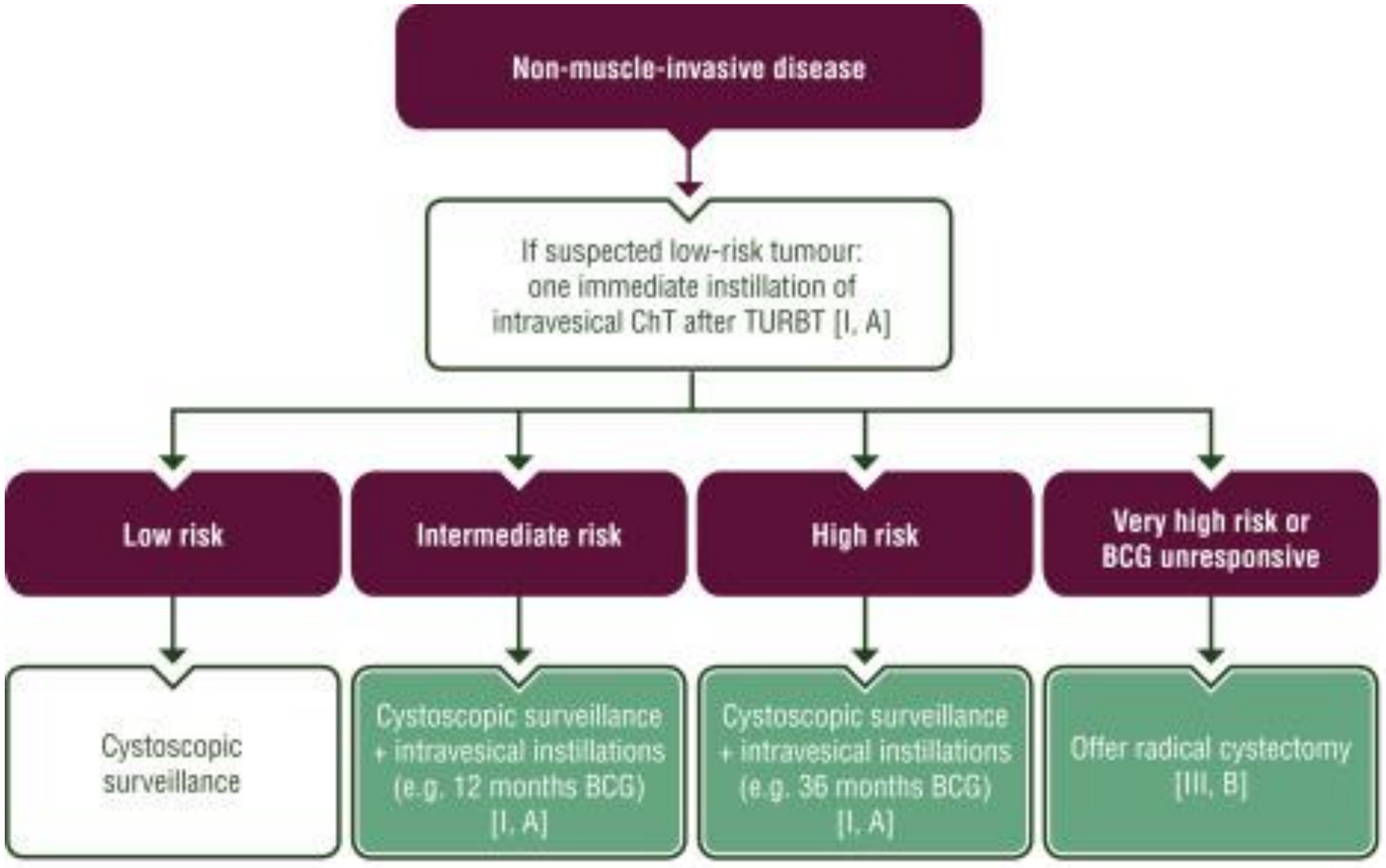
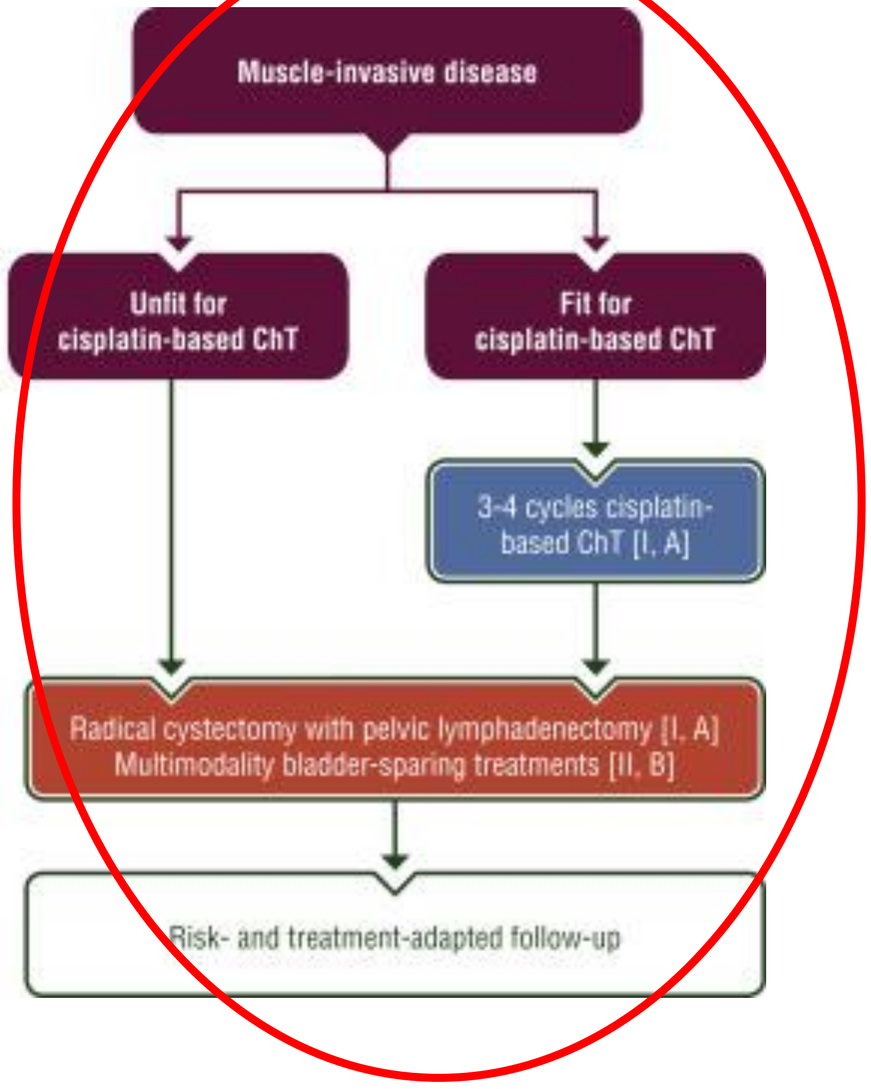
ASCO GU 2025: Bladder Cancer

New data





ESMO Guidelines 2023

Study design: CheckMate 274

- Phase 3, randomized, double-blind, multicenter study of adjuvant NIVO vs PBO for high-risk MIUC[a]

N = 709

Key inclusion criteria

- Patients with ypT2-ypT4a or ypN+ MIUC who had NAC chemotherapy
- Patients with pT3-pT4a or pN+ MIUC without prior NAC 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 NAC-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%

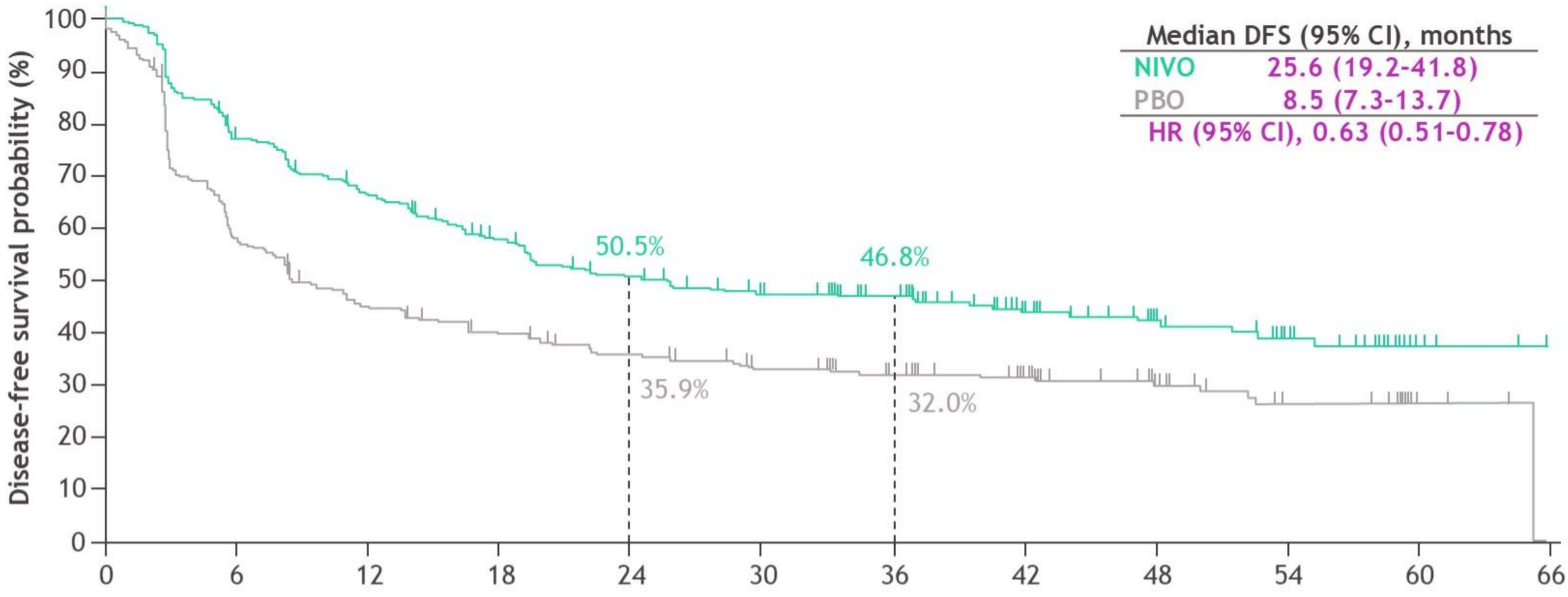
Post hoc analysis endpoints reported here:

- DFS in all randomized patients with MIBC, and in patients with MIBC according to prior NAC
- OS in all randomized patients with MIBC, patients with MIBC and tumor PD-L1 ≥ 1%, and MIBC according to prior NAC

[a]NCT02632409. [b]Defined by the percent of positive tumor cell membrane staining in a minimum of 100 evaluable tumor cells using the validated Dako PD-L1 IHC 28-8 pharmDx assay. [c]OS is being tested using a hierarchical procedure in each population (ITT and PD-L1 ≥ 1%), per the statistical analysis plan. OS data are from preplanned interim analyses for the ITT and PD-L1 ≥ 1% populations. OS follow-up is ongoing, as the prespecified statistical boundary for significance was not met at the time of these analyses.

Bajorin D, et al. *N Engl J Med* 2021;384:2102-2114.

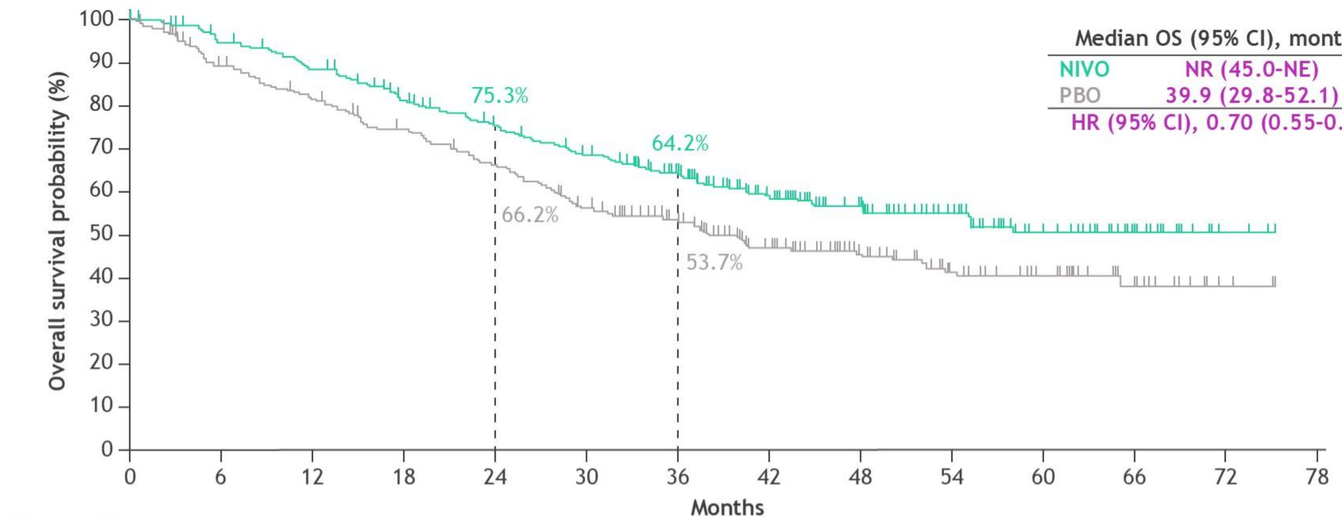
DFS: all randomized patients with MIBC



edian follow-up of 36.1 months in the ITT population and 34.5 months in the MIBC population.
alsky MD, et al. *J Clin Oncol* 2025;43:15-21.

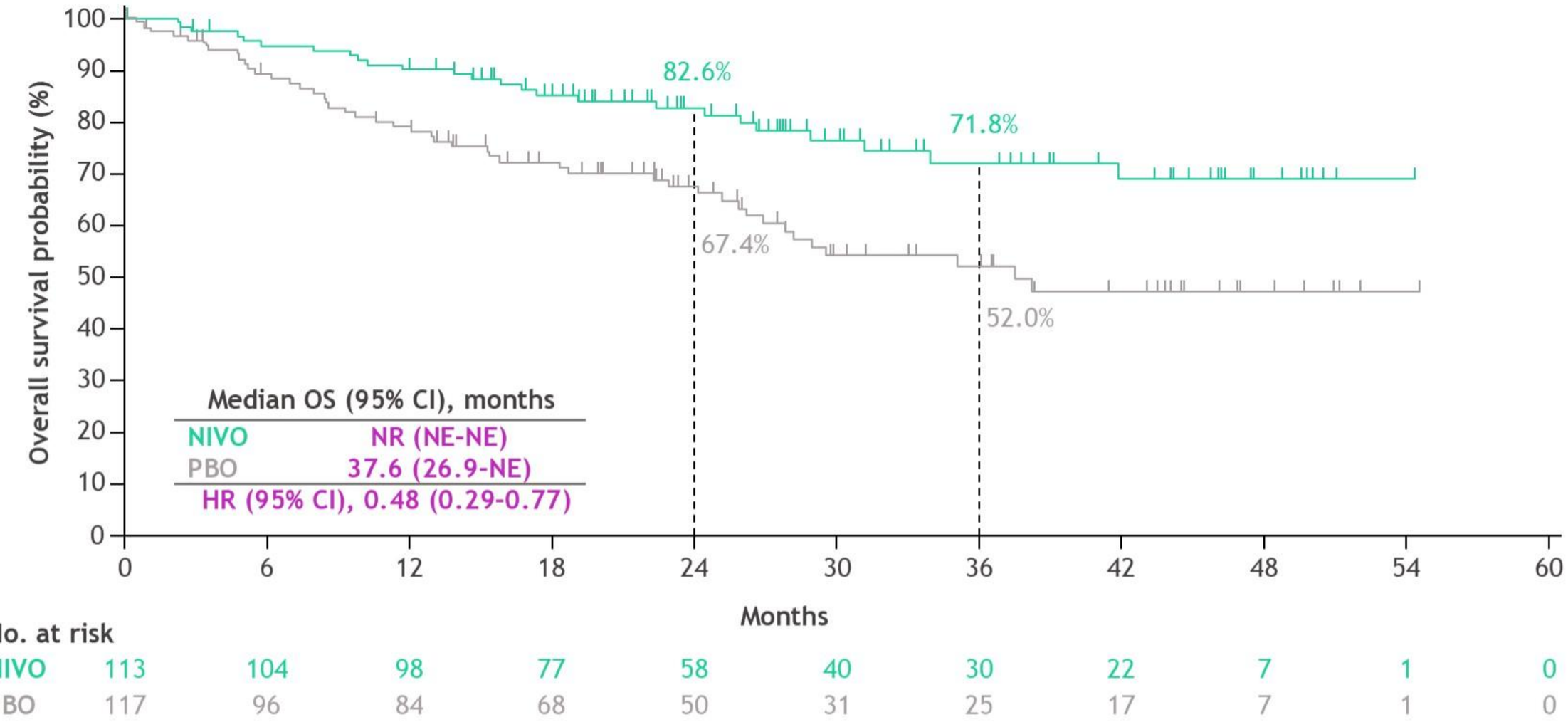
OSa: all randomized patients with MIBC

OS[a]: all randomized patients with 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.

OS[a]: all randomized patients with MIBC and tumor PD-L1 ≥ 1%



[a]Interim OS analysis.
Median follow-up of 36.1 months in the ITT population and 36.7 months in the MIBC and PD-L1 ≥ 1% population.

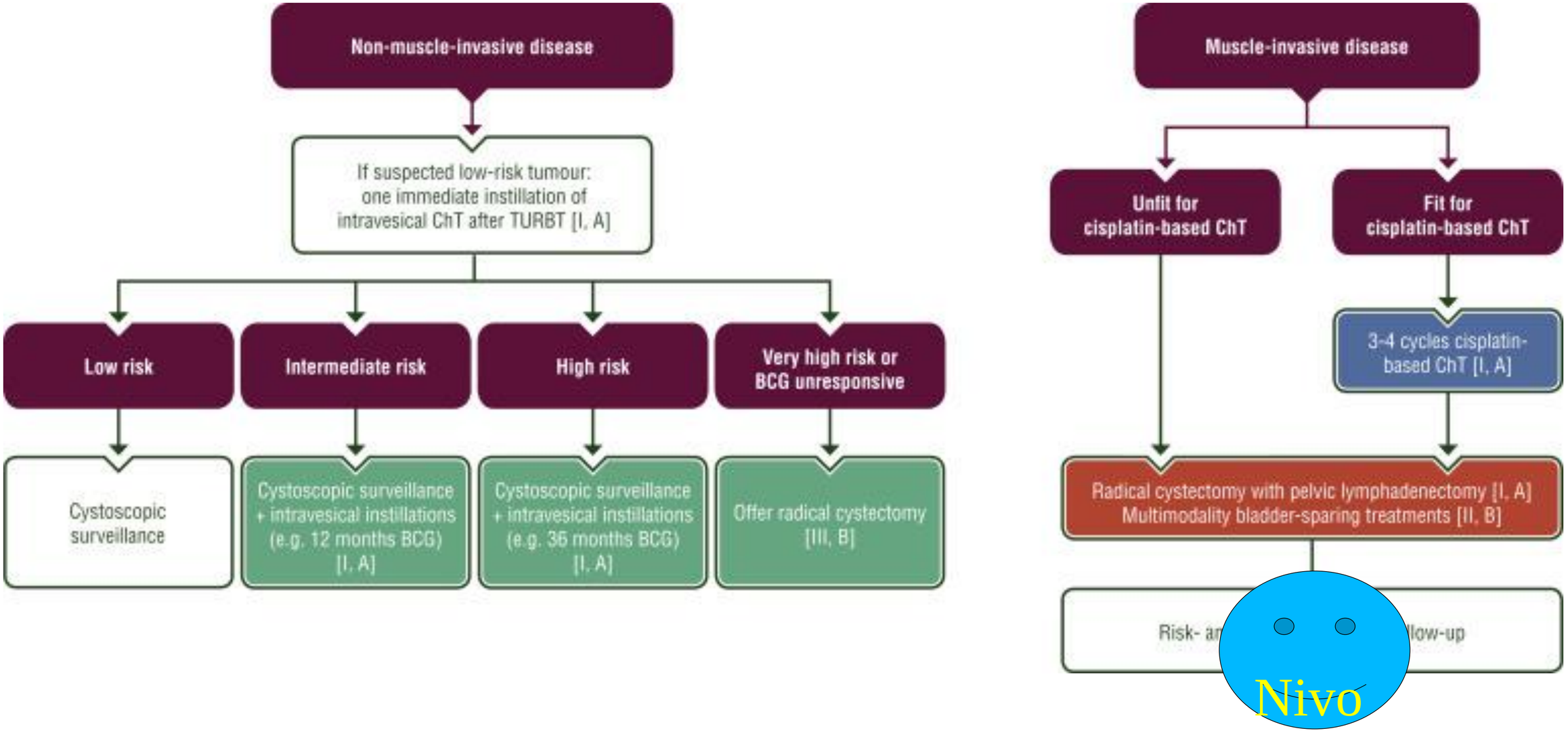
Summary

- With extended follow-up in CheckMate 274, adjuvant NIVO continued to show DFS benefits vs PBO in patients with MIBC, regardless of prior treatment with NAC[1,2]
- OS data from interim analyses favored adjuvant NIVO over PBO in the MIBC population, regardless of prior NAC, as well as in patients with MIBC and tumor PD-L1 expression ≥1%[2]
- No new safety signals were identified[1,2]
- The improveme…itional support for adjuvant NIVO as a stand…adical surgery and regardless of prior NAC
- Subcutaneous N…standard IV dosing and may provide an alter…[3-5]

El estudio CheckMate 274 ha redefinido la adyuvancia en cáncer urotelial músculo-invasivo, con nivolumab mostrando beneficio en supervivencia libre de enfermedad, pero aún sin madurez en OS.

Nivolumab tiene su valor, pero es crucial entender qué ha demostrado y qué no

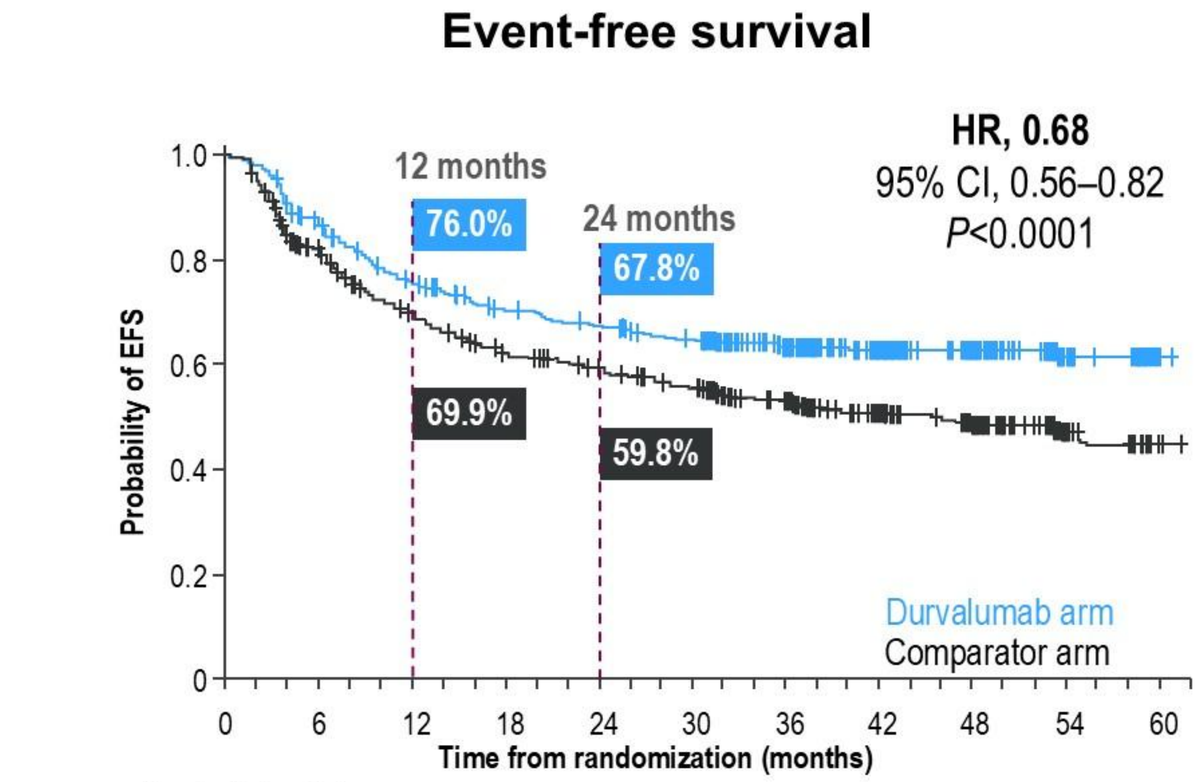
1. Bajorin D, et al. *N Engl J Med* 2021;384:2102-2114. 2. Galsky MD, et al. *J Clin Oncol* 2025;43:15-21. 3. Albigès L, et al. *Ann Oncol* 2025;36:99-107. 4. Lonardi S, et al. Poster presentation at the ASCO 2021 Annual Meeting; June 4-8, 2021; Virtual. Poster 2575. 5. Zhao Y, et al. Poster presentation at the SITC 2024 Annual Meeting; November 6-10, 2024; Houston, TX & Online. Poster 524.



ESMO Guidelines 2023

Background

- In NIAGARA, the addition of perioperative durvalumab to NAC demonstrated[1]:
  - Statistically significant and clinically meaningful 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 pathological complete response (pCR) rate
  - No delay to surgery and no impact on patients' ability to undergo/complete surgery
- Here, we report additional efficacy and safety results from NIAGARA



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

1. Powles T, et al. *N Engl J Med*. 2024;391:1773–1786.
EFS, event-free survival; HR, hazard ratio; MIBC, muscle-invasive bladder cancer; NAC, neoadjuvant chemotherapy; OS, overall survival.

NIAGARA: Study Design

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

R 1:1

Perioperative

	Neoadjuvant	Adjuvant
	Q3W, 4 cycles	Q4W, 8 cycles
Durvalumab arm (N=533)	Durvalumab 1500 mg IV + Gemcitabine + cisplatin	Durvalumab 1500 mg IV
Comparator arm (N=530)	Gemcitabine + cisplatin	No treatment

Radical cystectomy

Primary endpoints
- EFS
- pCR

Key secondary endpoint
- OS

Secondary endpoints
- Metastasis-free survival
- Disease-specific survival

Safety
- Immune-mediated AEs

Exploratory post-hoc analysis
- EFS by pCR
- OS by pCR

Full study design details are available in Powles T, et al. *N Engl J Med*. 2024;391:1773–1786.

ClinicalTrials.gov, NCT03732677; EudraCT number, 2018-001811-59.

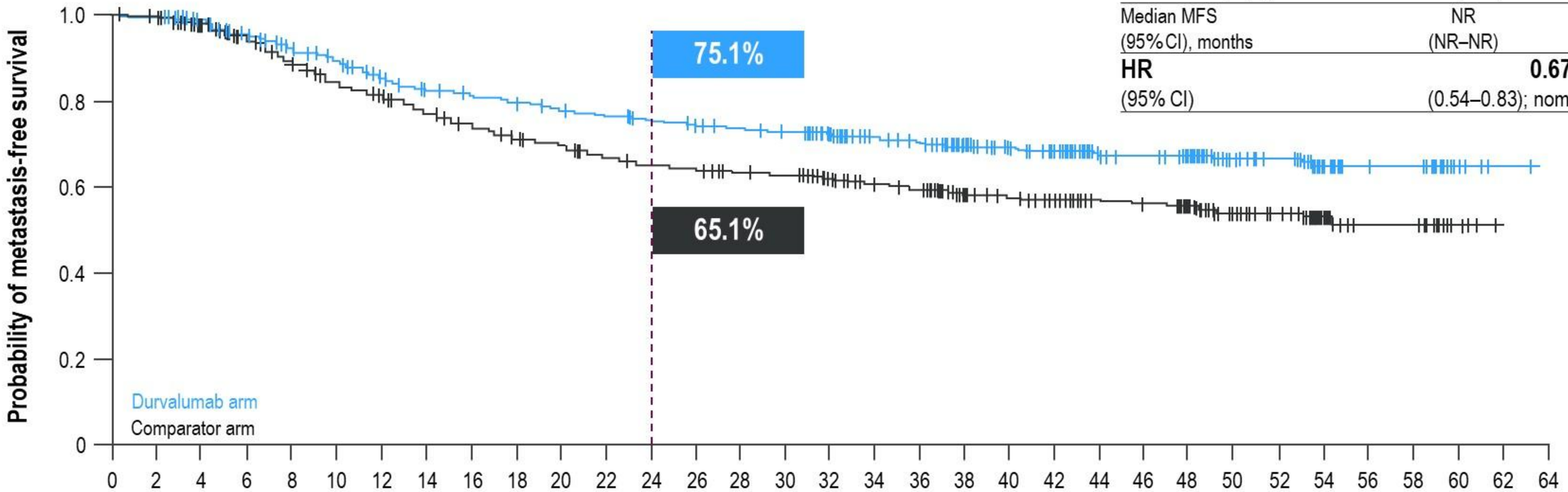
AE, adverse event; CrCl, creatinine clearance; EFS, event-free survival; IV, intravenous; MIBC, muscle-invasive bladder cancer; OS, overall survival; pCR, pathological complete response; Q3W, every 3 weeks; Q4W, every 4 weeks; R, randomized; RC, radical cystectomy; UC, urothelial carcinoma.

PRESENTED BY: Prof Matthew D. Galsky

NIAGARA: Metastasis-free Survival (ITT)

Perioperative D + NAC reduced the risk of distant metastases or death by 33%

	Durvalumab arm N=533	Comparator arm N=530
No. of events, n (%)	152 (28.5)	201 (37.9)
Median MFS (95% CI), months	NR (NR–NR)	NR (48.0–NR)
HR (95% CI)	**0.67** (0.54–0.83); nominal *P*<0.001	



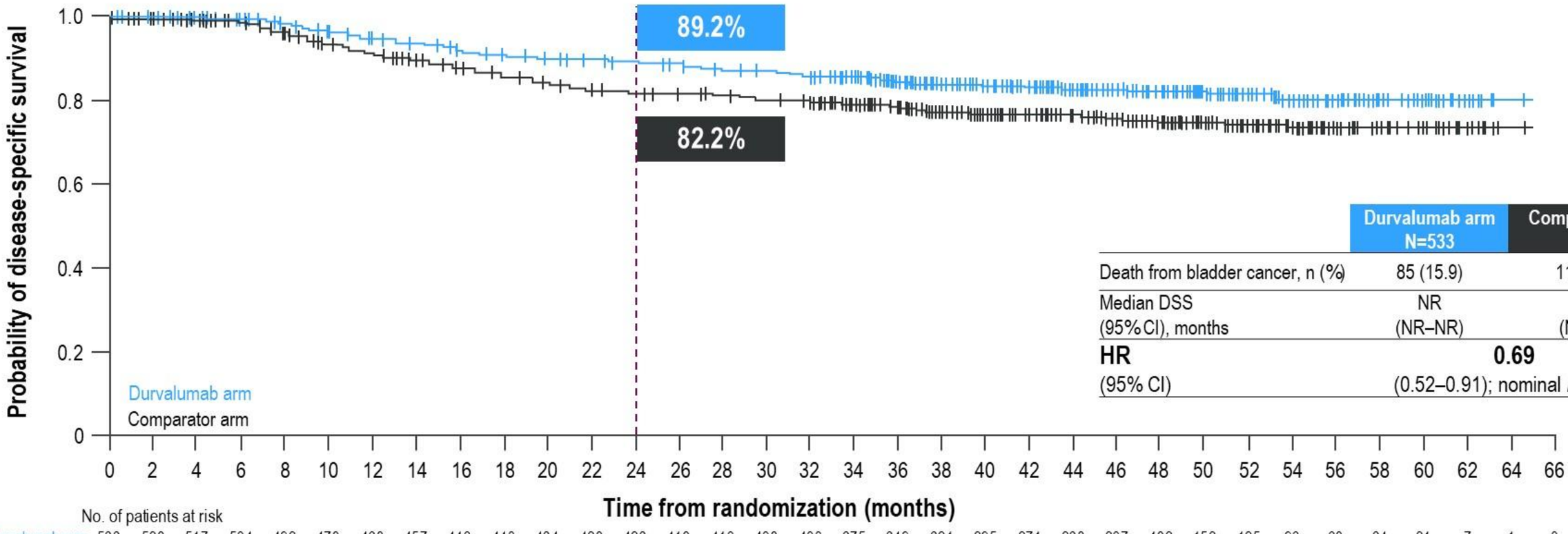
No. of patients at risk

Durvalumab arm	533	522	492	470	442	422	397	382	372	365	355	349	340	331	327	322	291	278	265	225	212	189	147	146	121	90	85	33	22	22	3	1	0
Comparator arm	530	498	473	443	409	384	365	350	332	315	309	293	286	279	274	271	240	231	224	184	178	163	136	134	99	72	64	27	21	19	3	0	0

Data cutoff Apr 29, 2024. Metastasis-free survival is defined as the time from date of randomization until the first recognition of distant metastases or death, whichever occurs first. Tick marks indicate patients with censored data. CI, confidence interval; D, durvalumab; HR, hazard ratio; ITT, intent-to-treat population; MFS, metastasis-free survival; NAC, neoadjuvant chemotherapy; NR, not reached.

NIAGARA: Disease-specific Survival (ITT)

Perioperative D + NAC reduced the risk of death from bladder cancer by 31%



	Durvalumab arm N=533	Comparator arm N=530
Death from bladder cancer, n (%)	85 (15.9)	114 (21.5)
Median DSS (95% CI), months	NR (NR–NR)	NR (NR–NR)
HR (95% CI)	**0.69** (0.52–0.91); nominal *P*=0.008	

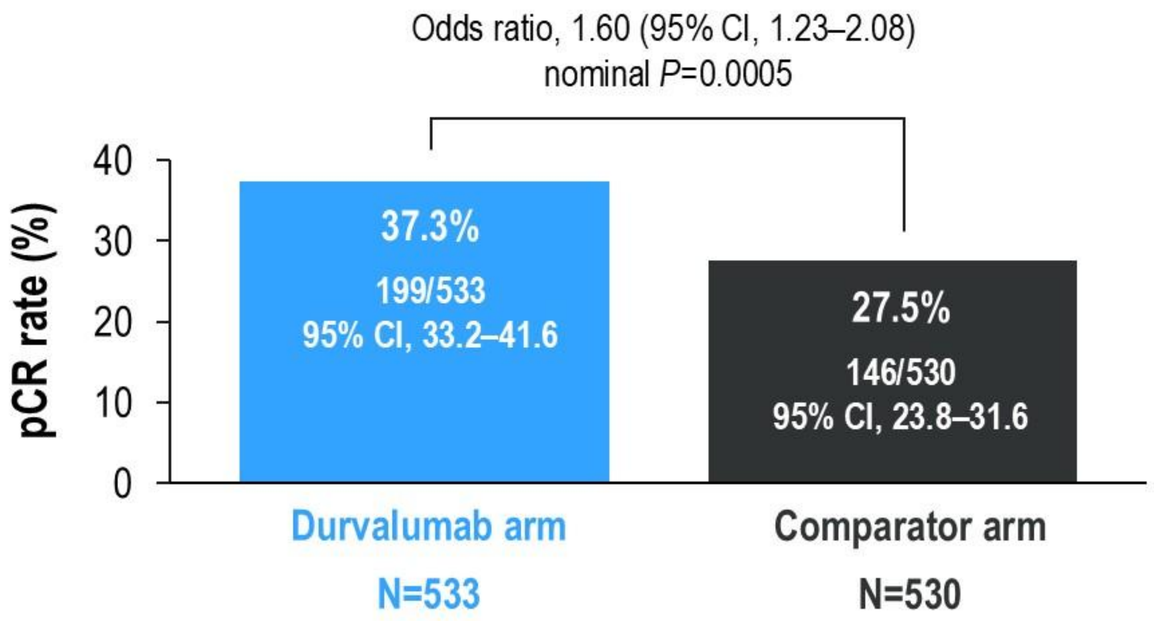
No. of patients at risk

Durvalumab arm	533	528	517	504	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	515	506	489	466	449	437	424	412	401	391	382	377	372	368	363	358	333	310	280	258	238	214	193	173	141	113	90	60	38	21	10	2	0

Data cutoff Apr 29, 2024. Disease-specific survival is defined as the time from the date of randomization until death due to bladder cancer. Tick marks indicate patients with censored data. CI, confidence interval; D, durvalumab; DSS, disease-specific survival; HR, hazard ratio; ITT, intent-to-treat population; NAC, neoadjuvant chemotherapy; NR, not reached.

NIAGARA: Pathological Complete Response (ITT)

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



From *N Engl J Med*, Powles T, Catto JWF, Galsky MD, et al. Perioperative Durvalumab with Neoadjuvant Chemotherapy in Operable Bladder Cancer, 391:1773–86. Copyright © (2024) Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

Further details are available in Powles T, et al. *N Engl J Med*. 2024;391:1773–1786.
Data cutoff Apr 29, 2024. Odds ratio, corresponding CI, and *P* value are obtained using logistic regression adjusted for the stratification factors (renal function, tumor 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.

NIAGARA: Patient Characteristics (pCR and Non-pCR Groups)

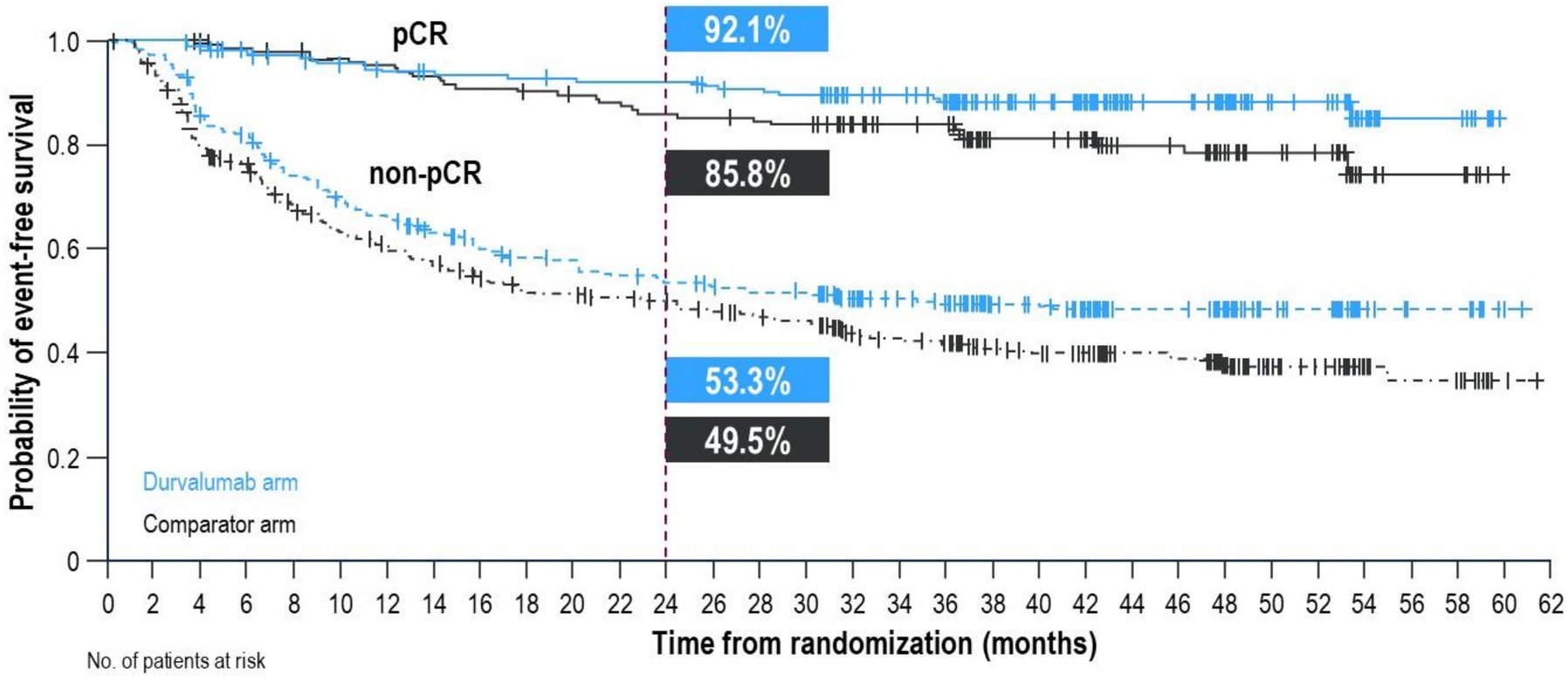
Demographic and disease characteristics were generally balanced between groups

Baseline characteristics		Patients with pCR		Patients without pCR	
		Durvalumab arm N=199	Comparator arm N=146	Durvalumab arm N=334	Comparator arm N=384
Age	Median (range), years	64.0 (34–83)	65.5 (37–83)	65.0 (35–84)	66.0 (32–82)
Sex, %	Male	87	79	79	83
Race, %	White	69	65	65	69
	Asian	26	27	30	28
	Black/Other	3	<1	2	1
	Not reported	3	8	3	3
ECOG PS, %	0	79	80	78	78
	1	21	20	22	22
Renal function, %	CrCl ≥60 mL/min	84	89	79	78
	CrCl ≥40–<60 mL/min	16	11	21	22
Tumor stage, %	T2N0	44	46	38	38
	>T2N0	56	54	62	62
Histology, %	UC	84	80	87	84
	UC with divergent differentiation or histologic subtypes	16	20	13	16
Regional lymph nodes, %	cN0	96	97	94	93
	cN1	4	3	6	7
PD-L1 expression*, %	TC/IC ≥25%	82	86	67	68
	TC/IC <25%	18	14	33	32

Data cutoff Apr 29, 2024. Exploratory post-hoc analysis. *Assessed with the VENTANA PD-L1 (SP263) Assay using the TC/IC25% algorithm; high PD-L1 expression was defined as ≥25% of TCs with any membrane staining or ICs staining for PD-L1 at any intensity. c, clinical; CrCl, creatinine clearance; ECOG PS, Eastern Cooperative Oncology Group performance status; IC, immune cell; PD-L1, programmed cell death ligand-1; TC, tumor cell; UC, urothelial carcinoma.

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

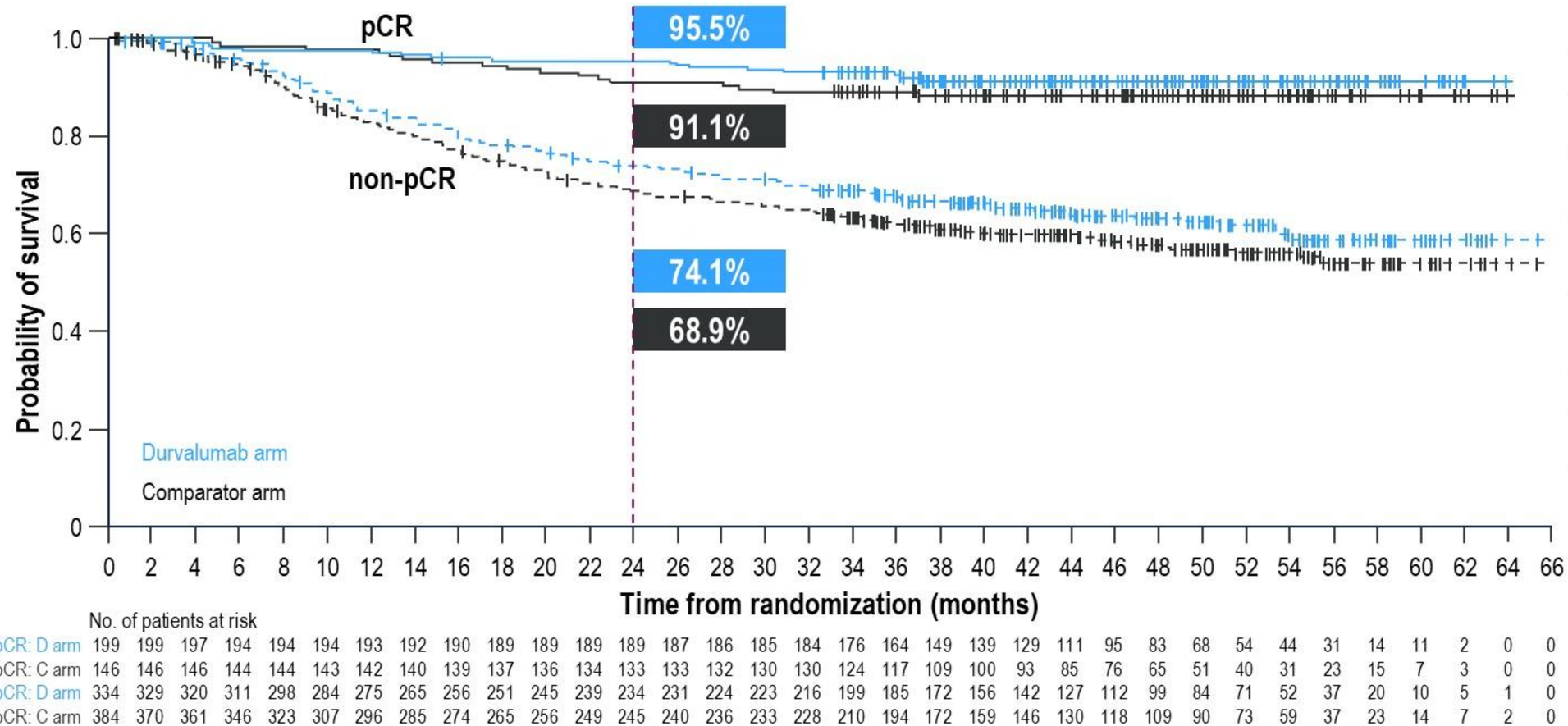
EFS HR	**0.68**
(95% CI)	(0.56–0.82)

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.

PRESENTED BY: Prof Matthew D. Galsky

NIAGARA: Overall Survival in pCR and Non-pCR Groups

Perioperative D + NAC improved OS in both groups



No. of patients at risk

pCR: D arm	199	199	197	194	194	194	193	192	190	189	189	189	189	187	186	185	184	176	164	149	139	129	111	95	83	68	54	44	31	14	11	2	0	0
pCR: C arm	146	146	146	144	144	143	142	140	139	137	136	134	133	133	132	130	130	124	117	109	100	93	85	76	65	51	40	31	23	15	7	3	0	0
non-pCR: D arm	334	329	320	311	298	284	275	265	256	251	245	239	234	231	224	223	216	199	185	172	156	142	127	112	99	84	71	52	37	20	10	5	1	0
non-pCR: C arm	384	370	361	346	323	307	296	285	274	265	256	249	245	240	236	233	228	210	194	172	159	146	130	118	109	90	73	59	37	23	14	7	2	0

pCR

	Durvalumab N=199	Comparator N=146
No. deaths, n (%)	17 (9)	17 (12)
Median OS (95% CI), months	NR (NR–NR)	NR (NR–NR)
OS HR (95% CI)	**0.72** (0.367–1.426)	

non-pCR

	Durvalumab N=334	Comparator N=384
No. deaths, n (%)	119 (36)	152 (40)
Median OS (95% CI), months	NR (NR–NR)	NR (53.9–NR)
OS HR (95% CI)	**0.84** (0.660–1.068)	

ITT

OS HR	**0.75**
(95% CI)	(0.59–0.93)

Data cutoff Apr 29, 2024. Exploratory post-hoc analysis. Tick marks indicate patients with censored data. C, comparator; D, durvalumab; HR, hazard ratio; ITT, intent-to treat; NAC, neoadjuvant chemotherapy; pCR, pathological complete response; OS, overall survival.

PRESENTED BY: Prof Matthew D. Galsky

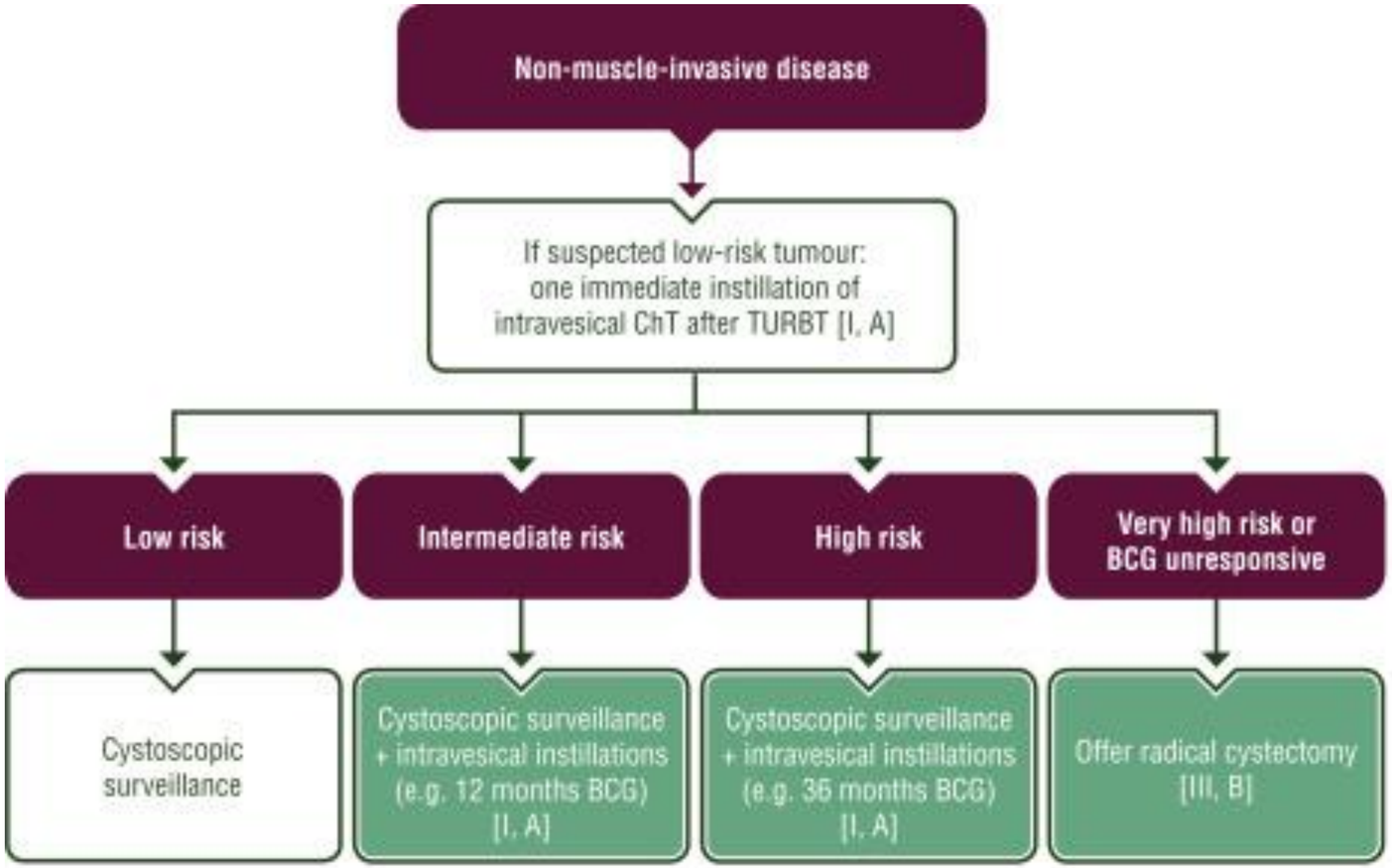
Conclusions

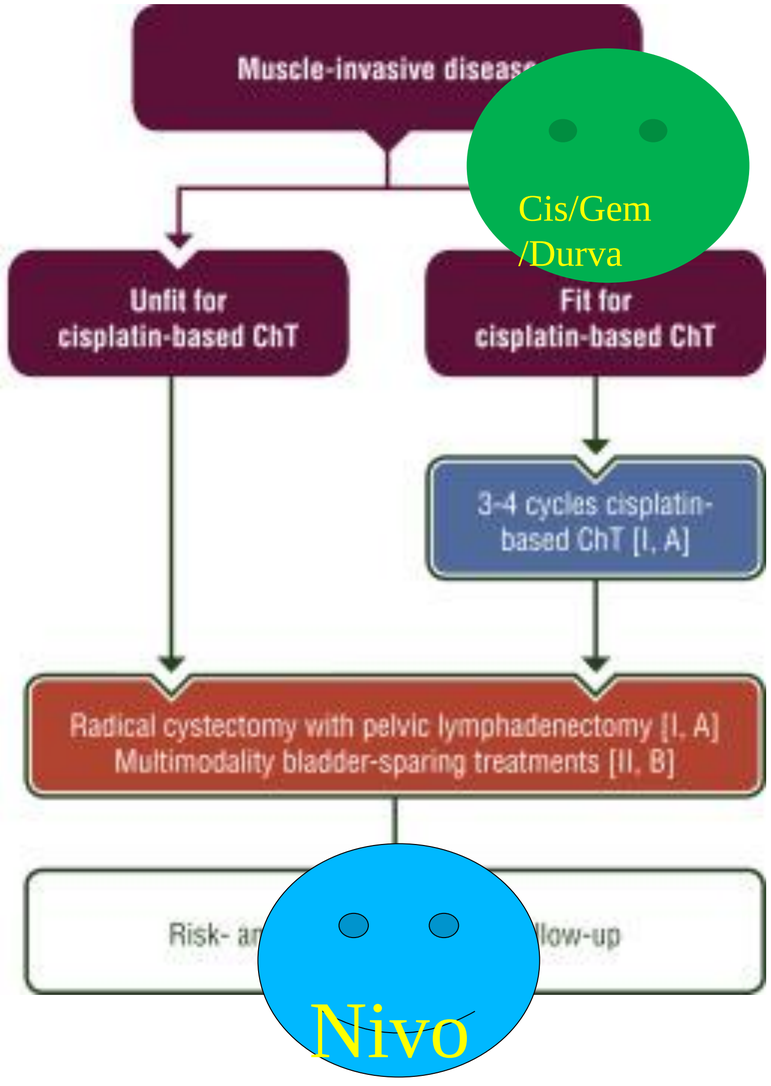
- NIAGARA demonstrated statistically significant and clinically meaningful improvement in EFS (HR, 0.68; 95% CI, 0.56–0.82) and OS (HR, 0.75; 95% CI, 0.59–0.93), with a 10% improvement in pCR rate[1]
- In the durvalumab arm, the risk of an MFS event was reduced by 22%, and the risk of a DSS event w
- Perioperative du and non-pCR groups in an exploratory post-hoc analysis
- imAEs were mostly low grade and consistent with the known profile of durvalumab

NIAGARA tiene la ventaja de aumentar la elegibilidad para cisplatino gracias al split-dose, permitiendo tratar a más pacientes

This additional NIAGARA data further supports perioperative durvalumab with NAC as a potential new treatment for patients with cisplatin-eligible MIBC

1. Powles T, et al. *N Engl J Med*. 2024;391:1773–1786. CI, confidence interval; DSS, disease-specific survival; EFS, event-free survival; HR, hazard ratio; imAE, immune-mediated adverse event; MFS, metastasis-free survival; MIBC, muscle-invasive bladder cancer; NAC, neoadjuvant chemotherapy; OS, overall survival; pCR, pathological complete response.





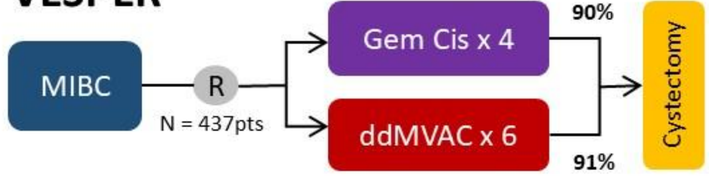
ESMO Guidelines 2023

NIAGARA in the context of currently available treatment options

NIAGARA

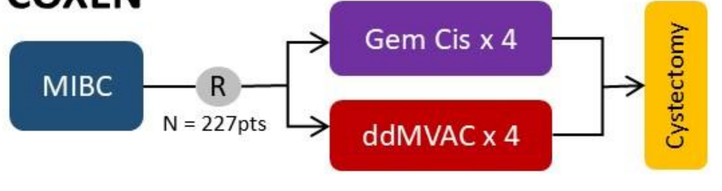
DGC “sandwich” vs GC
EFS benefit at 2 yrs: 8%
OS benefit at 2 yrs: 7%

VESPER

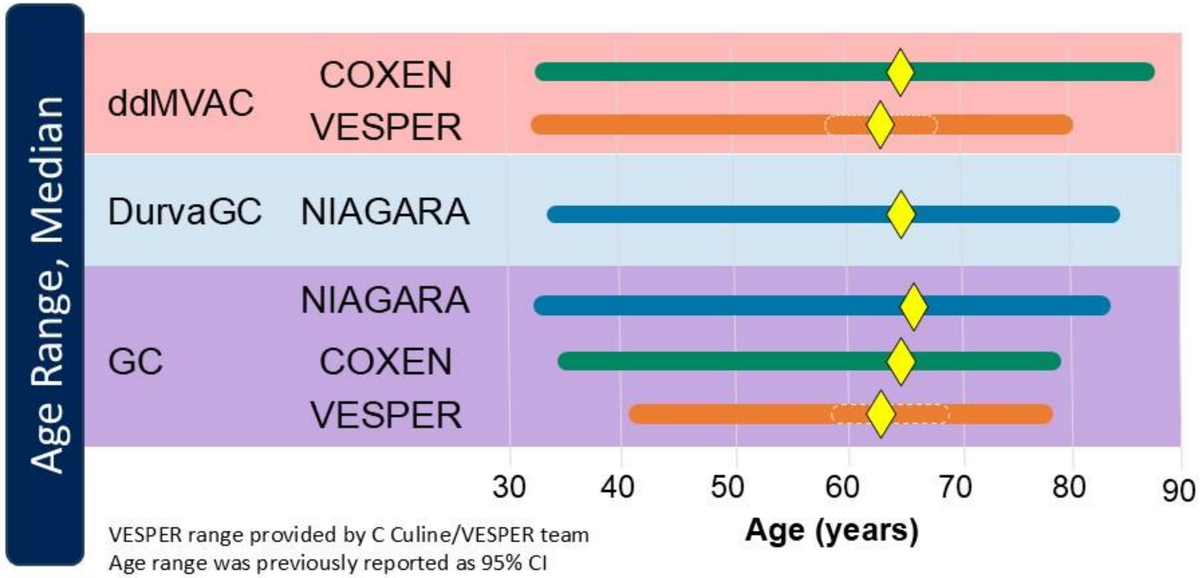


ddMVAC vs GC
EFS benefit at 5 yrs: 9%
OS benefit at 5 yrs: 9%

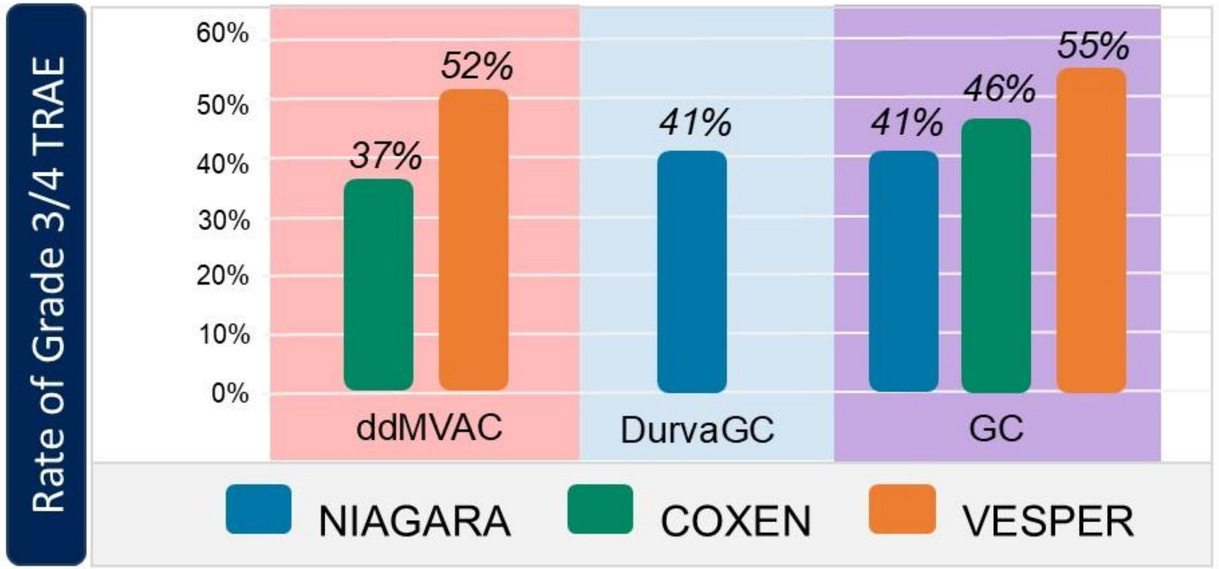
COXEN



ddMVAC vs GC
EFS benefit at 5 yrs: 4%
OS benefit at 5 yrs: 7%
Differences were not statistically significant



VESPER range provided by C Culine/VESPER team
Age range was previously reported as 95% CI



PRESENTED BY: Elizabeth Plimack, MD MS FASCO

NIAGARA Galsky et al. ASCO GU 2025
Pfister et al. The Lancet Onc 25, 255-264 (2024).
Flaig et al. Eur Urol 84, 341-347 (2023).

Take Home: 2 options for clinic on Monday

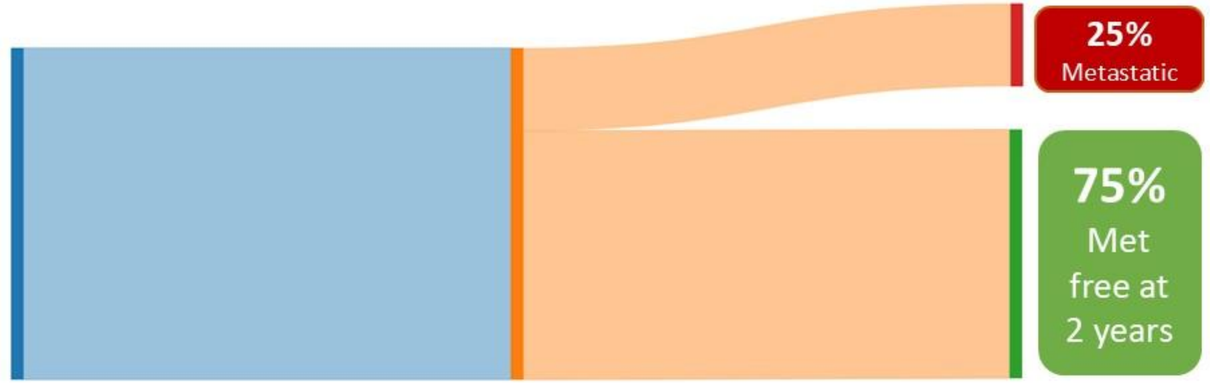
Neoadjuvant ddMVAC

Neoadj ddMVAC **Observation**

Benefits of risk adapted approach using ddMVAC

- **≥ypT2 35%** patients would qualify for and may gain additional benefit from adjuvant nivolumab or the MODERN trial
- Avoids overtreatment and IO toxicity for **<ypT2 65%**
- Cost and time saving

"Sandwich" Approach with GC Durva



Neoadj Gem Cis + Durva **Durvalumab x 8**

Benefits of a "sandwich" approach

- If using Gem Cis, adding durvalumab pre and post adds benefit in direct and cross trial comparison
- Adjuvant durvalumab may benefit some of the ~10% of <ypT2 who develop metastases but would not have qualified for adjuvant nivolumab

PRESENTED BY: Elizabeth Plimack, MD MS FASCO

NIAGARA Galsky et al. ASCO GU 2025
VESPER Pfister et al. LBA4507, ASCO 2023
S Culine and VESPER team personal communication

ASCO Genitourinary Cancers Symposium

Safety and Efficacy of Durvalumab (MEDI 4736) in combination with neoadjuvant chemotherapy (Gemcitabine / Cisplatin or Carboplatin) in patients with operable high-risk upper tract urothelial carcinoma

Nadine HOUEDE[1,2], Thierry CHEVALLIER[3,4,], Loïc JAFFRELOT[5], Constance THIBAULT[6], Yann NEUZILLET[7], Christine ABRAHAM[8], Alexandra MASSON-LECOMTE[9], Gwenaelle GRAVIS[10], Géraldine PIGNOT[11], Sophie TARTAS[12], Damien POUESSEL[13], Brigitte LAGUERRE[14], François AUDENET[6], Evanguelos XYLINAS[15], Guillaume LUQUIENS[3], Morgan ROUPRET[16]

[1]Department of Oncology, CHU Nîmes, Univ. Montpellier, Nîmes, France; [2]INSERM U1194, Université de Montpellier CHU Nîmes, [3]Department of Biostatistics, Epidemiology, Public Health and Innovation in Methodology30029 Nîmes, France; Univ. Montpellier, [4]NSERM, UMR 1302, Institute Desbrest of Epidemiology and Public Health, Montpellier, France; [5]AP-HP, Oncology, Pitie-Salpetriere Hospital, F-75013 PARIS, France; [6]Department of medical oncology, Hôpital Européen Georges Pompidou, AP-HP, University Paris Cité, Paris, France, Institut du Cancer Paris CARPEM, AP-HP Centre, Université Paris Cité, Paris; [7]Foch Hospital, Department of Urology, University of Paris-Saclay – UVSQ, Suresnes, France; [8]Foch Hospital, Department of Oncology, Suresnes, France; [9]Service d'Urologie Hôpital Saint Louis, Université Paris Cité, Service de Recherche en Hémato-Immunologie CEA - INSERM U976 HIPI; [10]Institut Paoli-Calmettes, Department of Medical Oncology, Aix Marseille Univ, INSERM, CNRS, CRCM, Immunity and Cancer Team, Marseille, France; [11]Department of Surgical Oncology, Paoli-Calmettes Institute, Marseille, France.[12]Department of Medical Oncology, IMMUCARE, Centre Hospitalier Lyon Sud, Institut de Cancérologie des Hospices de Lyon (IC-HCL), Pierre-Bénite, France; [13]Department of Medical Oncology, Institut Universitaire du Cancer -Toulouse- Oncopole, Toulouse, France; [14]Department of Medical Oncology, Centre Eugene - Marquis, Rennes, France; [15]Department of Urology, Bichat-Claude Bernard Hospital, APHP, Paris University; [16]Sorbonne University, GRC 5 Predictive Onco-Uro, AP-HP, Urology, Pitie-Salpetriere Hospital, F-75013 PARIS, France

PRESENTED BY: Houede N. MD PhD

Methods

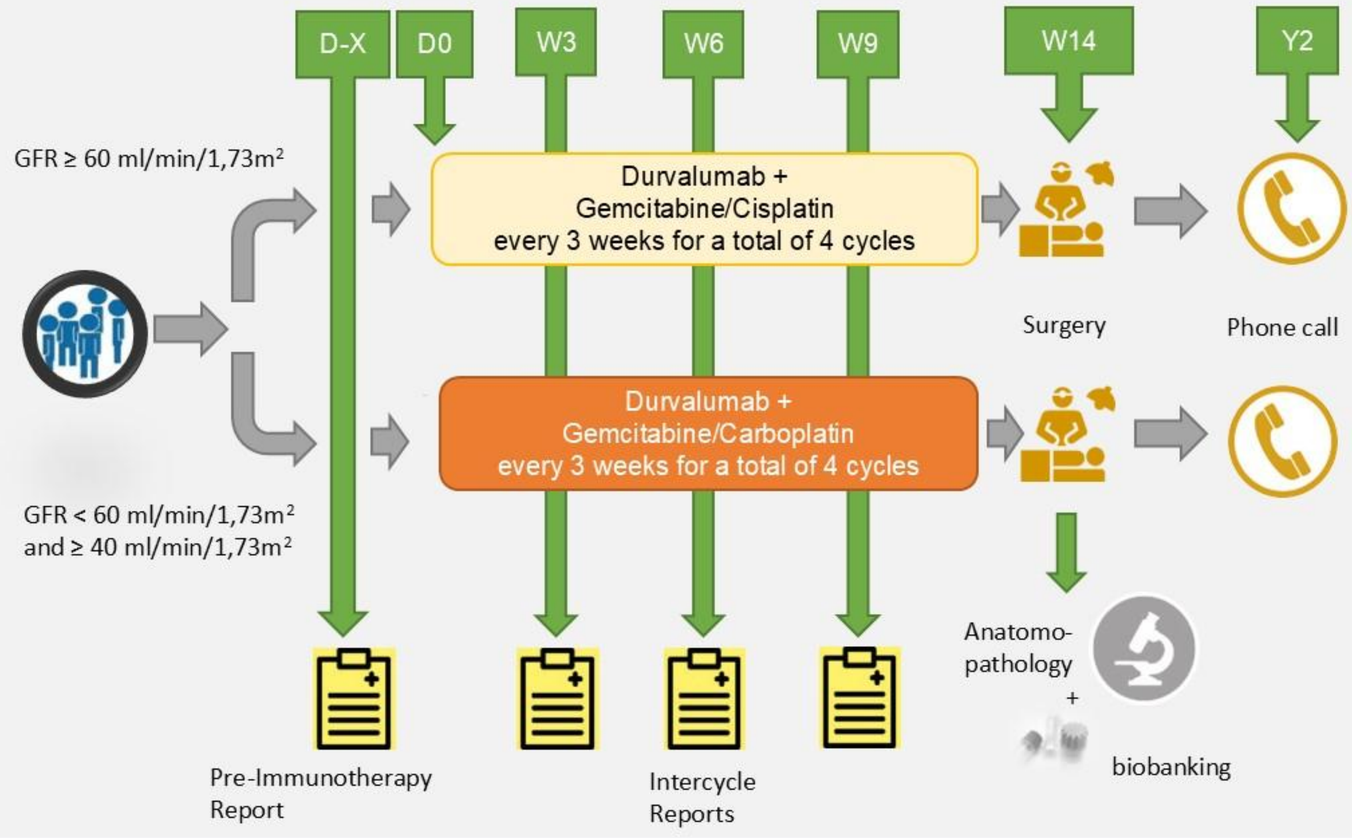
- iNDUCT – GETUG V 08 phase 2 clinical trial

Inclusions criteria:

- ECOG status ≤1
- Presence of either:
  - o High-grade disease on tumor biopsy or High-grade disease on urine cytology AND /OR
  - o Infiltrative aspect of renal pelvis/ureteral wall on imaging with negative cystoscopy.
- cTNM: ≤T3, ≤N1
- M0

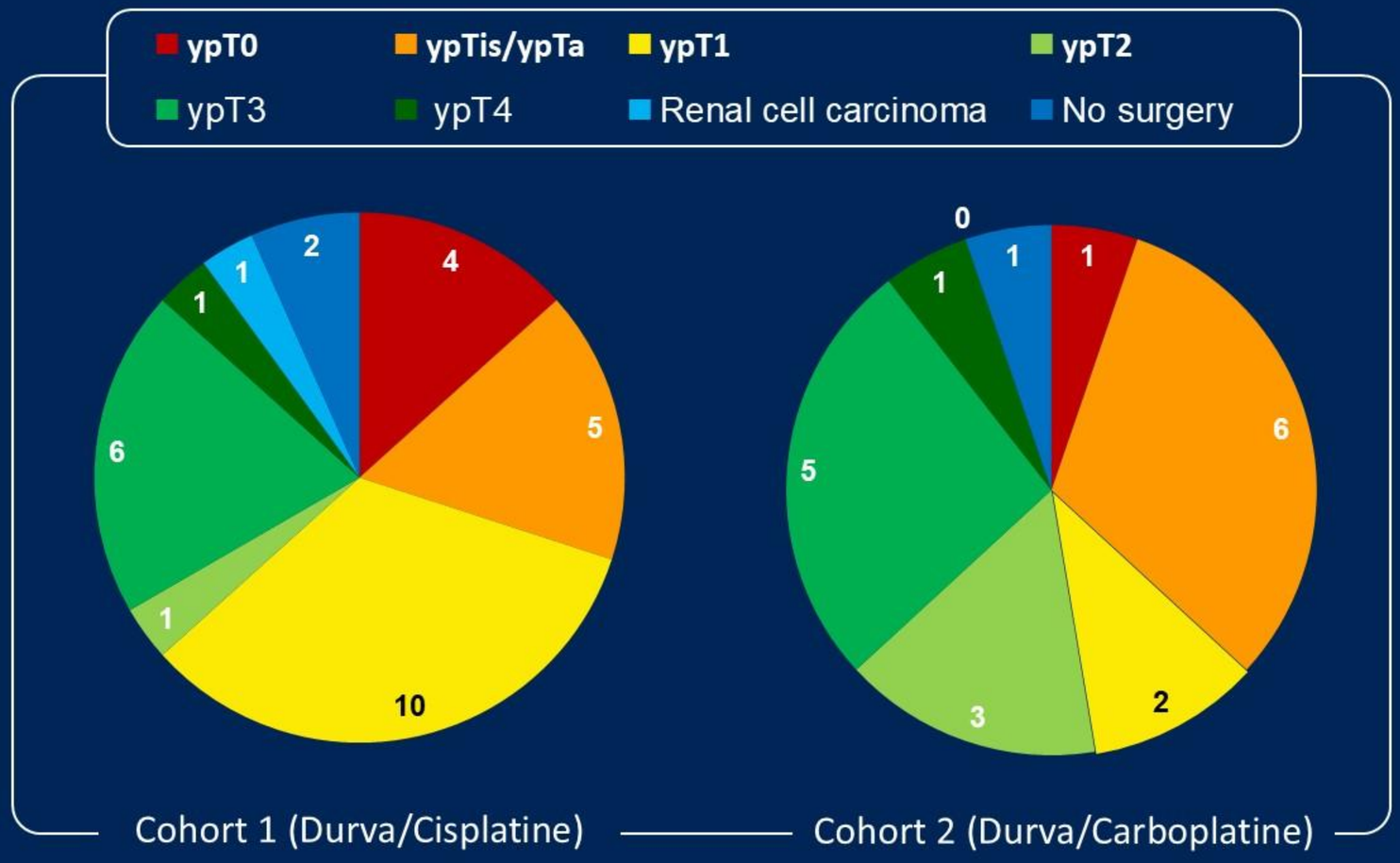
Primary endpoint:

- Rate of ypT0



Results

- Pathological response



	Cohort 1 (Durva /Cisplatine) (30)	Cohort 2 (Durva /Carboplatine) (19)
Pathological tumor stage at surgery No. (%)		
ypT0	**4 (13%) [95 CI 5%-30%]**	**1 (5%) [95 CI 1%-25%]**
ypTis/ypTa	5 (17%)	6 (31%)
ypT1	10 (34%)	2 (12%)
ypT2	1 (3%)	3 (16%)
ypT3	6 (20%)	5 (26%)
ypT4	1 (3%)	1 (5%)
Renal cell carcinoma	1(3%)	0
No surgery	2 (7%)	1 (5%)
Nodal status at surgery No. (%)		
Nx	8 (30%)	7 (39%)
N0	18 (67%)	9 (50%)
N1	0	2 (11%)
N2	1 (3%)	0 (%)

Key Points

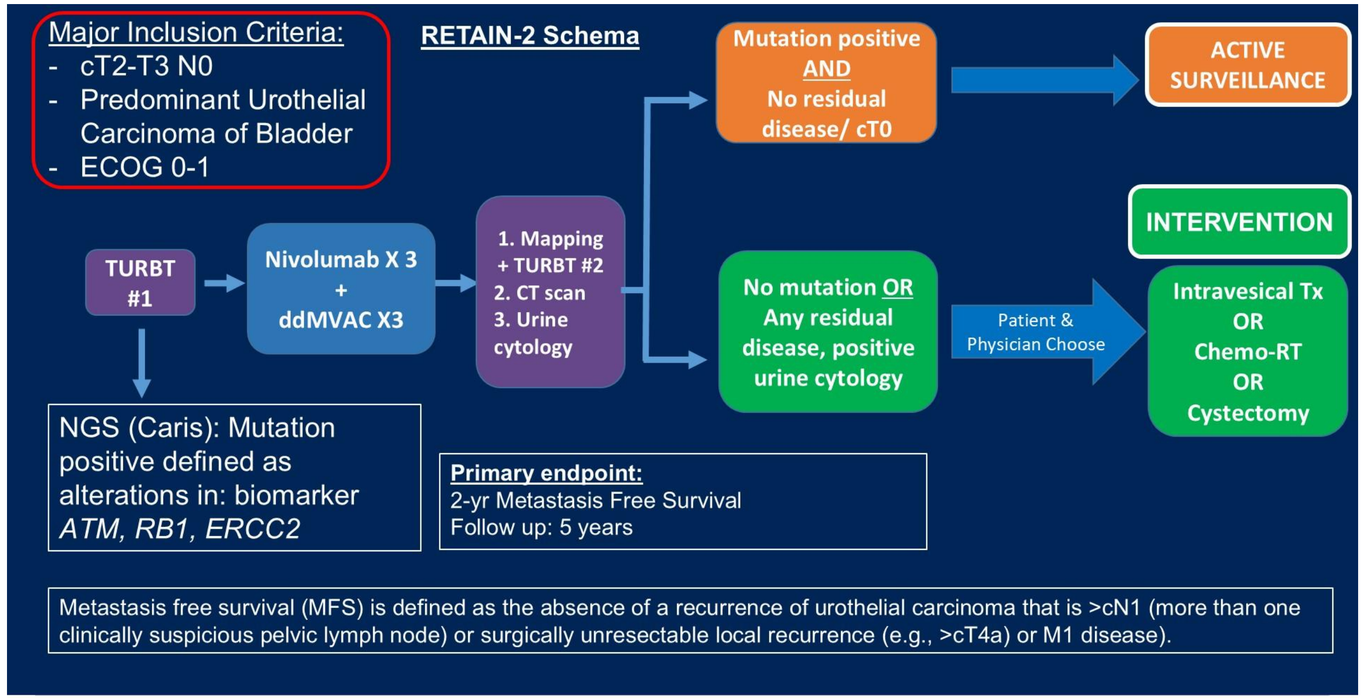
- First completed neoadjuvant phase 2 clinical trial in UTUC combining immunotherapy and platinum-based chemotherapy
- This combination is safe and do not impact negatively surgery
- Encouraging results in terms of residual disease, mainly when cisplatin-based chemotherapy is used
- Will follow a phase 3 comparing chemotherapy alone vs chemotherapy + immunotherapy: **iNDUCT-3** *(grant PHRC-K 2024 & MERCK sponsor)*

ASCO Genitourinary Cancers Symposium

A phase 2 trial of risk enabled therapy after neoadjuvant chemo-immunotherapy for muscle-invasive bladder cancer: RETAIN-2 Interim results

Pooja Ghatalia[1], Eric Ross[1], Matthew R. Zibelman[1], Fern Anari[1], Philip Abbosh[1], William J Tester[2], Patrick Mille[2], Tracy Rose[3], Suzanne Cole[4], James R. Mark[2], Rosalia Viterbo[1], Erika Jerome[1], Eric M. Horwitz[1], Mark Hallman[1], Andres Correa[1], Marc C. Smaldone[1], Robert Uzzo[1], David Chen[1], Alexander Kutikov[1], Elizabeth R. Plimack[1], Daniel M. Geynisman[1]

[1]*Fox Chase Cancer Center*
[2]*Thomas Jefferson University Hospital*
[3]*University of North Carolina- Chapel Hill*
[4]*UT Southwestern Medical Center*



ASCO Genitourinary Cancers Symposium #GU25 PRESENTED BY: Pooja Ghatalia, MD
Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org.
ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

Results: Baseline Characteristics

Characteristic	N = 71	(%)
Age		
Median	69	
Range	68-86	
Gender		
Male	55	77%
Female	16	23%
ECOG PS		
0	57	80%
1	14	20%
Histology		
Pure UC	48	68%
UC/Variant histology	23	32%
Clinical Stage		
cT2	41	58%
cT3	30	42%
Mutation		
positive	31	44%
negative	40	56.3%

Results: Baseline Characteristics

Characteristic	N = 71	(%)
Age		
Median	69	
Range	68-86	
Gender		
Male	55	77%
Female	16	23%
ECOG PS		
0	57	80%
1	14	20%
Histology		
Pure UC	48	68%
UC/Variant histology	23	32%
Clinical Stage		
cT2	41	58%
cT3	30	42%
Mutation		
positive	31	44%
negative	40	56.3%

Results: Baseline Characteristics

Characteristic	N = 71	(%)
Age		
Median	69	
Range	68-86	
Gender		
Male	55	77%
Female	16	23%
ECOG PS		
0	57	80%
1	14	20%
Histology		
Pure UC	48	68%
UC/Variant histology	23	32%
Clinical Stage		
cT2	41	58%
cT3	30	42%
Mutation		
positive	31	44%
negative	40	56.3%

Results: Baseline Characteristics

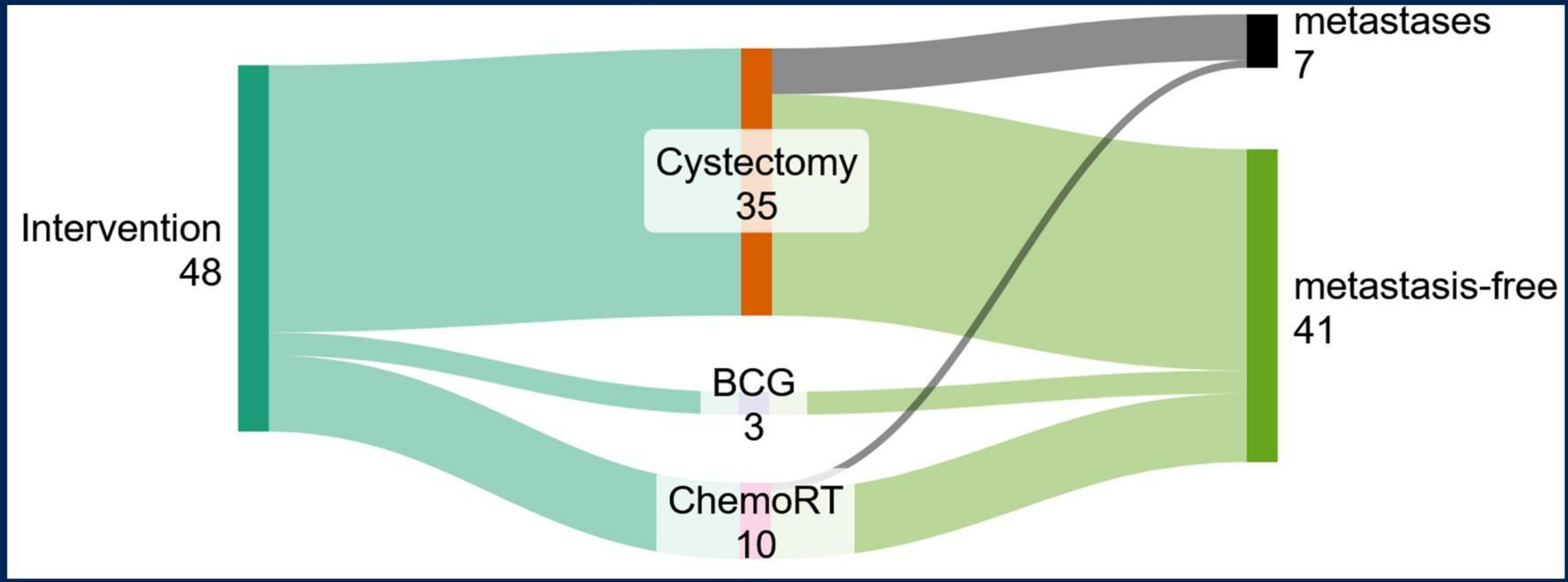
Characteristic	N = 71	(%)
Age		
Median	69	
Range	68-86	
Gender		
Male	55	77%
Female	16	23%
ECOG PS		
0	57	80%
1	14	20%
Histology		
Pure UC	48	68%
UC/Variant histology	23	32%
Clinical Stage		
cT2	41	58%
cT3	30	42%
Mutation		
positive	31	44%
negative	40	56.3%

Safety

- Grade 3/4 TRAE in 19% patients
- 2 deaths with ddMVAC/nivolumab after completing 3 cycles
  - Multi-organ failure
  - AKI
- 1 death in chemoRT patient likely related to pneumonitis
  - Pneumonitis within 1-2 months of starting chemoRT (with 5FU/mitomycin)

Results: Intervention

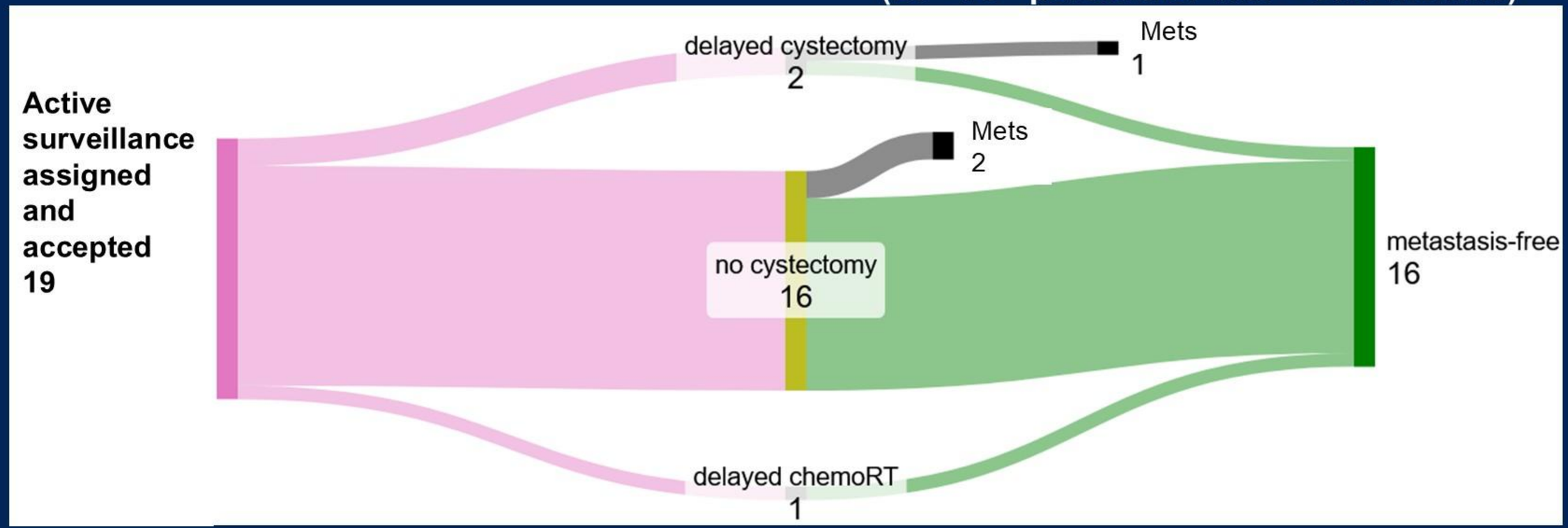
Median follow-up: 21.7 months
(25th-75th percentile: 13.6 – 30.3 months)



- **Among cystectomy pts, 40% are ypT0; 63% are ≤ ypT1**
- **Among intervention accepted pts, 85% are metastasis-free**

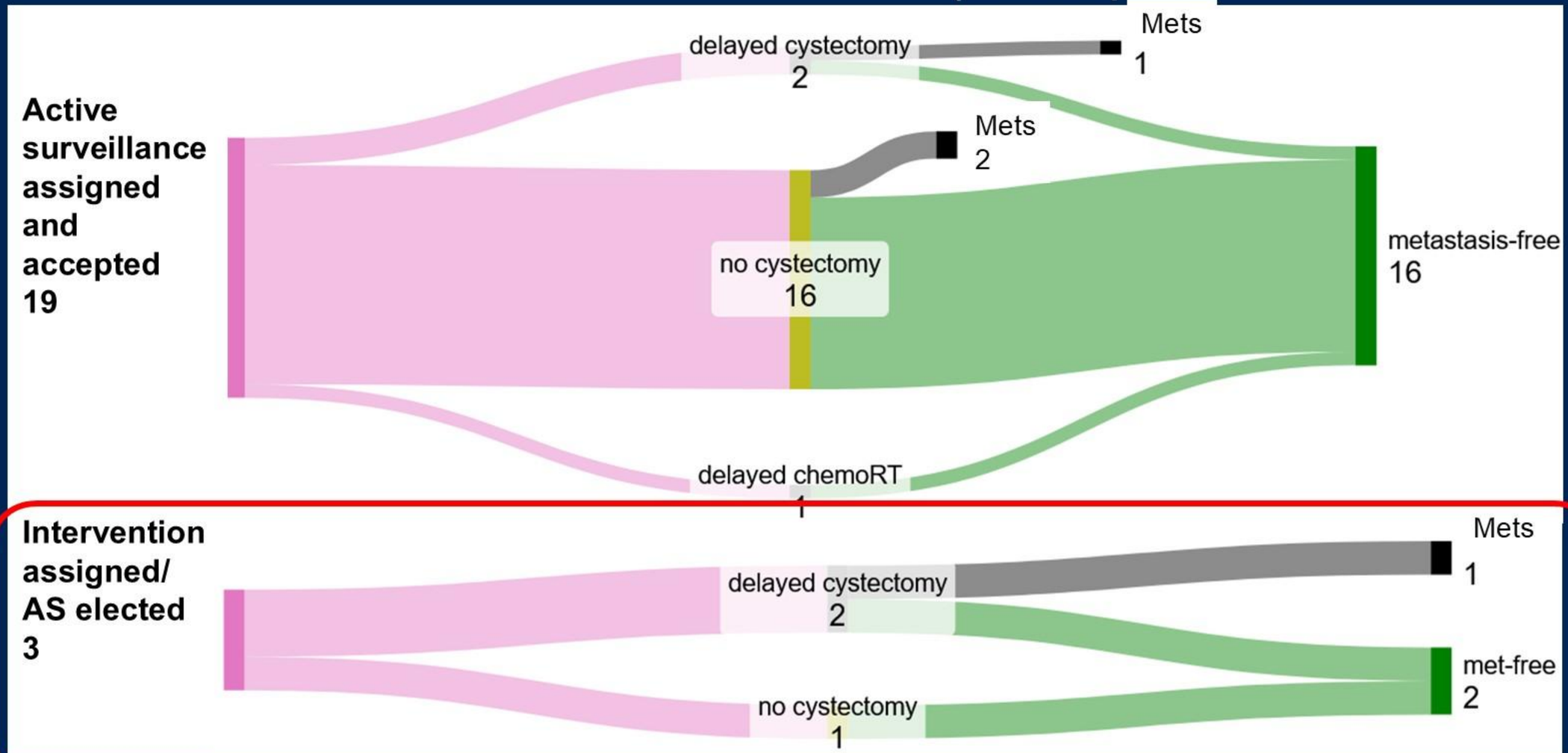
Results: Active Surveillance

Median follow-up: 21.7 months
(25th-75th percentile: 13.6 – 30.3 months)



Results: Active Surveillance

Median follow-up: 21.7 months
(25th-75th percentile: 13.6 – 30.3 months)

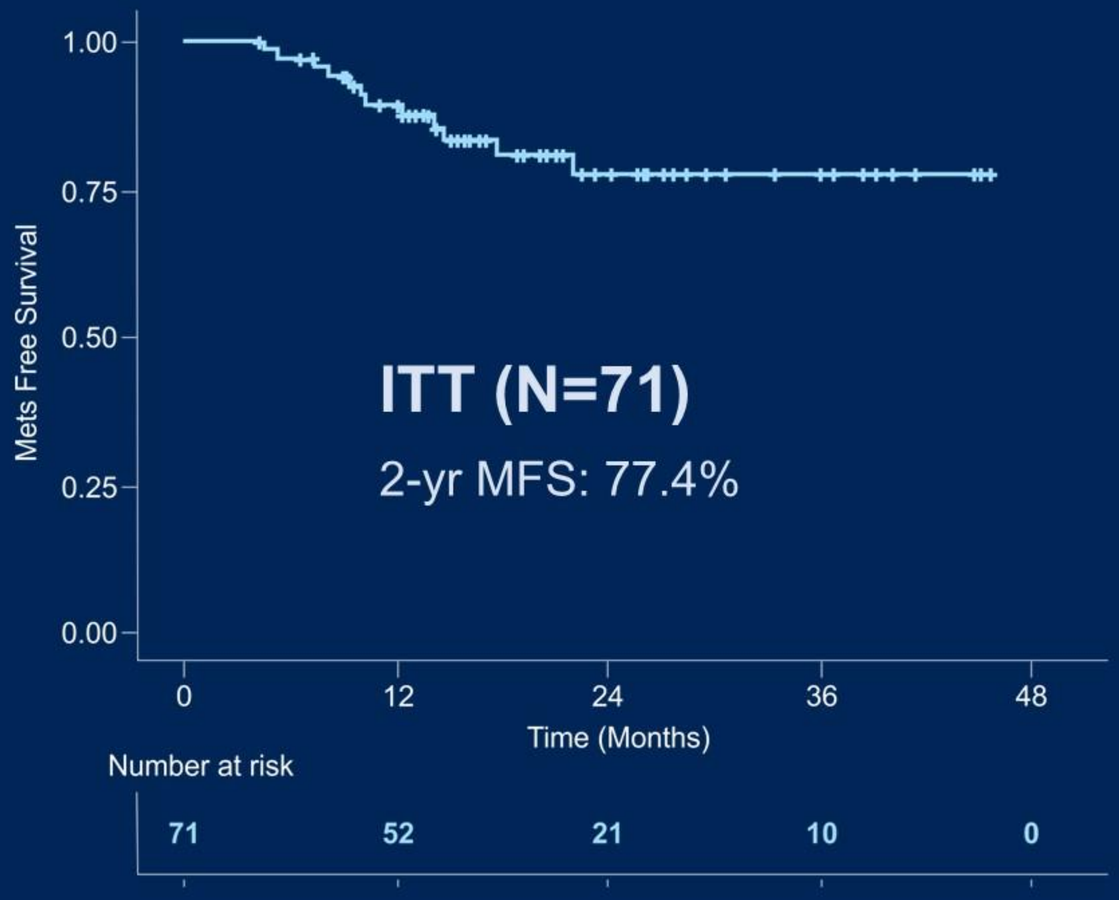


Among AS pts, 82% are metastases-free, 60% metastases-free and with an intact un-radiated bladder

Outcomes of patients on Active Surveillance

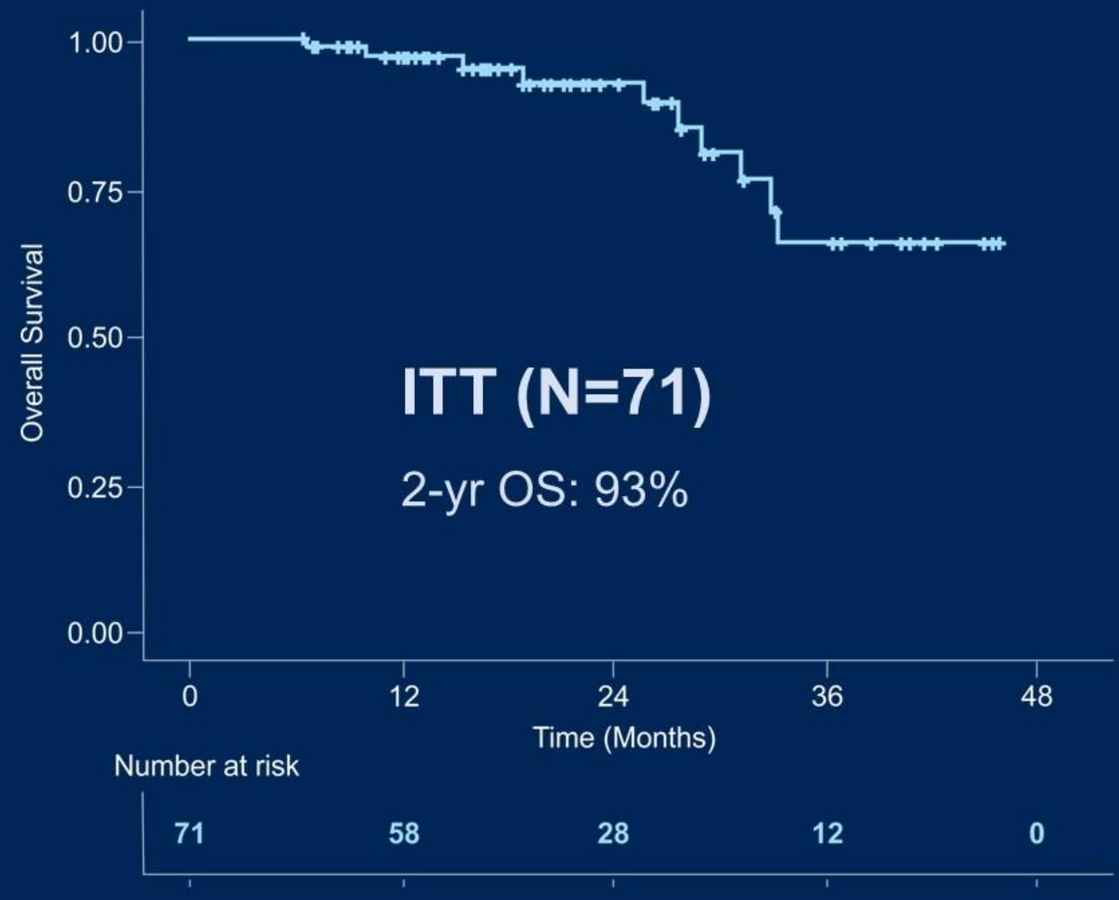
Median follow-up: 21.7 months (25th-75th percentile: 13.6 – 30.3 mo)

Interim Results: OS and MFS in ITT



ITT (N=71)

2-yr MFS: 77.4%



ITT (N=71)

2-yr OS: 93%

Median follow-up: 21.7 months (25th-75th percentile: 13.6 – 30.3 months)

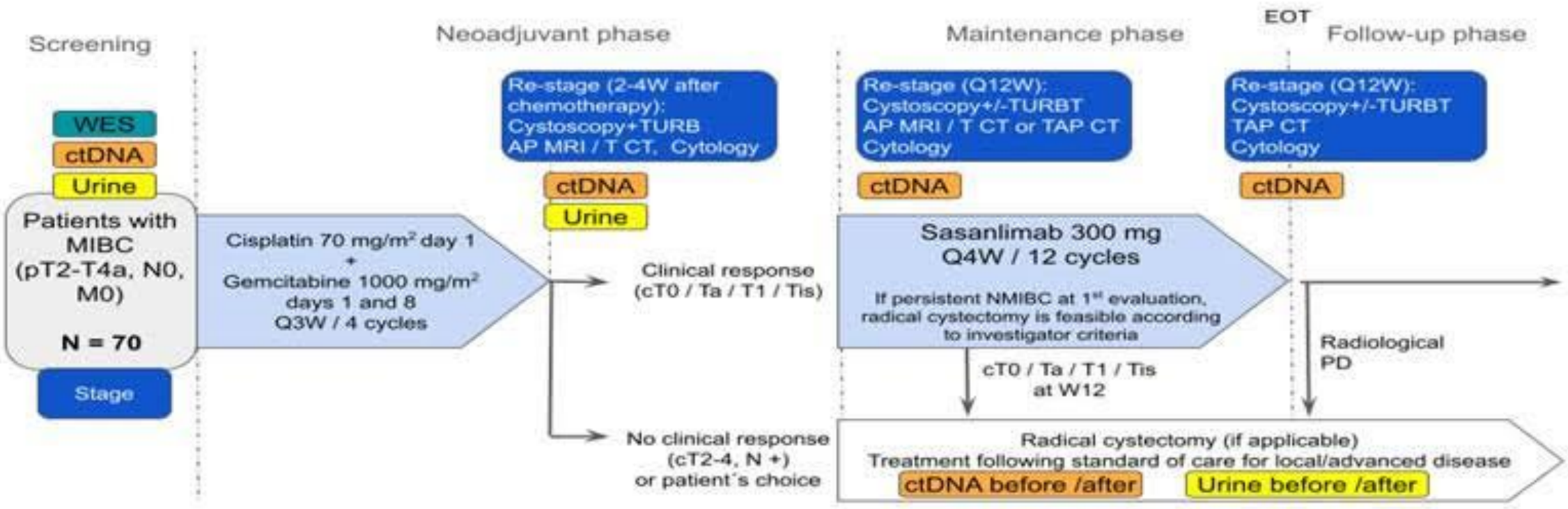
Comparison of RETAIN-1 vs RETAIN-2 results

	RETAIN-1 (ddMVAC)	RETAIN-2 (ddMVAC + nivolumab)
Mutation pos	47%	44%
% active surveillance	36%	31.4%
Median duration of f/u	40 mo	22 mo
In AS – mets free	64%	82%
In cystectomy – ypT0	15%	40%
In ITT – ypT0 + cCR	27%	54%
In AS – no local recurrence	38%	68%
In AS – metastases-free with intact unradiated bladder	48%	60%

Conclusions

- At the time of interim analysis, ddMVAC/ nivolumab was associated with metastases-free rate of **84.2%** in ITT and **82%** in the AS arm
- **60%** AS pts are metastases-free and with an intact un-radiated bladder
- Compared to RETAIN-1 the ypT0 rate was higher at **40%** and rate of ypT0 + cCR of **54%** in RETAIN-2 suggesting additive benefit of adding nivolumab to ddMVAC

SASAN-SPARING



PI: Elena Sevillano & Guillermo de Velasco

Nuevos combos

ASCO Genitourinary Cancers Symposium

Abstract number: 665

Neoadjuvant treatment with disitamab vedotin plus perioperative toripalimab in patients with muscle-invasive bladder cancer (MIBC) with HER2 expression: updated efficacy and safety results from the phase II RC48-C017 trial

Xinan Sheng[1*], Cuijian Zhang[2], Peng Du[3], Kaiwei Yang[2], Yongpeng Ji[3], Li Zhou[1], Benkui Zou[4], Hang Huang[5], Yonghua Wang[6], Xue Bai[7], Dan Feng[7], Yong Yang[3], Jiasheng Bian[4], Zhixian Yu[5], Haitao Niu[6], Jianmin Fang[8], Zhisong He[2], **Jun Guo[1**]**

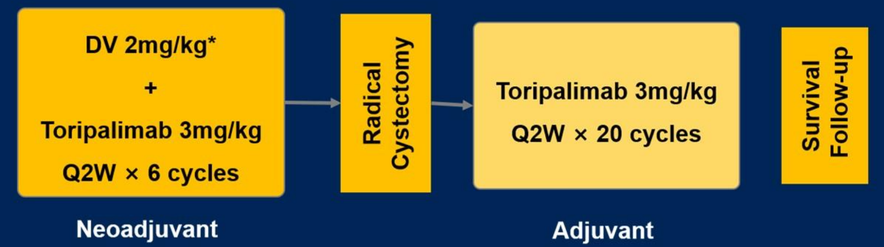
*presenting author **corresponding author

[1] Department of Genitourinary Oncology, Peking University Cancer Hospital & Institute, Beijing, China. [2] Department of Urology, Peking University First Hospital, Beijing, China. [3] Department of Urology, Peking University Cancer Hospital, Beijing, China. [4] Shandong Cancer Hospital and Institute, Beijing, China. [5] The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China. [6] The Affiliated Hospital of Qingdao University, Qingdao, China. [7] RemeGen Co., Ltd., Yantai, China. [8] School of Life Science and Technology, Tongji University, Shanghai, China.

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).

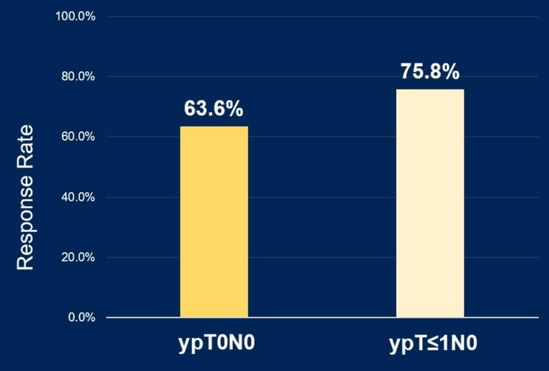
Pathological tumour response was assessed by the local pathologists and investigators based on the postoperative pathology. Radiological assessment was performed by the investigators per RECIST v1.1
*Equivalent to dose of 1.5 mg/kg using DV-based extinction coefficient outside of China. #Including complete 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

- Median time from end of neoadjuvant treatment to RC: 5.0 weeks (range: 2.6-13.1)

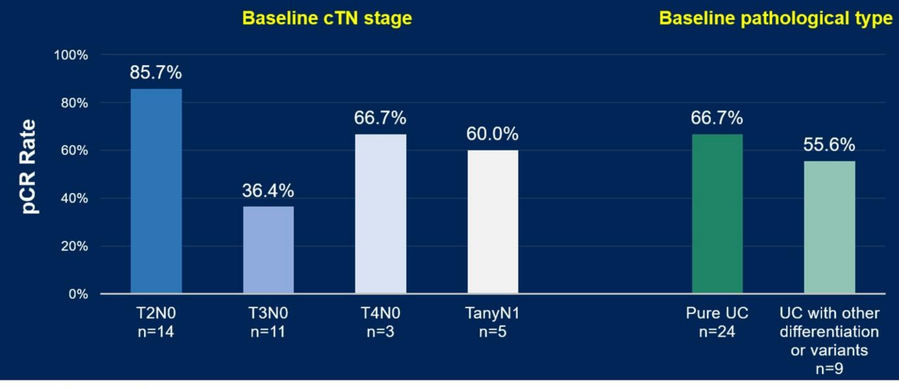
	Patients Received RC N=33
Pathological response	
pCR (ypT0N0), n (%)	**21 (63.6)**
95% CI	45.1-79.6
Pathological response (≤ypT1N0M0), n (%)	**25 (75.8)**
95% CI	57.7-88.9
Pathological staging, n (%)	
ypT0N0	21 (63.6)
ypT≤1N0	4 (12.1)
ypTisNx*	1 (3.0)
ypT2N0	4 (12.1)
ypT3N0	3 (9.1)
ypT4 or ypTanyN+	0

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



Subgroup analysis

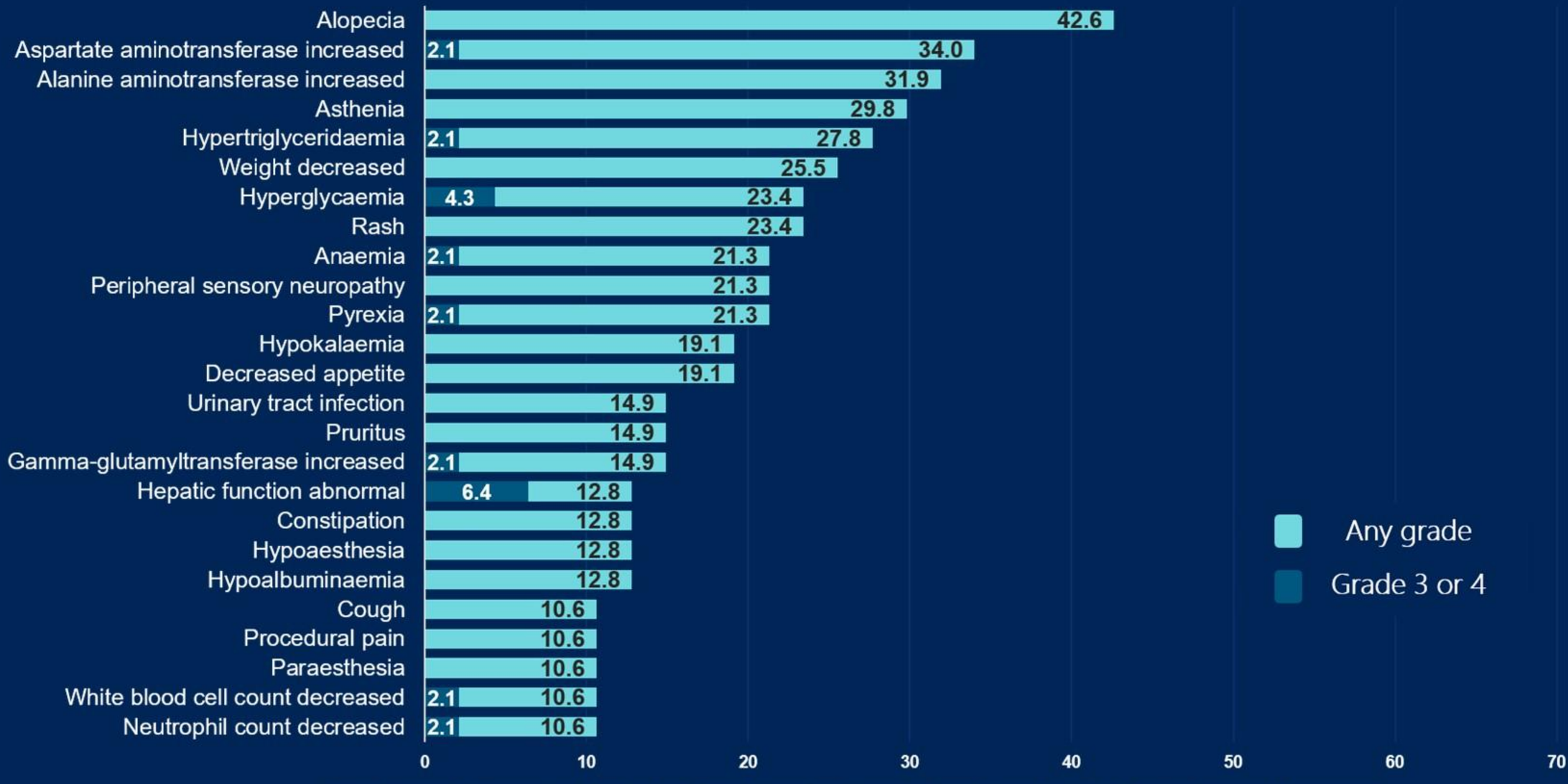
- The pCR rate for the T2N0 patients appeared higher than those for the other subgroups.
- The pCR rates were generally consistent between patients with pure UC and patients with UC with other differentiation or variants.



Postoperative complications

Characteristic	Patients Received RC(N=33)
Postoperative complications (Clavien Dindo), n (%)	
Ⅰ	8 (24.2)
Ⅱ	5 (15.2)
Ⅲa	1 (3.0)
Ⅲb	1 (3.0)
Type of postoperative complications, n (%)	
Postoperative pain	4 (12.1)
Stoma site infection	5 (15.2)
Clotting disorder	1 (3.0)
Pyrexia	1 (3.0)
Pneumonia	1 (3.0)
Intestinal obstruction	1 (3.0)
Urinary tract infection	1 (3.0)
Hydronephrosis	1 (3.0)
Septic shock	1 (3.0)

Most common TEAEs

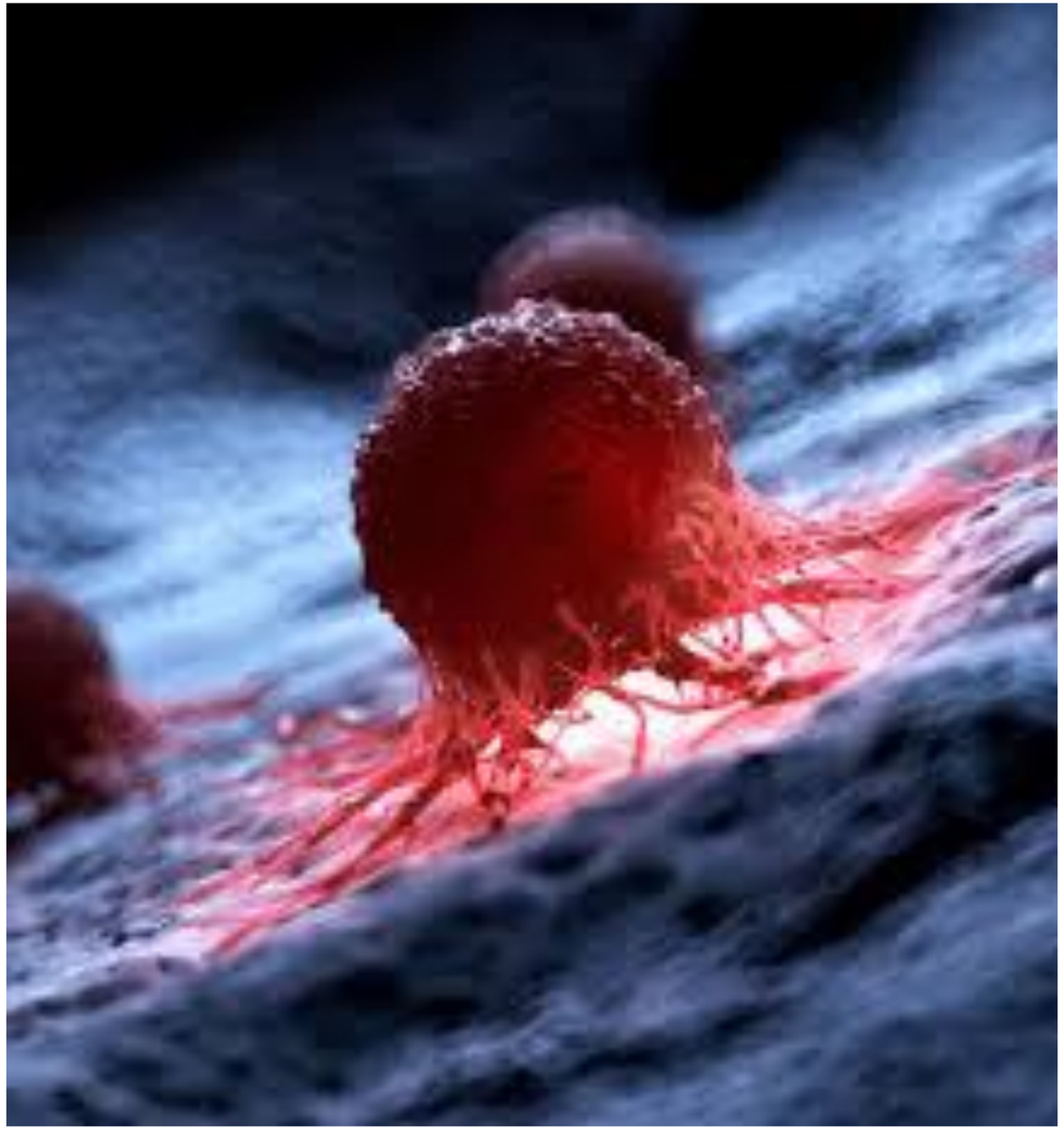


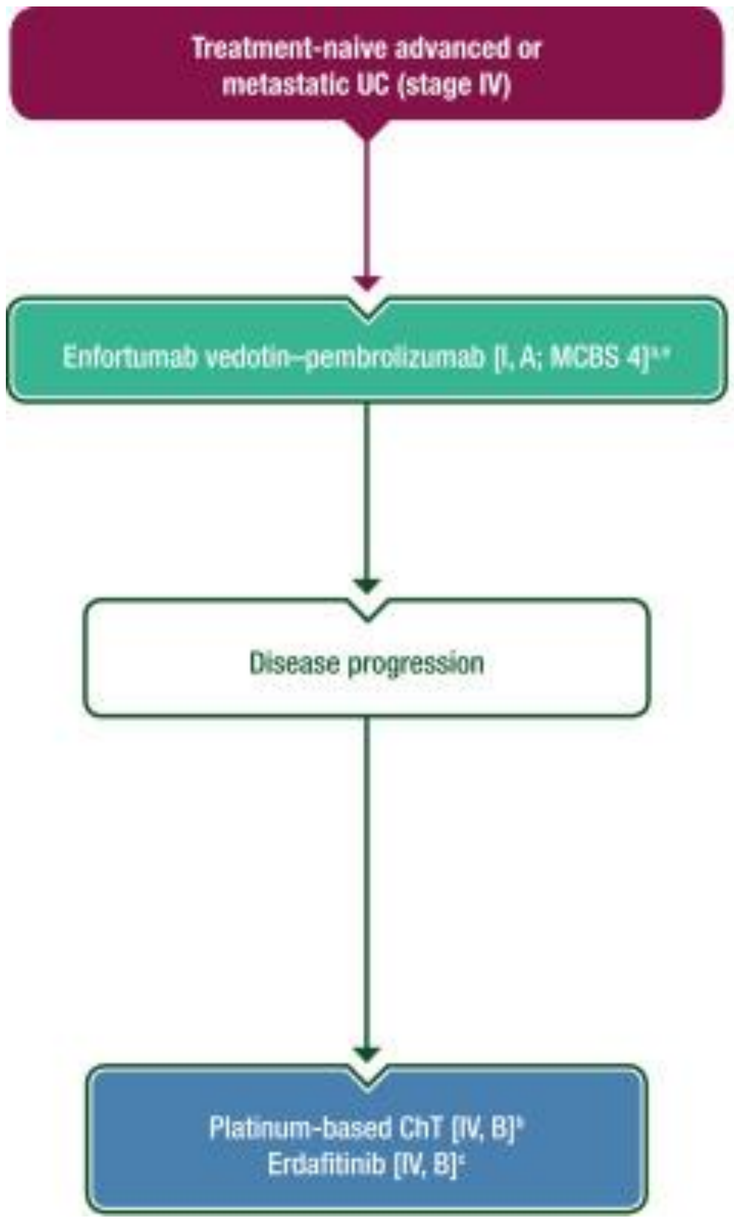
The most common TEAEs occurring in ≥10% patients during the overall study period are listed. Abbreviations: TEAEs=treatment-emergent adverse events.

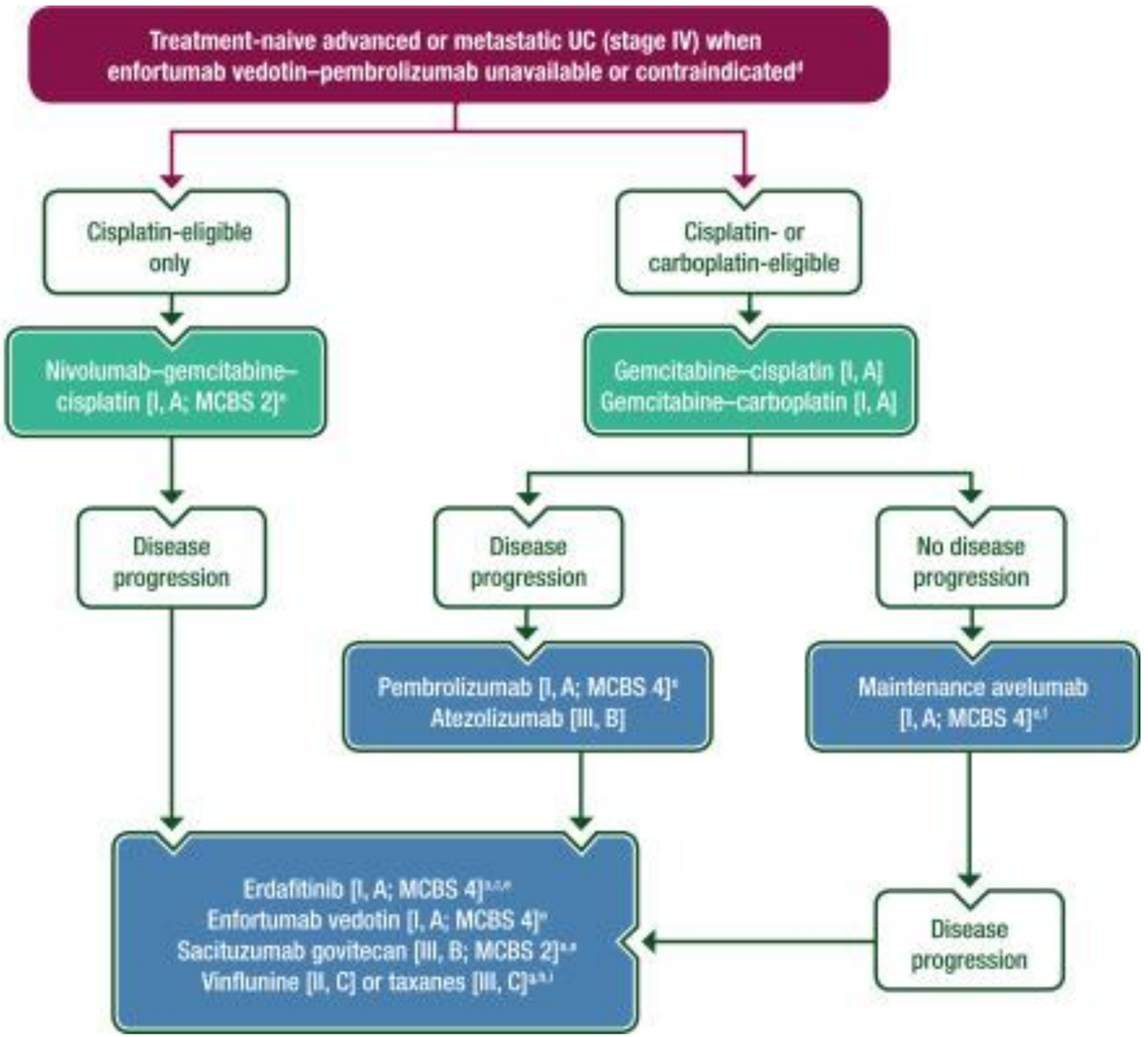
Conclusion

- RC48-017 is the first prospective study showing that ADC in combination with a PD-1 inhibitor as perioperative treatment provided prominent outcomes in operable MIBC.
  - pCR rate: 63.6% (95% CI: 45.1-79.6)
  - 12-month EFS rate: 92.5% (95% CI: 72.8- 98.1)
- Neoadjuvant DV plus toripalimab did not delay RC procedures or impact patients' ability to undergo RC. Safety profile was manageable with no new safety signals.
- The results indicated that neoadjuvant DV plus perioperative toripalimab had promising efficacy and acceptable safety in patients with HER2-expressing MIBC, warranting further investigation.

M1 disease







Esmo Guidelines 2024

ASCO Genitourinary Cancers Symposium

EV-302: Updated analysis from the phase 3 global study of enfortumab vedotin in combination with pembrolizumab (EV+P) vs chemotherapy (chemo) in previously untreated locally advanced or metastatic urothelial carcinoma (la/mUC)

Thomas B. Powles,[1] Michiel S. Van der Heijden,[2] Yohann Loriot,[3] Jens Bedke,[4] Begoña Pérez Valderrama,[5] Gopakumar Iyer,[6] Eiji Kikuchi,[7] Jean Hoffman-Censits,[8] Christof Vulsteke,[9] Alexandra Drakaki,[10] Steffen Rausch,[11] Waddah Arafat,[12] Se Hoon Park,[13] Umang Swami,[14] Jian-Ri Li,[15] Seema Gorla,[16] Blanca Homet Moreno,[17] Xuesong Yu,[18] Yi-Tsung Lu,[18] Shilpa Gupta[19]

[1]Barts Cancer Centre, Queen Mary University of London, London, UK; [2]Netherlands Cancer Institute, Amsterdam, the Netherlands; [3]Institut Gustave Roussy, Université Paris-Saclay, Villejuif, France; [4]Department of Urology & Eva Mayr-Stihl Cancer Center, Klinikum Stuttgart, Stuttgart, Germany; [5]Hospital Universitario Virgen del Rocio, Seville, Spain; [6]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [7]St. Marianna University School of Medicine, Kawasaki, Japan; [8]The Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins Medical Center, Baltimore, MD, USA; [9]Integrated Cancer Center Ghent, AZ Maria Middelares and Center for Oncological Research (CORE), Antwerp University, Antwerp, Belgium; [10]University of California, Los Angeles Medical Center, Los Angeles, CA, USA; [11]Eberhard Karls University, Tübingen, Germany; [12]Simmons Comprehensive Cancer Center, University of Texas Southwestern Medical Center, Dallas, TX, USA; [13]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [14]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA; [15]Taichung Veterans General Hospital, Taichung, Taiwan; [16]Astellas Pharma, Inc., Northbrook, IL, USA; [17]Merck & Co., Inc., Rahway, NJ, USA; [18]Pfizer Inc., Bothell, WA, USA; [19] The Cleveland Clinic, Cleveland, OH, USA

Background

- In the EV-302 primary analysis, EV+P nearly doubled mPFS and mOS in patients with previously untreated la/mUC versus platinum-based chemotherapy[1]
  - mPFS was 12.5 months (95% CI: 10.4, 16.6) with EV+P vs 6.3 months (95% CI: 6.2, 6.5) with platinum-based chemotherapy[1]
  - mOS was 31.5 months (95% CI: 25.4, NE) in the EV+P arm vs 16.1 months (95% CI: 13.9, 18.3) in the platinum-based chemotherapy arm[1]
- Based on these results, EV+P received approvals in many countries globally[2-5] and is the SOC in global treatment guidelines for patients with untreated la/mUC[6,7]

Here, we present 1 year of additional follow-up for EV-302 (~2.5 years of median follow-up) and an exploratory analysis of patients with confirmed complete response

EV, enfortumab vedotin; la/mUC, locally advanced or metastatic urothelial cancer; mOS, median overall survival; mPFS, median progression-free survival; NE, not estimable; P, pembrolizumab; SOC, standard of care.

1. Powles T, et al. N Engl J Med. 2024;390(10):875-88. 2. PADCEV. Highlights of Prescribing Information. 2023. 3. Padcev. Summary of Product Characteristics. 2024. 4. Astellas Pharma Inc. Japan's Ministry of Health, Labour and Welfare approves PADCEV (enfortumab vedotin) with KEYTRUDA (pembrolizumab) for first-line treatment of radically unresectable urothelial carcinoma. News release. Accessed January 23, 2025. https://www.astellas.com/en/news/29451. 5. Pfizer Canada. Padcev (enfortumab vedotin) in combination with pembrolizumab approved by Health Canada to treat advanced bladder cancer. News release. Accessed January 23, 2025. https://www.newswire.ca/news-releases/padcev-r-enfortumab-vedotin-in-combination-with-pembrolizumab-approved-by-health-canada-to-treat-advanced-bladder-cancer-862646661.html. 6. Powles T, et al. ESMO Clinical Practice Guideline. Ann Oncol. 2024;35(6):485-90. 7. Witjes J, et al. Eur Urol. 2024;85(1):17-31.

EV-302/KEYNOTE-A39 Design and Disposition

ITT Patient Population (N=886)

- Previously untreated la/mUC
- Eligible for platinum, EV, and P
- PD-(L)1 inhibitor-naive
- GFR ≥30 mL/min[a]
- ECOG PS ≤2

R 1:1

EV+P[b]
No maximum treatment cycles for EV
Maximum 35 cycles for P

Treatment until disease progression by BICR, clinical progression, unacceptable toxicity, or completion of maximum cycles

Chemotherapy[c]
(Cisplatin or carboplatin + gemcitabine)
Maximum 6 cycles

Stratification factors:
- *Cisplatin eligibility (eligible/ineligible)*
- *PD-L1 expression (high, CPS ≥10; low, CPS <10)*
- *Liver metastases (present/absent)*

Dual primary endpoints:
- PFS by BICR
- OS

Select secondary endpoints:
- ORR per RECIST 1.1 by BICR and INV assessment
- DOR
- Safety

With 29.1 months (95% CI: 28.5, 29.9) of median follow-up:

- 54 (12%) patients remained on EV+P treatment and no patients remained c
- 218 (49%) patients in the EV+P arm and 131 (30%) patients in the chemoth

Data cutoff: August 8, 2024. NCT04223856.

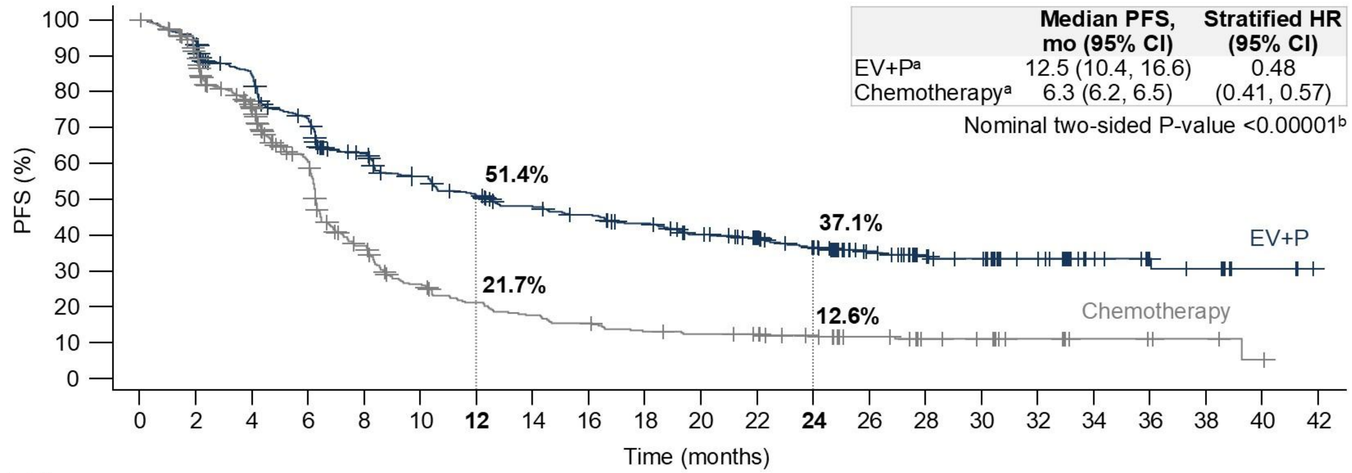
BICR, blinded independent central review; CPS, combined positive score; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group perforr INV, investigator; ITT, intent to treat; la/mUC, locally advanced or metastatic urothelial cancer; NYHA, New York Heart Association; ORR, objective response ra PFS, progress-free survival; RECIST, Response Evaluation Criteria in Solid Tumors.

[a]Patients with ECOG PS of 2 were required to also meet the additional criteria: hemoglobin ≥10 g/dL and GFR ≥50 mL/min but may not have NYHA class III he and P (200 mg; IV) on Day 1. [c]Cisplatin eligibility and assignment/dosing of cisplatin vs carboplatin were protocol defined.

Powles T, et al. N Engl J Med. 2024;390(10):875-88.

PFS by BICR in the Overall Population

PFS benefit with EV+P was maintained with 1 additional year of follow-up



	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]

No. at risk																					
EV+P	442	409	361	304	254	223	200	182	172	159	143	128	109	82	62	57	42	22	14	10	4
Chemotherapy	444	379	296	213	125	86	68	57	50	42	39	37	31	23	16	14	9	5	4	3	1

Data cutoff: August 8, 2024.

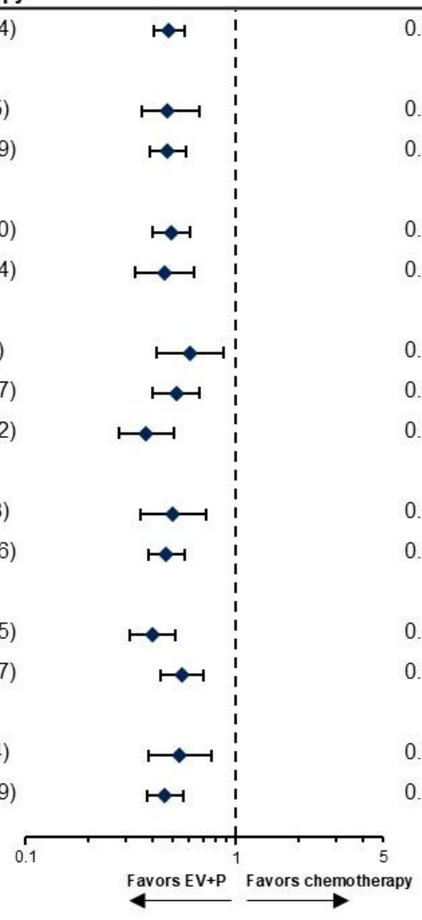
EV, enfortumab vedotin; P, pembrolizumab; PFS, progression-free survival.

[a]Events/N were 262/442 for EV+P and 317/444 for chemotherapy. [b]P-value is nominal and descriptive.

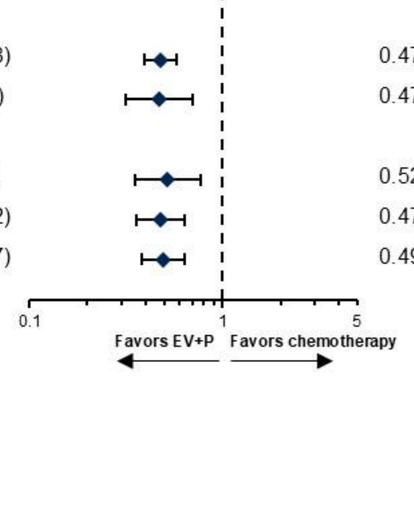
PFS by BICR in Prespecified Subgroups

PFS benefit was consistent across prespecified subgroups

	Median PFS, months (event/N) EV+P	Chemotherapy	HR (95% CI)
Overall	12.5 (262/442)	6.3 (317/444)	0.481 (0.407, 0.570)
Age			
<65 years	14.6 (87/144)	6.4 (90/135)	0.490 (0.358, 0.670)
≥65 years	12.3 (175/298)	6.2 (227/309)	0.478 (0.390, 0.585)
Race			
White	10.5 (191/308)	6.2 (214/290)	0.492 (0.401, 0.604)
Other	19.2 (71/134)	6.5 (103/154)	0.461 (0.335, 0.633)
Region			
North America	10.3 (72/103)	6.3 (57/85)	0.605 (0.418, 0.876)
Europe	10.4 (102/172)	6.3 (149/197)	0.523 (0.403, 0.678)
Rest of world	19.3 (88/167)	6.2 (111/162)	0.376 (0.279, 0.508)
Sex			
Female	10.4 (59/98)	6.1 (75/108)	0.505 (0.351, 0.727)
Male	14.0 (203/344)	6.3 (242/336)	0.468 (0.385, 0.569)
ECOG PS			
0	17.3 (121/223)	6.7 (151/215)	0.404 (0.314, 0.520)
1-2	9.3 (141/219)	6.1 (166/227)	0.555 (0.440, 0.699)
Primary disease site of origin			
Upper tract	12.3 (81/135)	6.2 (70/104)	0.542 (0.384, 0.763)
Lower tract	12.8 (179/305)	6.3 (246/339)	0.462 (0.379, 0.564)



	Median PFS, months (event/N) EV+P	Chemotherapy	HR (95% CI)
Overall	12.5 (262/442)	6.3 (317/444)	0.481 (0.407, 0.570)
Liver metastases			
Present	8.1 (74/100)	6.0 (80/99)	0.548 (0.392, 0.766)
Absent	16.4 (188/342)	6.4 (237/345)	0.458 (0.376, 0.557)
PD-L1 expression			
Low (CPS <10)	10.5 (122/184)	6.3 (131/185)	0.517 (0.400, 0.667)
High (CPS ≥10)	16.4 (138/254)	6.2 (182/254)	0.459 (0.365, 0.576)
Cisplatin eligibility			
Eligible	15.0 (140/244)	6.5 (155/234)	0.518 (0.409, 0.655)
Ineligible	10.6 (122/198)	6.1 (162/210)	0.455 (0.357, 0.580)
Metastatic disease site			
Visceral metastases	10.4 (203/318)	6.2 (242/318)	0.477 (0.393, 0.579)
Lymph node only	22.1 (50/103)	8.3 (60/104)	0.473 (0.317, 0.704)
Renal function			
Normal	18.7 (47/84)	6.7 (64/95)	0.520 (0.350, 0.774)
Mild	12.7 (91/165)	6.3 (118/162)	0.477 (0.358, 0.636)
Moderate/severe	10.5 (124/193)	6.2 (135/187)	0.493 (0.381, 0.637)



Data cutoff: August 8, 2024.

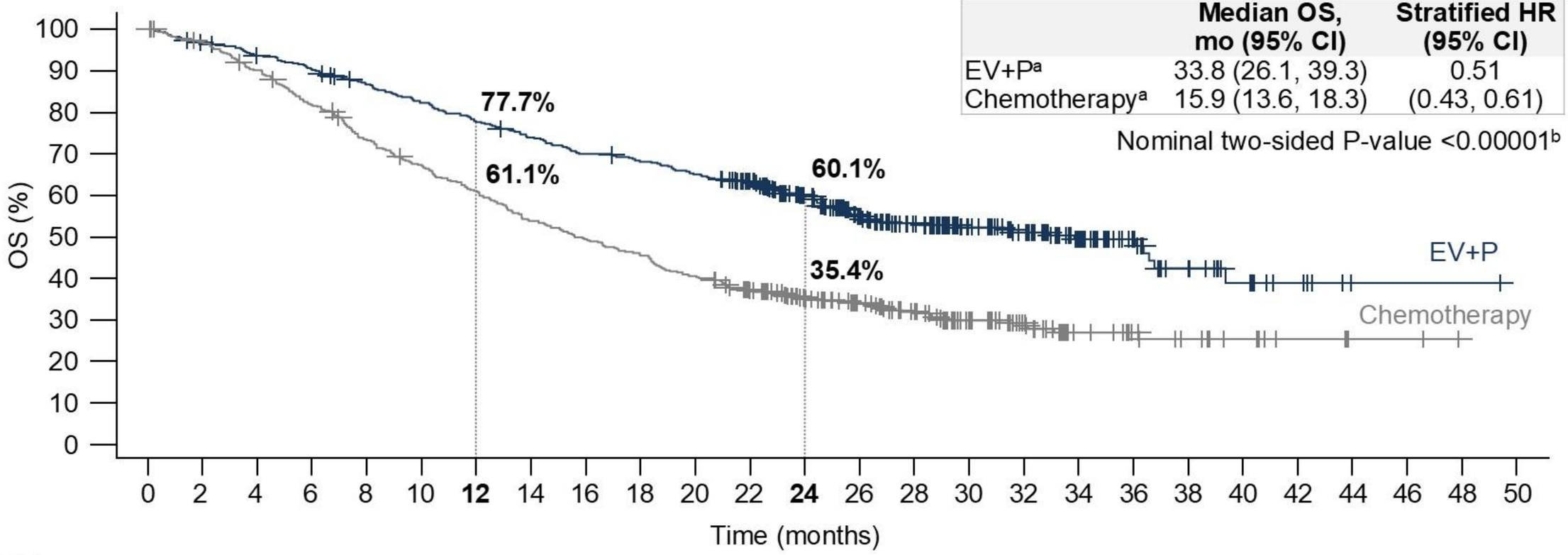
CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; EV, enfortumab vedotin; P, pembrolizumab; PD-L1, programmed death ligand 1; PFS, progression-free survival.

OS in the Overall Population

Risk of death was reduced by almost 50%

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

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



No. at risk

EV+P	442	426	409	394	375	356	336	319	302	293	280	252	206	161	133	102	79	52	32	19	11	6	1	1	1
Chemotherapy	444	423	393	356	317	290	263	233	214	197	176	148	121	102	81	59	43	24	18	13	9	5	2	2	

Data cutoff: August 8, 2024.

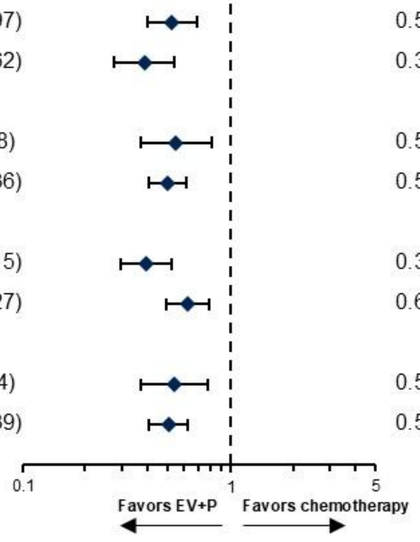
EV, enfortumab vedotin; P, pembrolizumab; OS, overall survival.

[a]Events/N were 203/442 for EV+P and 297/444 for chemotherapy. [b]P-value is nominal and descriptive.

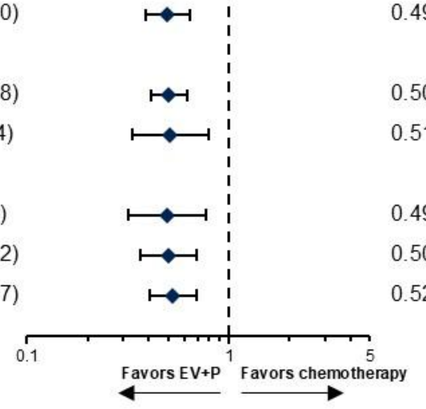
OS in Prespecified Subgroups

OS benefit was consistent across prespecified subgroups

	Median OS, months (event/N) EV+P	Chemotherapy	HR (95% CI)
Overall	33.8 (203/442)	15.9 (297/444)	0.513 (0.428, 0.614)
Age			
<65 years	39.3 (59/144)	18.7 (87/135)	0.434 (0.307, 0.614)
≥65 years	27.1 (144/298)	14.6 (210/309)	0.544 (0.439, 0.674)
Race			
White	26.1 (158/308)	15.1 (207/290)	0.521 (0.422, 0.644)
Other	36.3 (45/134)	19.1 (90/154)	0.436 (0.302, 0.629)
Region			
North America	25.7 (57/103)	21.0 (54/85)	0.672 (0.451, 1.000)
Europe	25.6 (90/172)	14.6 (140/197)	0.522 (0.397, 0.687)
Rest of world	NR (56/167)	15.5 (103/162)	0.386 (0.277, 0.539)
Sex			
Female	25.4 (46/98)	14.6 (70/108)	0.549 (0.371, 0.811)
Male	33.8 (157/344)	16.4 (227/336)	0.501 (0.407, 0.617)
ECOG PS			
0	36.5 (77/223)	18.7 (136/215)	0.394 (0.296, 0.524)
1-2	22.8 (126/219)	13.3 (160/227)	0.621 (0.490, 0.787)
Primary disease site of origin			
Upper tract	36.5 (60/135)	18.3 (63/104)	0.538 (0.371, 0.781)
Lower tract	32.9 (142/305)	15.6 (233/339)	0.504 (0.408, 0.623)



	Median OS, months (event/N) EV+P	Chemotherapy	HR (95% CI)
Overall	33.8 (203/442)	15.9 (297/444)	0.513 (0.428, 0.614)
Liver metastases			
Present	19.1 (68/100)	10.1 (82/99)	0.556 (0.399, 0.776)
Absent	39.3 (135/342)	18.3 (215/345)	0.496 (0.400, 0.615)
PD-L1 expression			
Low (CPS <10)	31.2 (91/184)	15.1 (136/185)	0.472 (0.361, 0.618)
High (CPS ≥10)	36.5 (111/254)	17.1 (158/254)	0.550 (0.431, 0.703)
Cisplatin eligibility			
Eligible	36.7 (101/244)	18.7 (143/234)	0.541 (0.419, 0.699)
Ineligible	25.6 (102/198)	12.7 (154/210)	0.498 (0.386, 0.642)
Metastatic disease site			
Visceral metastases	25.7 (163/318)	13.5 (235/318)	0.505 (0.412, 0.619)
Lymph node only	NR (34/103)	24.4 (54/104)	0.512 (0.332, 0.789)
Renal function			
Normal	39.3 (33/84)	18.6 (61/95)	0.496 (0.318, 0.773)
Mild	36.5 (69/165)	18.4 (101/162)	0.502 (0.365, 0.689)
Moderate/severe	25.6 (101/193)	13.3 (135/187)	0.528 (0.405, 0.689)



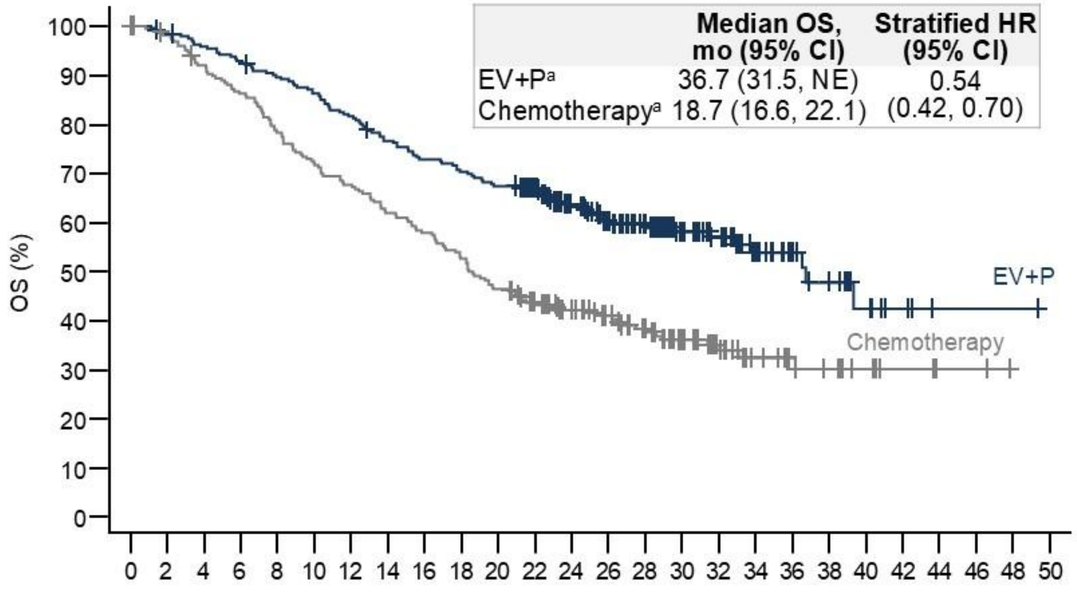
Data cutoff: August 8, 2024.

CPS, combined positive score; ECOG PS, Eastern Cooperative Oncology Group performance status; EV, enfortumab vedotin; P, pembrolizumab; PD-L1, programmed death ligand 1; OS, overall survival.

OS Subgroup Analysis: Cisplatin Eligibility

OS benefit was consistent with the overall population regardless of cisplatin eligibility

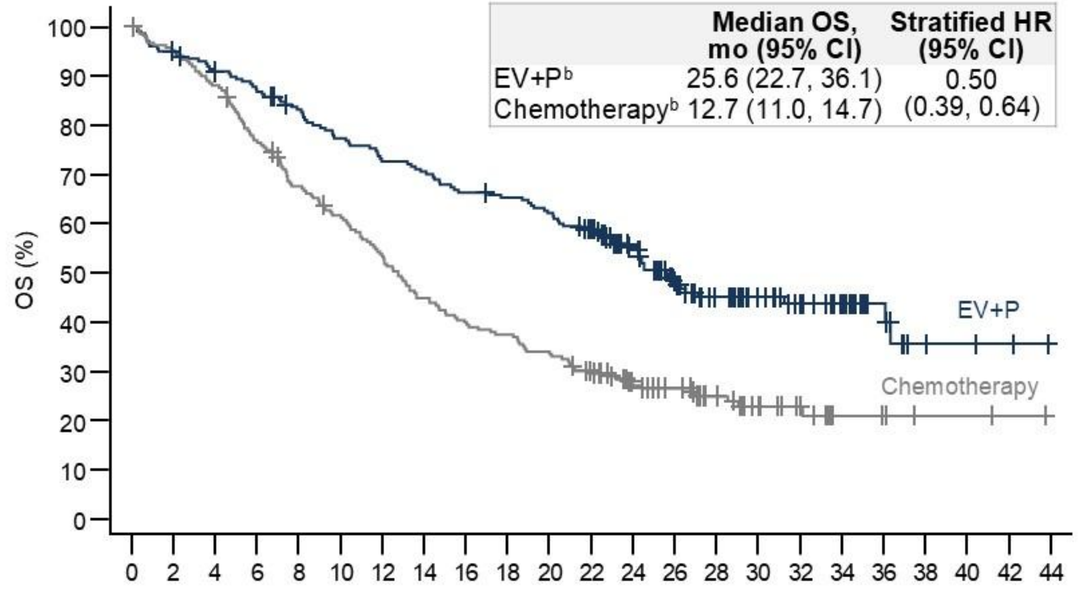
Cisplatin Eligible



No. at risk

EV+P	244	239	232	225	216	208	197	184	175	169	162	147	121	98	83	64	50	30	20	14	8	4	1	1	1
Chemotherapy	234	224	209	196	178	164	154	141	132	120	106	90	77	65	54	41	30	19	14	11	7	4	2	2	

Cisplatin Ineligible



No. at risk

EV+P	198	187	177	169	159	148	139	135	127	124	118	105	85	63	50	38	29	22	12	5	3	2	
Chemotherapy	210	199	184	160	139	126	109	92	82	77	70	58	44	37	27	18	13	5	4	2	2	1	

Data cutoff: August 8, 2024.

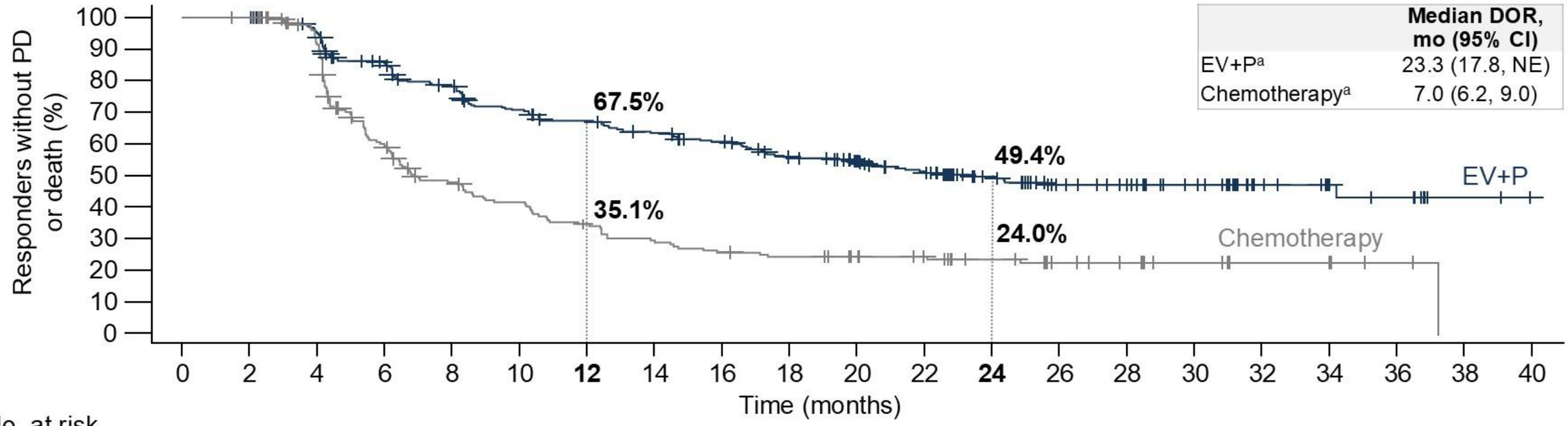
EV, enfortumab vedotin; NE, not estimable; OS, overall survival; P, pembrolizumab.

[a]Events/N in the cisplatin-eligible population were 101/244 for EV+P and 143/234 for chemotherapy. [b]Events/N in the cisplatin-ineligible population were 102/198 for EV+P and 154/210 for chemotherapy.

PRESENTED BY: Thomas B. Powles, MD

Duration of Response (CR or PR) by BICR

Among responders, the probability of maintained response at 24 months was ~50% with EV+P



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

	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.

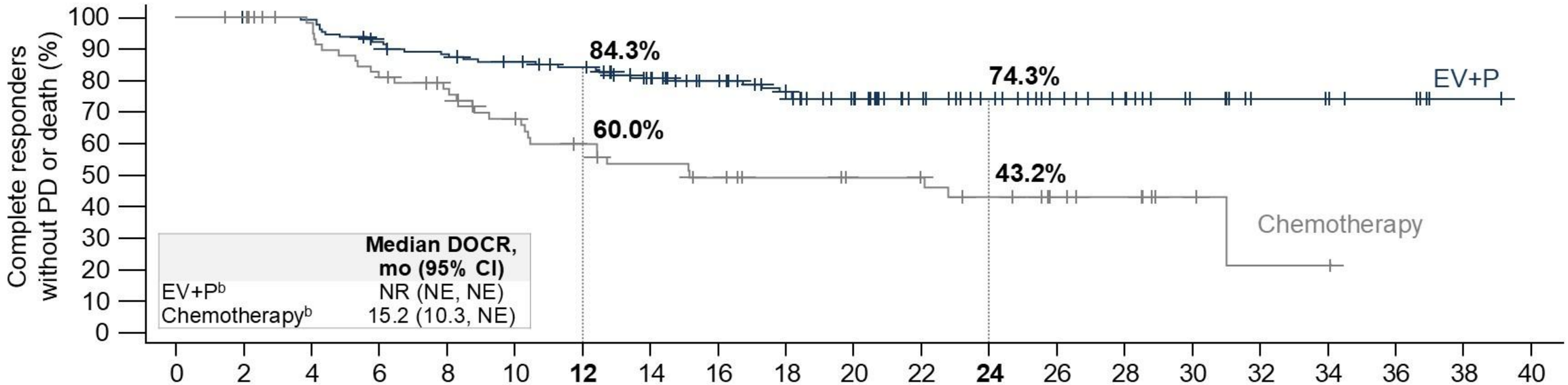
CR, complete response; EV, enfortumab vedotin; NE, not estimable; P, pembrolizumab; PR, partial response; ORR, objective response rate; SD, stable disease.

[a]Events/N were 137/295 for EV+P and 129/195 for chemotherapy. [b]P-value is nominal and descriptive.

PRESENTED BY: Thomas B. Powles, MD

Duration of Confirmed Completed Response (cCR)[a] by BICR

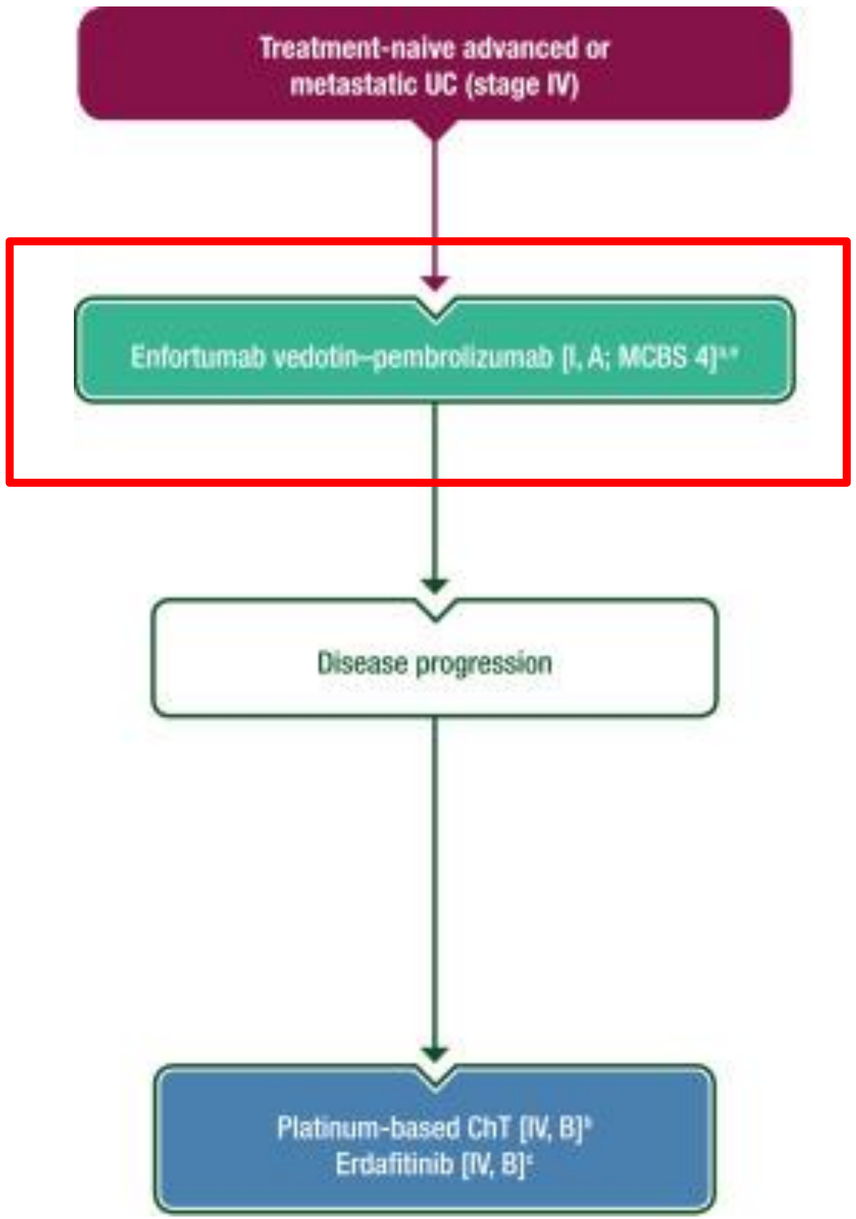
Probability of maintained CR at 24 months was 74% with EV+P

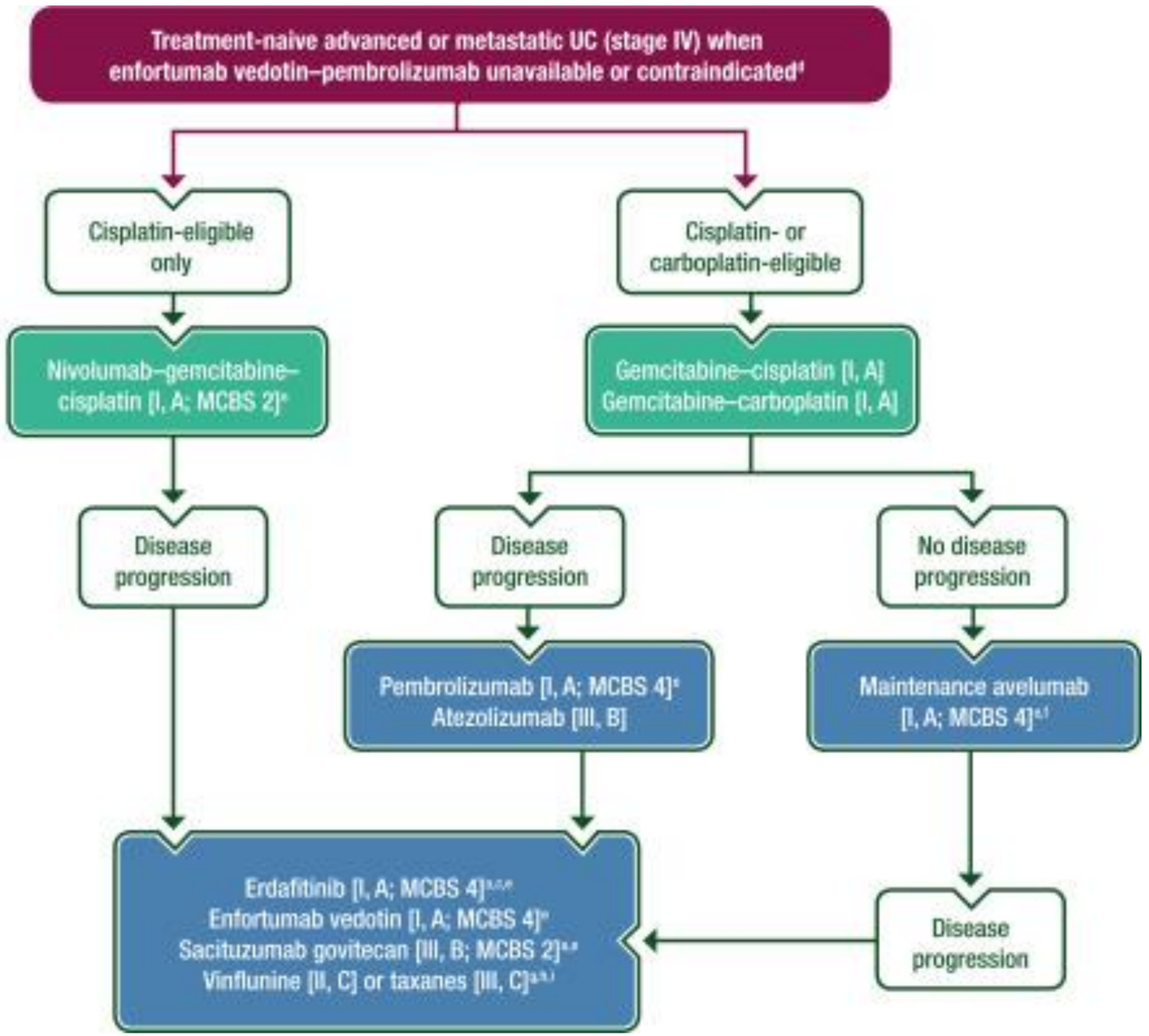


- For patients with cCR:
  - PFS HR=0.36; 95% CI: 0.21, 0.61; estimated 24-month PFS rate: 78.2% for EV+P vs 53.7% for chemotherapy
  - OS HR=0.37; 95% CI: 0.17, 0.80; estimated 24-month OS rate: 95.4% for EV+P vs 85.8% for chemotherapy

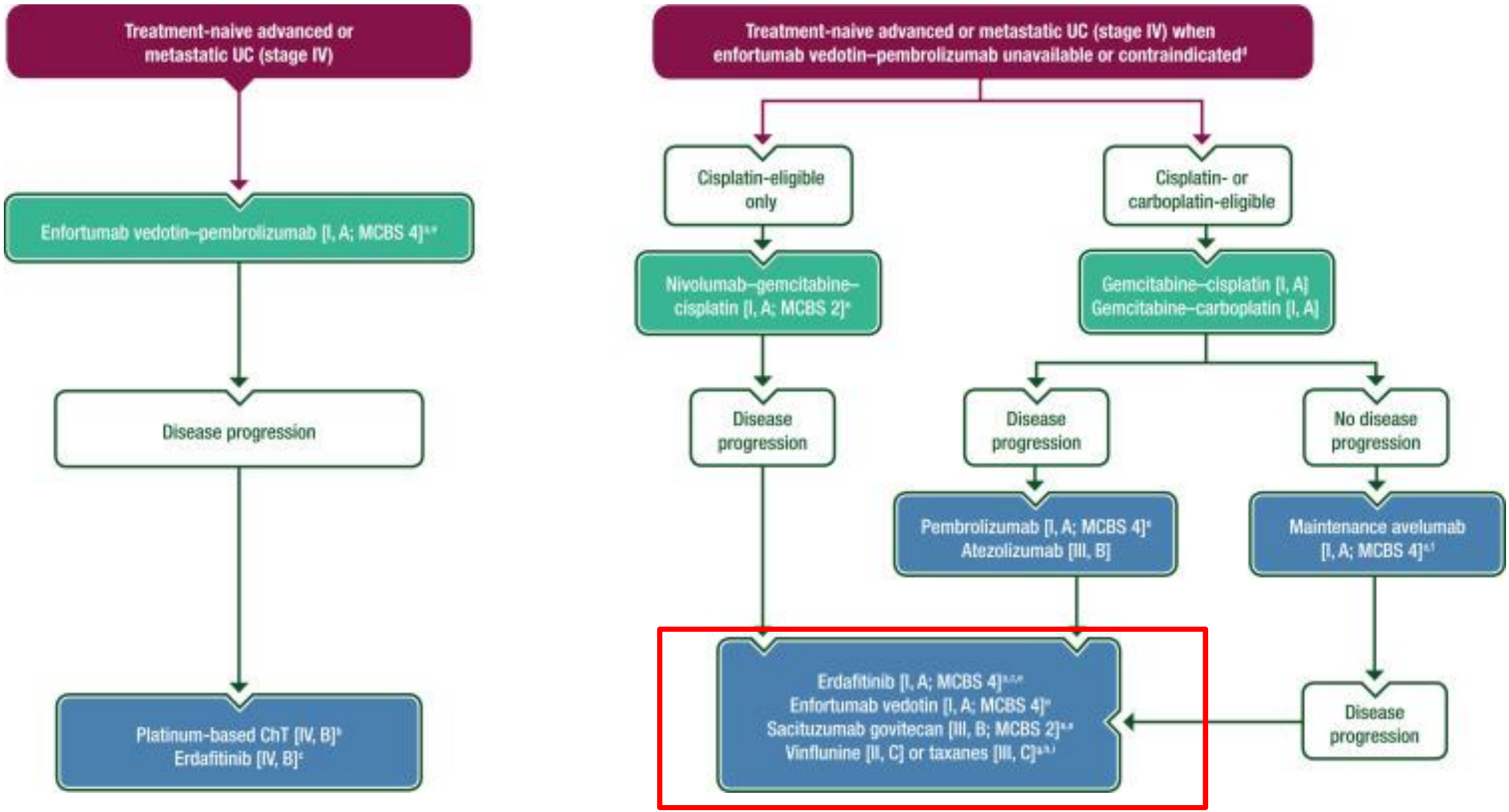
Data cutoff: August 8, 2024.

DOCR, duration of complete response; EV, enfortumab vedotin; HR, hazard ratio; NE, not estimable; NR, not reached; OS, overall survival; P, pembrolizumab; PD, disease progression; PFS, progression-free survival.
[a]For patients with a best overall response of confirmed CR. [b]Events/N were 30/133 for EV+P and 30/64 for chemotherapy.





Esmo Guidelines 2024



Esmo Guidelines 2024

ASCO® Genitourinary Cancers Symposium

Datopotamab deruxtecan (Dato-DXd) in locally advanced/metastatic urothelial cancer: updated results from the phase 1 TROPION PanTumor01 study

Funda Meric-Bernstam,[1] Omar Alhalabi,[2] Aaron Lisberg,[3] Alexandra Drakaki,[3] Benjamin Garmezy,[4] Takahiro Kogawa,[5] Alexander Spira,[6] Mohamad Salkeni,[6] Xin Gao,[7] Anthony Tolcher,[8] Manali Bhave,[9] Deborah Doroshow,[10] Jeannie Hoffman-Censits,[11] Gunnar Klauss,[12] Yoshiaki Kaga,[13] Yasuyuki Kakurai,[14] Takahiro Kojima[15]

[1]Department of Investigational Cancer Therapeutics, MD Anderson Cancer Center, University of Texas, Houston, TX, USA; [2]Department of Genitourinary Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]Department of Medicine, Division of Hematology and Oncology, David Geffen School of Medicine, University of California Los Angeles (UCLA), Los Angeles, CA, USA; [4]Sarah Cannon Research Institute, Nashville, TN, USA; [5]Department of Advanced Medical Development, Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan; [6]Virginia Cancer Specialists (VCS) Research Institute, Fairfax, VA, USA; [7]Department of Medicine, Division of Hematology and Oncology, Massachusetts General Hospital, Harvard Medical School, Harvard University, Boston, MA, USA; [8]NEXT Oncology, San Antonio, TX, USA; [9]Department of Hematology/Oncology, Emory University, Atlanta, GA, USA; [10]Division of Hematology & Medical Oncology, The Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, NY, USA; [11]Departments of Medical Oncology & Urology, The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Johns Hopkins Medical Institutions, Baltimore, MD, USA; [12]Global Oncology, R&D, Daiichi Sankyo, Inc., Basking Ridge, NJ, USA; [13]Clinical Science, Daiichi Sankyo, Inc., Basking Ridge, NJ, USA; [14]Data Intelligence, Daiichi Sankyo, Co., Ltd., Tokyo, Japan; [15]Department of Urology, Aichi Cancer Center, Nagoya, Japan

Study Design

- Datopotamab deruxtecan (Dato-DXd) is a TROP2-directed ADC composed of an anti-TROP2 mAb covalently linked to a highly potent topoisomerase I inhibitor payload via a plasma-stable, tumor-selective, tetrapeptide-based cleavable linker[1]
- TROPION-PanTumor01 is an ongoing, phase 1, multi-cohort, multicenter, open-label, dose-escalation and dose-expansion study evaluating Dato-DXd in patients with several types of previously treated advanced solid tumors, including urothelial cancer

Key eligibility criteria

- Unresectable locally advanced/metastatic (stage III or IV) urothelial carcinoma (included renal pelvis, ureter, urinary bladder, and urethra)
- Previous treatment with ≥1 line of therapy including an immune checkpoint inhibitor
- ECOG PS 0–1
- Unselected for TROP2 expression
- No prior treatment with DXd-ADCs or TROP2-directed therapies

→ **Dato-DXd**
6 mg/kg Q3W
(N=40)

Primary endpoints

- Safety and tolerability

Secondary endpoints (by BICR[a])

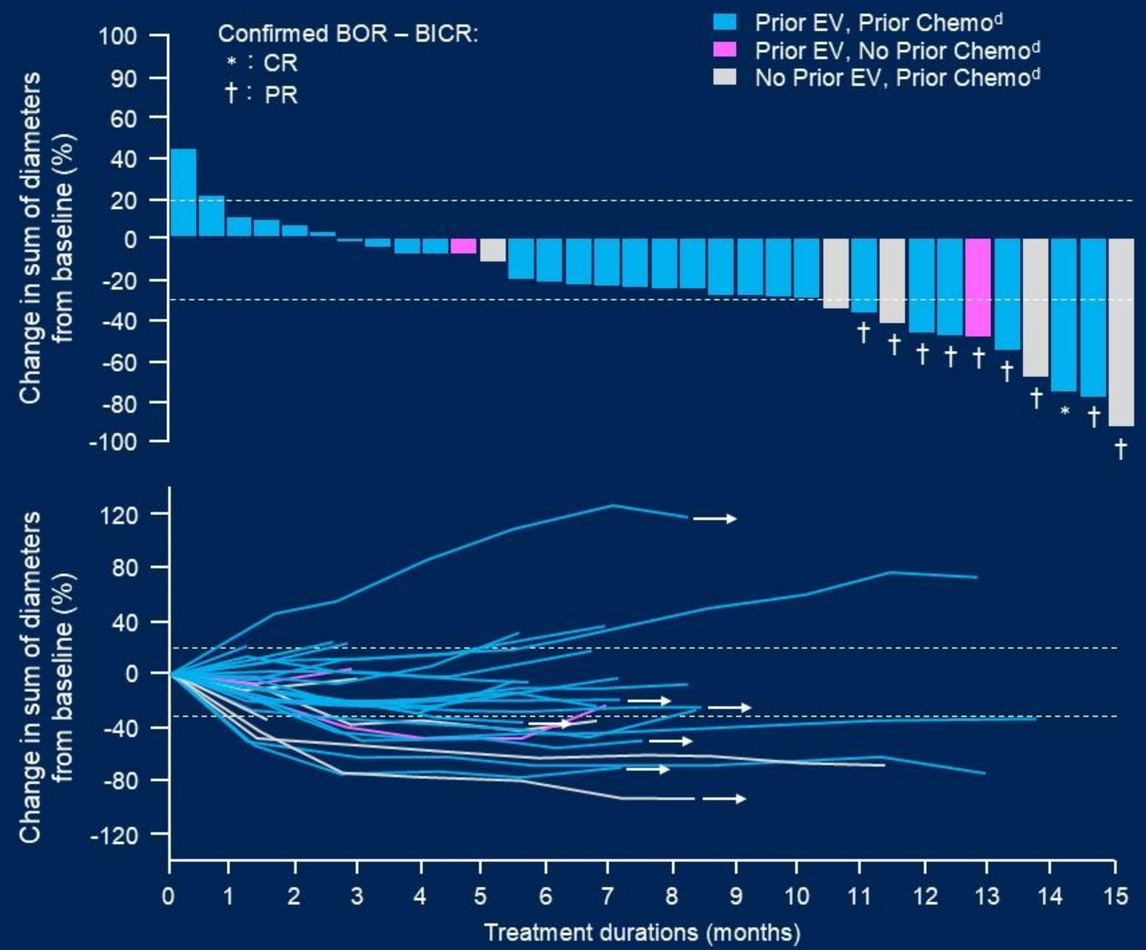
- ORR
- DOR
- DCR
- PFS

BICR, blinded independent review committee; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; ORR, objective response rate; Q3W, every 3 weeks.
Data cut off: April 22, 2024. Median follow-up was 10.0 months (range, 5.0–28.2). [a]Evaluated per RECIST v1.1. 1. Okajima D, et al. Mol Cancer Ther. 2021;20:2329–40.

Response and Change in Tumor Burden

Response by BICR[a]	Dato-DXd (N=40)
ORR[b], n (%) [95% CI]	**10 (25.0)** [12.7–41.2]
DCR[c], n (%) [95% CI]	**31 (77.5)** [61.5–89.2]
BOR, n (%)	
CR	1 (2.5)
PR	9 (22.5)
SD	20 (50.0)
Non-CR/non-PD	1 (2.5)
PD	5 (12.5)
NE	4 (10.0)
DOR, median (95% CI)**, months**	NE (2.6–NE)
6-month DOR rate, % (95% CI)	76.2 (33.2–93.5)

ORR by investigator was 30.0% (n=12); all were PR



BOR, best overall response; CI, confidence interval; CR, complete response; NE, non-evaluable; PD, progressive disease; PR, partial response; SD, stable disease.
[a]Evaluated by BICR per RECIST v1.1. [b]Responses with confirmation of CR/PR. [c]CR + PR + SD + non-CR/non-PD. [d]All patients received prior immunotherapy.

ASCO® Genitourinary Cancers Symposium

A first-in-human phase 1 study of LY3866288 (LOXO-435), a potent, highly isoform-selective FGFR3 inhibitor (FGFR3i) in advanced solid tumors with FGFR3 alterations: Initial results from FORAGER-1

Gopa Iyer[1], Hiromichi Ebi[2], Natalie Cook[3], Xin Gao[4], Shigehisa Kitano[5], Nobuaki Matsubara[6], Melissa A. Reimers[7], Arlene O. Siefker-Radtke[8], Miso Kim[9], Matthew D. Galsky[10], Debbie GJ. Robbrecht[11], Jun Guo[12], Bernhard J. Eigl[13], Clare Schaverien[14], Brent D. Butts[14], Eunice Yuen[14], Sylwia Szymczak[14], Xiang Zhao[14], Ryan C. Widau[14], Alexandra Drakaki[15]

[1]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Division of Molecular Therapeutics, Aichi Cancer Center Research Institute, Nagoya, Japan; [3]The Christie NHS Foundation Trust and Division of Cancer Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK; [4]Massachusetts General Hospital Cancer Center, Boston, MA, USA; [5]Department of Advanced Medical Development, The Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan; [6]National Cancer Center Hospital East, Chiba, Japan; [7]Department of Internal Medicine, Washington University in St Louis, St. Louis, MO, USA; [8]Department of Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [9]Seoul National University Hospital, Seoul, Republic of Korea; [10]Division of Hematology and Medical Oncology, Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [11]Medical Oncology, Erasmus MC Cancer Institute, Rotterdam, the Netherlands; [12]Peking University Cancer Hospital & Institute, Beijing, China; [13]British Columbia Cancer Agency, Vancouver, Canada[14]; Eli Lilly and Company, Indianapolis, IN, USA; [15]Division of Hematology/Oncology, Department of Medicine, UCLA David Geffen School of Medicine, Los Angeles, CA, USA

Key Takeaway Points

- LY3866288 (LOXO-435) is an oral, potent, highly isoform-selective, small molecule FGFR3 inhibitor designed to limit off-target toxicities
- Here, we report initial phase 1a dose escalation results from FORAGER-1, a phase 1a/b study of LY3866288 in *FGFR3*-altered advanced solid tumors (NCT05614739)
- In patients treated at 200 mg BID and higher, LY3866288 demonstrates a favorable safety profile and promising preliminary antitumor activity in patients with *FGFR3*-altered metastatic urothelial carcinoma
  - 41% (16/39) of patients with an activating *FGFR3* mutation or fusion had a confirmed response with a 90% DCR
  - 50% (6/12) of patients who previously received an FGFR inhibitor had a confirmed response
  - LY3866288 was well-tolerated; grades 1-2 diarrhea were the most common TEAEs, and high-grade FGFR-1, 2, and 4 mediated AEs typical of erdafitinib and other pan-FGFR inhibitors were very rare

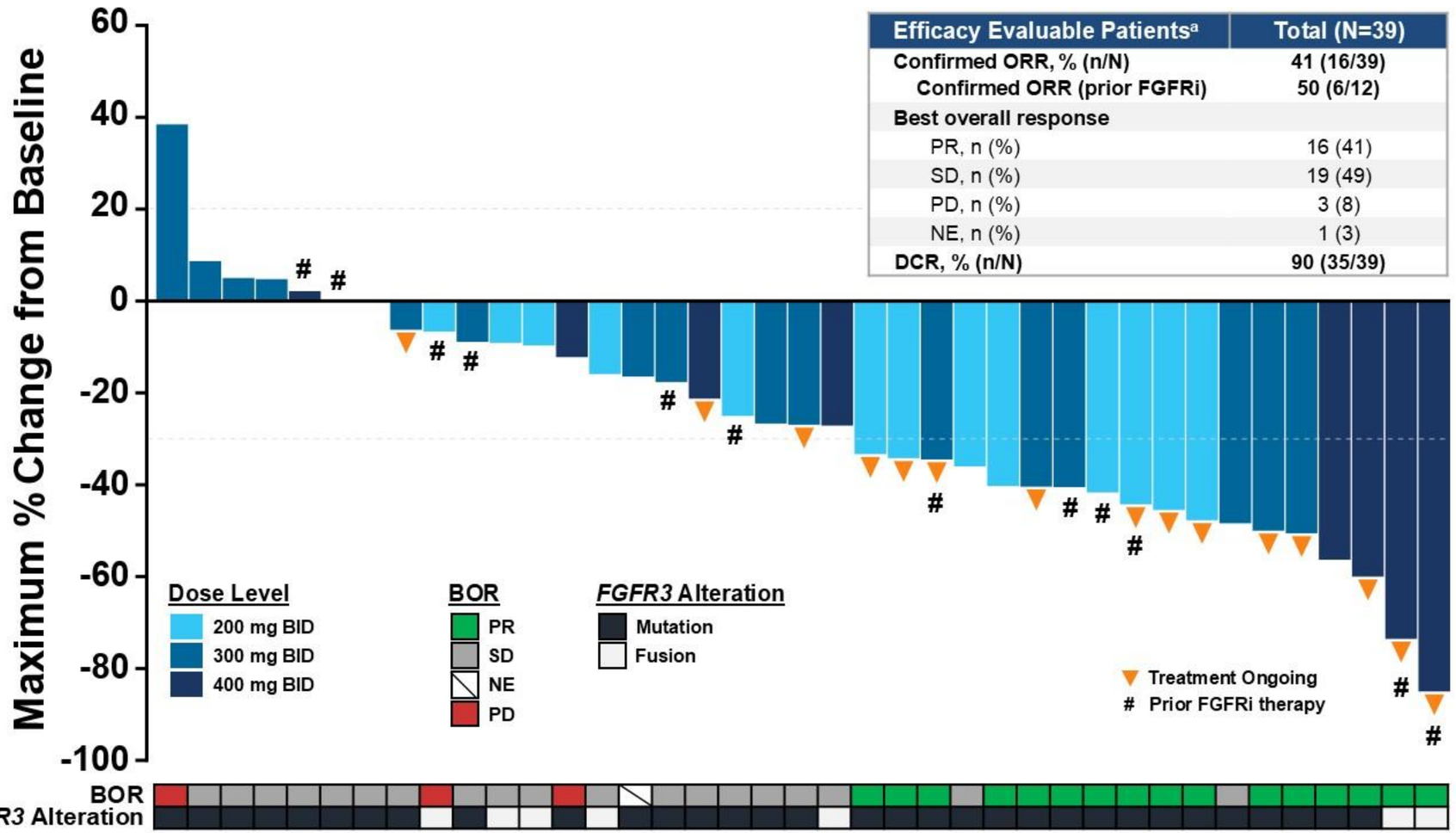
Safety

Treatment-Emergent AEs ≥20%				
	All Patients (N=107)		200 mg, 300 mg, 400 mg BID (n=70)	
All TEAEs, %	**Any Grade**	**Grade ≥3**	**Any Grade**	**Grade ≥3[e]**
Any	98	45	100	46
Diarrhea	63	3	76	4
Fatigue	26	<1	29	1
ALT increased	22	7	29	9
AST increased	22	7	29	9
Decreased appetite	21	3	24	1
AEs of interest, %				
Skin disorders[a]	42	3	46	4
Hand-foot (PPE)	6	2	9	3
Hyperphosphatemia[b]	26	<1	36	1
Eye disorders[c]	19	-	21	-
Retinopathy	4	-	4	-
Stomatitis	18	<1	23	1
Nail disorders[d]	16	-	19	-
Dry mouth	14	-	17	-
Dose modifications, %				
Dose reductions due to TEAEs	10		14	
Discontinuations due to TEAEs	5		6	

- Median follow-up time: 5.0 (0.4-19.9+) months
- 10 dose levels evaluated (6 mg QD – 400 mg BID)
- No DLTs observed during dose escalation
- At the higher dose levels (200, 300, 400 mg BID)
  - 25 (36%) remain on treatment at data cutoff
  - Most TEAEs were grade 1-2
  - High-grade FGFR-1, 2, and 4 related AEs typical for erdafitinib[f] were very rare
  - Dose reductions/discontinuations were uncommon[g]

Data cutoff date of 02 Dec 2024. Safety was evaluated across all patients dosed, regardless of dose or tumor type. [a]Includes rash, dry skin, PPE, rash maculo-popular, alopecia, pruritus, decubitus ulcer, night sweats, skin fissures, blister, dermatitis acneiform/allergic, hyperhidrosis, hyperkeratosis, neurodermatitis, seborrheic dermatitis, and skin ulcer. [b]13 patients received pharmacologic intervention (1 at 200 mg, 6 at 300 mg, 6 at 400 mg). [c]Includes vision blurred, dry eye, blepharitis, eye pruritus, lacrimation increased, ocular hyperemia, retinal hemorrhage, subretinal fluid, swelling of eyelid, visual acuity reduced, and vitreous floaters. [d]Includes nail ridging, discoloration, onycholysis, onychalgia, and onychoclasis. [e]4 patients had grade 4 events – ALT/AST increased, hyponatremia, hypotension, and neutrophil count decreased; 2 unrelated grade 5 events occurred – septic shock and cardiac failure. [f]Includes retinopathy, onycholysis, and PPE. [g]ALT/AST increased (n=2), diarrhea (n=2), and stomatitis (n=2) were most common reasons for dose reduction. ALT, alanine aminotransferase; AST, aspartate aminotransferase; PPE, palmar-plantar erythrodysesthesia.

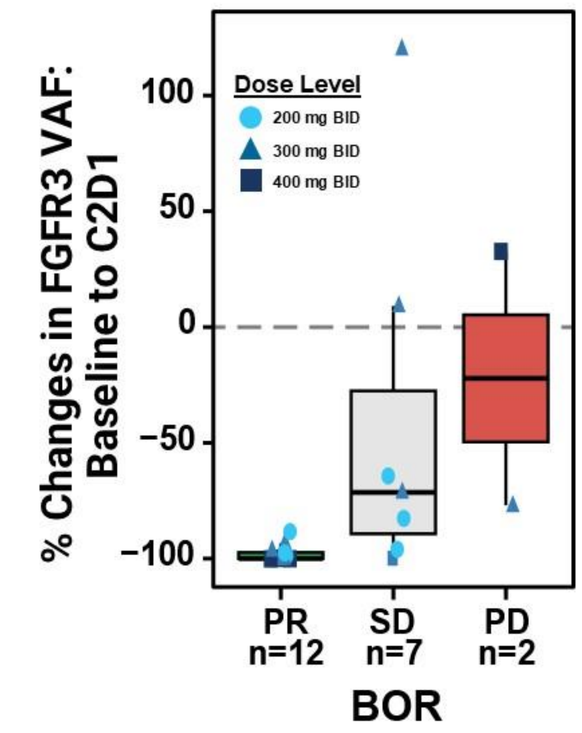
Radiographic Response and *FGFR3* Variant Allele Frequency in *FGFR3*-Altered Efficacy Evaluable mUC Patients Receiving ≥200 mg BID (n=39)



Efficacy Evaluable Patients[a]	Total (N=39)
Confirmed ORR, % (n/N)	41 (16/39)
Confirmed ORR (prior FGFRi)	50 (6/12)
Best overall response	
PR, n (%)	16 (41)
SD, n (%)	19 (49)
PD, n (%)	3 (8)
NE, n (%)	1 (3)
DCR, % (n/N)	90 (35/39)

- Responses were also observed in non mUC patients: intrahepatic cholangiocarcinoma and ovarian (Brenner) cancer (n=1 each).

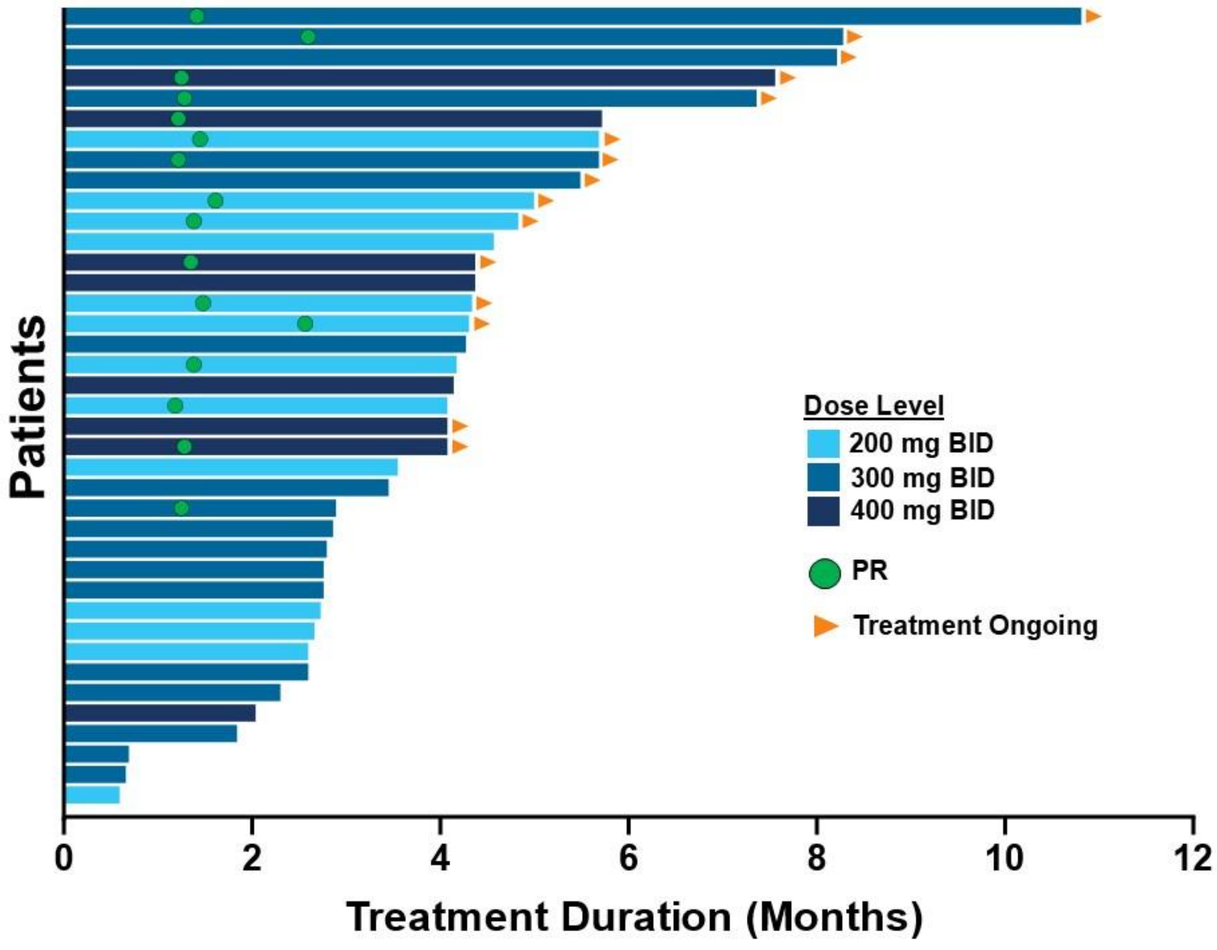
***FGFR3* Variant Allele Frequency[b]**

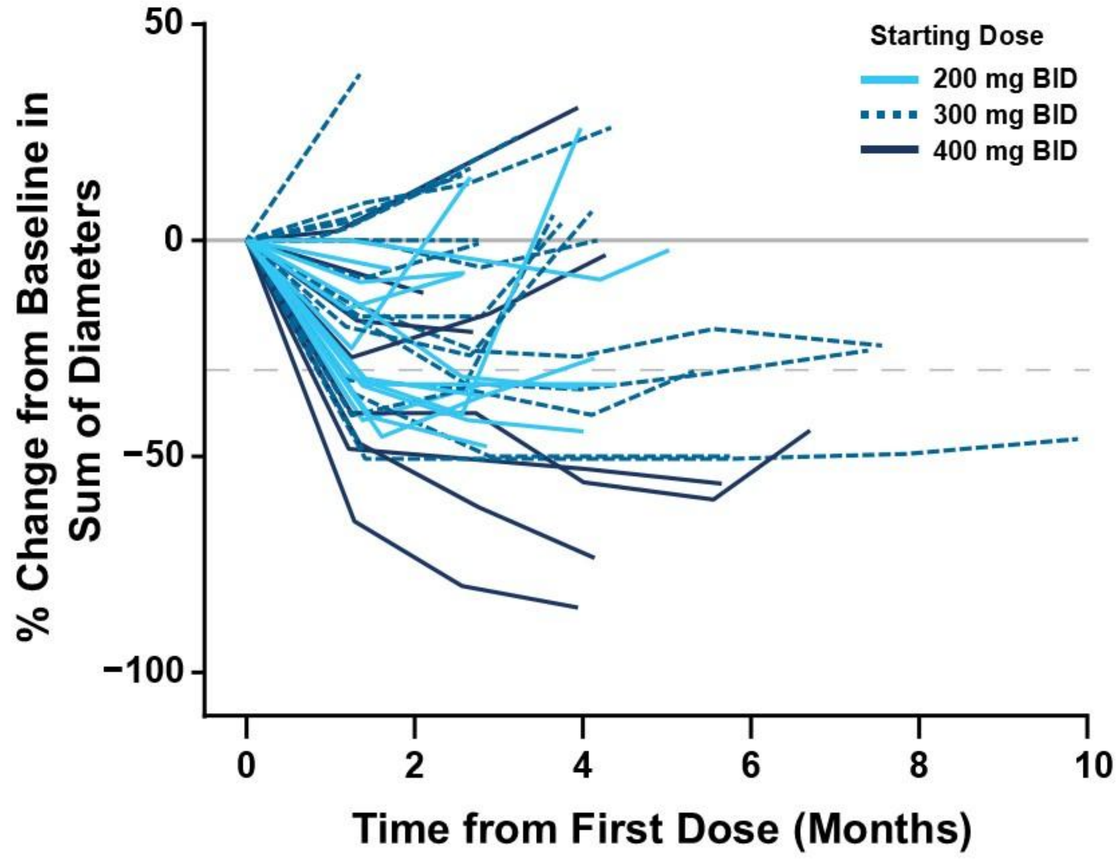


- Decreases in FGFR3 Variant Allele Frequency (VAF) at C2D1 correlate with BOR
- 21/39 patients had detectable FGFR3 VAF at baseline

Data cutoff date of 02 Dec 2024. [a]Efficacy evaluable patients are those with measurable disease who had at least 1 post-baseline response assessment or had discontinued treatment before the first post-baseline response assessment. [b]Changes in ctDNA were assessed using Guardant 360 from patients' plasma samples.

Treatment Duration and Treatment Response in *FGFR3*-Altered Efficacy Evaluable mUC Patients Receiving ≥200 mg BID (n=39)

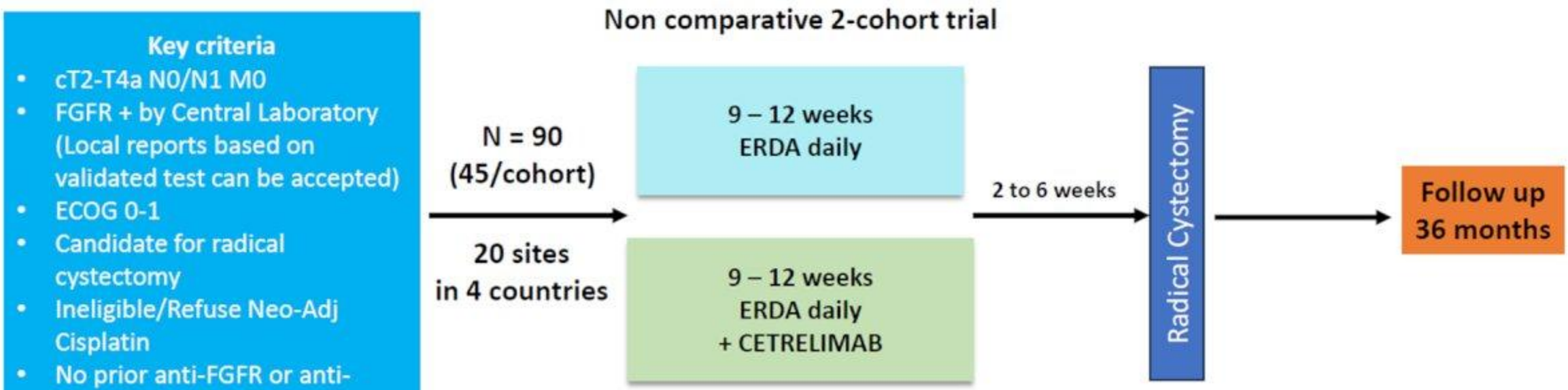




- Median time to response was 1.4 (1.2-2.6) months
- 12 (75%) of 16 confirmed responders remain on treatment; median duration of response is immature

Data cutoff date of 02 Dec 2024.

Neowin



Total Study Duration: 63 months from FPI to LPO
Estimated accrual: 24 months

Co-primary endpoints:
- pCR & Downstaging Rate (<ypT2)

Secondary endpoints:
- Any downstaging rate
- Event-free survival (EFS)
- Overall Survival (OS)
- Objective Response Rate (ORR) according to RECIST v1.1, after neo-adj. treatment
- Safety
- Rate of delay to surgery

Exploratory endpoint:
- Tumor response via PET-MRI
- Quality of Live (QoL)
- Biomarkers of response
- Changes in Biomarkers expression
- Genomic data in plasma, urine and feces

NMIBC

Abstract 667

ASCO Genitourinary Cancers Symposium

A Phase 1/2 Trial Of Durvalumab Plus Intravesical Gemcitabine And Docetaxel In BCG-Unresponsive Non-muscle Invasive Bladder Cancer Patients (HCRN GU16-243: ADAPT-BLADDER Cohort 4)

Noah M. Hahn[1,2,3], Marianna Zahurak[1], Hristos Z. Kaimakliotis[4], Timothy A. Masterson[4], Nabil Adra[5], David YT Chen[6], Alexander Kutikov[6], Daniel M. Geynisman[7], Woodson W. Smelser[8], Melissa A. Reimers[9], Christopher B. Anderson[10,11], Mark N. Stein[10,12], Alex S. Baras[1,2,3,13], Gabriela Colocho[1,2,3], Debbie G. Schwartz[1,2,3], David J. McConkey[1,2,3], Sunil H. Patel[1,2,3], Bilal Rahim[14], Michael A. O'Donnell[15], Max R. Kates[1,2,3]

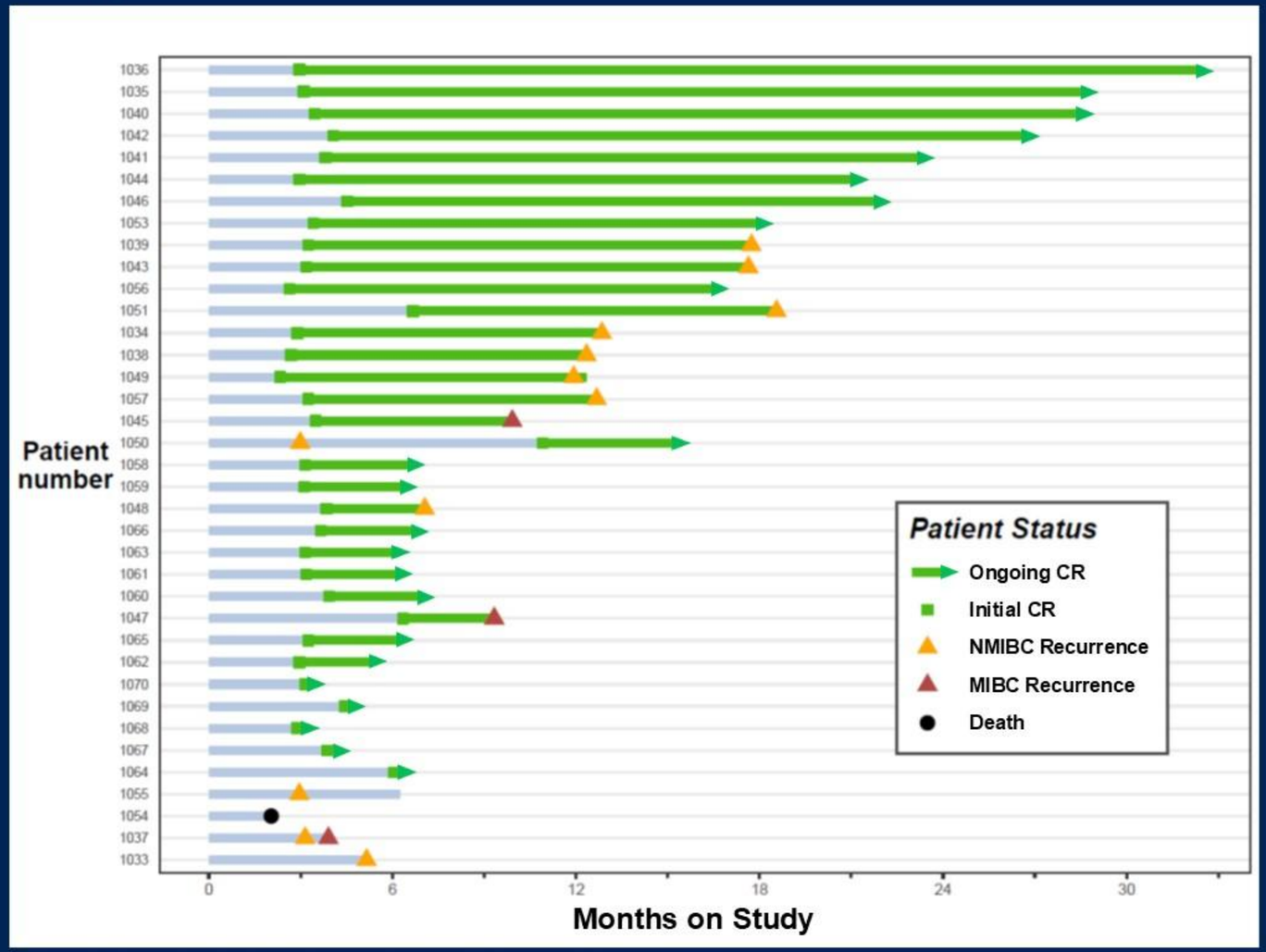
[1]Johns Hopkins University Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD; [2]The Johns Hopkins Greenberg Bladder Cancer Institute, Baltimore, MD; [3]The James Buchanan Brady Urological Institute, Baltimore, MD; [4]Indiana University Simon Cancer Center, Department of Urology, Indianapolis, IN; [5]Indiana University Simon Cancer Center, Department of Hematology and Oncology, Indianapolis, IN; [6]Fox Chase Cancer Center, Department of Urology, Philadelphia, PA; [7]Fox Chase Cancer Center, Department of Hematology and Oncology, Philadelphia, PA; [8]Washington University School of Medicine, Department of Surgery, Division of Urology, St. Louis, MO; [9]Washington University School of Medicine, Department of Medicine, Division of Oncology, St. Louis, MO; [10]Herbert Irving Comprehensive Cancer Center, Columbia University, New York, NY; [11]Columbia University, Department of Urology, New York, NY; [12]Columbia University, Department of Medicine, Division of Hematology and Oncology, New York, NY; [13]Johns Hopkins School of Medicine, Department of Pathology, Baltimore, MD; [14]University of Iowa Carver College of Medicine, Department of Internal Medicine, Division of Hematology and Oncology, Iowa City, IA; [15]University of Iowa Carver College of Medicine, Department of Urology, Iowa City, IA

Complete Response Rates

	All Patients (N=37)	CIS (n=20)	Pure Papillary (n=17)
Any Time point (n=37)			
Complete Response, n (%)	**33 (89.2)** *(90% CI: 77.0, 96.2)*	**18 (90.0)** *(90% CI: 71.7, 98.2)*	**15 (88.2)** *(90% CI: 67.4, 97.9)*
Non-Response, n (%)	4 (10.8)	2 (10.0)	2 (11.8)
3-month (n=36)			
Complete Response, n (%)	30 (83.3)	17 (89.5)	13 (76.5)
Indeterminate Response, n (%)	5 (13.9)	2 (10.5)	3 (17.6)
Non-response, n (%)	1 (2.8)	0 (0.0)	1 (5.9)
6-month (n=28)			
Complete Response, n (%)	25 (89.3)	15 (93.8)	10 (83.3)
Recurrence, n (%)	3 (10.7)	1 (6.3)	2 (16.7)
12-month (n=16)			
Complete Response, n (%)	11 (68.8)	6 (66.7)	5 (71.4)
Recurrence, n (%)	5 (31.3)	3 (33.3)	2 (28.6)

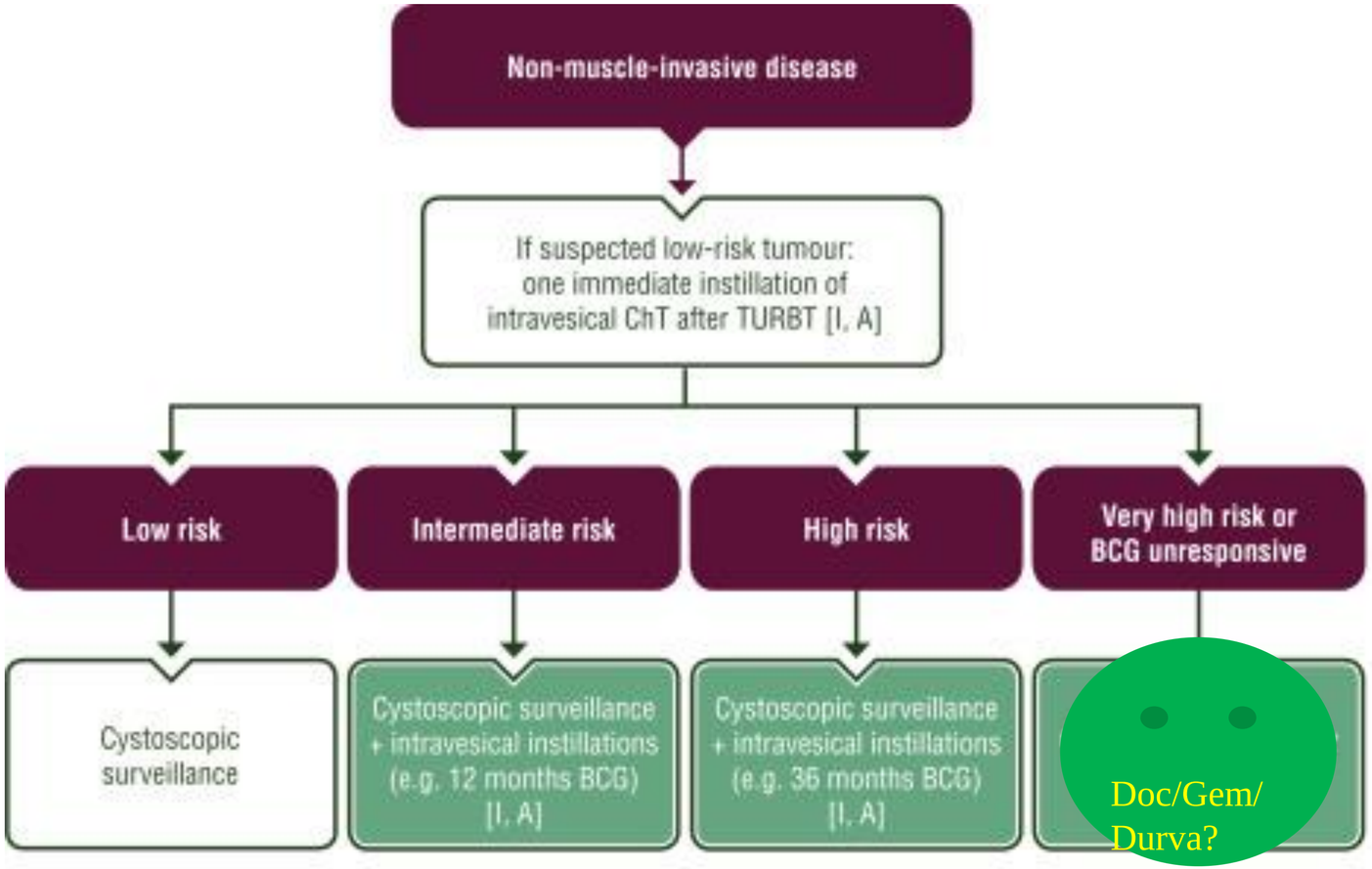
CI = Confidence Interval; CIS = Carcinoma In Situ

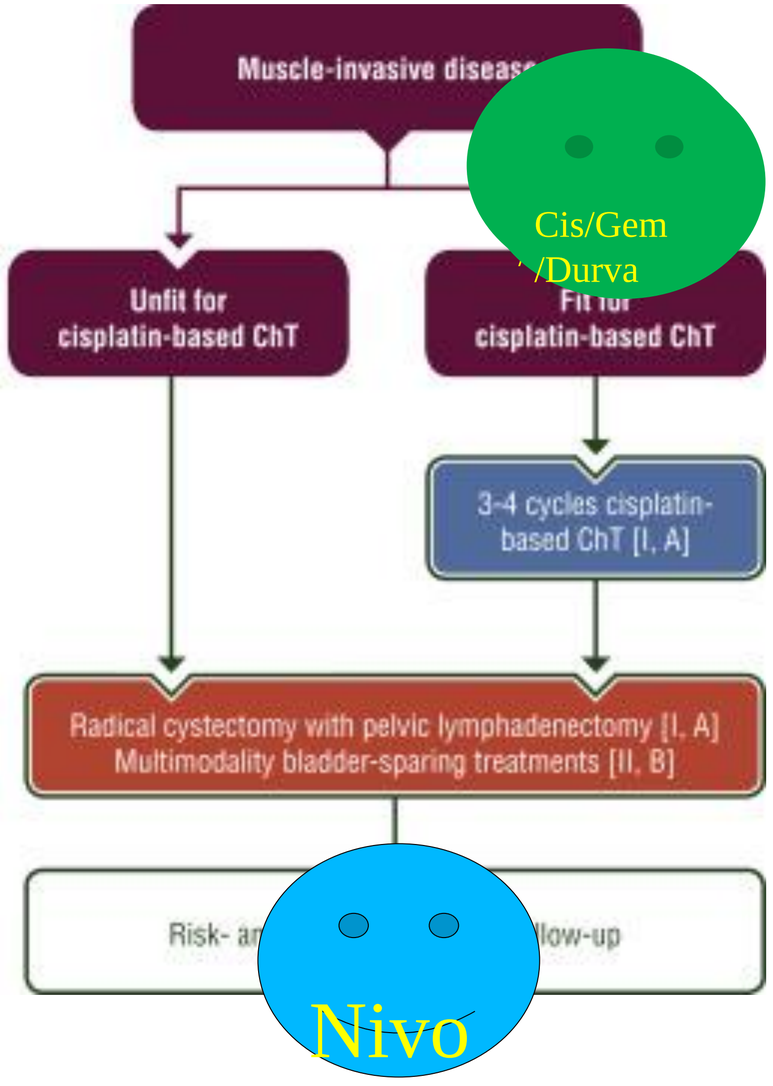
Response Duration and Recurrence Events



- 23 of 33 (69.7%) CRs ongoing
- 10 (27.0%) NMIBC recurrences and 3 (8.1%) MIBC recurrences observed
- Of the 4 recurrences detected at the 12-month time point, 1 had a normal cystoscopy and (-) cytology

CR = Complete Response; NMIBC = Non-muscle Invasive Bladder Cancer; MIBC = Muscle Invasive Bladder Cancer





ESMO Guidelines 2023

5 preguntas para la discusión

¿Es OS imprescindible para decidir o ya tenemos suficiente?

pCR: ¿basta por sí solo este endopoint para tomar decisiones?

EV/Pem: ¿realmente tiene competencia?

FGFR3: ¿se avecina una revolución?

¿El ADC definitivo está por llegar?