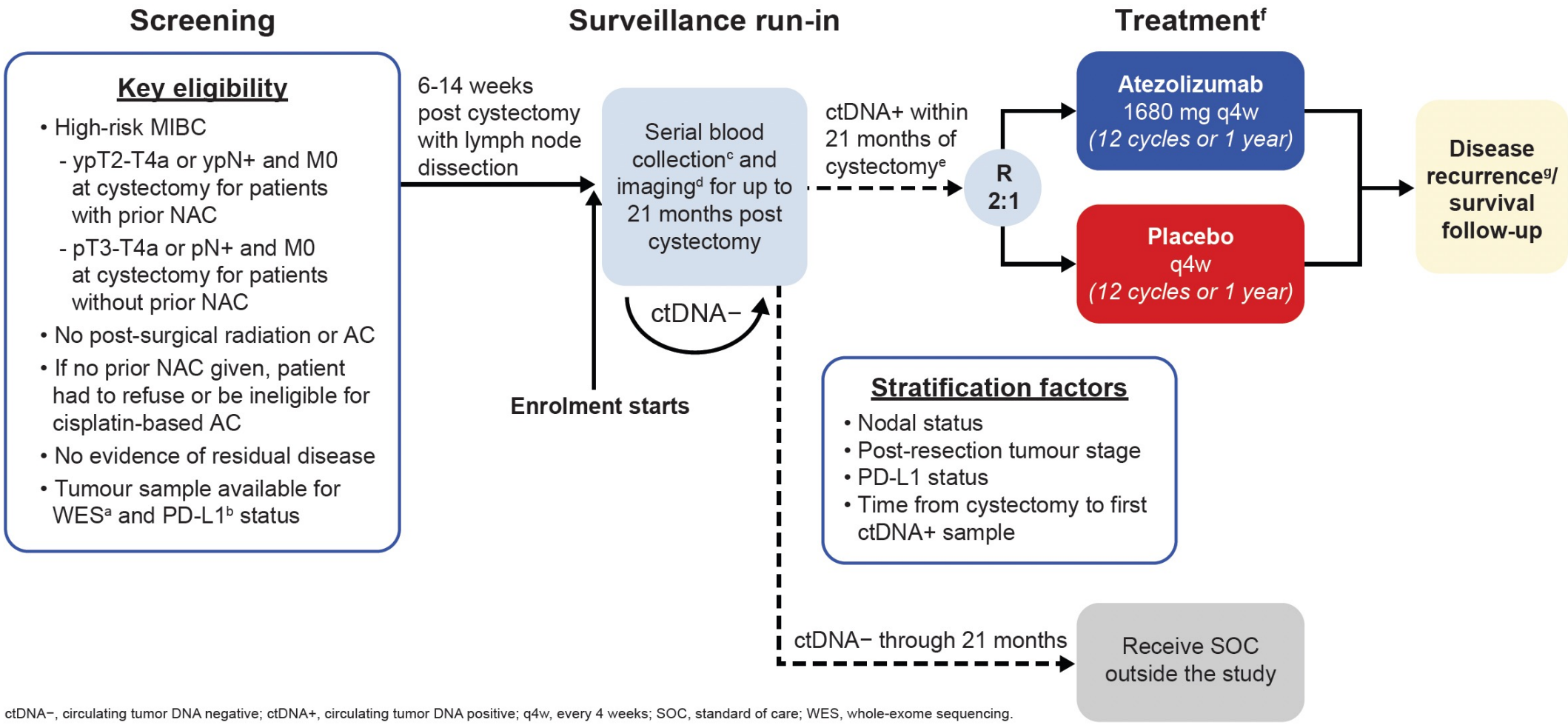




- ctDNA clearance was associated with improved DFS and OS outcomes in the atezolizumab arm

Powles et al. ESMO IO Congress 2020.

IMvigor011 Study Design



ctDNA−, circulating tumor DNA negative; ctDNA+, circulating tumor DNA positive; q4w, every 4 weeks; SOC, standard of care; WES, whole-exome sequencing.

[a] Evaluable WES data for development of a personalised multiplex PCR (mPCR) ctDNA assay from post-surgical blood samples (Signatera assay) are required.

[b] Per the VENTANA SP142 IHC assay.

[c] Every 6 weeks up to 36 weeks and q12w (every 12 weeks) up to 21 months.

[d] q12w up to Week 84 or until 21 months from date of cystectomy, whichever occurs first.

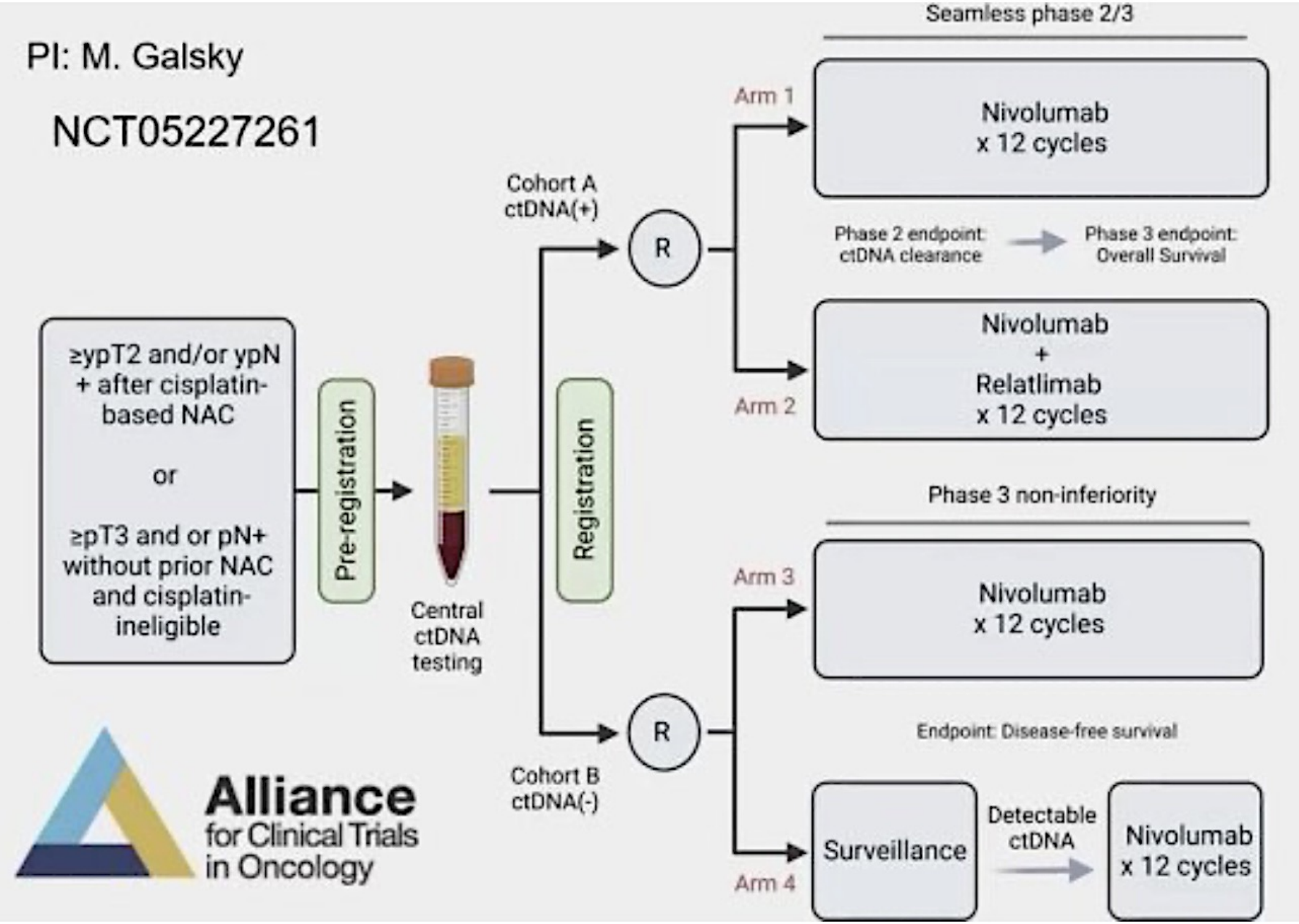
[e] ctDNA positivity is defined as ≥2 mutations per ctDNA mPCR assay. Patients will be randomised to treatment at the first ctDNA+ sample; full recovery from cystectomy and no evidence of disease recurrence within 28 days of treatment initiation is required.

[f] Imaging and blood draws q9w (every 9 weeks) starting at Week 9 up to Week 54.

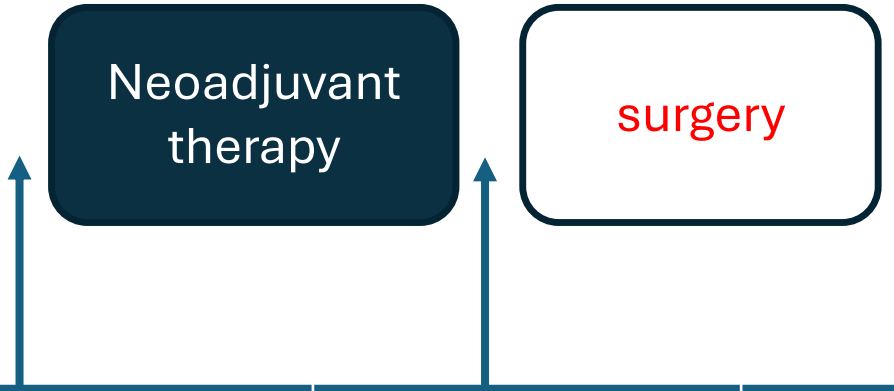
[g] Assessed q9w up to Year 3; less often up to Year 6.

Powles et al. ESMO 2021;Abstract 716TiP.

MODERN Study Design



About half of MIBC patients are ctDNA positive prior to treatment



- Higher T and N stage is associated with higher ctDNA expression
- Chemotherapy appears to have higher ctDNA clearance

	Pre treatment % ctDNA positive	Pre surgery % ctDNA positive	Post surgery % ctDNA positive	pCR rates
Chemotherapy (n=68)	**44%**	**17%**	**9%**	**~30%**
Atezolizumab (n=40)	**60%**	**47%**	**14%**	**31%**
EV Durva Treme (n=17)*	**62%**	**21%**	**NA**	**46%**

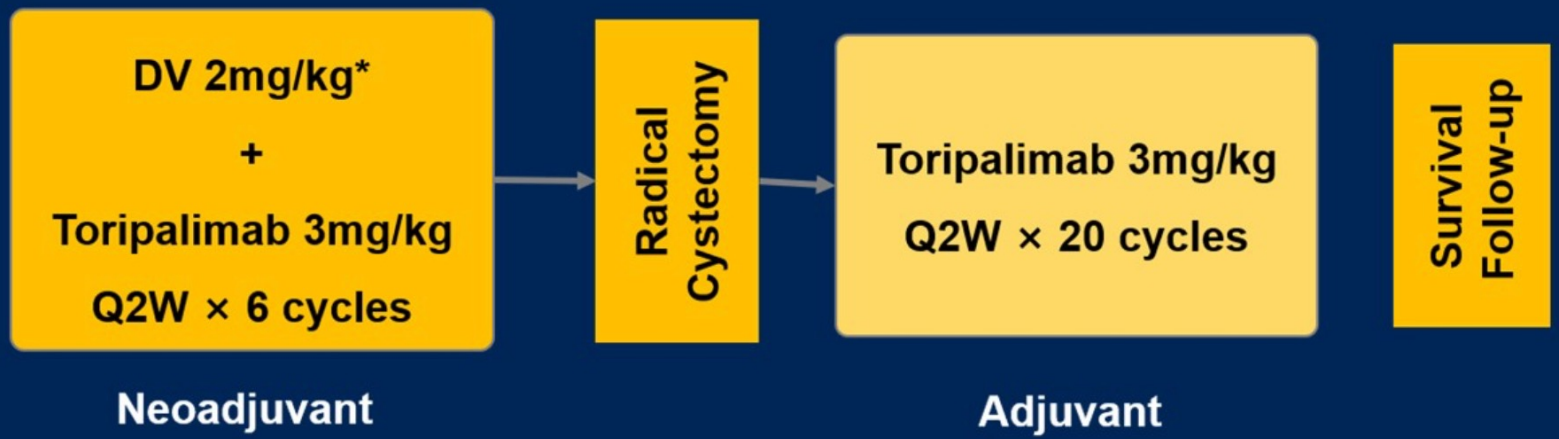
* Uninformed approach

Powles et al ASCO 2021, Chrisiensen et al JCO 2018, Drakaki et al ASCO 2024

Study design

Key Eligible Criteria:

- Histologically confirmed urothelial carcinoma;
- MIBC at stage of cT2-T4a, N0-1, and M0;
- Eligible for radical cystectomy (RC) + pelvic lymph node dissection (PLND);
- HER2 expression: IHC 1+, 2+, or 3+.



- **Primary endpoint:** Pathologic complete response (pCR, defined as ypT0N0) rate.
- **Secondary endpoints:** Pathological response rate (defined as ≤ypT1N0M0)#; event-free survival (EFS); overall survival (OS)^; adverse events.

The preliminary results of this trial showed promising efficacy and acceptable safety.[1] Herein, we present updated results including the pathological response, event-free survival, safety, and other outcomes with a longer follow-up (data cutoff: Dec 3, 2024).

Pathological tumour response was assessed by the local pathologists and investigators based on the postoperative pathology. Radiological assessment was performed by the investigators per RECIST v1.1
*Equivalent to dose of 1.5 mg/kg using DV-based extinction coefficient outside of China. #Including complete or partial pathological response. ^OS data was not mature and not reported here. 1. Sheng, et al. J Clin Oncol. 2024, 42(16_suppl):4568.
Abbreviations: IHC=immunohistochemistry, Q2W=every two weeks, RECIST=Response Evaluation Criteria in Solid Tumors.

Pathological response

- 11 pts refused RC (8 pts received TURBT and 5 of them achieved pT0); 2 pts did not undergo surgery due to distant metastases; 1 patient did not recover from the AE within the operative window, then received TURBT and achieved pT0.
- Median time from end of neoadjuvant treatment to RC: 5.0 weeks (range: 2.6-13.1)

	Evaluable patients N=33*
Pathological response	
pCR (ypT0N0), n (%)	**21 (63.6)**
95% CI	45.1-79.6
Pathological response (≤ypT1N0M0), n (%)	**25 (75.8)**
95% CI	57.7-88.9
Pathological staging, n (%)	
ypT0N0	21 (63.6)
ypT≤1N0	4 (12.1)
ypTisNx*	1 (3.0)
ypT2N0	4 (12.1)
ypT3N0	3 (9.1)
ypT4 or ypTanyN+	0

Pathological tumor response was assessed by the local pathologists based on the postoperative pathology.
*Pelvic lymph-node dissection was not performed.

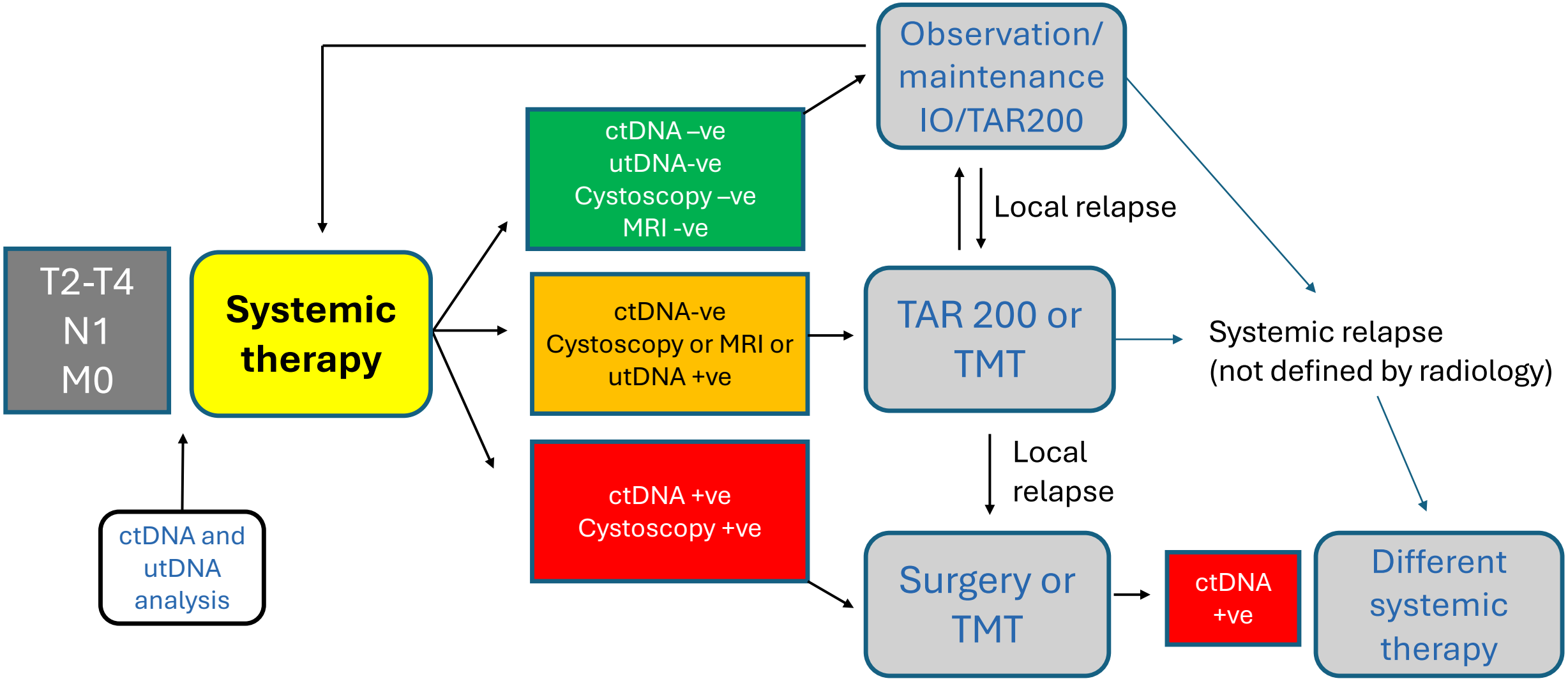
Ongoing Phase 3 Neoadjuvant IO-based Trials in MIBC

	Clinical Trial	N	Treatment Arms	Eligibility
CISPLATIN ELIGIBLE	**KEYNOTE-866**	870	Pembro + GC vs GC	T2-4aN0M0
	KEYNOTE-B15/EV-304	784	Pembro +EV vs GC	T2-T4aN0M0 T1-T4aN1M0
	NIAGARA	1050	Durva+ GC vs GC	T2-4aN0M0
	ENERGIZE	1200	Nivo + GC vs GC	T2-4aN0M0
CISPLATIN-INELIGIBLE	**KEYNOTE-905/ EV-303**	836	RC vs Pembro+EV vs Pembro	T2-4aN0M0
	VOLGA	830	RC vs Durva/Treme+EV vs Durva+EV	T2-4aN0M0
	SWOG GAP	196	Surgery vs Gem-Carbo+ Avelumab	T2-4aN0M0

There are also RIII trials with TMT and ICI therapy:
These studies may have wider influences.

ADC in platinum advanced bladder cancer	Enfortumab Vedotin (301)	Sacituzumab Govitecan (n=355)	Disitamab Vedotin (n=109)	T-DXD (n=16)	zelenectide pevedotin (n=45)	BL-B01D1 (n=27)	SHR-A2102 (n=81)	Sacituzumab Tirumotecan (n=49)
Target	NECTIN4	TROP-2	HER-2	HER-2	NECTIN-4	HER3/EGFR	NECTIN-4	TROP-2
Payload	MMAE	TOPO-1	MMAE	TOPO-1	MMAE	TOPO-1	TOPO-1	TOPO-1
Biomarker selection	None	None	HER2:1-3+	HER2:3+	None	None	None	None
% pior ADC	<10%	<10%	<10%	<10%	<10%	<10%	50%	<10%
Randomised phase III studies	*301, VOLGA 302,303,304*	TROPICS-4	1st line R3 awaited	None	1st line R3 awaited	None	None	None
Grade 3+ TRAEs	*51%*	77%	45%	45-55%	22%	52%	~50%	*59%*
Response rates in platinum refractory disease	*41%*	*23%*	*50%*	*56%*	*45%*	*41%*	38%	31%
Response rate for ADC/PD1 combo	**68% (420)**	**34% (41)**	**75% (20)**	**36% (26)**				

Curing most patients with MIBC without surgery or RT



A 65-year-old patient presents with persistent hematuria. Cystoscopy reveals a mass in the urinary bladder. Biopsy shows muscle-invasive bladder cancer (MIBC). Creatinine clearance is 72 mL/min. Regulatory and reimbursement issues aside, what would you most likely recommend?

 Dr Galsky	Neoadjuvant durvalumab with platinum-based chemotherapy → cystectomy → adjuvant durvalumab
 Prof Necchi	Neoadjuvant enfortumab vedotin/pembrolizumab → cystectomy → adjuvant pembrolizumab
 Prof Powles	Neoadjuvant durvalumab with platinum-based chemotherapy → cystectomy → adjuvant durvalumab
 Dr Friedlander	Neoadjuvant durvalumab with cisplatin-based chemotherapy → cystectomy → adjuvant durvalumab
 Dr Grivas	Neoadjuvant durvalumab with cisplatin-based chemotherapy → cystectomy → adjuvant durvalumab
 Dr Rosenberg	Neoadjuvant durvalumab with platinum-based chemotherapy → cystectomy → adjuvant durvalumab

Regulatory and reimbursement issues aside, what would you most likely recommend for a 65-year-old patient with MIBC who has received neoadjuvant cisplatin-based chemotherapy followed by cystectomy with the postoperative imaging results described below?

	Evidence of residual disease	No evidence of disease
 Dr Galsky	≥ pT2 adjuvant nivolumab	Decide treatment or observation based on pathologic stage
 Prof Necchi	Order a ctDNA assay and decide based on results	Observation
 Prof Powles	Nivolumab	Observation
 Dr Friedlander	Nivolumab	Observation
 Dr Grivas	≥ pT2 consider adjuvant nivolumab	≥ pT2 consider adjuvant nivolumab
 Dr Rosenberg	pT0N0 observation; ≥ pT2 adjuvant nivolumab	Decide treatment or observation based on pathologic stage

ctDNA = circulating tumor DNA

Based on available data and your personal experience, how would you compare the sensitivity of serial ctDNA monitoring to that of radiological assessments for detecting disease progression in patients with MIBC?

 Dr Galsky	ctDNA is more sensitive with a lead time of ~3-6 months, depending on the assay
 Prof Necchi	ctDNA is useful for anticipating the imaging evidence of tumor recurrence
 Prof Powles	ctDNA is probably better and more sensitive
 Dr Friedlander	ctDNA is likely more sensitive than imaging. The challenge is knowing what to do with the results
 Dr Grivas	Serial ctDNA monitoring is highly prognostic as shown in many trials and seems strongly associated with radiologic recurrence
 Dr Rosenberg	ctDNA finds recurrence earlier, about 3-6 months lead time

RTP RESEARCH TO PRACTICE

In general, outside of a clinical trial, for which patients with MIBC, if any, would you order ctDNA testing?

 Dr Galsky	All patients
 Prof Necchi	All comers pre/post neoadjuvant therapy
 Prof Powles	Postcystectomy
 Dr Friedlander	I now order ctDNA on the majority of my patients as a monitoring tool
 Dr Grivas	I would order ctDNA in highly selected cases in which the patient has a very hard time deciding on adjuvant anti-PD-1/PD-L1
 Dr Rosenberg	Patients for whom I would not be recommending adjuvant immunotherapy based on their pathologic stage

RTP RESEARCH TO PRACTICE

Agenda

MODULE 1: Current and Future Management of Muscle-Invasive Bladder Cancer — Prof Powles

MODULE 2: Novel Intravesical Therapies Under Evaluation for Nonmetastatic Urothelial Bladder Cancer (UBC) — Prof Necchi

MODULE 3: Selection and Sequencing of Therapy for Metastatic UBC — Dr Galsky

RTP RESEARCH TO PRACTICE



Novel Intravesical Therapies Under Evaluation in Nonmetastatic UBC

Andrea Necchi, MD

Vita-Salute San Raffaele University
Director of Genitourinary Medical Oncology
IRCCS San Raffaele Hospital, Milan, Italy

Unmet Needs Across the Disease Spectrum

- Only one-third of patients with **NMIBC** receive intravesical BCG[1]
- Many of those with **NMIBC** who are unresponsive to BCG experience recurrence or progression[2]

- Close to half of patients with **MIBC** worldwide may not receive curative-intent therapy[3]
- Patients who have undergone radical cystectomy for **MIBC** often have impaired HRQOL and a high risk of recurrence[4,5]

- More than half of patients with **mUC** may not receive first-line systemic treatment[4,5]
- Many patients with **mUC** who progress on 1L or 2L therapy do not receive subsequent treatment[4,5]

- In NMIBC, development of effective, safe, and durable intravesical treatment remains a critical unmet clinical need for patients who want to avoid radical cystectomy
- In MIBC, effective consolidation approaches post neoadjuvant therapy in patients who refuse to undergo radical cystectomy are key to improve disease control and QoL
- Clinical trial enrollment allows for modern advances to reach patients

1. Tyson M et al. *J Clin Oncol*. 2019;37(suppl 15):e16012. 2. Shore ND et al. *Urol Oncol*. 2021;39(10):642-663. 3. Westergren DO et al. *J Urol*. 2019;202:905-912.
4. Choi H et al. *Transl Androl Urol*. 2020;9:2997-3006. 5. Roupret M et al. *Eur Urol*. 2021;79:62-79. 4. Morgans AK. ESMO 2021. Abstract 704P.
5. Bilen M. ESMO 2021. Abstract 701P.

Background

High-Risk NMIBC Is Defined as High-grade Ta, Any T1, and/or Carcinoma in situ

- **Standard of care for high-risk NMIBC:** TURBT followed by intravesical BCG
- Prognosis is poor for patients whose disease does not respond to BCG or relapses within 12 months[1]; these patients are directed to radical cystectomy

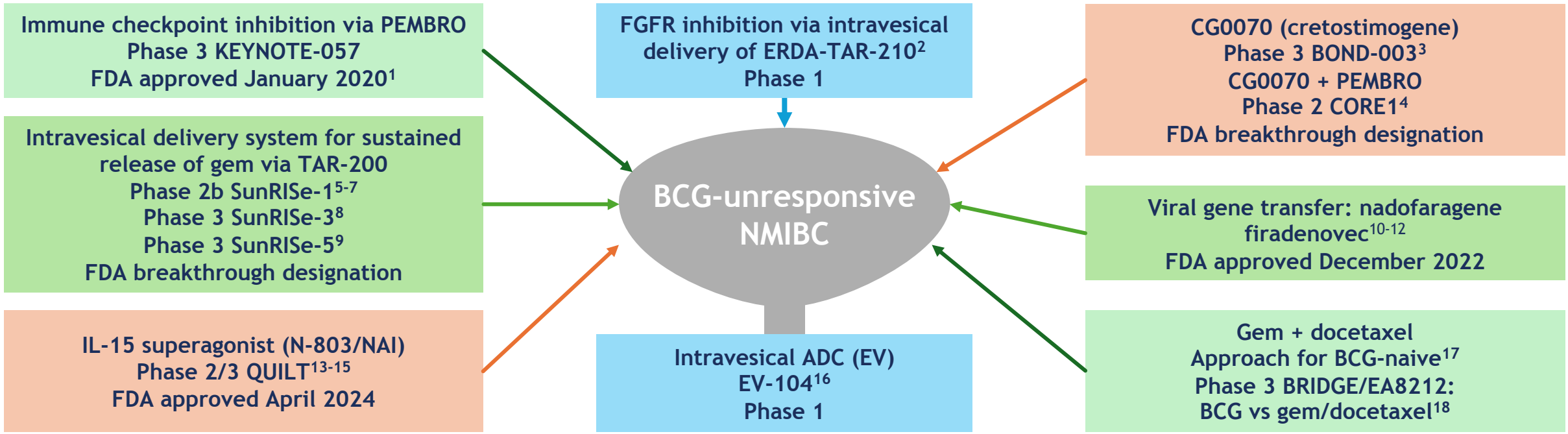
Criteria for the Definition of Adequate BCG and BCG-Unresponsive, High-Risk NMIBC Are Well Established and Endorsed by the FDA[2]

- **Adequate BCG induction:** ≥5 instillations of BCG and ≥7 instillations within 9 months of the first instillation of induction therapy
- **BCG-unresponsive, high-risk NMIBC** is defined as one of the following
  - Stage progression at 3 months despite adequate BCG induction
  - High-grade T1 disease at first evaluation after adequate BCG induction
  - Persistent high-risk NMIBC at 6 months after adequate BCG
  - Recurrent high-risk NMIBC within 9 months of the last BCG instillation despite adequate BCG

BCG, Bacillus Calmette-Guerin; NMIBC, nonmuscle-invasive bladder cancer; RC, radical cystectomy; TURBT, transurethral resection of bladder tumor.

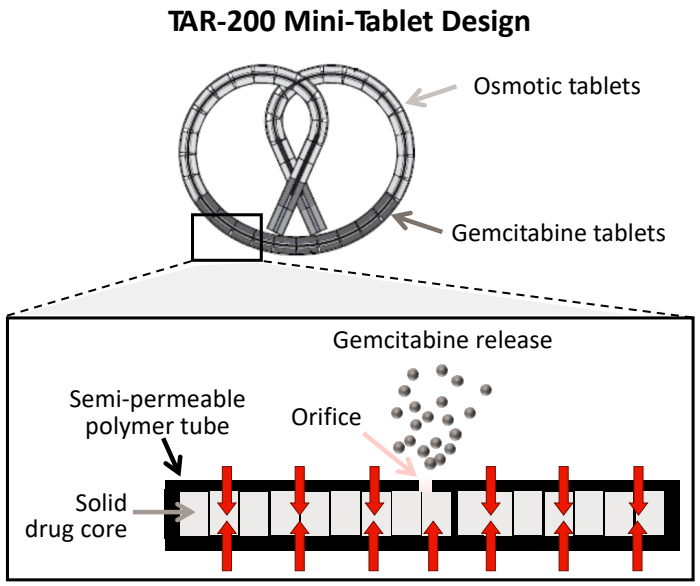
1. Jeong et al. *BMC Cancer*. 2022;22:361. 2. Kamat AM et al. *J Clin Oncol.* 2016;34:1935–1944.

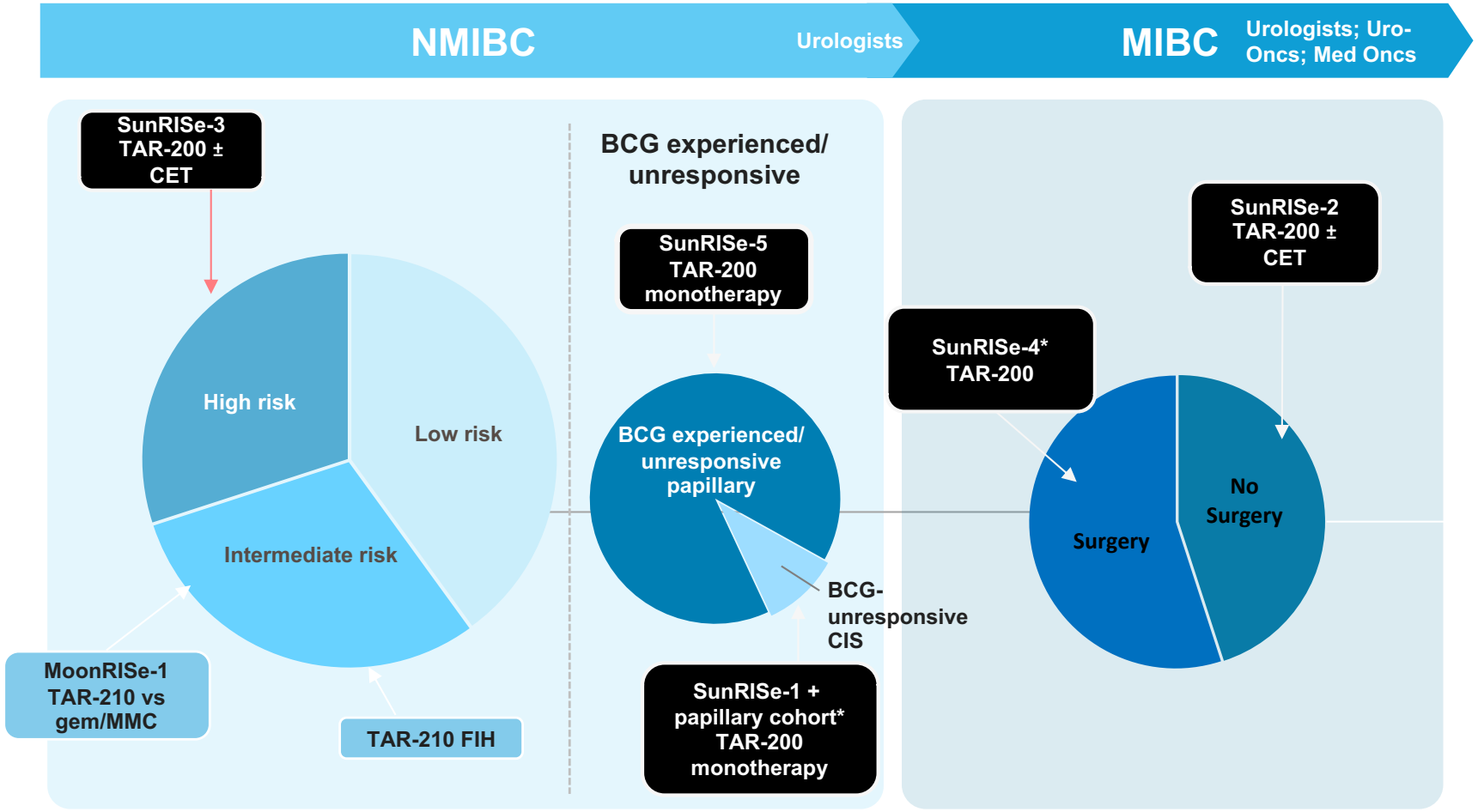
Treatment approaches for high-risk NMIBC unresponsive to BCG



- ADC, antibody-drug conjugate; BCG, Bacillus Calmette-Guerin; ERDA, erdafitinib; EV, enfortumab vedotin; FGFR, fibroblast growth factor receptor; gem, gemcitabine; IL, interleukin; NAI, nogapendekin alfa inbakicept; NMIBC, nonmuscle-invasive bladder cancer; PEMBRO, pembrolizumab. 1. Balar AV et al. *Lancet Oncol*. 2021;22:919-930. 2. Vilaseca A et al. AUA 2024. Abstract PD48-02. 3. Tyson MD et al. AUA 2024. Abstract P2-02. 4. Li R et al. *Nat Med*. 2024 Jun 6. doi: 10.1038/s41591-024-03025-3. Online ahead of print. 5. Daneshmand S et al. AUA 2023. LBA 02-03. 6. Necchi A et al. ESMO 2023. LBA105. 7. Jacob J et al. AUA 2024. Abstract P2-01. 8. ClinicalTrials.gov https://clinicaltrials.gov/study/NCT05714202. 9. ClinicalTrials.gov https://clinicaltrials.gov/study/NCT06211764. 10. Boorjian SA et al. *Lancet Oncol*. 2021;22:107–117. 11. Mitra AP et al. AUA 2022. Abstract MP54-05. 12. ADSTILADRIN® (nadofaragene firadenovec-vncg) [package insert]. Kastrup, Denmark: Ferring Pharmaceuticals; August 2024. 13. Chamie K. *NEJM Evidence*. 2022;2(1):1–11. 14. ClinicalTrials.gov https://clinicaltrials.gov/study/NCT03022825. 15. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-nogapendekin-alfa-inbakicept-pmln-bcg-unresponsive-non-muscle-invasive-bladder-cancer. Accessed August 29, 2024. 16. Kamat AM et al. *J Clin Oncol*. 2023;41(suppl 16). Abstract 4596. 17. McElree IM et al. *J Urol*. 2022;208:589-599. 18. Kates M et al. *Eur Urol Focus*. 2023;9(4):561–563.

TAR development in Nonmetastatic Bladder Cancer





*Nonregistrational. **Size of bubbles roughly represents the proportion of eligible patients.** BCG, bacillus Calmette–Guerin; CET, cetrelimab; CIS, carcinoma in situ; CRT, chemoradiotherapy; FIH, first-in-human; gem, gemcitabine; MIBC, muscle-invasive bladder cancer; MMC, mitomycin C; mUC, metastatic urothelial carcinoma; NMIBC, non–muscle-invasive bladder cancer.

SunRISe-3 (NCT05714202) Is a Phase 3, Open-Label, Multicenter Randomized Study

Key eligibility criteria

- Patients with histologically confirmed HR NMIBC (high grade Ta, any T1, or CIS)
- BCG naive (no prior BCG or last exposure >3 years prior to randomization)

Additional criteria:

- Aged ≥18 years
- ECOG PS of 0, 1, or2
- All visible papillary disease must be fully resected (absent) prior to randomization and documented at baseline cystoscopy
- Local urine cytology at screening must be negative or atypical for high-grade urothelial carcinoma in patients with papillary-only disease
- All adverse events associated with any prior surgery and/or intravesical therapy must have resolved to CTCAE v5.0 grade <2 prior to date of randomization

1:1:1 (N≈1050)

R

Group A (n≈350)
TAR-200 + cetrelimab[a]

Group C (n≈350)
TAR-200

Group B (n≈350)
BCG

Primary end point

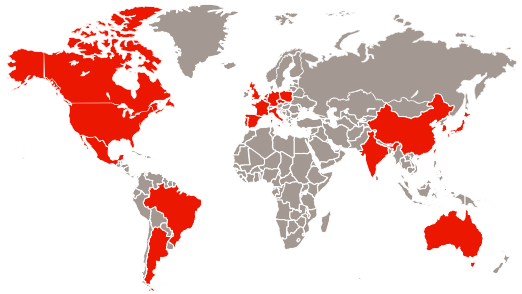
Event-free survival

Time from randomization to first occurrence of:

- High-risk disease recurrence
- Disease progression[b]
- Any-cause death
- For patients with CIS, persistent disease at 6 months is also an EFS event

Secondary end points

- Overall CR rate (CIS only)[c]/duration of CR[d]
- Recurrence-free survival
- Time to progression
- Overall survival
- Cancer-specific survival
- Safety and tolerability
- Patient-reported outcomes



CR, complete response, CTCAE, Common Terminology Criteria for Adverse Events; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival.
[a]Cetrelimab is an anti–programmed death-1 antibody. [b]Progression is defined as stage increase from Ta to T1 or from CIS to T1 or progression to MIBC (T≥2) or to lymph node (N+) or distant (M+) disease (whichever occurs first).
[c]Proportion of patients with CIS who have no presence of high-risk disease at 6 months. [d]Time from first CR achieved to first evidence of recurrence, progression, or any-cause death, whichever occurs first.

Presented by SS Chang at the 119th AUA Annual Meeting; May 3-6, 2024; San Antonio, TX, USA

SunRISe-5 (NCT06211764) Is an Open-Label, Multicenter Phase 3 Study

Key eligibility criteria

- Histologically confirmed, papillary-only HR NMIBC (high grade Ta or any T1),[1,2] recurrent within the first year of last dose of BCG
- No CIS at time of papillary recurrence
- RC refusing or ineligible
- ECOG PS <3

Stratification factors

- T-stage
- Prior BCG

1:1
(N≈250)

R

Group A (n≈125)
TAR-200 monotherapy
Q3W during an induction phase
Q12W during a maintenance phase

Crossover
Patients in Group B may receive TAR-200 after positive study result at any planned analyses

Group B (n≈125)
Intravesical gemcitabine
OR
Intravesical mitomycin
Weekly during an induction phase
Monthly during a maintenance phase

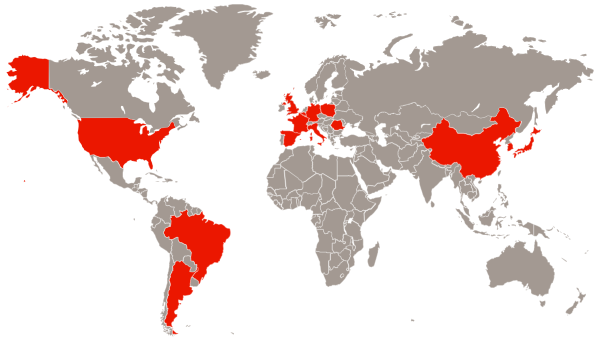
Primary end point

Disease-free survival

Secondary end points

- Recurrence-free survival
- Time to next intervention
- Time to progression
- Time to disease worsening
- Overall survival
- Safety and tolerability
- PROs/HRQoL

- Disease-free survival is defined as time from randomization to first recurrence of HR NMIBC (high grade Ta, any T1 or CIS), progression, or any cause death, whichever occurs first



The study will evaluate whether TAR-200 will prolong disease-free survival when compared with intravesical chemotherapy in patients with papillary-only HR NMIBC recurrent after BCG therapy who refuse or are unfit for RC

ECOG PS, Eastern Cooperative Oncology Group performance status; PRO, patient-reported outcome; HRQoL, health-related quality of life; Q3W, every 3 weeks; Q12W, every 12 weeks.

1. NCCN Clinical Practice Guidelines in Oncology. Bladder Cancer. Version 1. 2024. 2. EAU Guidelines. Edn. presented at the EAU Annual Congress Milan 2023. ISBN 978-94-92671-19-6.

Presented by S Porten at the 119th AUA Annual Meeting; May 3-6, 2024; San Antonio, TX, USA

Phase 2b SunRISe-1 Study: Cohort 2 BCG-Unresponsive HR NMIBC CIS ± Papillary Disease

NCT04640623

Population:
- Aged ≥18 years
- Histologically confirmed HR NMIBC CIS (with or without papillary disease)
- ECOG PS of 0-2
- Persistent or recurrent disease within 12 months of completion of BCG
- Unresponsive to BCG[1,2] and not receiving RC

R

- TAR-200 + Cetrelimab[b] *Cohort 1* (N=53)[c] — *Cohort 1 was closed*
- **TAR-200 Monotherapy *Cohort 2* (N=85)** — ***Enrollment completed***
- Cetrelimab[b] Monotherapy *Cohort 3* (N=28) — *Cohort 3 was closed*
- TAR-200 Monotherapy *Cohort 4* (N=52) — *Enrollment completed*

Population:
- Papillary-only HR NMIBC (no CIS)[a]

TAR-200 dosing: Q3W (indwelling) for the first 24 weeks; then Q12W through Week 96

Cohorts 1-3:
Primary end point
- Overall CR rate

Key secondary end points
- Duration of response
- Overall survival
- Safety
- Tolerability
- HRQoL

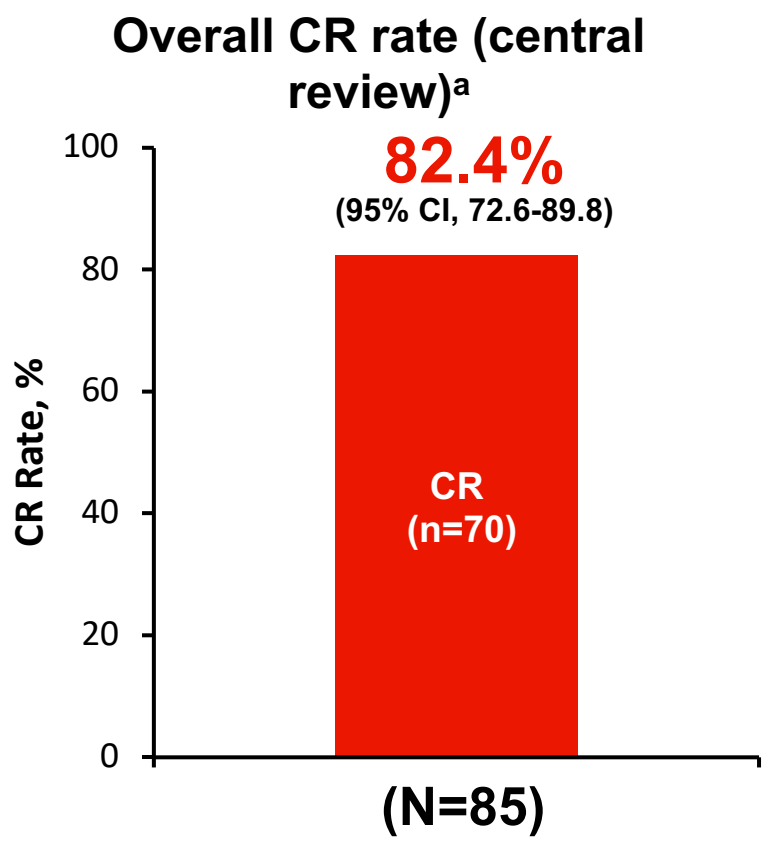
Cohort 4:
Primary end point
- DFS

- **Here we report *1-year durability data from the TAR-200 monotherapy cohort (Cohort 2) of SunRISe-1***
- Response is determined by quarterly cystoscopy, quarterly central cytology, **mandated bladder biopsy by central assessment at Weeks 24 and 48**, and local imaging Q24W
- The study protocol **did not allow re-induction for nonresponders**, consistent with US FDA guidance[2]
- As of June 2023, Cohorts 1 and 3 were closed for enrollment, and Cohort 2 enrollment continued to achieve N=85, per protocol amendment

The clinical data cutoff was March 31, 2025.
DFS, disease-free survival; ECOG PS, Eastern Cooperative Oncology Group performance status; HRQoL, health-related quality of life; Q3W, every 3 weeks; Q12W, every 12 weeks; Q24W, every 24 weeks; R, randomization.
[a]Patients with BCG-unresponsive papillary-only HR NMIBC (high-grade Ta, any T1) per protocol amendment 4. [b]Cetrelimab is an anti–programmed cell death-1[3,4]; cetrelimab dosing was Q3W through Week 78. [c]Number of patients enrolled in Cohort 1 was N=55 and number of patients treated was N=53.
1. Lerner SP, et al. *Urol Oncol*. 2009;27:155-159. 2. US Food and Drug Administration. Available at: https://www.fda.gov/media/101468/download. 3. DeAngelis N, et al. *Cancer Chemother Pharmacol*. 2022;89:515-527.
4. Felip E, et al. *Cancer Chemother Pharmacol*. 2022;89:499-514.

Presented by JM Jacob at the 120th AUA Annual Meeting; April 26-29, 2025; Las Vegas, NV, USA

Highest CR Rate to Date With Rapid Onset After TAR-200 Monotherapy in BCG-Unresponsive HR NMIBC CIS ± Papillary Disease



CR Rate From Treatment Initiation	Observed Overall CR Rate, % (n/N)
12 months[b]	**45.9** (39/85)

	KM Estimated Overall CR Rate, % (95% CI)
12 months	**52.4** (40.7-62.8)
24 months	**44.7** (33.1-55.7)

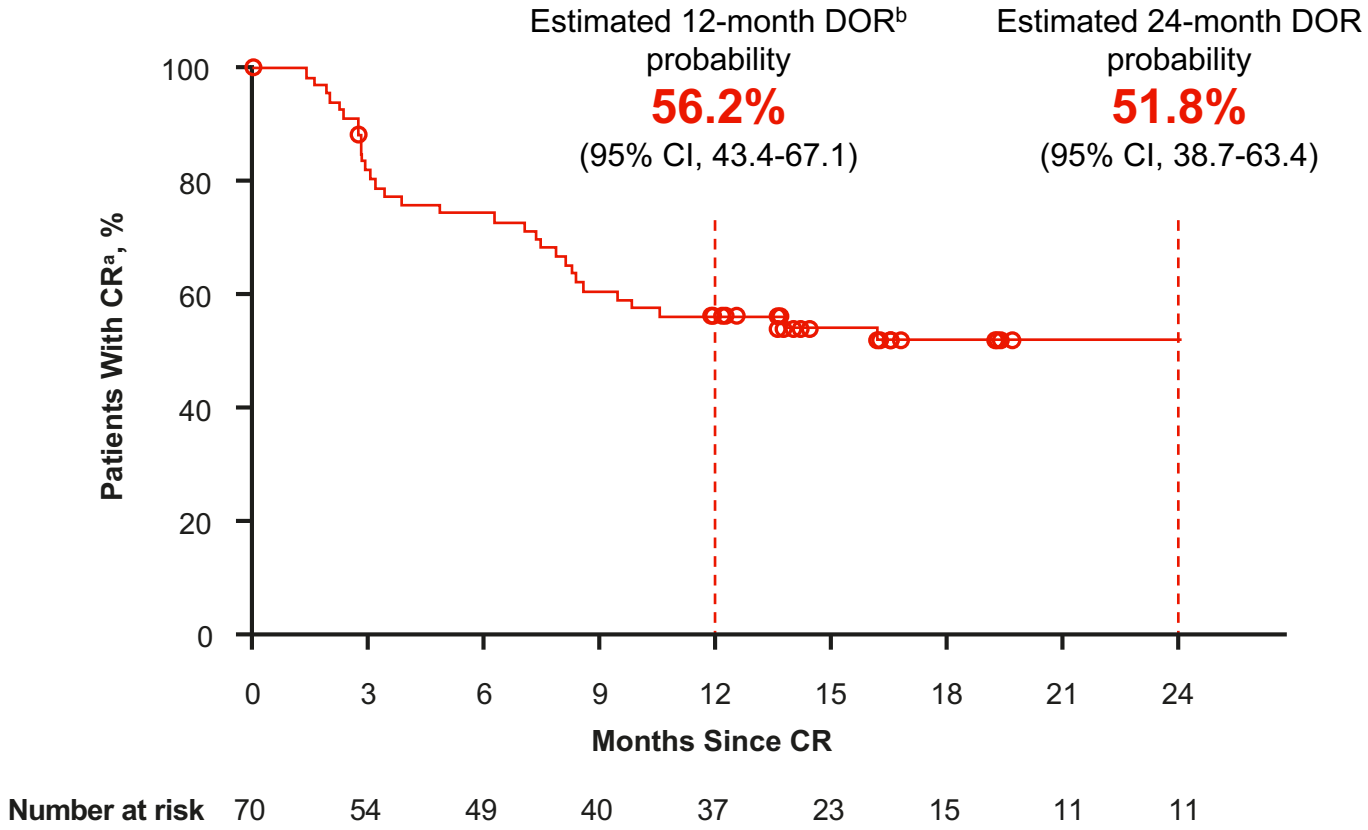
- Rapid onset of response: median time to onset, **2.8 months** (range, 2.1-8.3)
- **95.7%** (67 of 70) CRs achieved at the first (3 month) disease assessment

FDA Breakthrough Therapy Designation

CI, confidence interval; KM, Kaplan-Meier.
[a]Response is based on centrally reviewed urine cytology, local cystoscopy, and central biopsy (if available). CRs do not have to be confirmed. A CR is defined as having a negative cystoscopy and negative (including atypical) centrally read urine cytology, or positive cystoscopy with biopsy-proven benign or low-grade NMIBC and negative (including atypical) centrally read cytology at any time point. [b]The CR rate at 12 months is represented by disease evaluation occurring at 48 weeks from first dose.

Presented by JM Jacob at the 120th AUA Annual Meeting; April 26-29, 2025; Las Vegas, NV, USA

Durable Responses With TAR-200 Monotherapy



- **25.8 months** (95% CI, 8.3-NE) median DOR
- Of 70 responders:
  - 23 (32.9%) had HR NMIBC recurrence[c]
  - 4 (5.7%) had ≥T2 progression[c]
- **86.6%** (95% CI, 76.6-92.6) cystectomy-free rate at 12 months

DOR, duration of response; MIBC, muscle-invasive bladder cancer; NE, not estimable.
[a]Response is based on centrally reviewed urine cytology, local cystoscopy, and central biopsy (if available). CRs do not have to be confirmed. A CR is defined as having a negative cystoscopy and negative (including atypical) centrally read urine cytology, or positive cystoscopy with biopsy-proven benign or low-grade NMIBC and negative (including atypical) centrally read cytology at any time point. [b]Median follow-up in responders was 20.2 months (range, 5-48). [c]Stage based on investigator assessment. Three patients with no evidence of disease had recurrence/progression based on central review but was not indicated by local assessment.

Presented by JM Jacob at the 120th AUA Annual Meeting; April 26-29, 2025; Las Vegas, NV, USA

TAR-200 Monotherapy Safety Profile

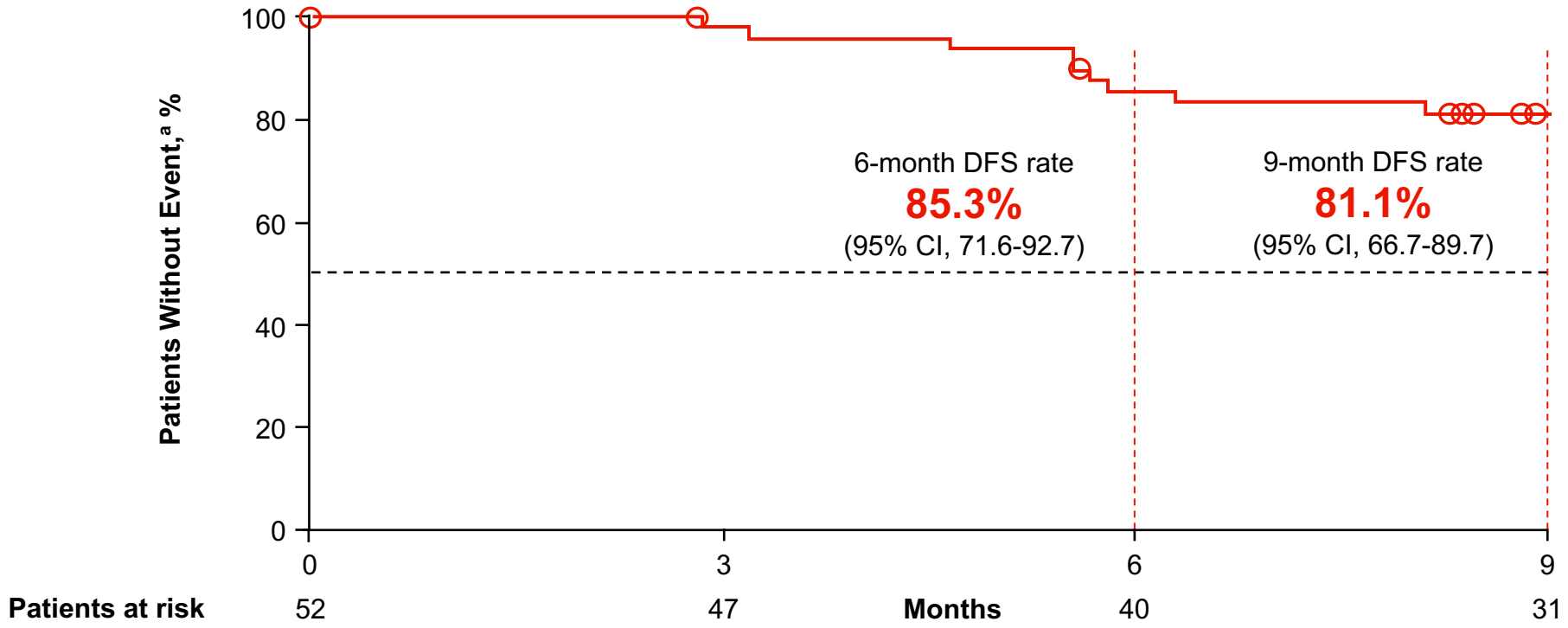
- Most TEAEs were grade 1 or 2
  - TEAEs resolved after a median of 3.1 weeks
- 99% (745 of 755) insertion success rate
- 5 patients (5.9%) had ≥1 serious TRAEs[a]
- Few patients (n=3; 3.5%) discontinued treatment due to TRAEs[b]
- No treatment-related deaths were reported

Patients With Events, n (%)	TAR-200 Monotherapy *Cohort 2* (N=85)[c]	
	Any Grade	Grade ≥3
≥1 TRAE[d]	71 (83.5)	11 (12.9)
Most frequent TRAEs[e,f]		
Pollakiuria	37 (43.5)	0
Dysuria	34 (40.0)	0
Micturition urgency	21 (24.7)	0
Urinary tract infection	19 (22.4)	1 (1.2)
Hematuria	14 (16.5)	0
Urinary tract pain	9 (10.6)	4 (4.7)
Bladder pain	7 (8.2)	2 (2.4)
Bladder spasm	7 (8.2)	0
Noninfective cystitis	6 (7.1)	0
Urinary incontinence	5 (5.9)	0

TEAE, treatment emergent adverse event; TRAE, treatment-related adverse event.
[a]1 event each of acute kidney injury, bladder pain, cystitis, cystitis pseudomonal, urinary tract infection, urinary tract pain, and urosepsis. Note, patients may have had ≥1 serious TRAE. [b]TRAEs leading to discontinuation were noninfective cystitis (n=2), bladder pain (n=1), pollakiuria (n=1), and urinary tract disorder (n=1). Note, patients who discontinued may have had ≥1 TRAE. [c]Safety is shown for all patients who received at least 1 dose of TAR-200 in the safety analysis set (N=85). [d]An AE was categorized as related if the investigator determined that there was a possible, probable, or causal relationship between the AE and TAR-200 or the insertion or removal procedure or urinary placement catheter. [e]Reported in ≥5% of patients. [f]TRAEs of grade ≥3 reported in ≥2% of patients. All other TRAEs of grade ≥3 were reported in only 1 patient each and included acute kidney injury, cystitis, urinary retention, cystitis pseudomonal, and urosepsis. Note, patients may have had ≥1 grade ≥3 TRAE.

Presented by JM Jacob at the 120th AUA Annual Meeting; April 26-29, 2025; Las Vegas, NV, USA

Cohort 4 interim results: 6- and 9-Month DFS Rates With TAR-200 Monotherapy in Papillary Disease–Only HR NMIBC



- Median follow-up was 12.8 months
- **Median DFS was not reached** (95% CI, 12.1-NE)
- Overall, only **5.8%** (3 of 52) of patients had **RC**

NE, not estimable.
[a]**An event is defined as recurrence, progression, or death.**

Presented by F Guerrero-Ramos at the 120th AUA Annual Meeting; April 26-29, 2025; Las Vegas, NV, USA

New Drug Application initiated with U.S. FDA for TAR-200, the first and only intravesical drug releasing system for patients with BCG-unresponsive high-risk non-muscle-invasive bladder cancer

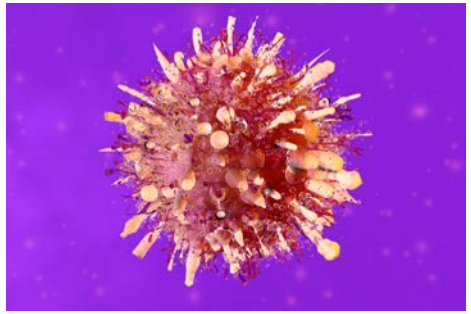
Press Release: January 15, 2025

"January 15, 2025 – [the manufacturer] announced it has initiated the submission of an original New Drug Application with the U.S. Food and Drug Administration (FDA) for TAR-200 for the treatment of patients with Bacillus Calmette-Guérin (BCG)-unresponsive high-risk non-muscle-invasive bladder cancer (HR-NMIBC) with carcinoma in situ (CIS), with or without papillary tumors.

The submission of this innovative intravesical drug releasing system is supported by data from the Phase 2b SunRISe-1 registration study.

In December 2023, the FDA granted Breakthrough Therapy Designation (BTD) to TAR-200 for the treatment of adult patients with BCG-unresponsive HR-NMIBC with CIS who are ineligible for or have elected not to undergo radical cystectomy."

https://www.jnj.com/media-center/press-releases/new-drug-application-initiated-with-u-s-fda-for-tar-200-the-first-and-only-intravesical-drug-releasing-system-for-patients-with-bcg-unresponsive-high-risk-non-muscle-invasive-bladder-cancer



Cretostimogene Grenadenorepvec – BOND-003 Trial

FDA Breakthrough Therapy Designation

US-based clinical trial

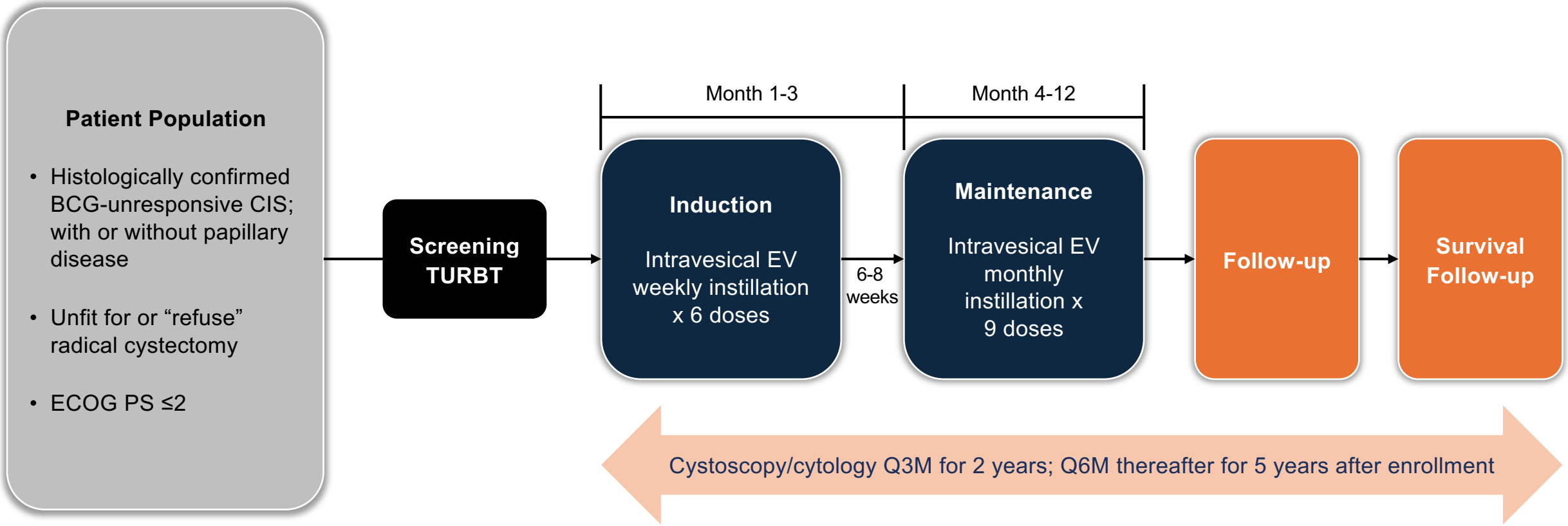
76% CR at Any Time; 74.4% of Responders Maintained Response ≥ 6 Months

Response Evaluation	Cretostimogene Monotherapy	
	%, (n/N)	Confidence Interval (CI)
Complete Response		
Complete Response, Any Time	75.7% (50/66)	95% CI: 63% - 85%
Complete Response, 3 Months	68.2% (45/66)	95% CI: 55% - 79%
Complete Response, 6 Months	63.6% (42/66)	95% CI: 51% - 75%
Duration of Complete Response		
Duration of Response ≥ 3 Months	84.0% (42/50)	95% CI: 70% - 92%
Duration of Response ≥ 6 Months	74.4% (32/43)[1]	95% CI: 58% - 86%

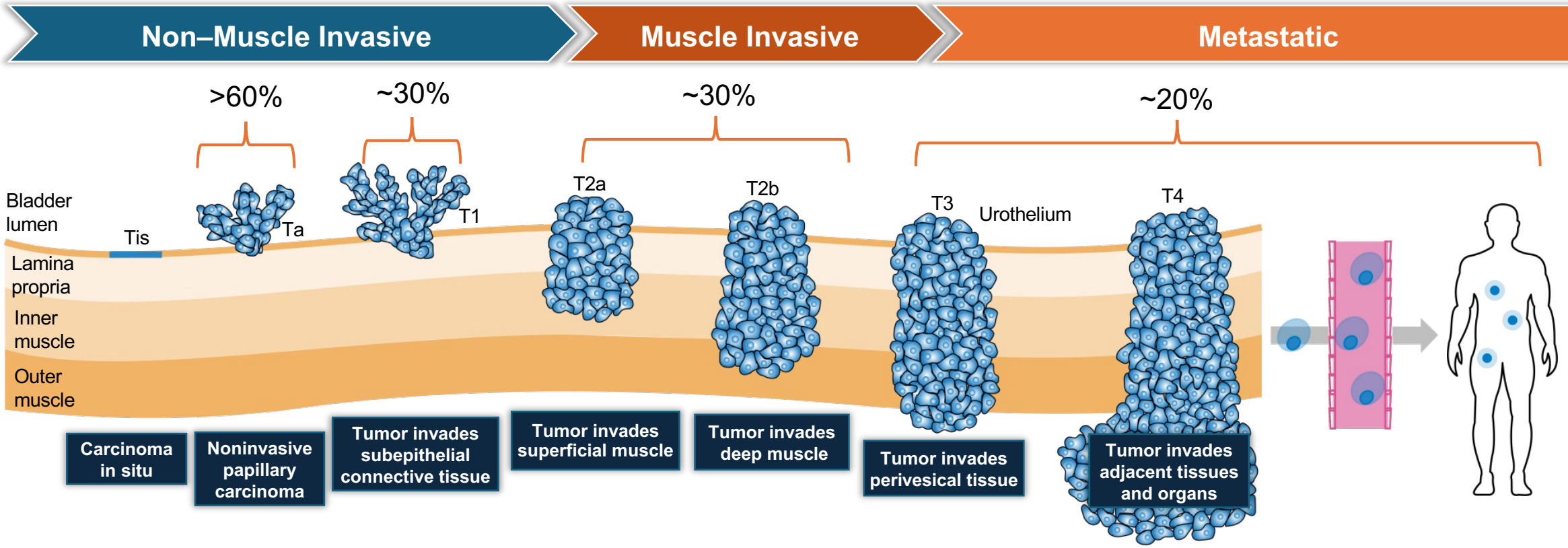
Tyson MD, et al. AUA 2024

Intravesical ADC Approach: EV-104[1]

EV-104 (NCT05014139) is a phase 1, open-label, multicenter, dose-escalation and dose-expansion study designed to evaluate the safety, tolerability, PK, and antitumor activity of intravesical enfortumab vedotin in adults with NMIBC



FGFR Mutations Are Frequently Observed in Bladder Cancer[1]



FGFR inhibitors can be effective across the disease spectrum

1. Knowles MA et al. *Nat Rev Cancer*. 2015;15:25-41.

THOR-2: Oral Erdafitinib Versus Intravesical Chemotherapy[1-6]

BCG-Unresponsive High-Risk NMIBC
- *FGFR* mutations or fusions
- **Cohort 1:** papillary tumor only
- **Cohort 2:** with or without papillary tumor
- **Cohort 3:** intermediate-risk NMIBC with papillary tumor

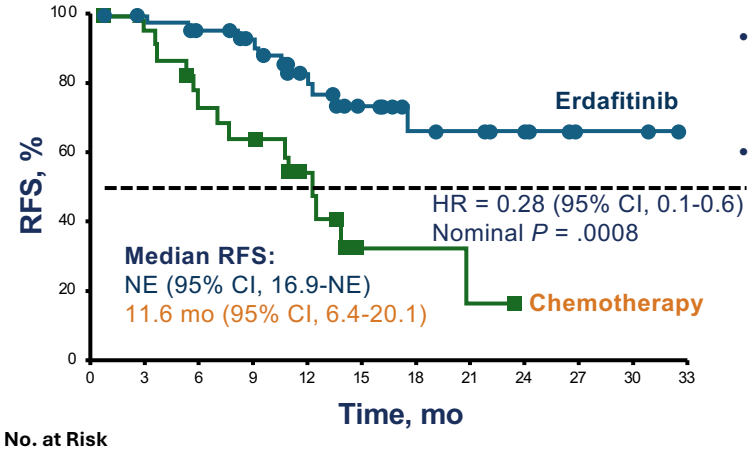
R

Erdafitinib 6 mg/d

Investigator's choice of intravesical chemotherapy

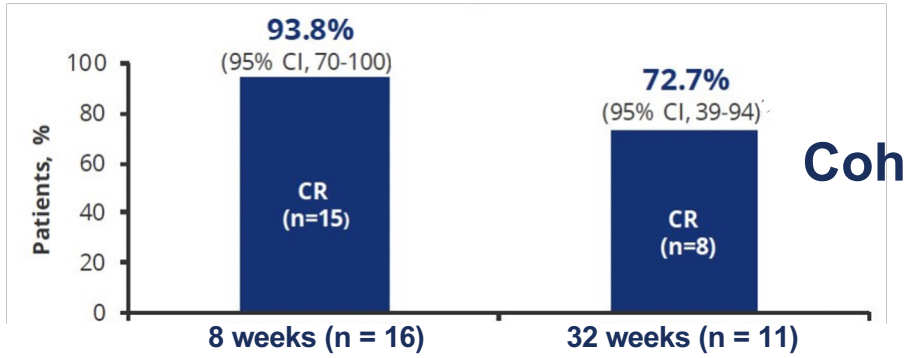
- **Primary endpoint**
  - Cohort 1: RFS
- **Exploratory endpoints**
  - Cohort 2: C3D1 = 100%; C6D1 = 75%
  - Cohort 3: CR = 75%

Cohort 1

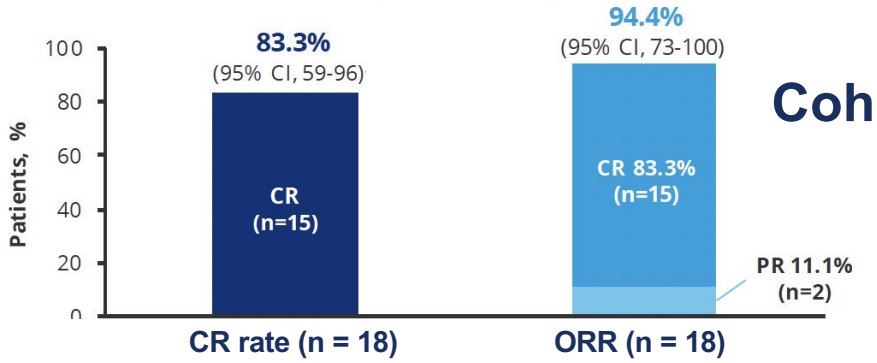


- At median follow-up of 13.4 mo, **median RFS was not reached for erdafitinib** and was 11.6 mo for chemotherapy
- At clinical cutoff, 25 total RFS events had occurred (11, erdafitinib; 14, chemotherapy)

RFS Rate (95% CI), %	Erda (n = 49)	Chemo (n = 24)
At 6 mo	96 (84-99)	73 (50-87)
At 12 mo	77 (60-87)	41 (19-62)



Cohort 2



Cohort 3

[a] Patient still on treatment. [b] DOR for patient is currently censored.
https://clinicaltrials.gov/study/NCT04172675.
Catto JWF, et al. *Ann Oncol*. 2024 Jan;35(1):98-106.

TAR-210 erdafitinib intravesical delivery first-in-human phase 1 trial[1-4]

Molecular eligibility

- *FGFR* alterations: flexible molecular eligibility strategy used
  - Local or central fresh/archival **tissue-based** testing by NGS or PCR or
  - Central **urine cell-free DNA** NGS testing

HR-NMIBC (cohort 1)

- Recurrent, high-grade Ta/T1, papillary only, no CIS
- BCG-experienced/unresponsive and not undergoing RC
- TURBT with complete resection of all visible disease prior to treatment

IR NMIBC (cohort 3)

- Recurrent, history of low-grade only Ta/T1 disease
- **Visible target lesions** prior to treatment (chemoablation design)

Part 1: dose escalation

BOIN

TAR-210-D
≈ 4 mg/day

TAR-210-B
≈ 2 mg/day

- Placement every 3 months

Part 2: dose expansion

- Expansion of both dose levels

Response assessed every 3 months with continued treatment for up to 1 year if recurrence free (cohort 1) or CR (cohort 3)

Interim results: Cohort 1

- **90% estimated 12-month RFS rate**[a] (n = 21)
  - Median RFS was not estimable
  - 2 of 21 patients recurred
  - Median duration of follow-up was 8.9 months
- No difference was observed in RFS between the TAR-210 dose levels

Interim results: Cohort 3

31 patients were evaluable for response[b]

90% CR rate, with 28/31 patients achieving a CR at week 12

- Overall, **100% of patients achieved a clinical response**; 3 patients had a non-CR/non-PD response

Consistent CR rate across both doses

86% (24/28) of CRs are ongoing at time of clinical cutoff

NCT06319820

Phase 3 MoonRISe-1 underway: TAR-210 vs IV chemo in *FGFR*-altered IR NMIBC

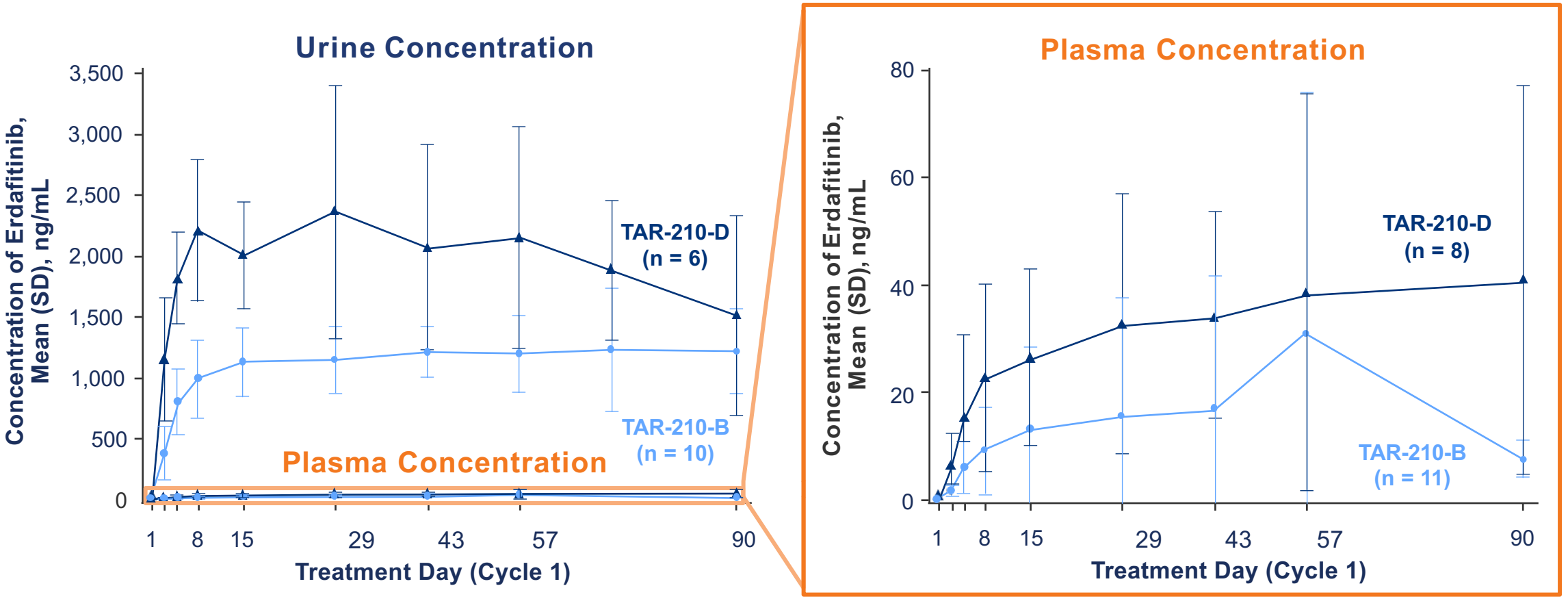
NCT06919965

Phase 3 MoonRISe-3 underway: TAR-210 vs IV chemo in BCG-treated, *FGFR*-altered Papillary only HR NMIBC

- BOIN, Bayesian Optimal Interval; CR, complete response; HR, high risk; IR, intermediate-risk; NGS, next-generation sequencing; NMIBC, nonmuscle-invasive bladder cancer; PCR, polymerase chain reaction; RC, radical cystectomy.

1. Liu S and Yuan Y. *J R Stat Soc Ser C Appl Stat*. 2015;64:507–523. 2. Yuan Y et al. *Clin Cancer Res*. 2016;22:4291–4301. 3. Vilaseca A et al. Presentation at the American Urological Association Annual Meeting; May 3–6, 2024; San Antonio, TX. Abstract 1343. 4. ClinicalTrials.gov. Accessed August 27, 2024. https://clinicaltrials.gov/study/NCT05316155.

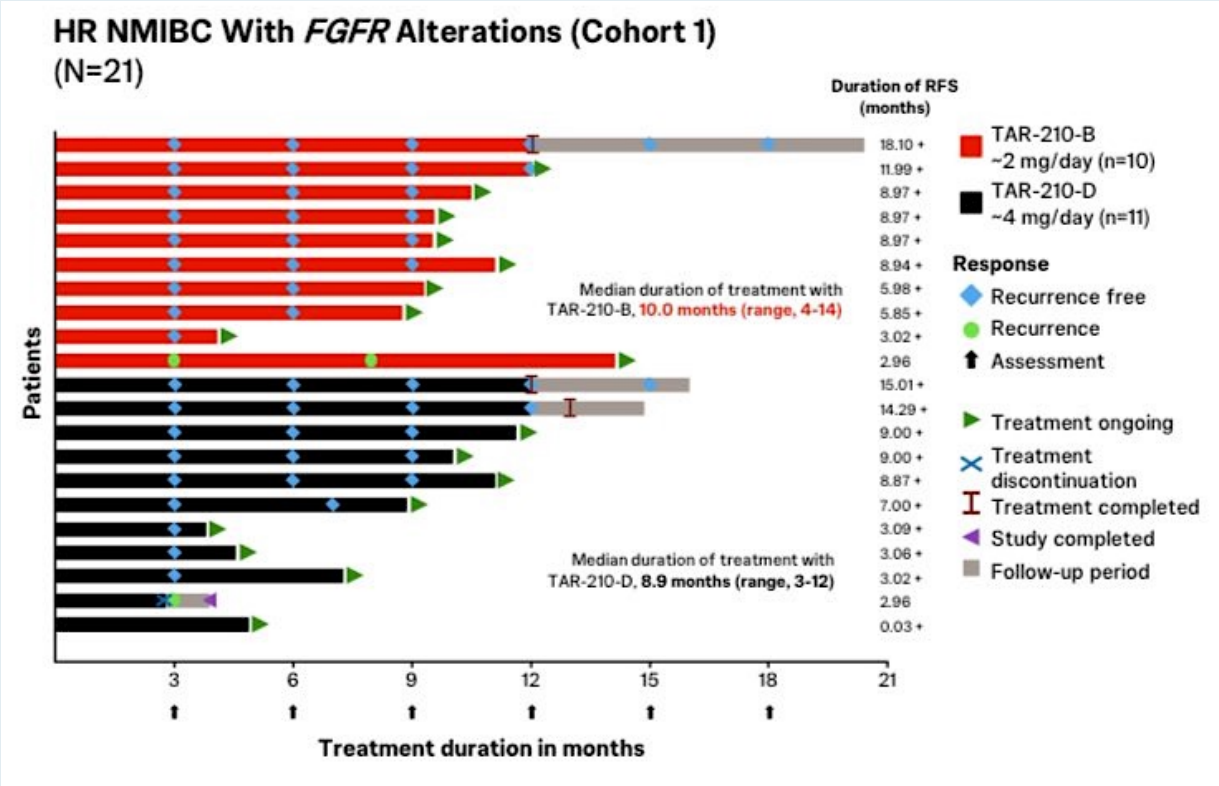
TAR-210 Provides Sustained Erdafitinib Release in Urine Over 90 Days With Very Low Plasma Concentrations

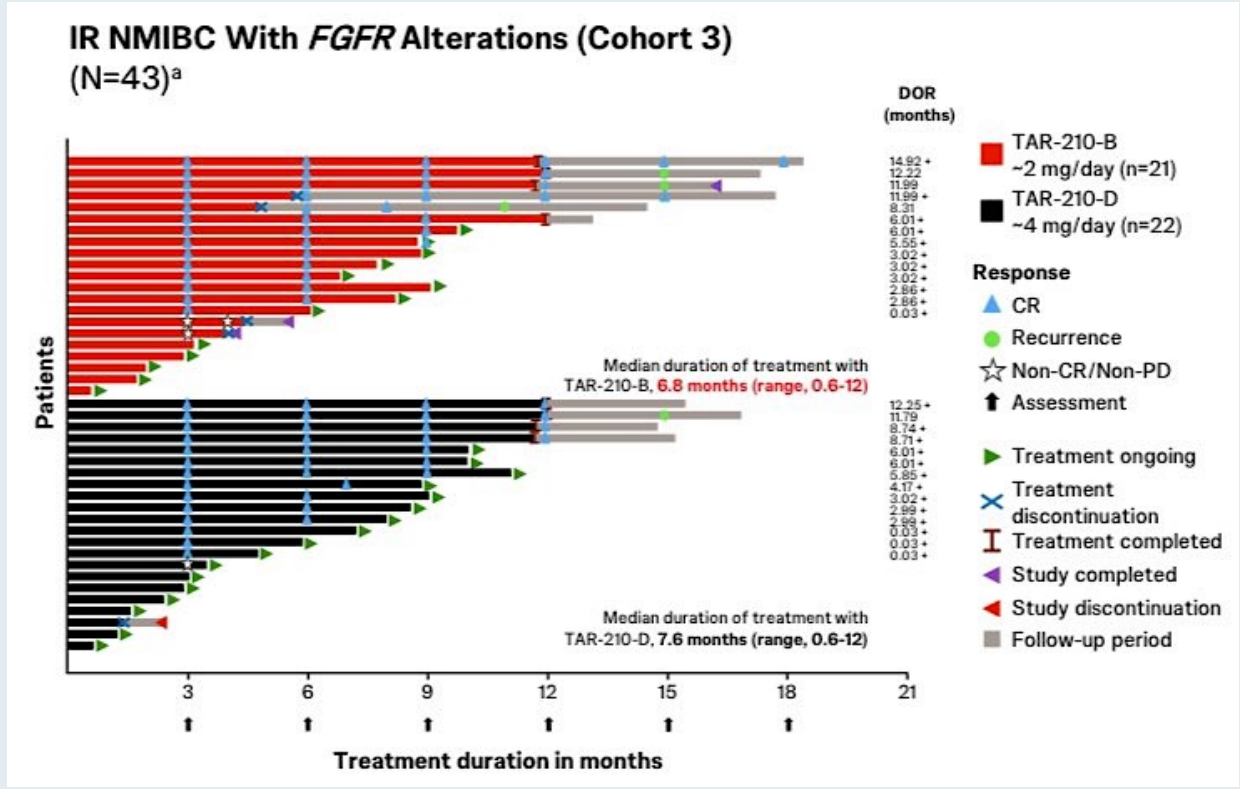


- Steady-state mean plasma concentrations are >50x lower than oral erdafitinib 9 mg daily
- No hyperphosphatemia was observed

1. Vilaseca A et al. ESMO 2023. Abstract LBA104.

TAR-210: Efficacy from Cohorts 1 and 3





Vilaseca A et al. AUA 2024;Abstract 1343.

RTP RESEARCH TO PRACTICE

TAR-210: Safety by Cohort

Patients with events, n (%)	HR NMIBC (Cohort 1)		IR NMIBC (Cohort 3)		All patients (N=64)
	TAR-210-B ~2 mg/day (n=10)	TAR-210-D ~4 mg/day (n=11)	TAR-210-B ~2 mg/day (n=21)	TAR-210-D ~4 mg/day (n=22)	
≥1 AE	10 (100)	9 (82)	20 (95)	15 (68)	54 (84)
≥1 TRAE[a]	9 (90)	5 (55)	9 (43)	6 (27)	30 (47)
Hematuria	5 (50)	2 (18)	7 (33)	4 (18)	18 (28)
Dysuria	4 (40)	2 (18)	4 (19)	2 (9)	12 (19)
Micturition urgency	2 (20)	1 (9)	5 (24)	0	8 (13)
UTI	0	1 (9)	3 (14)	1 (5)	5 (8)
Urethral pain	1 (10)	1 (9)	1 (5)	0	3 (5)
Cystitis noninfective	0	0	1 (5)	1 (5)	2 (3)
≥1 TRAE of grade ≥2	3 (30)	3 (27)	6 (29)	2 (9)	14 (22)

Vilaseca A et al. AUA 2024;Abstract 1343.

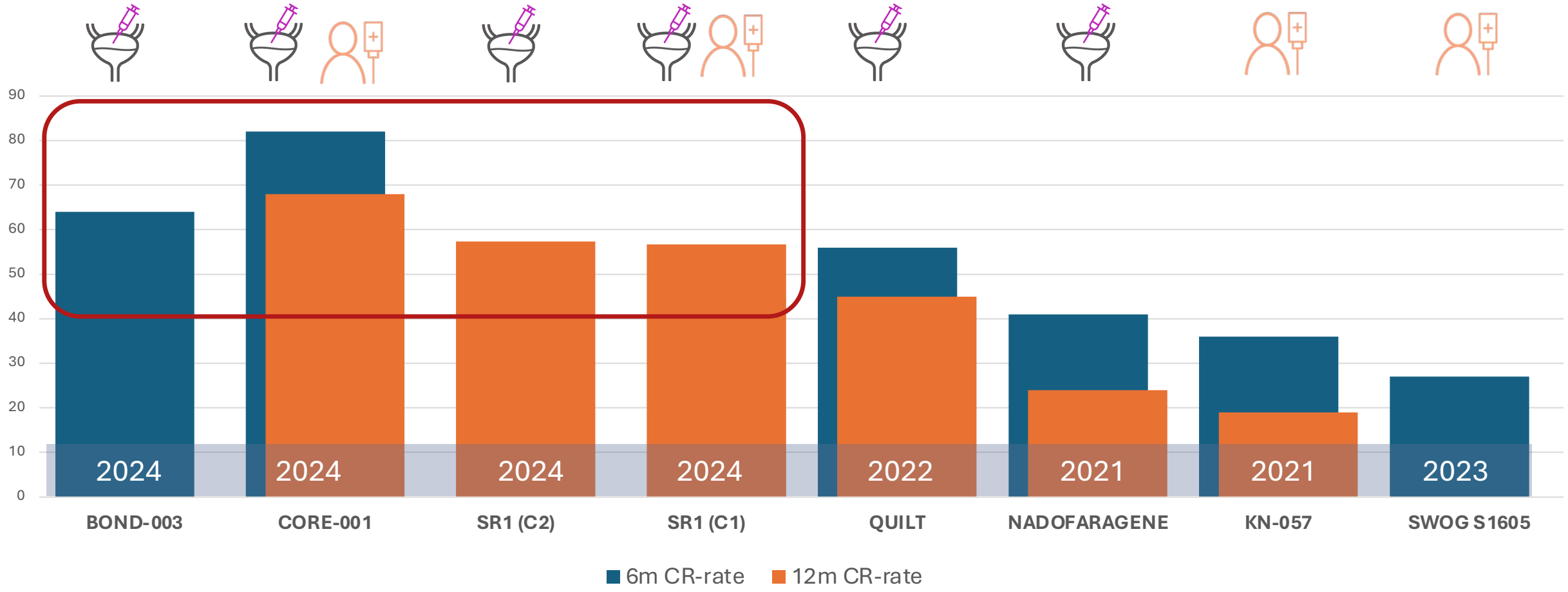
Summary of the Key Efficacy and Safety Outcomes of Novel Therapies for the Treatment of HR NMIBC

Trial	BOND-003[1]	CORE-001[2]	Sunrise-1[3]	Sunrise-1[3]	QUILT 3.032[4]	NCT02773849[5]	Keynote-057[6,7]	SWOG S1605[8]
Intervention	Cretostimogene	Cretostimogene + pembrolizumab	TAR-200	TAR-200 Cetrelimab	N-803+BCG	Nadofaragene	Pembrolizumab	Atezolizumab
Mechanism	Oncolytic immunotherapy	Oncolytic immunotherapy + ICI	Chemotherapy	Chemotherapy + ICI	IL-15 superagonist + BCG	Gene therapy secreting IFN	ICI	ICI
Delivery	Intravesical	Intravesical + intravenous	Intravesical	Intravesical + intravenous	Intravesical	Intravesical	Intravenous	Intravenous
Stage	Phase 3 **FDA BTD***	Phase 2	Phase 2 **FDA BTD**	Phase 2	**FDA approved** April 22, 2024	**FDA approved**	**FDA approved** (CIS)	Phase 2
N	116	35	85	53	77	98	96 (A)	129
6m CR-rate	**64%**	**82%**	**N/A**	**N/A**	**56%**	**41%**	**36%**	**27%**
12m CR-rate	**N/A**	**68%**	**57.4%**	**56.7%**	**45%**	**24%**	**19% (A)**	**N/A**
Safety	0% G3-4 TRAE	14.3% G3 TRAE	9.4% G3-4 TRAE	35.8% G3-4 TRAE	16% SAE	4% G3-4 TRAE	A: 11% G3 TRAE; 2% G4 TRAE	16% G3-5 TRAE

*BTD: breakthrough therapy designation; ICI: immune-checkpoint inhibitor

1. Tyson MD et al. AUA 2024. Abstract P2-02. 2. Li R et al. *Nat Med.* 2024 Aug;30(8):2216-2223. 3. Presented by MS van der Heijden at the European Society of Medical Oncology Congress 2024; September 13-17, 2024; Barcelona, Spain. 4. Chamie K. *NEJM Evidence*. 2022;2. 5. Boorjian SA et al. *Lancet Oncol*. 2021;22:107-117. 6. Balar AV et al. *Lancet Oncol*. 2021 Jul;22:919-930. 7. Necchi A et al. *Lancet Oncol*. 2024;S1470-2045:00178-5. 8. Black PC et al. *Eur Urol*. 2023;84:536-544.

BCG-unresponsive CIS: do we measure the IO effect?

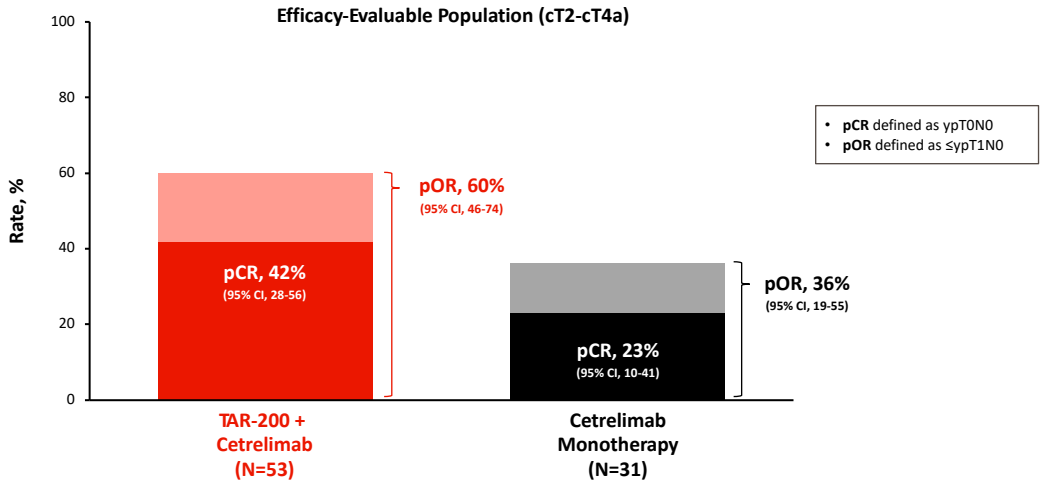


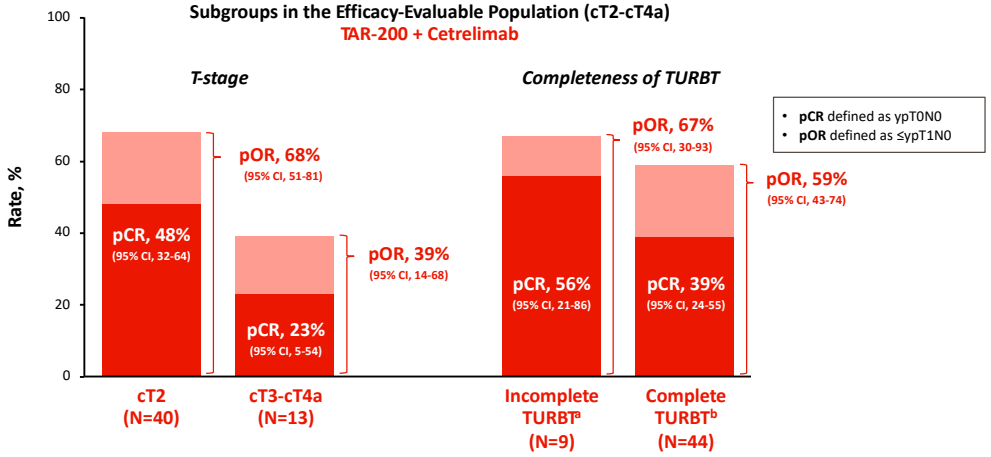
- Thus far the results favor the intravesical monotherapy strategy
- Uncertainties related to the contribution of systemic ICI towards monotherapies

1. Tyson MD et al. AUA 2024. Abstract P2-02. 2. Li R et al. *Nat Med.* 2024 Aug;30(8):2216-2223. 3. Presented by MS van der Heijden at the European Society of Medical Oncology Congress 2024; September 13-17, 2024; Barcelona, Spain. 4. Chamie K. *NEJM Evidence*. 2022;2. 5. Boorjian SA et al. *Lancet Oncol*. 2021;22:107-117. 6. Balar AV et al. *Lancet Oncol*. 2021 Jul;22:919-930. 7. Necchi A et al. *Lancet Oncol*. 2024;S1470-2045:00178-5. 8. Black PC et al. *Eur Urol*. 2023;84:536-544.

Combining intravesical and systemic therapy in MIBC:

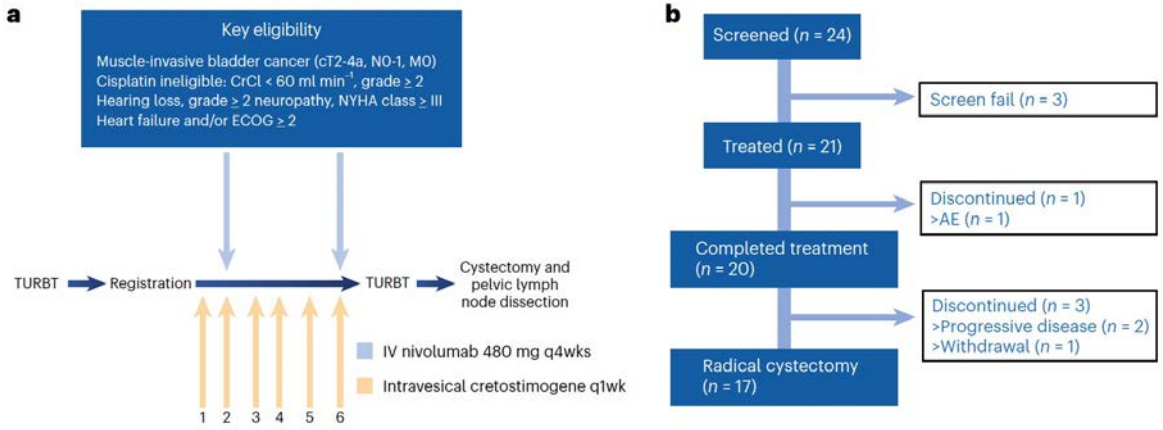
SunRISe-4: TAR-200 + Cetrelimab





Necchi A, et al. ESMO 2024

CORE-002 trial: cretostimogene + nivolumab



- Primary Endpoint: Safety (CTCAE)
- 68% cT2N0 stage
- Chemotherapy refusal for eligibility: 9.5%
- ypT0N0 rate: 8/19 (42.1%)
- 1-y RFS rate: 70.4%
- Grade 3-4 TRAE: 57%

Li R, et al. Nat Med. 2025 Jan;31(1):176-188.

Conclusions of the 2025 highlights for NMIBC and MIBC:

Unmet Needs in the Treatment of NMIBC:

- **The struggle of intravesical vs systemic therapies**
- **BCG-naive HR-NMIBC: the future is uncertain, phase 3 studies are ongoing**
- **Geographical disparities in therapeutic access (as standard therapy or clinical trial therapy) are huge! A US-based trial will very unlikely set a global standard-of-care**

Unmet Needs in the Treatment of MIBC:

- **Raising the bar of therapeutic success by avoiding RC or chemoRT in well-selected patients**

Regulatory and reimbursement issues aside, what would you most likely recommend for a 65-year-old patient with high-grade T1 NMIBC with persistent disease after completing induction BCG who is not amenable to cystectomy?

	FGFR wild type	FGFR mutated
 Dr Galsky	TAR-200 + cetrelimab	TAR-210 (intravesical erdafitinib)
 Prof Necchi	TAR-200	TAR-210 (intravesical erdafitinib)
 Prof Powles	TAR-200	TAR-200
 Dr Friedlander	TAR-200 + cetrelimab	TAR-210 (intravesical erdafitinib)
 Dr Grivas	Intravesical chemotherapy	Intravesical chemotherapy
 Dr Rosenberg	TAR-200	TAR-210 (intravesical erdafitinib)

Based on available data and your personal experience, what is your global perspective on the overall efficacy, tolerability and patient experience with the TAR-200 delivery system compared to standard chemotherapy?

	Efficacy	Tolerability	Patient experience
 Dr Galsky	TAR-200 is more effective	Tolerability is equal	Patient experience is equal
 Prof Necchi	TAR-200 is more effective	TAR-200 is more tolerable	Patient experience is better with TAR-200
 Prof Powles	TAR-200 is more effective	Tolerability is equal	Patient experience is equal
 Dr Friedlander	TAR-200 is more effective	Tolerability is equal	Patient experience is better with TAR-200
 Dr Grivas	Efficacy is equal	Tolerability is equal	Patient experience is better with TAR-200
 Dr Rosenberg	Efficacy is equal	TAR-200 is more tolerable	Patient experience is better with TAR-200

Given the FDA breakthrough therapy designation for TAR-200 for NMIBC, do you believe this agent will receive regulatory approval in the near future?

Would you like to be able to access TAR-200 today?

	Regulatory approval soon?	Access to TAR-200 today?
 Dr Galsky	Yes	Yes
 Prof Necchi	Yes	Yes
 Prof Powles	Yes	Yes
 Dr Friedlander	Yes	Yes
 Dr Grivas	Yes	Yes
 Dr Rosenberg	Yes	Yes

Based on available data and your personal experience, what is your global perspective on the overall efficacy of the TAR-210 (intravesical erdafitinib) delivery system?

 Dr Galsky	Highly effective
 Prof Necchi	Possibly more effective than TAR-200 in FGFR3-mutated disease
 Prof Powles	Too early to tell
 Dr Friedlander	Pretty effective, similar in many respects to TAR-200
 Dr Grivas	Promising but data are immature
 Dr Rosenberg	Quite active in FGFR3-mutated disease

RTP RESEARCH TO PRACTICE

Agenda

MODULE 1: Current and Future Management of Muscle-Invasive Bladder Cancer — Prof Powles

MODULE 2: Novel Intravesical Therapies Under Evaluation for Nonmetastatic Urothelial Bladder Cancer (UBC) — Prof Necchi

MODULE 3: Selection and Sequencing of Therapy for Metastatic UBC — Dr Galsky

RTP RESEARCH TO PRACTICE

Selection and Sequencing of Therapy for Metastatic Urothelial (Bladder) Cancer

Matthew D. Galsky, MD FASCO

Lillian and Howard Stratton Professor of Medicine

Icahn School of Medicine at Mount Sinai

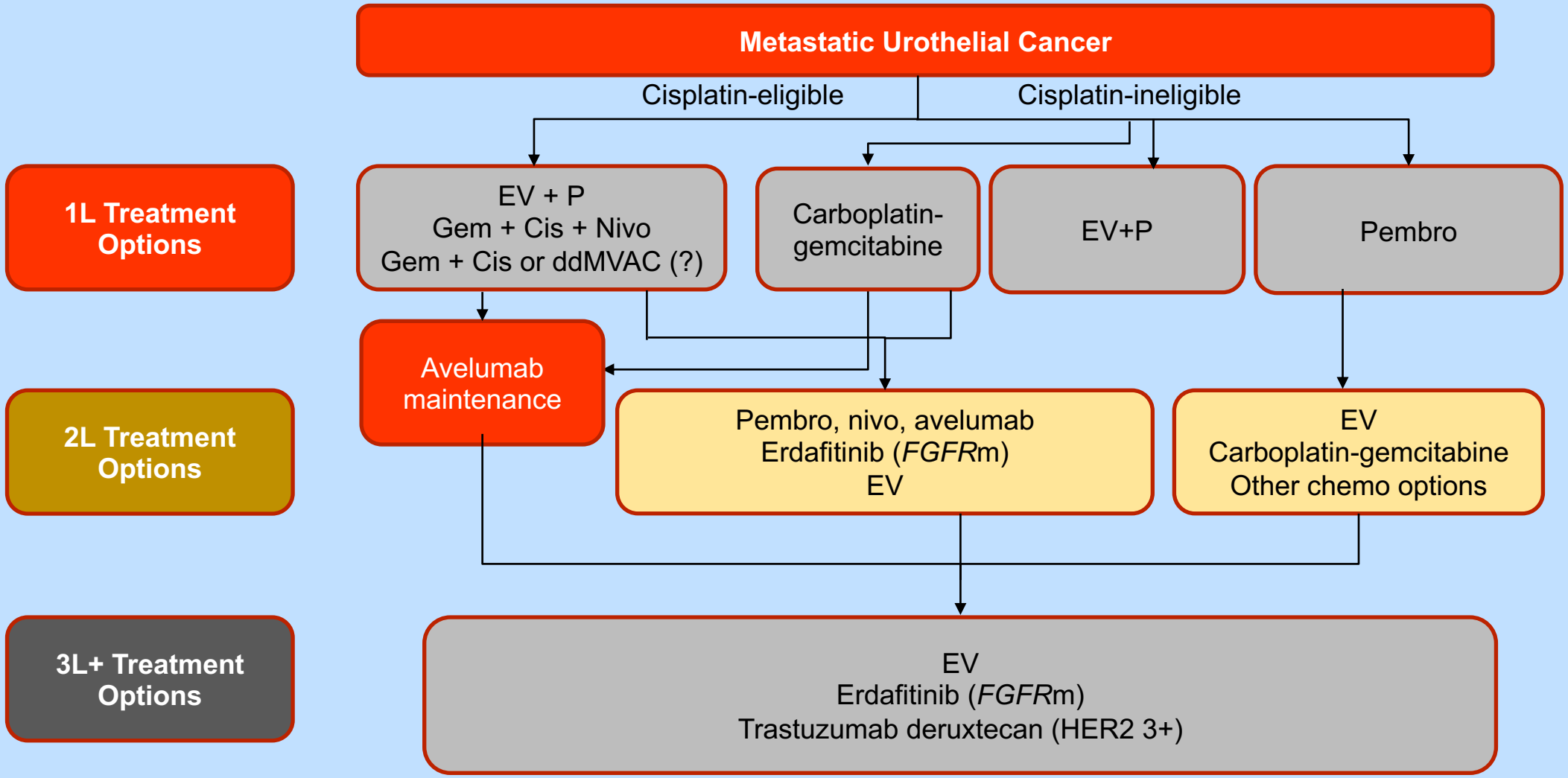
Director, Genitourinary Medical Oncology

Co-Leader, Cancer Clinical Investigation Program

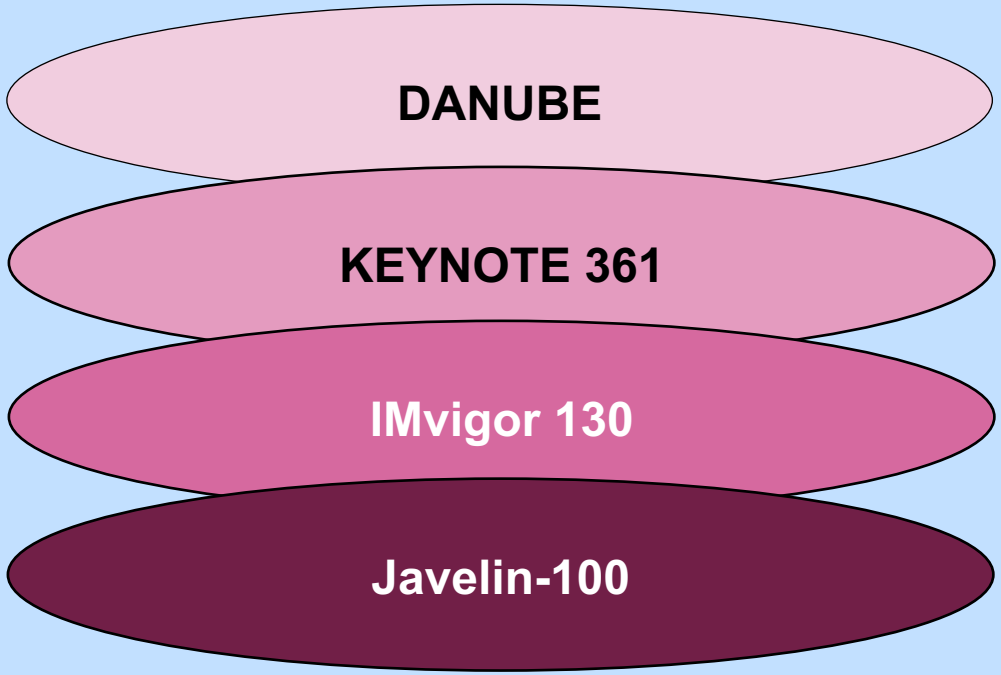
Associate Director for Translational Research

Tisch Cancer Institute

Contemporary Management of Metastatic Urothelial Cancer



Pre-ESMO 2023, what had we learned from this series of contemporary phase 3 trials in mUC?



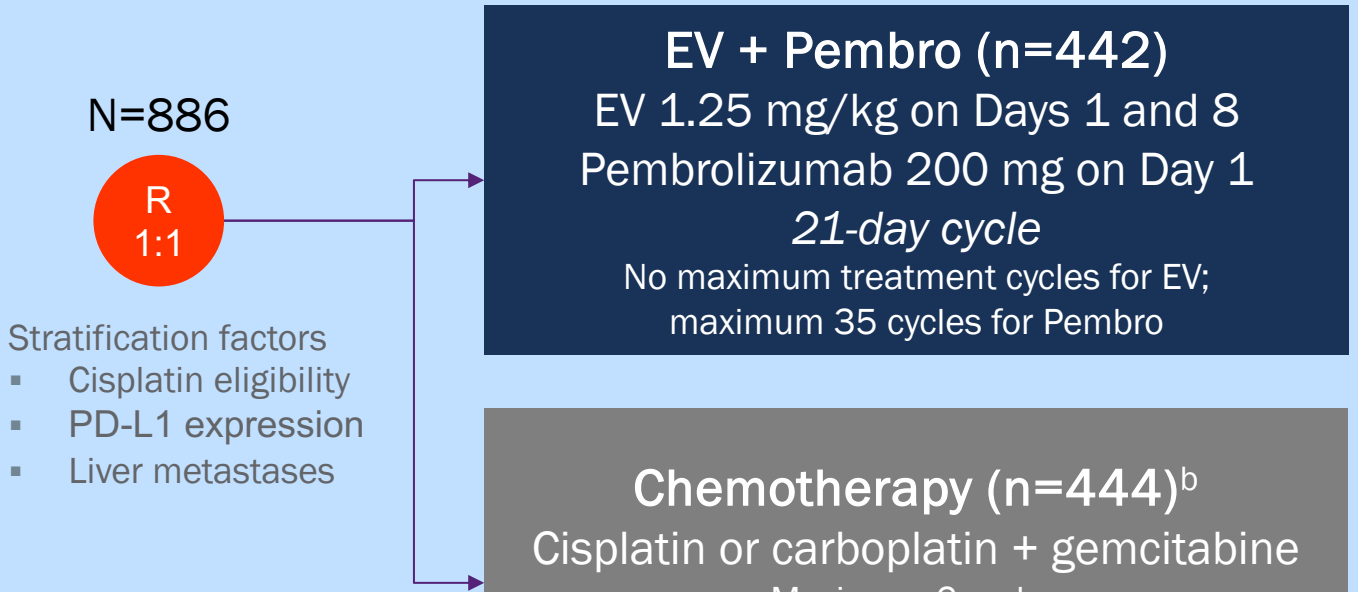
- Single agent PD-1/PD-L1 blockade not ideal strategy and hard to define population for whom sufficient
- Early second line (i.e., ”switch maintenance”) PD-1/PD-L1 is a good strategy.
- Combination CTLA4 + PD-1/PD-L1 blockade not an ideal strategy (?)
- Concurrent combination platinum-based chemotherapy + PD-1/PD-L1 blockade not an ideal strategy

EV-302: Phase 3 Trial of EV + Pembrolizumab

- Previously untreated la/mUC
- Eligible for platinum, EV, and pembrolizumab
- PD-1/L1 inhibitor naive
- ECOG PS 0-2[a]

Dual primary endpoints
- PFS per BICR
- OS

Select secondary endpoints
- ORR per RECIST v1.1 by BICR and investigator assessment
- Safety



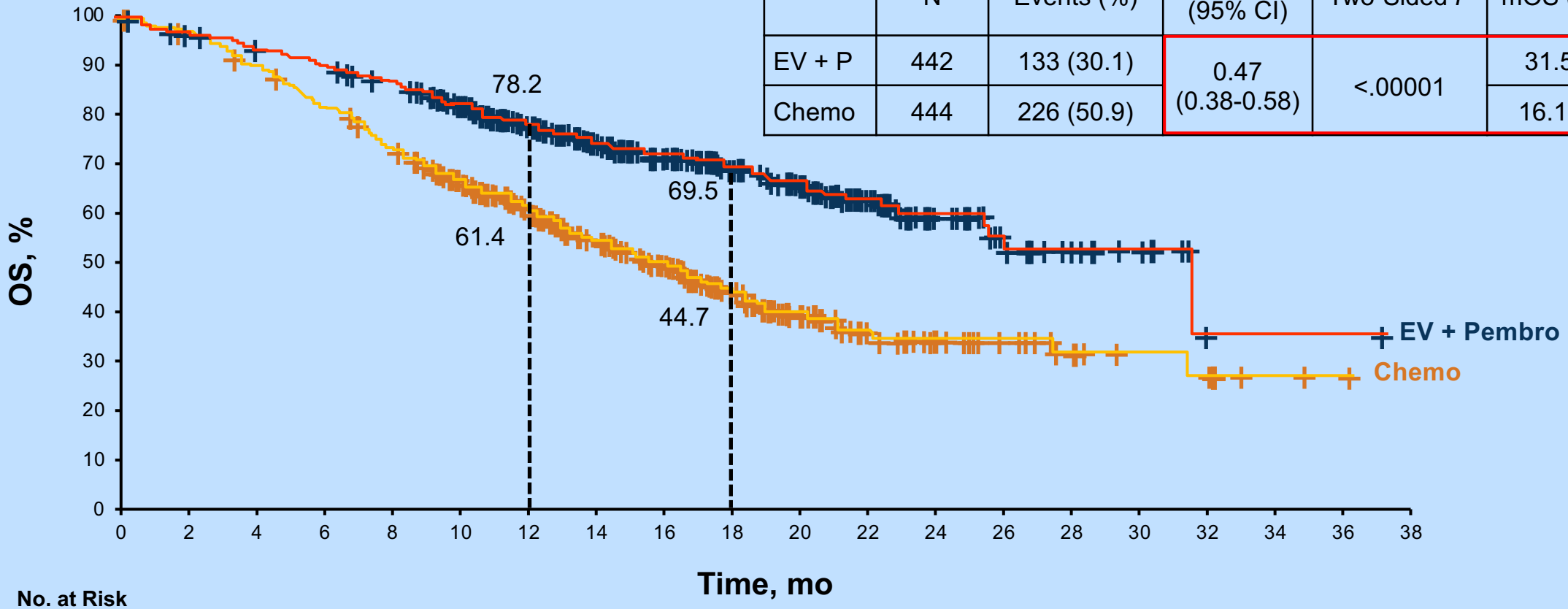
[b] Maintenance therapy could be used following completion and/or discontinuation of platinum-containing therapy

[a] Patients with ECOG PS of 2 were required to also meet the additional criteria: hemoglobin ≥10 g/dL, GFR ≥50mL/min, may not have NYHA class III heart failure.

Powles et al, NEJM, 2024

Phase 3 EV-302: Improved OS With Enfortumab Vedotin Plus Pembrolizumab

	N	Events (%)	HR[b] (95% CI)	Two-Sided *P*	mOS (95% CI), mo
EV + P	442	133 (30.1)	0.47 (0.38-0.58)	<.00001	31.5 (25.4-NR)
Chemo	444	226 (50.9)			16.1 (13.9-18.3)



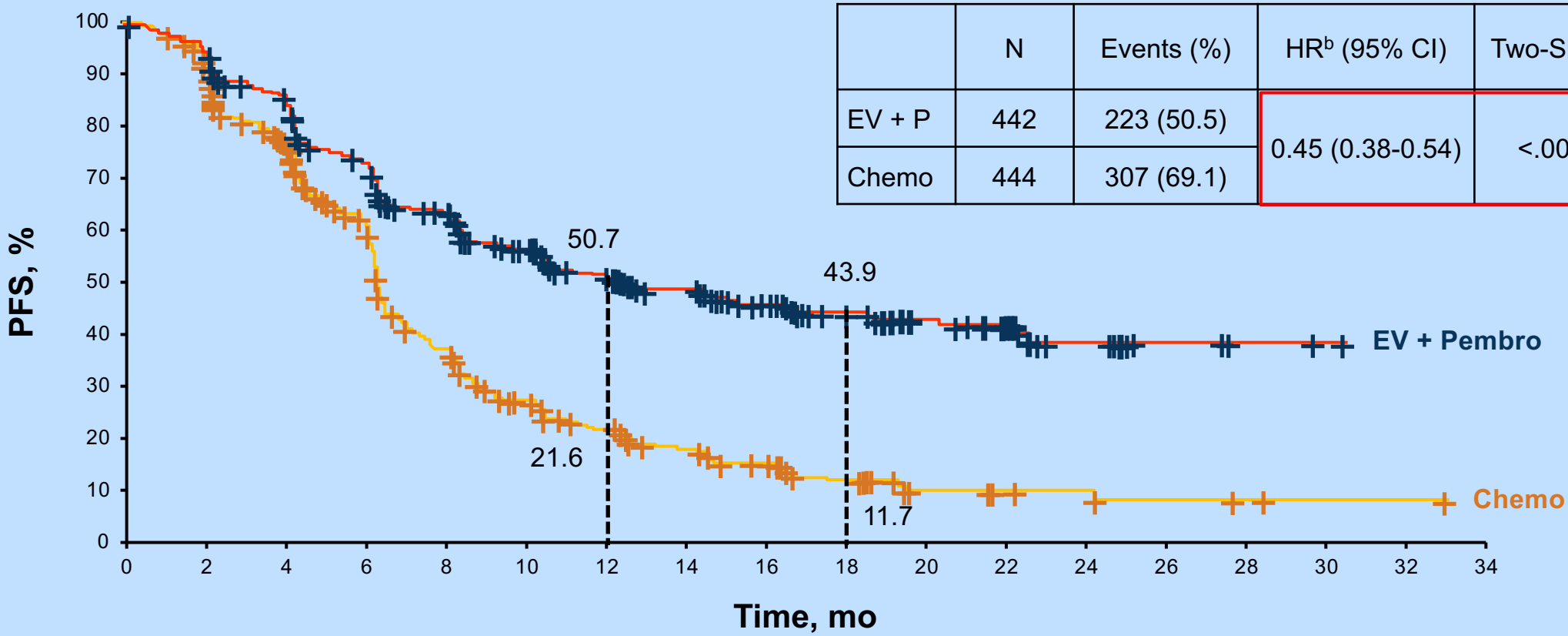
No. at Risk

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

Powles et al, NEJM, 2024

Phase 3 EV-302: Improved PFS With Enfortumab Vedotin Plus Pembrolizumab

	N	Events (%)	HR[b] (95% CI)	Two-Sided *P*	mPFS (95% CI), mo
EV + P	442	223 (50.5)	0.45 (0.38-0.54)	<.00001	12.5 (10.4-16.6)
Chemo	444	307 (69.1)			6.3 (6.2-6.5)

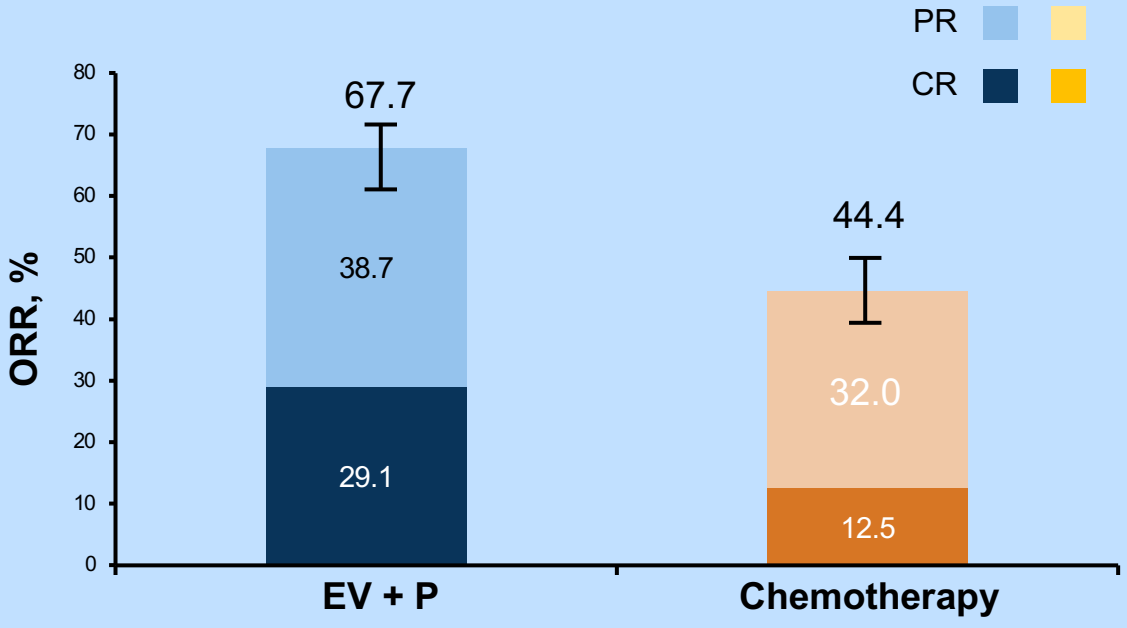


No. at Risk

EV + P	442	409	361	303	253	204	167	132	102	73	45	33	17	6	3	1	—
Chemo	444	380	297	213	124	78	56	41	30	19	8	6	5	3	2	1	1

Powles et al, NEJM, 2024

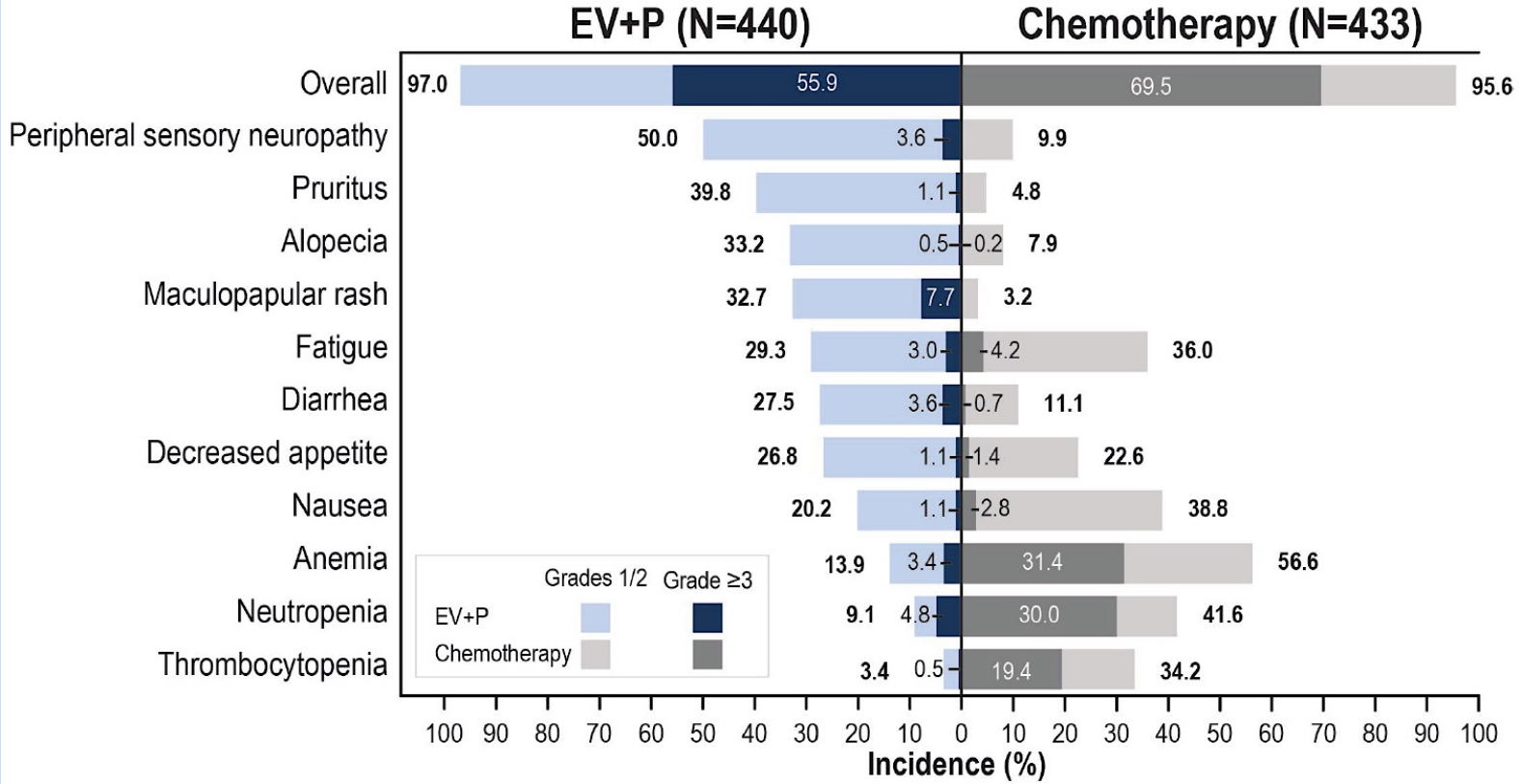
Phase 3 EV-302: Improved Response Rate



	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*	<.00001	
BOR[b], n (%)		
CR	127 (29.1)	55 (12.5)
PR	169 (38.7)	141 (32.0)
SD	82 (18.8)	149 (33.8)
PD	38 (8.7)	60 (13.6)
NE/NA[c]	21 (4.8)	36 (8.2)
mDOR (95% CI)	NR (20.2-NR)	7.0 (6.2-10.2)

Powles et al, NEJM, 2024

EV-302: Treatment-Related Adverse Events



Median number of cycles (range)

- **EV+P: 12.0 (1-46)**
- **Chemo: 6.0 (1-6)**

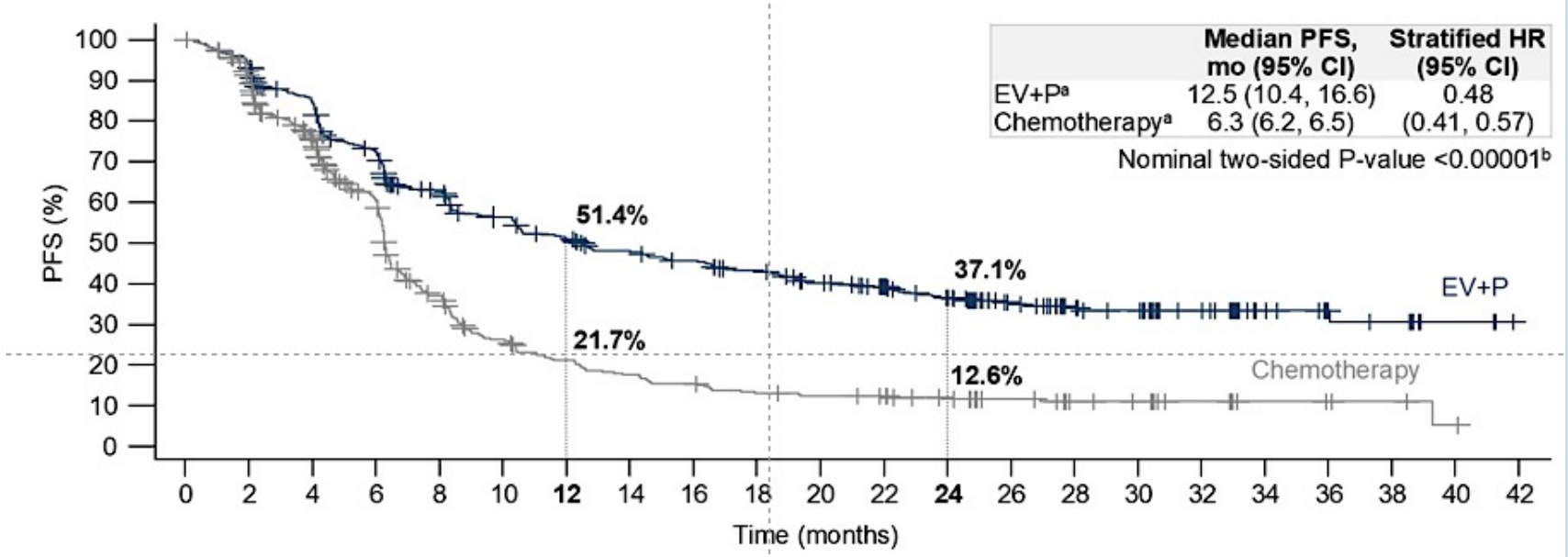
Treatment-related AEs leading to death per investigator

- **EV+P: 4 (0.9%)** – asthenia, diarrhea, immune-mediated lung disease, multiorgan dysfunction syndrome
- **Chemo: 4 (0.9%)** – febrile neutropenia, MI, neutropenic sepsis, sepsis

Powles et al, NEJM, 2024

EV-302: Longer-term follow-up (median ~2.5 years)

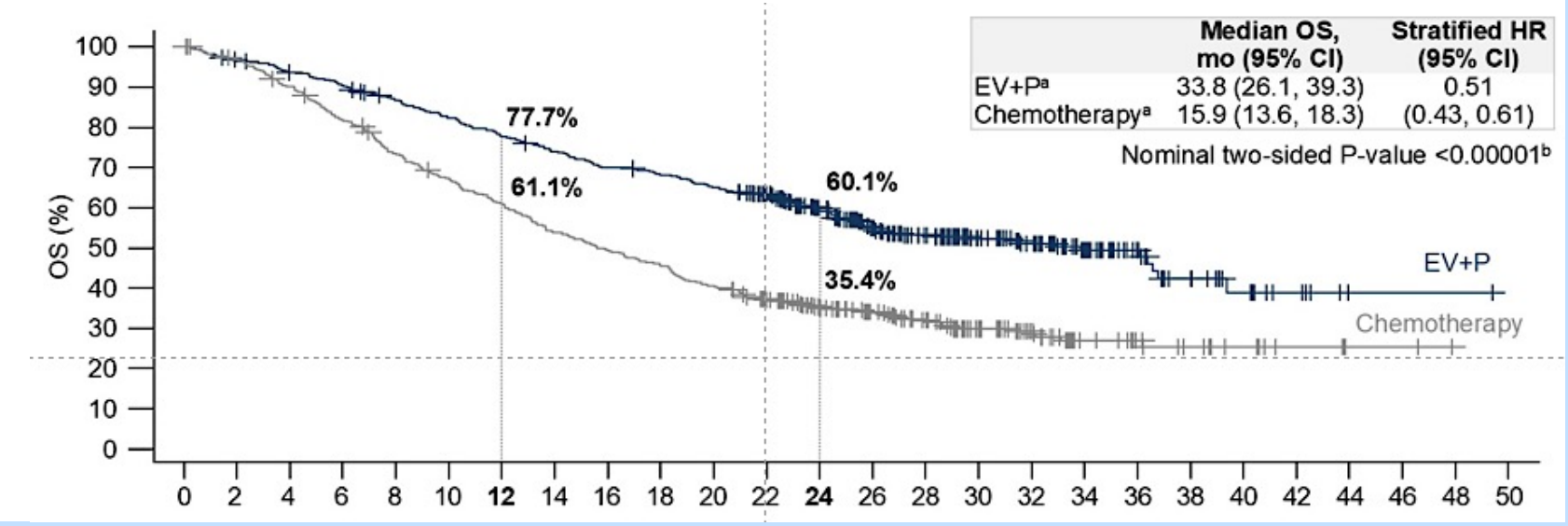
PFS



	Median PFS, mo (95% CI)	Stratified HR (95% CI)
EV+P[a]	12.5 (10.4, 16.6)	0.48
Chemotherapy[a]	6.3 (6.2, 6.5)	(0.41, 0.57)

Nominal two-sided P-value <0.00001[b]

OS

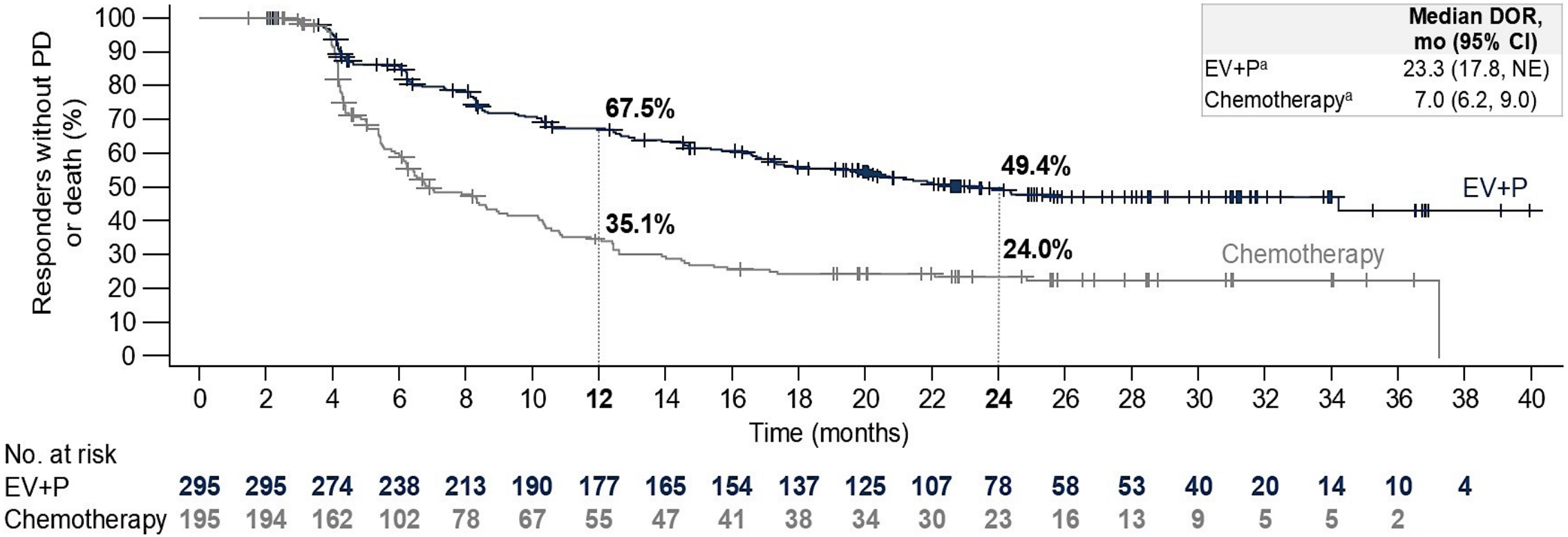


	Median OS, mo (95% CI)	Stratified HR (95% CI)
EV+P[a]	33.8 (26.1, 39.3)	0.51
Chemotherapy[a]	15.9 (13.6, 18.3)	(0.43, 0.61)

Nominal two-sided P-value <0.00001[b]

Powles T, et al. ASCO GU 2025. Abstract 664.

EV-302: Duration of Response



	Median DOR, mo (95% CI)
EV+P[a]	23.3 (17.8, NE)
Chemotherapy[a]	7.0 (6.2, 9.0)

No. at risk

EV+P	295	295	274	238	213	190	177	165	154	137	125	107	78	58	53	40	20	14	10	4
Chemotherapy	195	194	162	102	78	67	55	47	41	38	34	30	23	16	13	9	5	5	2	

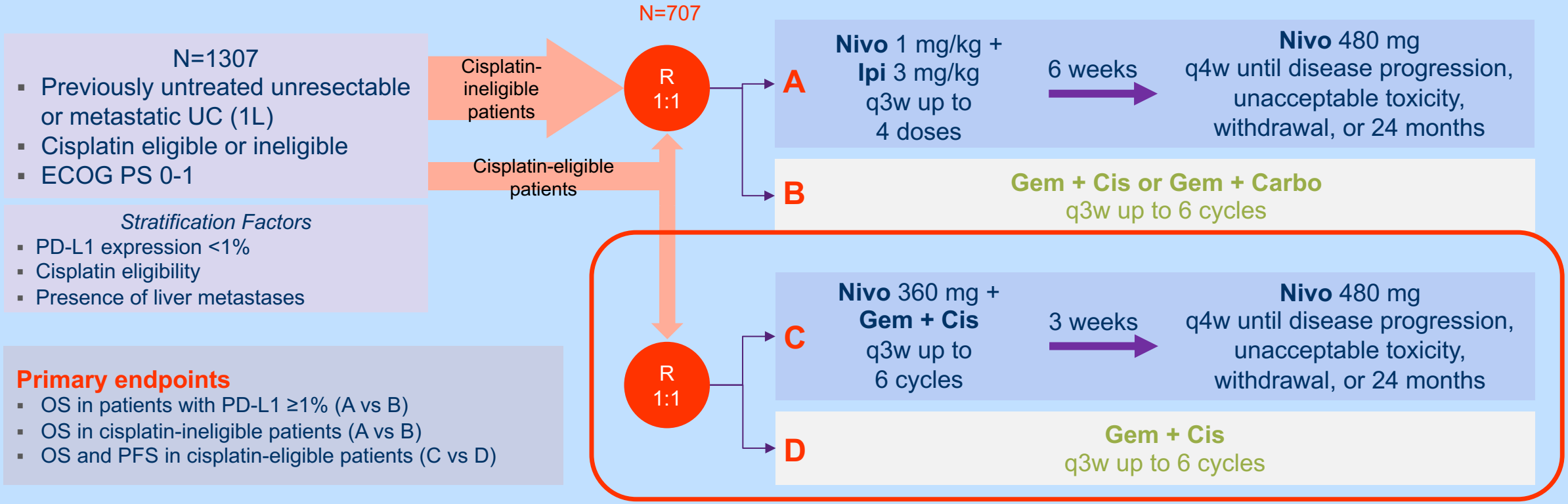
	EV+P (n=437)	Chemotherapy (n=441)	Nominal two-sided P-value
Confirmed ORR (CR or PR), n (%) [95% CI]	295 (67.5) [62.9, 71.9]	195 (44.2) [39.5, 49.0]	<0.00001[b]
Best overall response, n (%)			
CR	133 (30.4)	64 (14.5)	
PR	162 (37.1)	131 (29.7)	
SD	83 (19.0)	149 (33.8)	

Data cutoff: August 8, 2024.

CR, complete response; EV, enfortumab vedotin; NE, not estimable; P, pembrolizumab; PR, partial response; ORR, objective response rate; SD, stable disease.
[a]Events/N were 137/295 for EV+P and 129/195 for chemotherapy. [b]P-value is nominal and descriptive.

Powles T, et al. ASCO GU 2025. Abstract 664.

CheckMate 901: Phase 3 Trial of Nivolumab in Combination

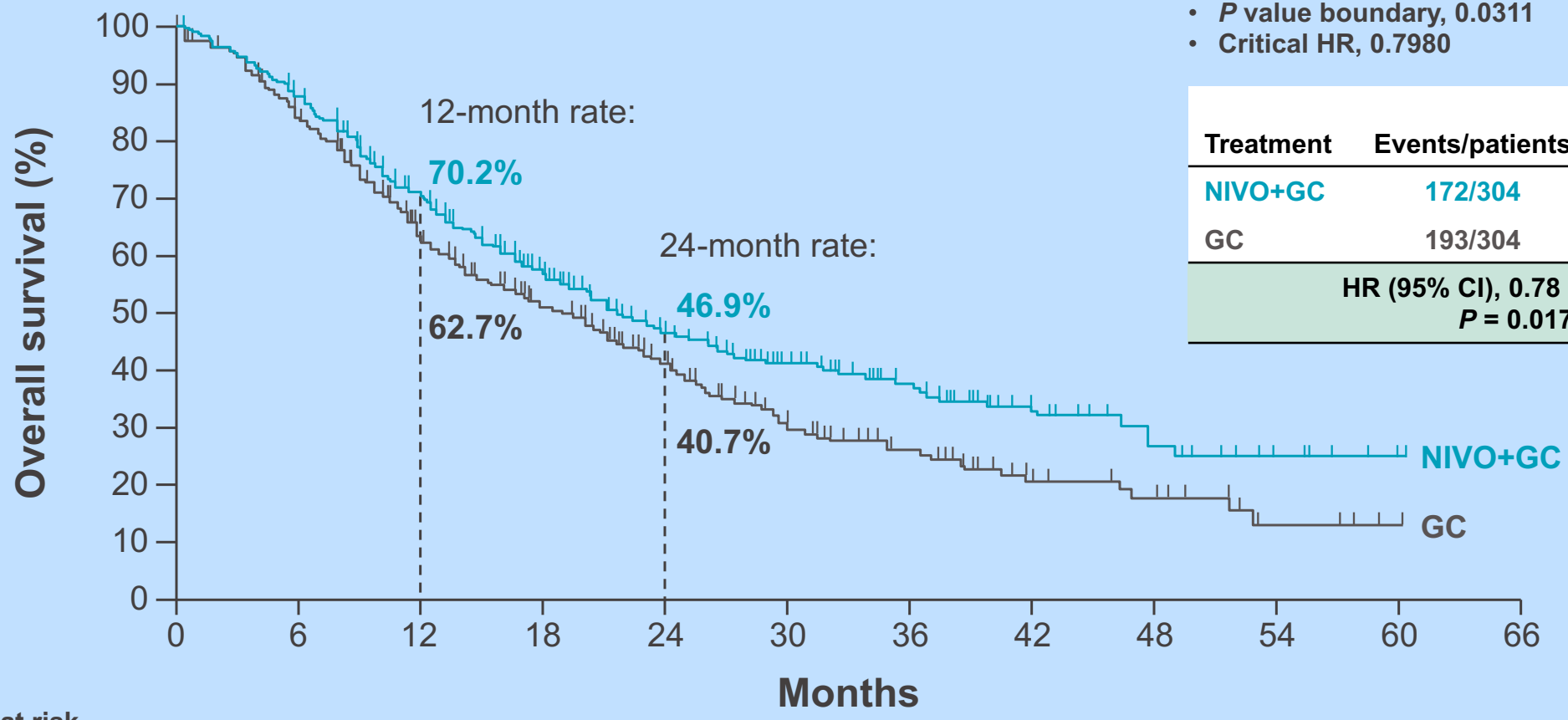


van der Heijden et al, NEJM, 2023

CheckMate 901: Overall Survival

OS final analysis statistical boundaries:
- ***P* value boundary, 0.0311**
- **Critical HR, 0.7980**

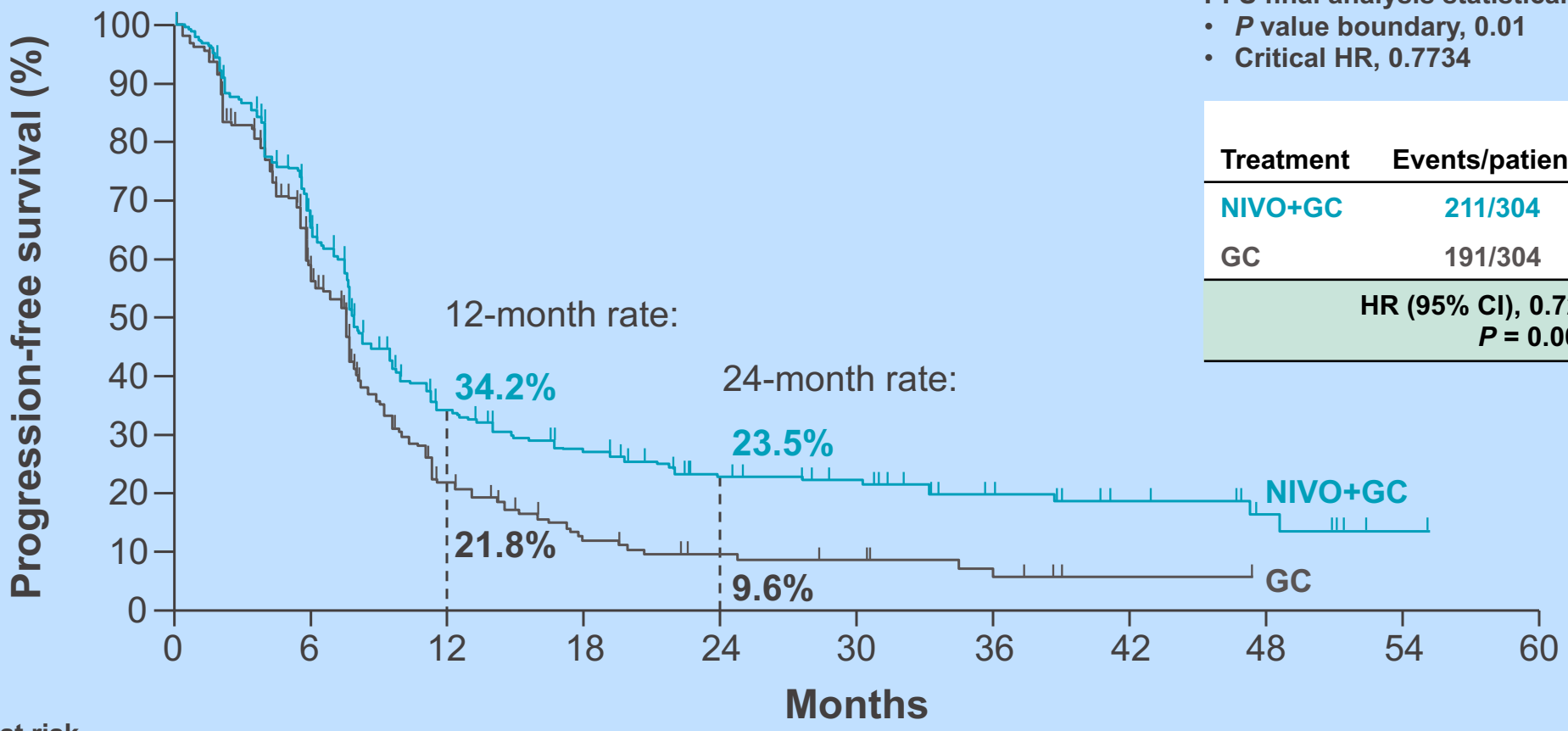
Treatment	Events/patients	Median OS (95% CI), months
NIVO+GC	172/304	21.7 (18.6-26.4)
GC	193/304	18.9 (14.7–22.4)
HR (95% CI), 0.78 (0.63–0.96) *P* = 0.0171		



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 et al, NEJM, 2023

CheckMate 901: Progression-free Survival



No. at risk

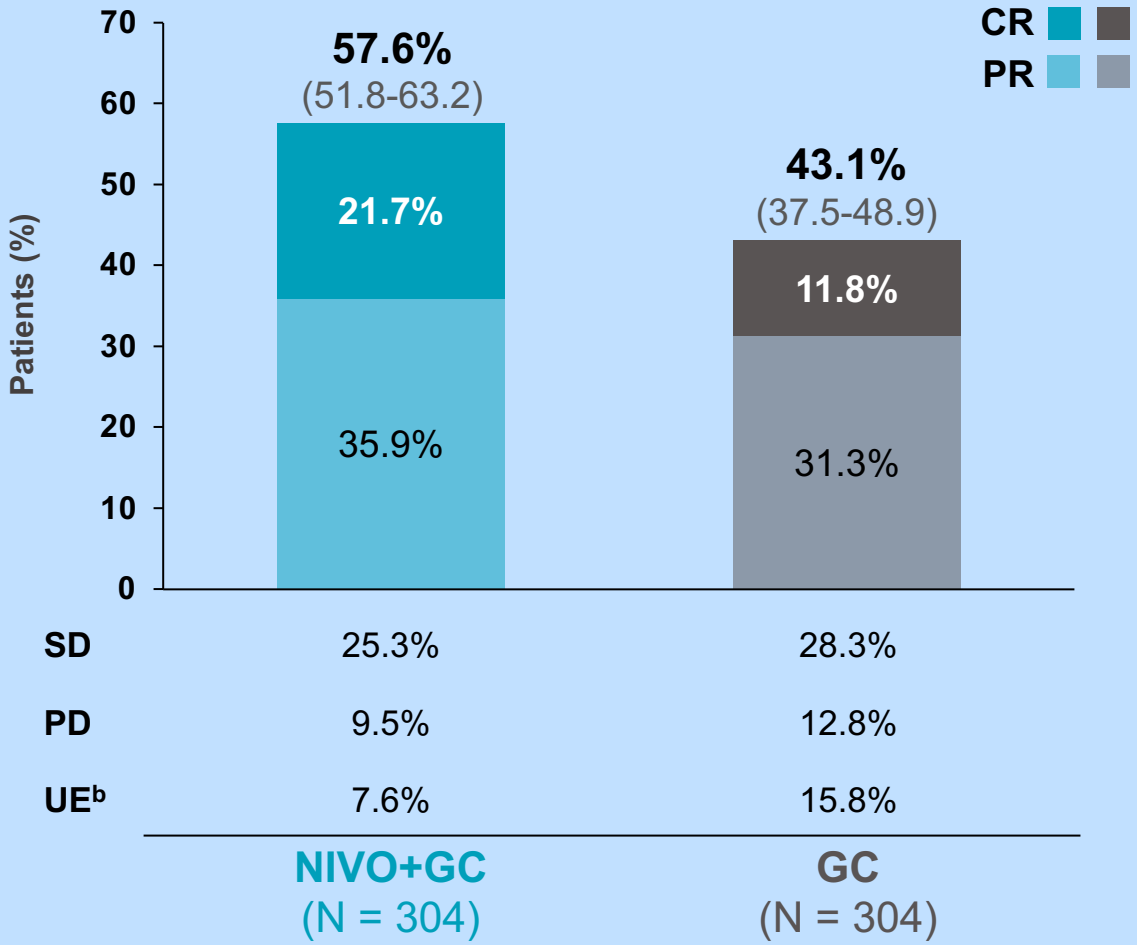
NIVO+GC	304	179	82	57	41	31	19	11	6	1	0
GC	304	119	35	17	10	8	5	1	0	0	0

PFS final analysis statistical boundaries:
- ***P* value boundary, 0.01**
- **Critical HR, 0.7734**

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

van der Heijden et al, NEJM, 2023

The quantity and quality of complete responses are different when nivolumab is added to gemcitabine plus cisplatin



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 et al, NEJM, 2023

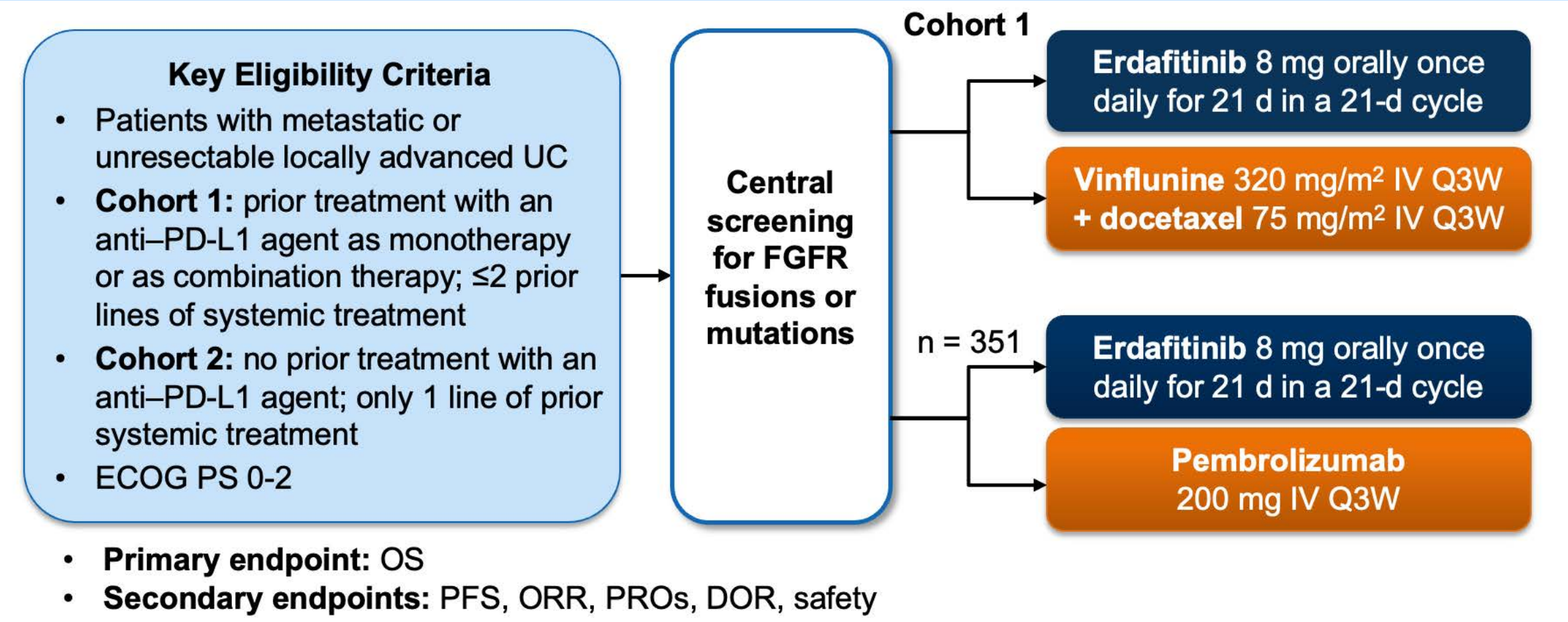
CheckMate 901: Treatment-Related AEs

TRAEs occurring in ≥20% (any grade) or ≥5% (grade ≥3)	Nivo + Gem-Cis (N=304)		Gem-Cis (N=288)	
	Any grade	**Grade ≥3**	**Any grade**	**Grade ≥3**
Any AE	296 (97.4)	188 (61.8)	267 (92.7)	149 (51.7)
Anemia	174 (57.2)	67 (22.0)	137 (47.6)	51 (17.7)
Nausea	142 (46.7)	1 (0.3)	138 (47.9)	3 (1.0)
Neutropenia	93 (30.6)	57 (18.8)	86 (29.9)	44 (15.3)
Decreased neutrophil count	75 (24.7)	44 (14.5)	60 (20.8)	32 (11.1)
Fatigue	74 (24.3)	6 (2.0)	69 (24.0)	4 (1.4)
Decreased appetite	68 (22.4)	4 (1.3)	45 (15.6)	1 (0.3)
Decreased platelet count	66 (21.7)	23 (7.6)	43 (14.9)	14 (4.9)
Decreased white cell count	64 (21.1)	30 (9.9)	40 (13.9)	11 (3.8)
Thrombocytopenia	45 (14.8)	20 (6.6)	35 (12.2)	13 (4.5)

van der Heijden et al, NEJM, 2023

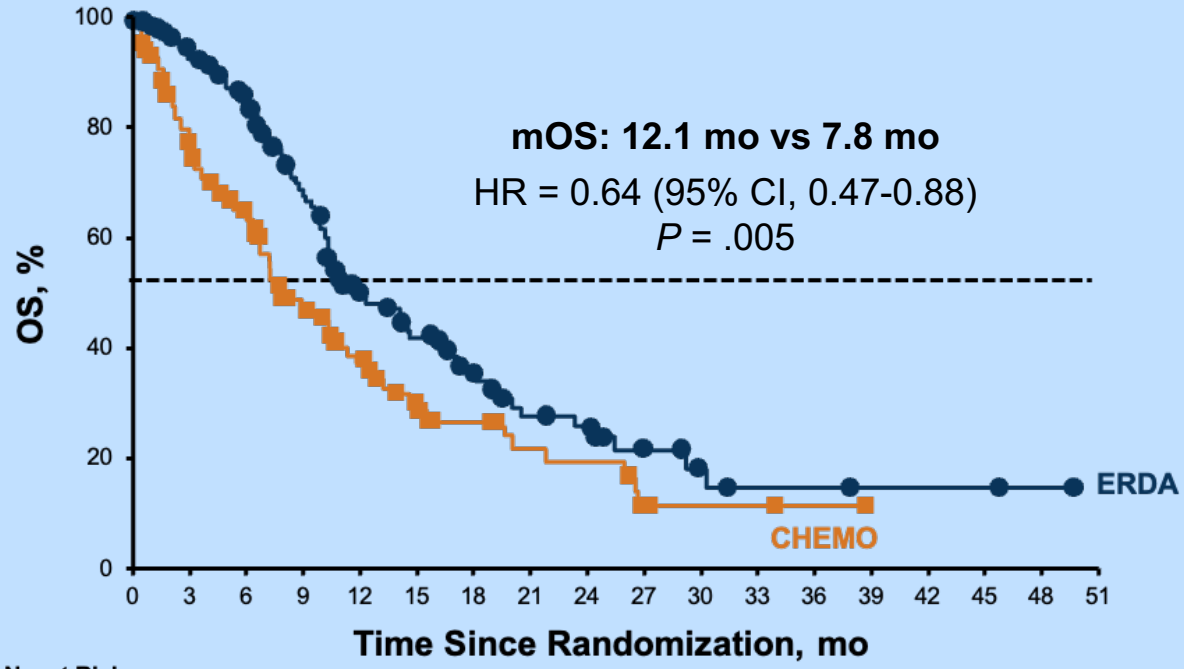
Erdafitinib in *FGFR*-Altered Metastatic or Unresectable UC

Phase 3 THOR

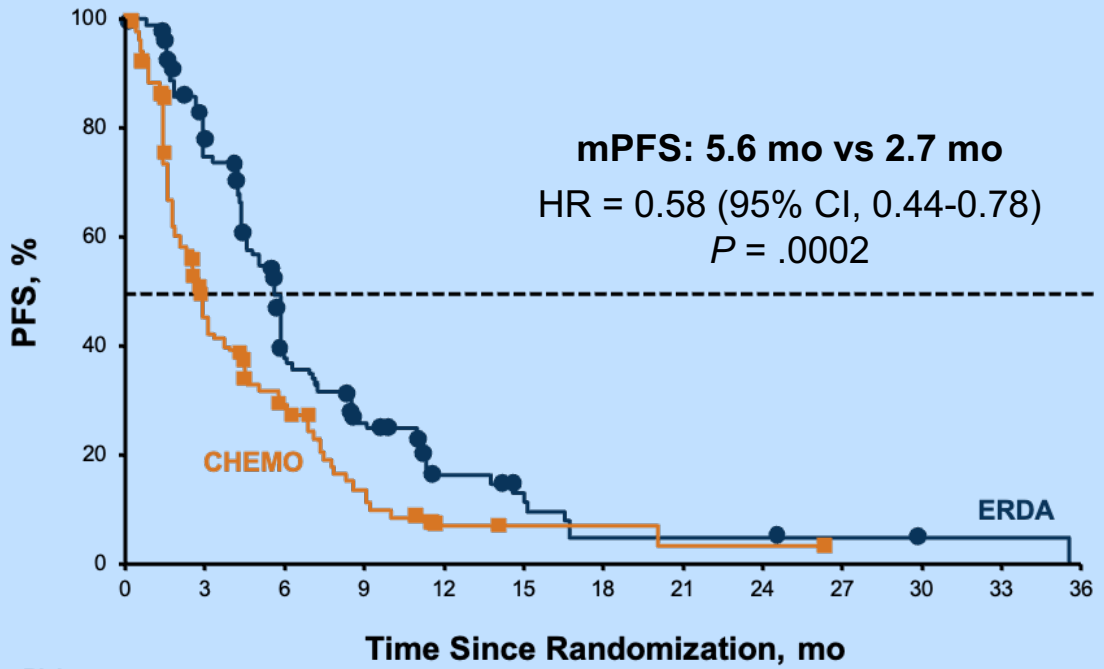


Loriot T et al. *N Engl J Med.* 2023

Phase 3 THOR: Cohort 1 (Erdafitinib Versus Chemotherapy)



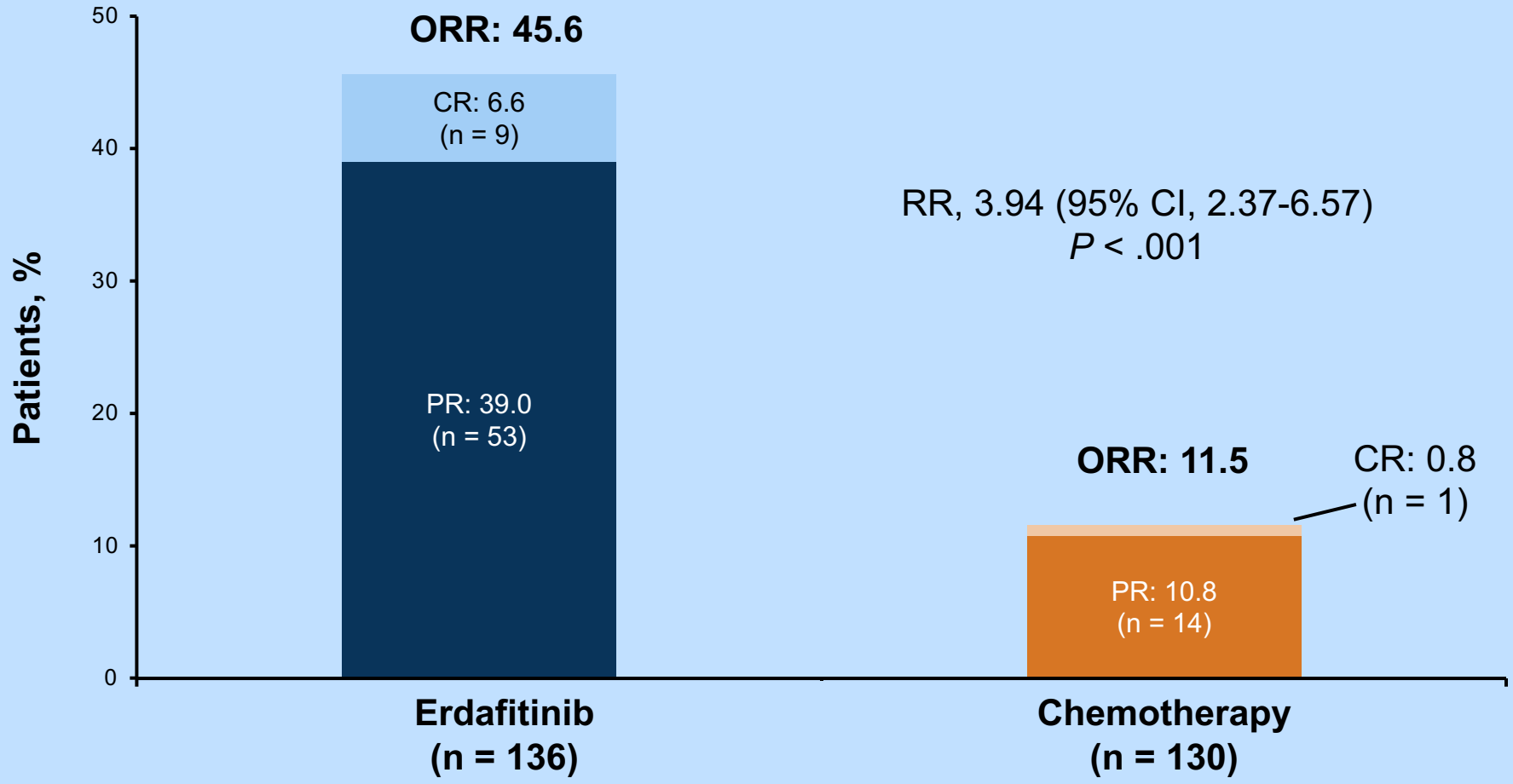
No. at Risk																		
Erda	136	117	97	74	46	35	25	17	15	9	5	3	3	2	2	2	1	0
Chemo	130	87	66	43	30	18	13	9	8	3	2	2	1	0	0	0	0	0



No. at Risk													
Erda	136	90	39	24	12	7	3	3	3	2	1	1	0
Chemo	130	43	23	9	4	2	2	1	1	0	0	0	0

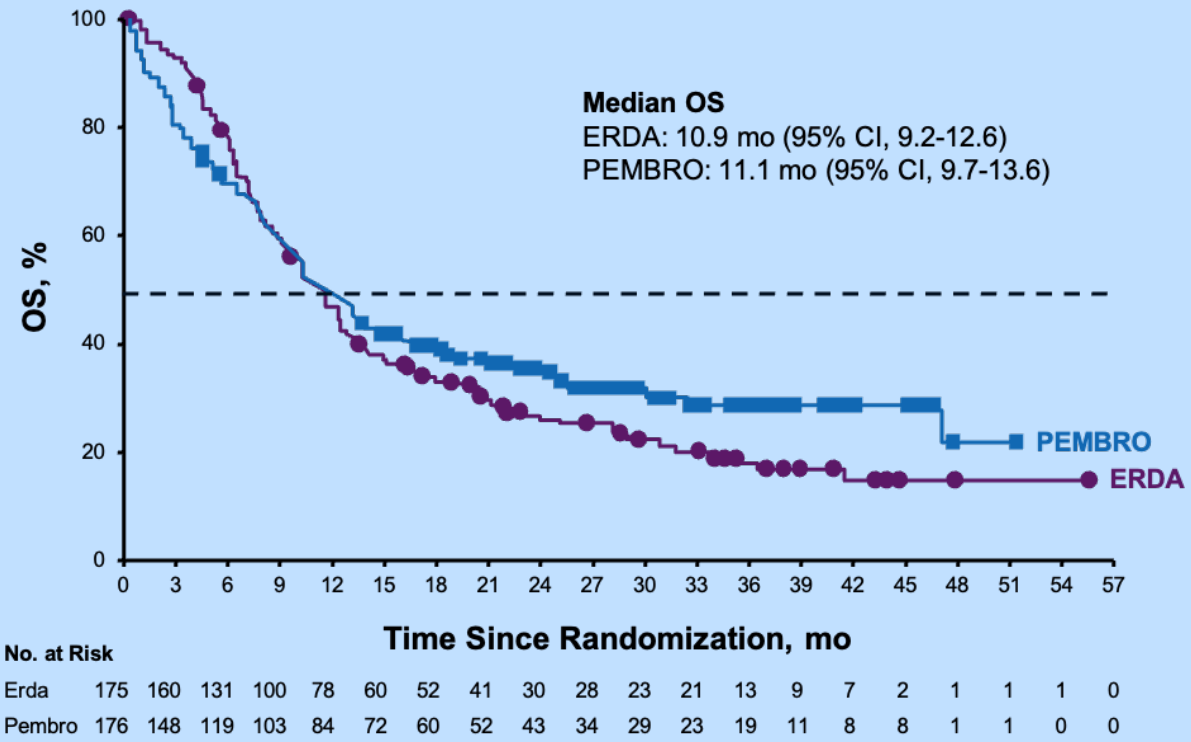
1. Loriot Y et al. *N Engl J Med*. 2019;381:338-348. 2. Necchi A et al. *Ann Oncol*. 2020;31(suppl 4):s550. 3. Siefker-Radtke et al. *Lancet Oncol*. 2022;23:248-258. 4. Loriot T et al. *N Engl J Med*. 2023;389:1961-1971.

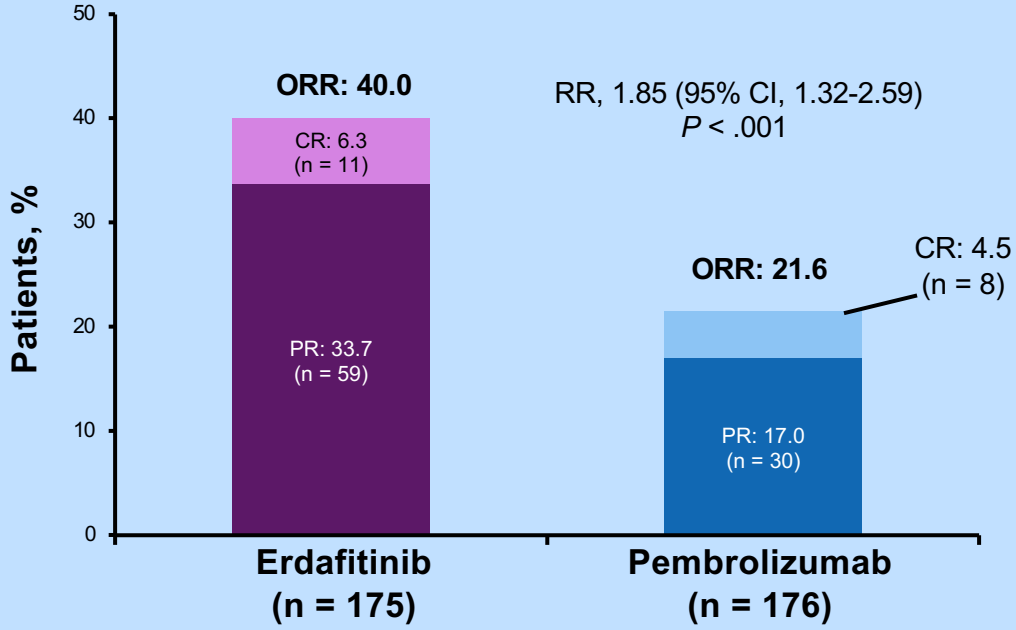
Phase 3 THOR: Cohort 1 (Erdafitinib Versus Chemotherapy)



Loriot T et al. *N Engl J Med.* 2023;389:1961-1971.

Phase 3 THOR: Cohort 2 (Erdafitinib Versus Pembrolizumab)





	Erdafitinib	Pembrolizumab
mPFS, mo	4.4	2.7
mDOR, mo	4.3	14.4

Siefker-Radtke A et al. *Ann Oncol.* 2023

Phase II DESTINY-PanTumor02 Trastuzumab Deruxtecan

T-DXd
5.4 mg/kg Q3W

40 per cohort[b]

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

Primary endpoint

- Confirmed ORR (investigator)

Secondary endpoints

- DOR, DCR, PFS, OS
- Safety

Exploratory analysis

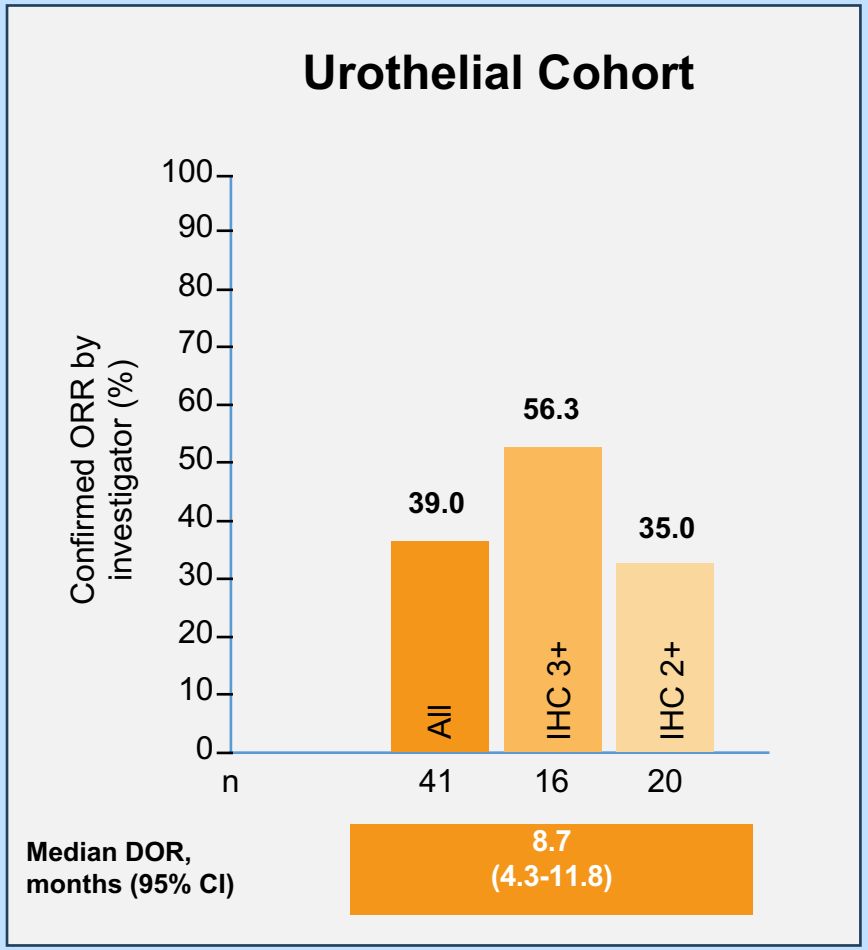
- Subgroup analyses by HER2 status

Primary analysis
data cutoff: Jun 8, 2023
Median follow up: 12.75 mo

Herceptest, 2017 ASCO/CAP gastric scoring guidelines, local testing permitted

Meric-Bernstam et al, JCO, 2024

Phase II DESTINY-PanTumor02 Trastuzumab Deruxtecan



All Patients

	All patients (N=267)	IHC 3+ (n=75)	IHC 2+ (n=125)
ORR, % (95% CI)	37.1 (31.3, 43.2)	61.3 (49.4, 72.4)	27.2 (19.6, 35.9)
Median DOR, months (95% CI)[b]	11.3 (9.6, 17.8)	22.1 (9.6, NR)	9.8 (4.3, 12.6)

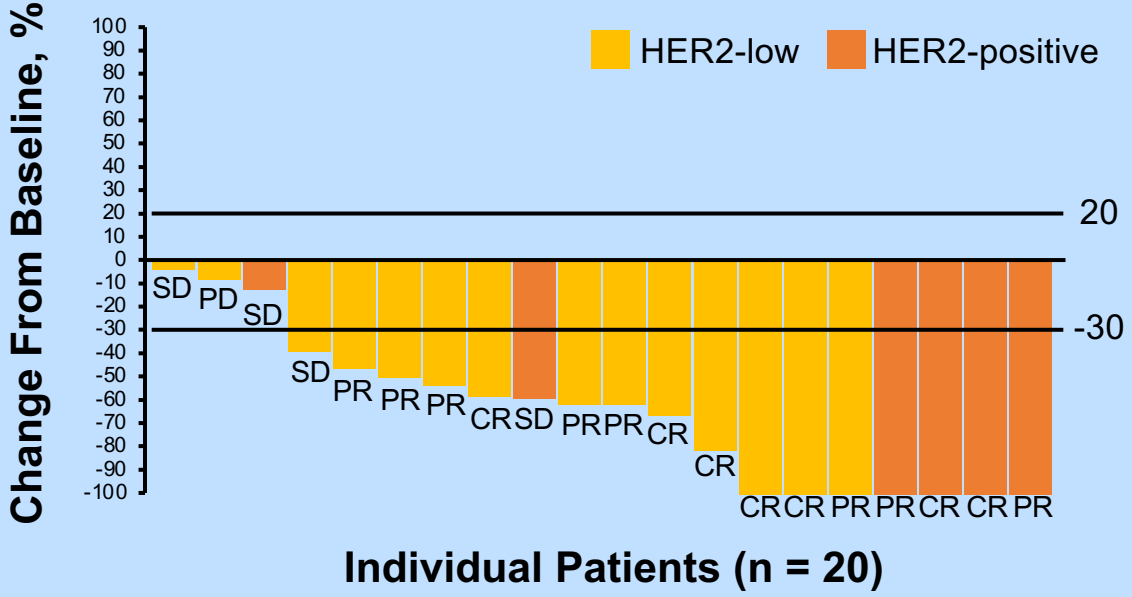
Meric-Bernstam et al, JCO, 2024

Disitamab Vedotin

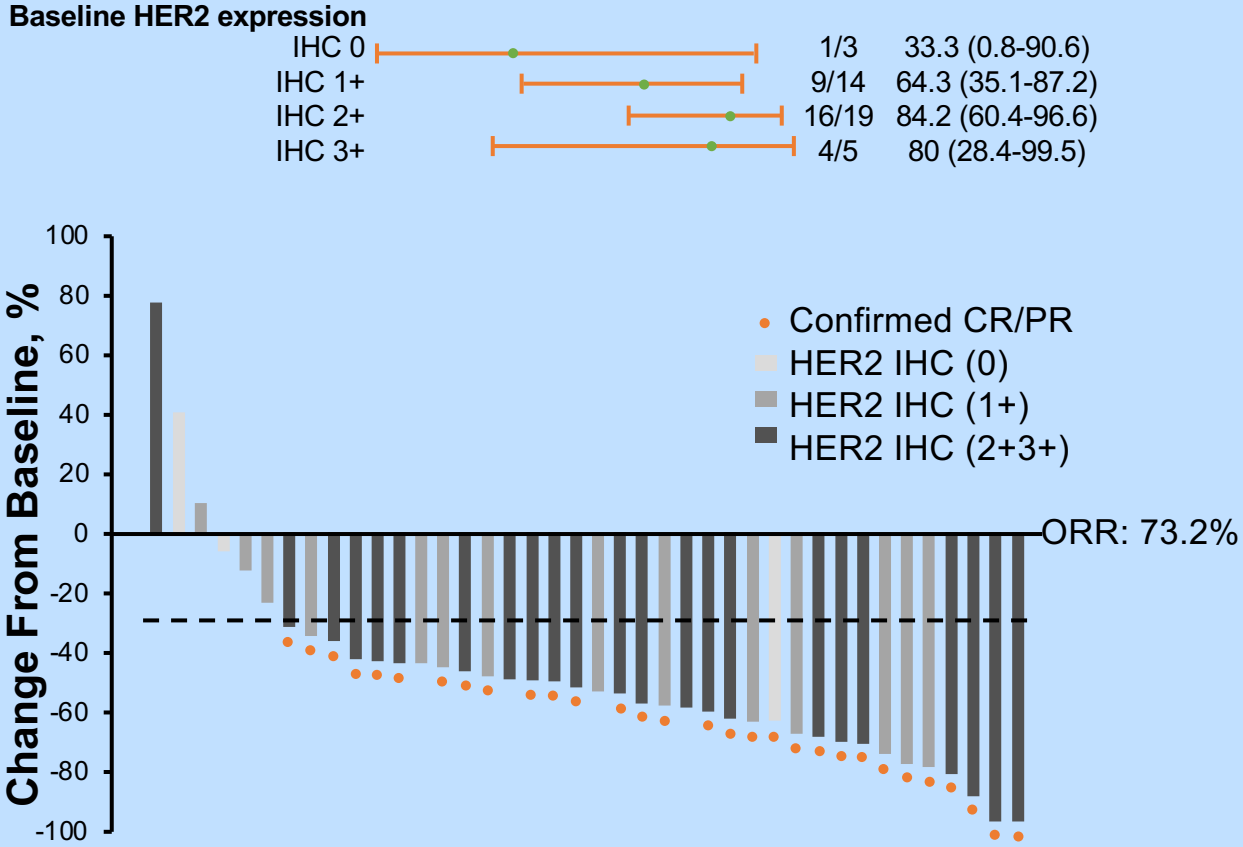
1L mUC:
Disitamab Vedotin (Anti-HER2) + Pembrolizumab in HER2-Expressing mUC[1]

Lead in cohort

Best Change in Sum of Diameters From Baseline per BICR, %

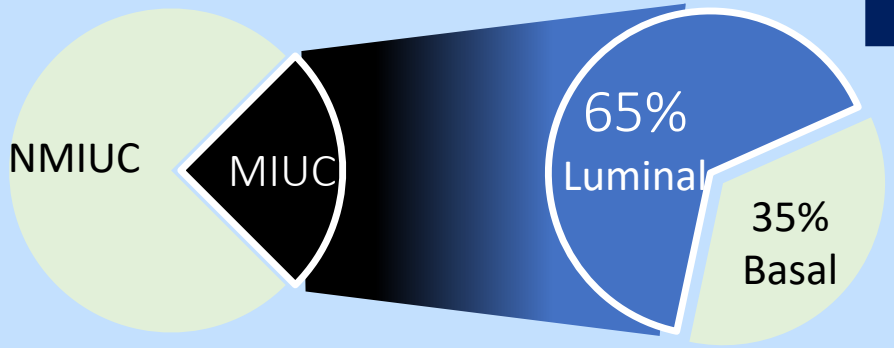


≥1L mUC:
Disitamab Vedotin + Toripalimab

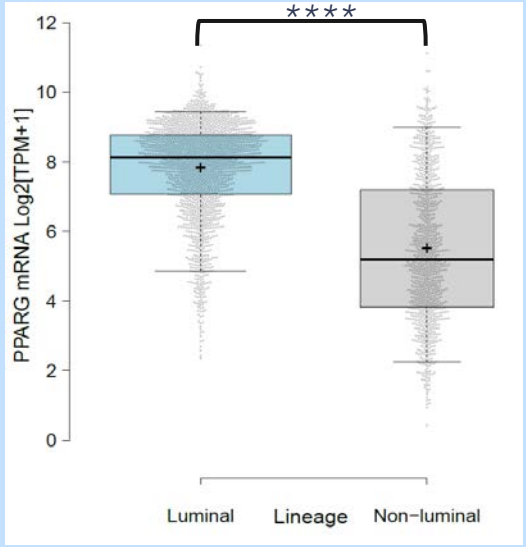


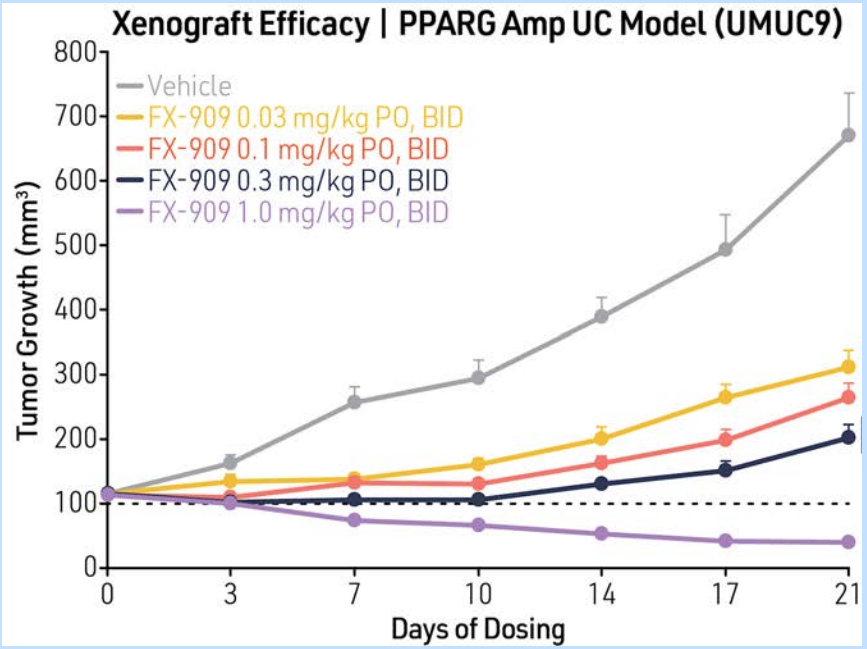
Galsky et al, ESMO, 2024
Zhou, Ann Oncology, 2025

FX-909 (PPARg inverse agonist) in Luminal Bladder Cancer



Luminal Cancers Express High **PPARG**





PART A: Dose Escalation

Advanced Solid Malignancies, Including Advanced UC

3+3 design 30-100mg dose range; QD dosing, 28-day cycle enriching for advanced UC via backfills

☑ Enrollment completed

PART B: Dose Expansion

Luminal Advanced UC*

2-Stage, 40pts; 1:1 randomization in Stage 1 and advance the dose with higher observed responses in Stage 2 as long as that dose has ≥4 OR; success criterion: ≥7 OR in 25 patients

Motley et al. *European Journal of Cancer* (2022) 333 (PB113)

In general, what is your preferred first-line treatment regimen for a 65-year-old patient with metastatic UBC and a PS of 0 who has received no prior systemic therapy?

	FGFR wild type	FGFR mutated
 Dr Galsky	Enfortumab vedotin/pembrolizumab	Enfortumab vedotin/pembrolizumab
 Prof Necchi	Enfortumab vedotin/pembrolizumab	Enfortumab vedotin/pembrolizumab
 Prof Powles	Enfortumab vedotin/pembrolizumab	Enfortumab vedotin/pembrolizumab
 Dr Friedlander	Enfortumab vedotin/pembrolizumab	Enfortumab vedotin/pembrolizumab
 Dr Grivas	Enfortumab vedotin/pembrolizumab	Enfortumab vedotin/pembrolizumab
 Dr Rosenberg	Enfortumab vedotin/pembrolizumab	Enfortumab vedotin/pembrolizumab

Regulatory and reimbursement issues aside, what would be your preferred first-line treatment regimen for a 90-year-old patient with FGFR-mutated metastatic UBC and a history of coronary artery disease?

 Dr Galsky	Enfortumab vedotin/pembrolizumab
 Prof Necchi	Carboplatin/gemcitabine → maintenance avelumab
 Prof Powles	Enfortumab vedotin/pembrolizumab
 Dr Friedlander	Enfortumab vedotin/pembrolizumab
 Dr Grivas	Pembrolizumab
 Dr Rosenberg	Pembrolizumab

RTP RESEARCH TO PRACTICE

A 65-year-old patient receives neoadjuvant chemotherapy followed by cystectomy and then adjuvant nivolumab for UBC but develops disease recurrence in the liver 12 months after starting nivolumab. Regulatory and reimbursement issues aside, what would you likely recommend?

	FGFR wild type	FGFR mutated
 Dr Galsky	Enfortumab vedotin	Enfortumab vedotin
 Prof Necchi	Enfortumab vedotin/pembrolizumab	Enfortumab vedotin/pembrolizumab
 Prof Powles	Enfortumab vedotin/pembrolizumab	Enfortumab vedotin/pembrolizumab
 Dr Friedlander	Enfortumab vedotin/pembrolizumab	Enfortumab vedotin/pembrolizumab
 Dr Grivas	Enfortumab vedotin	Erdafitinib
 Dr Rosenberg	Cisplatin/gemcitabine	Erdafitinib

What would you generally recommend as second-line therapy for a 65-year-old patient with metastatic UBC whose disease progresses on first-line enfortumab vedotin/pembrolizumab?

	FGFR wild type	FGFR mutated
 Dr Galsky	Platinum-based chemotherapy	Erdafitinib
 Prof Necchi	Platinum-based chemotherapy	Erdafitinib
 Prof Powles	Platinum-based chemotherapy	Platinum-based chemotherapy
 Dr Friedlander	Platinum-based chemotherapy	Erdafitinib
 Dr Grivas	Platinum-based chemotherapy	Erdafitinib
 Dr Rosenberg	Platinum-based chemotherapy	Platinum-based chemotherapy

Cases from the Community: Investigators Discuss Available Research Guiding the Care of Patients with Non-Hodgkin Lymphoma

Saturday, May 31, 2025
7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Joshua Brody, MD
Christopher Flowers, MD, MS
Ann LaCasce, MD, MMSc
Tycel Phillips, MD, FASCO

Moderator

Jeremy S Abramson, MD, MMSc

RTP
RESEARCH TO PRACTICE

Data + Perspectives: Clinical Investigators Discuss the Current and Future Clinical Care of Patients with Prostate Cancer

Saturday, May 31, 2025
7:00 PM – 9:00 PM CT (8:00 PM – 10:00 PM ET)

Faculty

Neeraj Agarwal, MD, FASCO
Andrew J Armstrong, MD, ScM
Himisha Beltran, MD
Fred Saad, MD

Moderator

Rana R McKay, MD

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RESEARCH
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