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

Part 2 of a 2-Part CME Symposium Series Held in Conjunction with the 2024 ASCO Genitourinary Cancers Symposium

Friday, January 26, 2024

7:00 PM – 9:00 PM PT (10:00 PM – 12:00 AM ET)

Faculty

Matthew Milowsky, MD, FASCO

Peter H O'Donnell, MD

Jonathan E Rosenberg, MD

Arlene Siefker-Radtke, MD

Moderator

Evan Y Yu, MD

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Dr Milowsky — Disclosures
Faculty

Contracted Research	Accuray, Acrivon Therapeutics, ALX Oncology, Amgen Inc, Arvinas, Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Clovis Oncology, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Incyte Corporation, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Mirati Therapeutics Inc, MorphoSys, Novartis, Seagen Inc
Nonrelevant Financial Relationships	Alliance for Clinical Trials in Oncology, Alliance Foundation Trials LLC, Elsevier (Co-Editor-in-Chief, *Clinical Genitourinary Cancer*), Hoosier Cancer Research Network Inc, Medscape, The Prostate Cancer Clinical Trials Consortium

Dr O'Donnell — Disclosures
Faculty

Advisory Committees	Merck, Seagen Inc
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Dr Rosenberg — Disclosures
Faculty

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Speakers Bureaus	EMD Serono Inc, Pfizer Inc
Nonrelevant Financial Relationships	Clinical Care Options, Medscape, MJH Life Sciences

Dr Siefker-Radtke — Disclosures
Faculty

No relevant conflicts of interest to disclose.

Dr Yu — Disclosures
Moderator

Consulting Agreements	Aadi Bioscience, Advanced Accelerator Applications, Bayer HealthCare Pharmaceuticals, Janssen Biotech Inc, Merck, Oncternal Therapeutics
Contracted Research	Bayer HealthCare Pharmaceuticals, Blue Earth Diagnostics, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Lantheus, Merck, Seagen Inc, Surface Oncology, Taiho Oncology Inc, Tyra Biosciences

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Dr Friedlander — Disclosures
Survey Participant

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Consulting Agreement	Merck
Contracted Research	Bristol Myers Squibb, Roche Laboratories Inc, Seagen Inc, Trishula Therapeutics Inc
Data and Safety Monitoring Board/Committee	AstraZeneca Pharmaceuticals LP

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Dr Plimack — Disclosures
Survey Participant

Advisory Committees and Consulting Agreements	Astellas, AstraZeneca Pharmaceuticals LP, Eisai Inc, EMD Serono Inc, IMV Inc, Merck, Pfizer Inc, Seagen Inc, Synthekine
Contracted Research	Merck

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Dr Sharma — Disclosures
Video Participant

Consulting Agreements	AstraZeneca Pharmaceuticals LP, Genzyme Corporation, Gilead Sciences Inc, GSK, Merck, Novartis, Pfizer Inc, Sanofi
Contracted Research	Gilead Sciences Inc, Merck, Novartis
Stock Options/Stock — Public Company	Amgen Inc, Janssen Biotech Inc, Johnson & Johnson Pharmaceuticals, Sanofi

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Commercial Support

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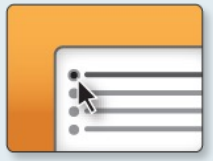

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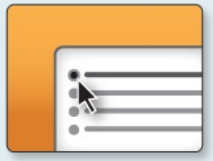

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Agenda

Module 1: Role of Anti-PD-1/PD-L1 Antibodies in Therapy for Nonmetastatic Urothelial Bladder Cancer (UBC) — Dr Milowsky

Module 2: Other Novel Strategies Under Investigation for Nonmetastatic UBC — Dr O'Donnell

Module 3: Front-Line Treatment for Metastatic UBC (mUBC) — Dr Rosenberg

Module 4: Emerging Role of HER2-Targeted Therapy for mUBC — Dr Yu

Module 5: Selection and Sequencing of Therapy for Relapsed/Refractory mUBC — Dr Siefker-Radtke

Consulting Faculty

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MODULE 1: Role of Anti-PD-1/PD-L1 Antibodies in Therapy for Nonmetastatic Urothelial Bladder Cancer (UBC) – Dr Milowsky

Consulting Faculty Questions

Adjuvant nivolumab after neoadjuvant chemoradiation and surgery for muscle-invasive bladder cancer (MIBC); discussing with patients

Neil Love, MD

Elizabeth R Plimack, MD, MS

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QUESTIONS FOR THE FACULTY

Elizabeth R Plimack, MD, MS

How do you discuss the benefits and risks of using adjuvant nivolumab with patients receiving neoadjuvant chemoradiation therapy?

Do you use adjuvant nivolumab for patients with upper tract urothelial cancer?

What are your thoughts on the emerging results of the Phase III AMBASSADOR trial of adjuvant pembrolizumab and the potential choice of IO in this setting?

Consulting Faculty Questions

Ongoing evaluation of the role of cell-free DNA assays to enhance adjuvant treatment strategies

Neil Love, MD

Terence Friedlander, MD

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QUESTIONS FOR THE FACULTY

Terence Friedlander, MD

Do you anticipate that subcutaneous immune checkpoint inhibitors will soon be available? What impact do you see this having on the patient experience and flow in the oncology clinic?

How do you think through the risk-benefit ratio surrounding the use of adjuvant nivolumab? Do you anticipate that ctDNA will eventually be used in UBC, and what are your thoughts about the design of ongoing trials evaluating this strategy?

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For a 65-year-old patient who receives neoadjuvant chemotherapy for MIBC and undergoes cystectomy, in general how do presence or absence of residual disease and PD-L1 status affect your decision whether the patient should receive postoperative adjuvant immunotherapy and which immunotherapy to administer? For how long do you generally administer adjuvant nivolumab?

	Presence or absence of residual disease (pCR or not)	PD-L1 status	Treatment duration
 Dr Milowsky	Use eligibility from study – ≥ypT2	Do not routinely check	1 year
 Dr O'Donnell	Residual pT2 disease or greater	Typically no but will order if "on the fence"	1 year
 Dr Rosenberg	Presence of invasive disease is key	No effect	1 year
 Dr Siefker-Radtke	More likely to consider it for ≥T3b or nodes	Not done	1 year
 Dr Yu	Residual pT2 disease or greater	No effect	1 year
 Dr Friedlander	Very important – if T3+ then we offer adjuvant nivolumab	Less important, not a major driver of decision	1 year
 Dr Plimack	Don't offer adjuvant Tx to patient with pCR; nivolumab	Little to no effect	1 year

pCR = pathologic complete response

Please describe the last patient in your practice diagnosed with muscle-invasive bladder cancer (MIBC) who received adjuvant nivolumab after neoadjuvant therapy and surgery.

	Age	PD-L1 status	One year of adjuvant nivolumab completed?	IO tolerability issues
 Dr Milowsky	74 years	Unknown	Yes	No irAEs
 Dr O'Donnell	65 years	Unknown	3 weeks in	None
 Dr Rosenberg	80 years	Negative	Yes	None
 Dr Siefker-Radtke	65 years	Unknown	Still on Tx	—
 Dr Yu	67 years	Unknown	4 months in	No significant IO-related, mild rash
 Dr Friedlander	75 years	Negative	4 months in	Infusion reaction
 Dr Plimack	43 years	Unknown	Ongoing	No irAEs

IO = immunotherapy; irAEs = immune-related adverse events

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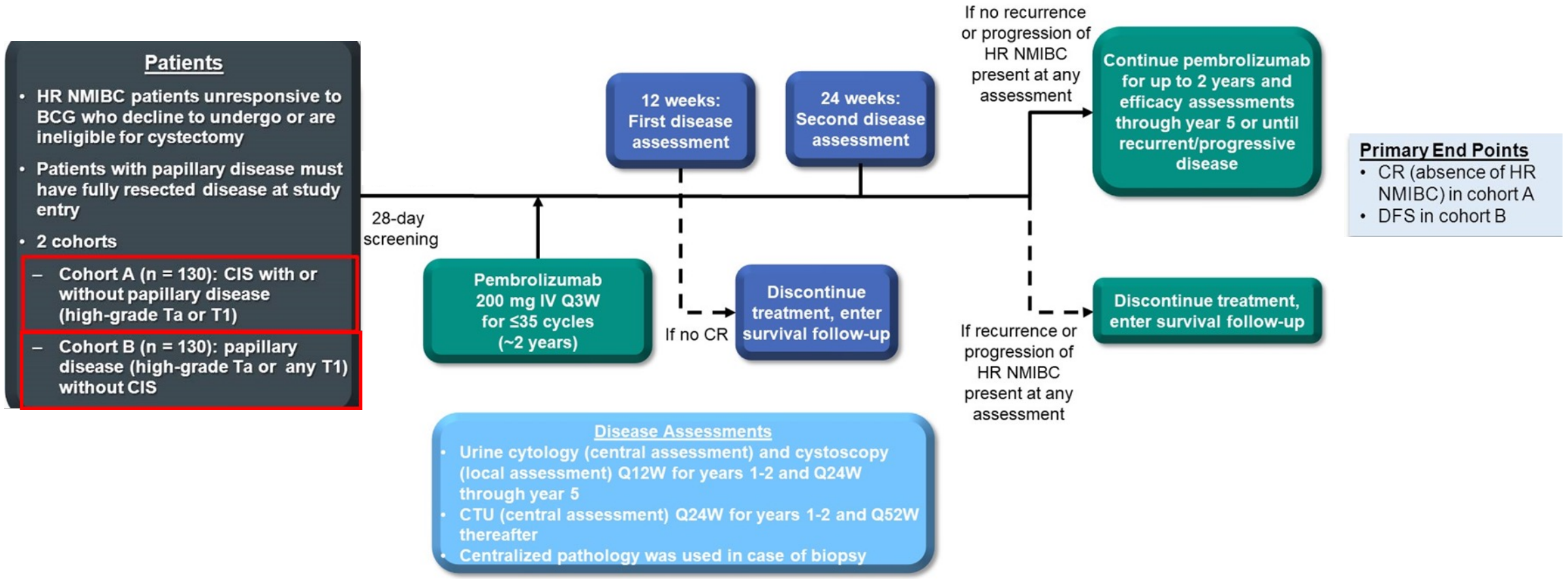
Role of Anti-PD-1/PD-L1 Antibodies in Nonmetastatic Urothelial Bladder Cancer

Matthew Milowsky, MD
George Gabriel and Frances Gable Villere Distinguished Professor
Section Chief, Genitourinary Oncology

KEYNOTE-057: Single-Arm, Open-Label Phase 2 Study (NCT02625961)

KEYNOTE-057 Study Design

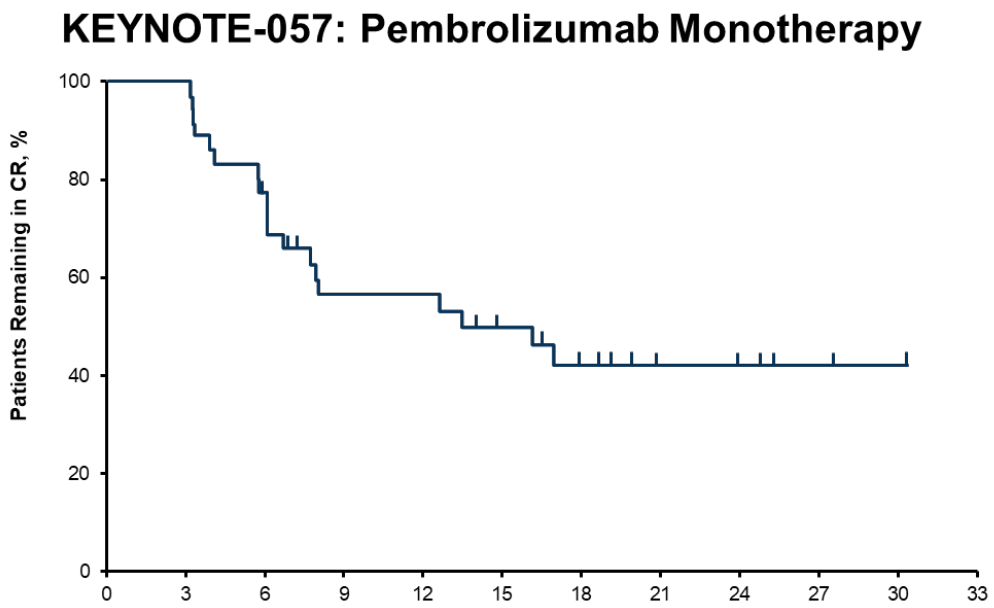


CTU, computed tomography urography; ECOG PS, Eastern Cooperative Oncology Group performance status.

Necchi A et al. Genitourinary Cancers Symposium 2023;Abstract LBA442.

KEYNOTE-057 Cohort A & B Results

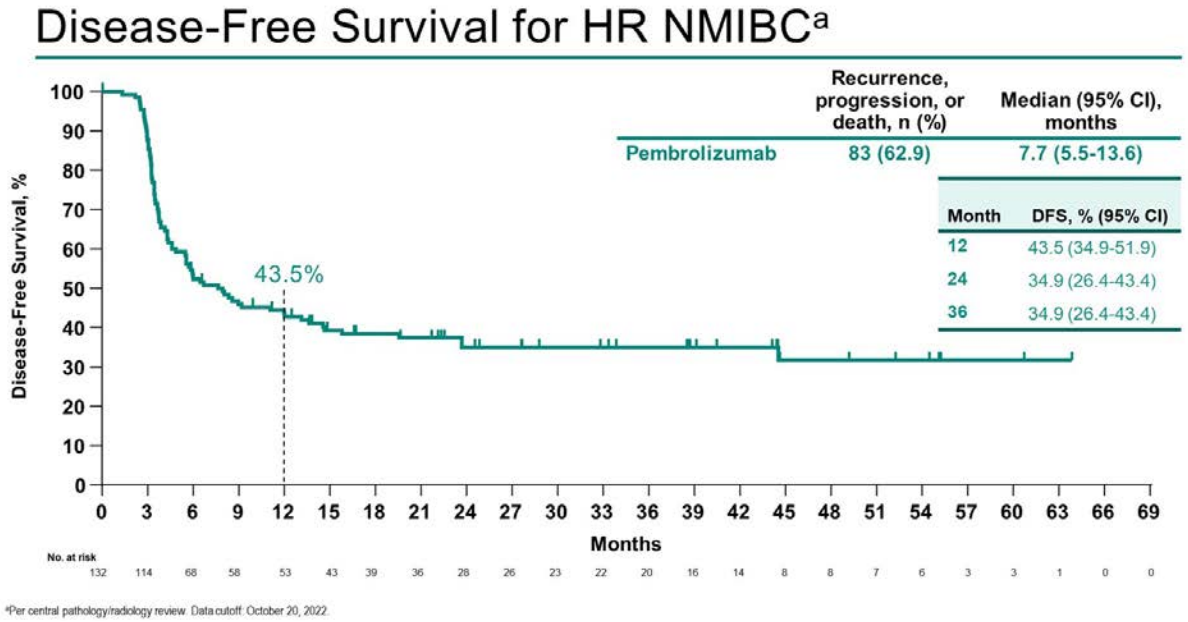
COHORT A



Median follow-up of 36.4 months

- Of 96 patients with BCG-unresponsive NMIBC, 39 (41%) had a CR at 3 mo
- Median DOR: 16.2 mo
- Of 39 responders, 18 (46%) remained in CR ≥12 mo; 11 (28%) remained in CR at the time of data cutoff

COHORT B



[a]Per central pathology/radiology review. Data cutoff: October 20, 2022.

January 2020: Pembrolizumab was FDA approved for the treatment of patients with BCG-unresponsive, high-risk NMIBC with carcinoma in situ with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy

Balar AV et al. *Lancet Oncol* 2021;22:919-930
Necchi A et al. Genitourinary Cancers Symposium 2023;Abstract LBA442.

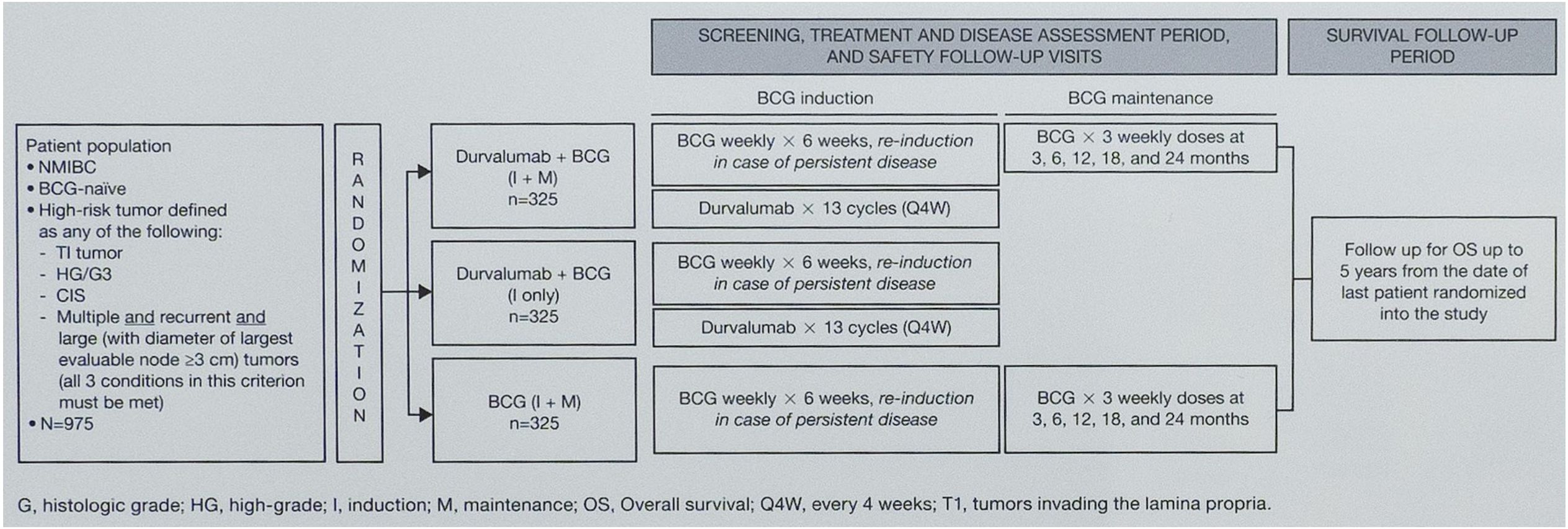
Ongoing phase III trials of anti-PD-(L)1 plus BCG in BCG-naïve NMIBC

PD-(L)1 inhibitors in phase 3 trials—first-line therapy for BCG-naïve, high-risk NMIBC.

	Durvalumab	Atezolizumab	Sasanlimab	Pembrolizumab
NCT number (familiar name)	NCT03528694 (POTOMAC)	NCT03799835 (ALBAN)	NCT04165317 (CREST)	NCT03711032 (KEYNOTE-676)[a]
Start/estimated primary completion dates	May 2018/Oct 2024	Jan 2019/Apr 2024	Dec 2019/Jun 2024	Dec 2018/Dec 2025
Trial design	Randomized, open-label, parallel-group, multicenter	Randomized, open-label, parallel-group, multicenter	Randomized, open-label, parallel-group, multicenter	Randomized, open-label, parallel-group, multicenter
Enrolled pts	n = 1018 (actual)	n = 516 (estimated)	n = 1160 (estimated)	n = 1405 (estimated)
Treatment arms	Durvalumab + BCG (IND + MAIN) or + BCG (IND) vs. BCG control	Atezolizumab + BCG (IND + MAIN) vs. BCG control	Sasanlimab + BCG (IND + MAIN) or + BCG (IND) vs. BCG control	Pembrolizumab + BCG (IND + MAIN) or + BCG (IND + reduced MAIN) vs. BCG (IND + MAIN)
PD-(L)1 regimen	Intravenous	Intravenous	Subcutaneous	Intravenous
Primary endpoint	DFS	RFS	EFS	EFS
Secondary endpoints[b]	DFS at 24 months; OS at 5 years	PFS, OS, DSS, CR, DW	OS, CR (pts with CIS), DSS, time to cystectomy	CR, DOR, 12-month DOR (CIS pts), RFS, OS, DSS

Bedke et al. *Urologic Oncology*. 2023;41:461-75.

POTOMAC: Phase III Study of Durvalumab with BCG versus BCG Alone for High-Risk, BCG-Naïve NMIBC



G, histologic grade; HG, high-grade; I, induction; M, maintenance; OS, Overall survival; Q4W, every 4 weeks; T1, tumors invading the lamina propria.

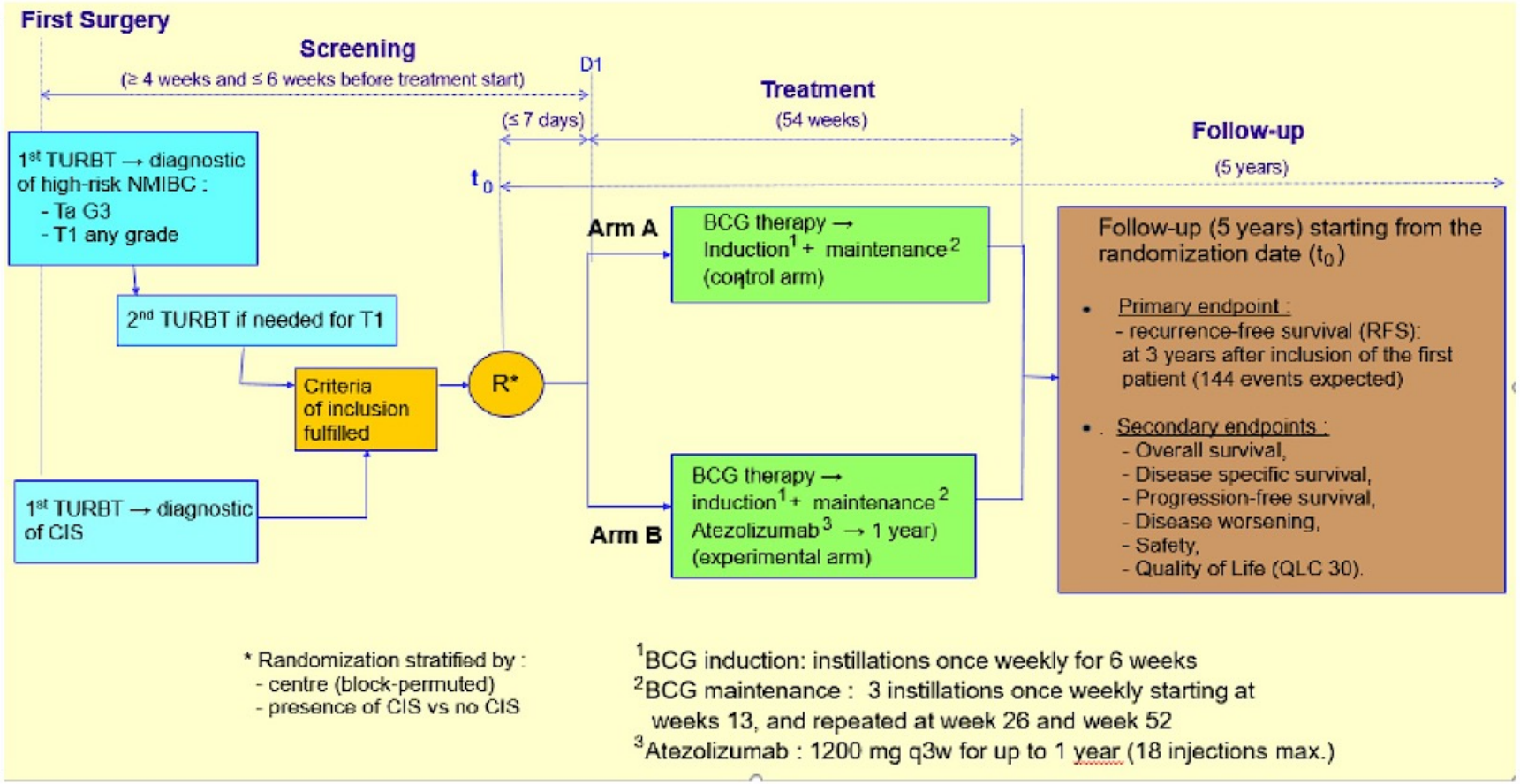
De Santis M et al. Genitourinary Cancers Symposium 2019;Abstract TPS500.

ALBAN: Phase III Trial of Atezolizumab with BCG versus BCG Alone for BCG-Naïve, High-Risk NMIBC

Patient population

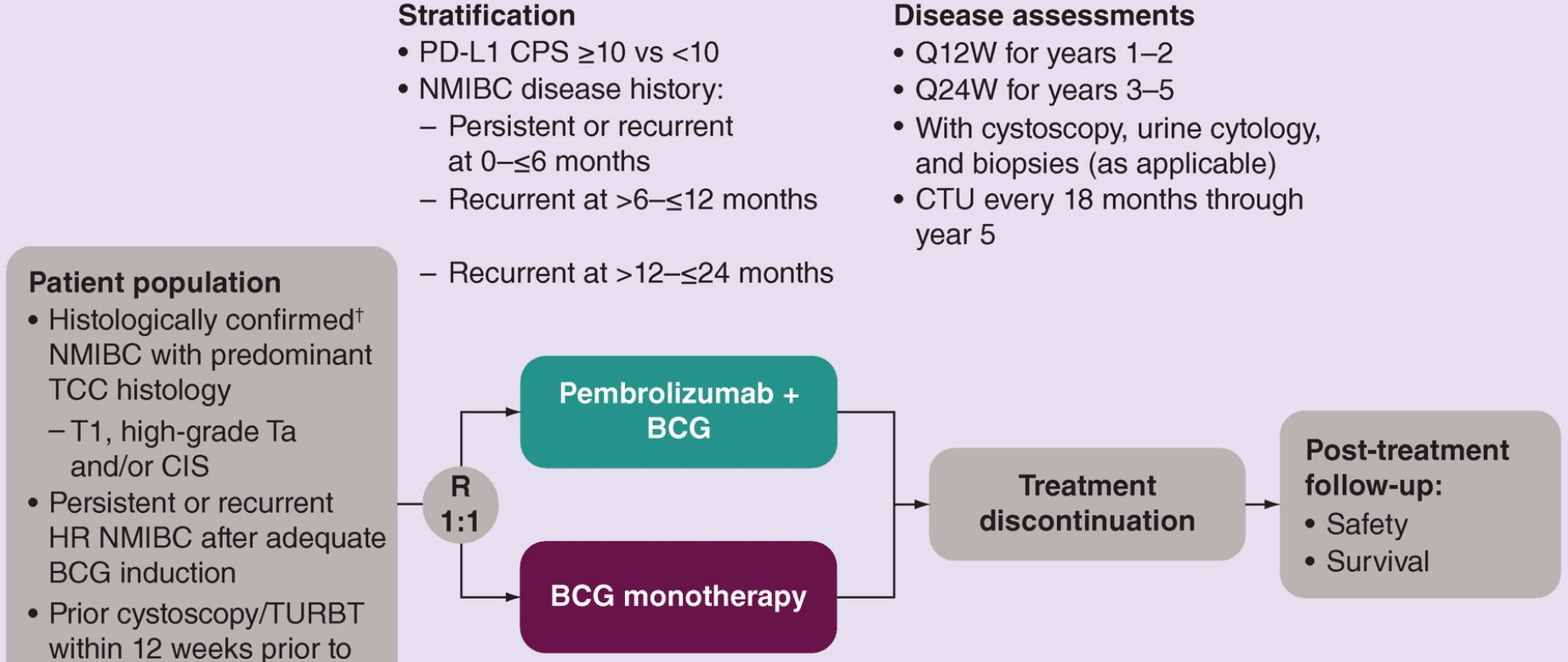
N=614

- Histologicall-confirmed NMIBC with predominant TCC histology
- **High risk NMIBC** defined
  - High grade and/or
  - T1 and/or
  - In situ carcinoma
- PS 0-2
- BCG naive
- Prior TURBT ≥ 4 weeks but ≤ 6 weeks before therapy
- Tumor samples available for PDL1 status assessment



Roupret M et al. ASCO 2019;Abstract TPS4589.

KEYNOTE-676 – Phase III trial of pembrolizumab plus BCG versus BCG monotherapy in patients with persistent/recurrent high-risk NMIBC after BCG induction



Primary Endpoint: CR rate in patients with CIS
Secondary Endpoints: EFS, 12-month EFS rate
RFS, OS, DSS, time to cystectomy, DOR, 12-mo DOR rate, HRQoL

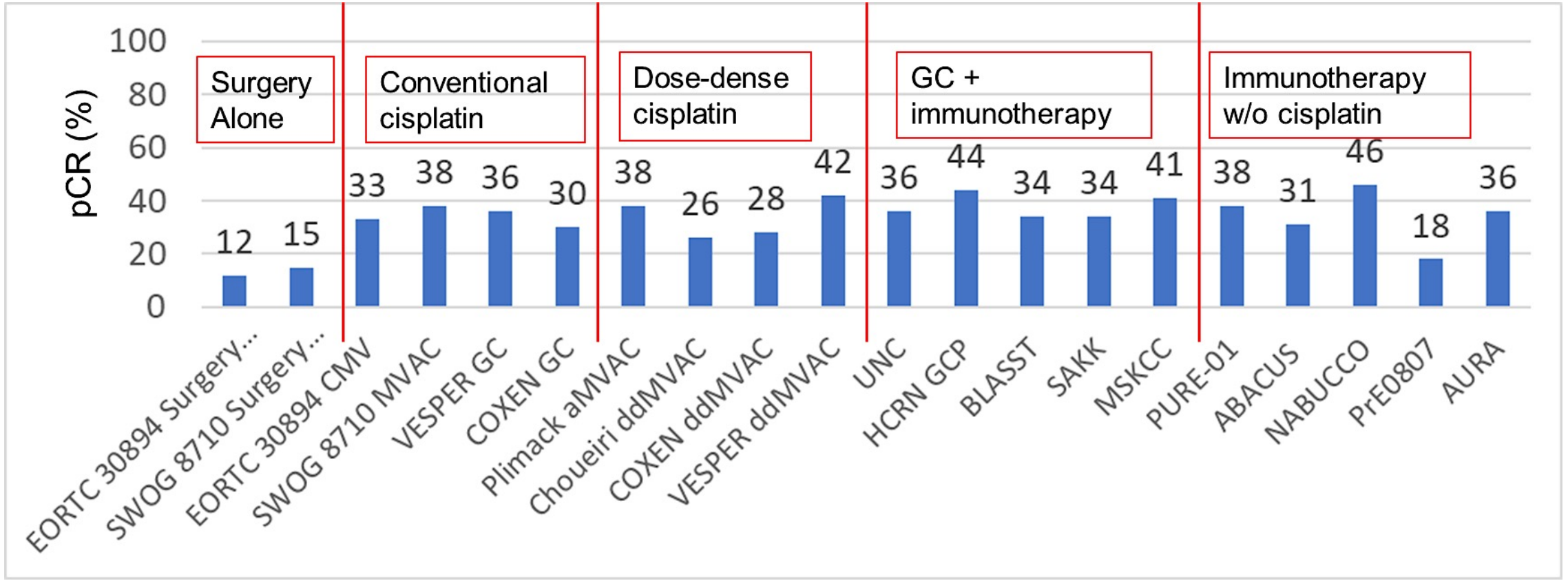
Kamat et al. *Future Oncology*. 2020;16.

Neoadjuvant ICI in patients with MIBC

Study	PURE-01	ABACUS	NABUCCO	AURA
# patients	50	95	24 (14)	28
IO agent	Pembrolizumab	Atezolizumab	Ipilimumab + nivolumab	Avelumab
# cycles	3 (9 weeks)	2 (6 weeks)	3 I -> I+N -> N (3, I+N x 2 -> N)	4 (8 weeks)
pCR (pT0)	38%	31%	46% (43%)	36%*
pRR (<pT2)	54%	Not reported	58% (57%)	39%

* pCR defined as pT0/is

Necchi et al, JCO 2018, Powles et al, Nat Med 2019, Kaimakliotis et al, ASCO Annual Mtg 2020;abstr 5019, van Dorp et al, ESMO 2021;abstr 5132, Van Dijk et al, ASCO Annual Mtg 2020;abstr 5020, Milowsky ASCO Annual Meeting 2022.



Grossman et al, NEJM 2003
Flaig et al, CCR 2021
Gupta et al, JCO 38,6_supp (Feb 2020)
Necchi et al, JCO 2018
Grivas et al, ASCO Annual Mtg 2021, abstr 4518

EORTC 30894, JCO 2011
Rose et al, GU ASCO 2021, abstr 396
Cathomas et al, GU ASCO 2021, abstr 430
Powles et al, Nat Med 2019
Kaimakliotis et al, ASCO Annual Mtg 2020, abstr 5019

Pfister et al, Euro Urol 2021
Hoimes et al, ESMO 2018, abstr 5681
Funt et al, ASCO Annual Mtg 2021, abstr 4517
Van Dijk et al, ASCO Annual Mtg 2020, abstr 5020
Milowsky ASCO Annual Mtg 2022

	ypT0	<ypT2	2y PFS/EFS	2y DFS	2y OS	3y PFS
VESPER						
dd-MVAC	42%	63%	~ 77%		~ 88%	66%
GC	36%	50%	~ 62%		~ 79%	56%
SAKK						
GC-D	34%	60%	76%		87%	NA
ABACUS						
Atezo	31%			68% (85% with CR)	77%	

VESPER: PFS at 3 years (time to detection bladder cancer progression or death)
SAKK: EFS at 2 years (PD during neoadjuvant treatment, locoregional or metastatic recurrence or death)

Pfister et al. J Clin Oncol. 2022, Szabados et al. Eur Urol. 2022,
Milowsky ASCO Annual Meeting 2022.

Ongoing Phase III studies – ICI + chemo

Randomized trials are investigating combination chemo-immunotherapy in MIBC

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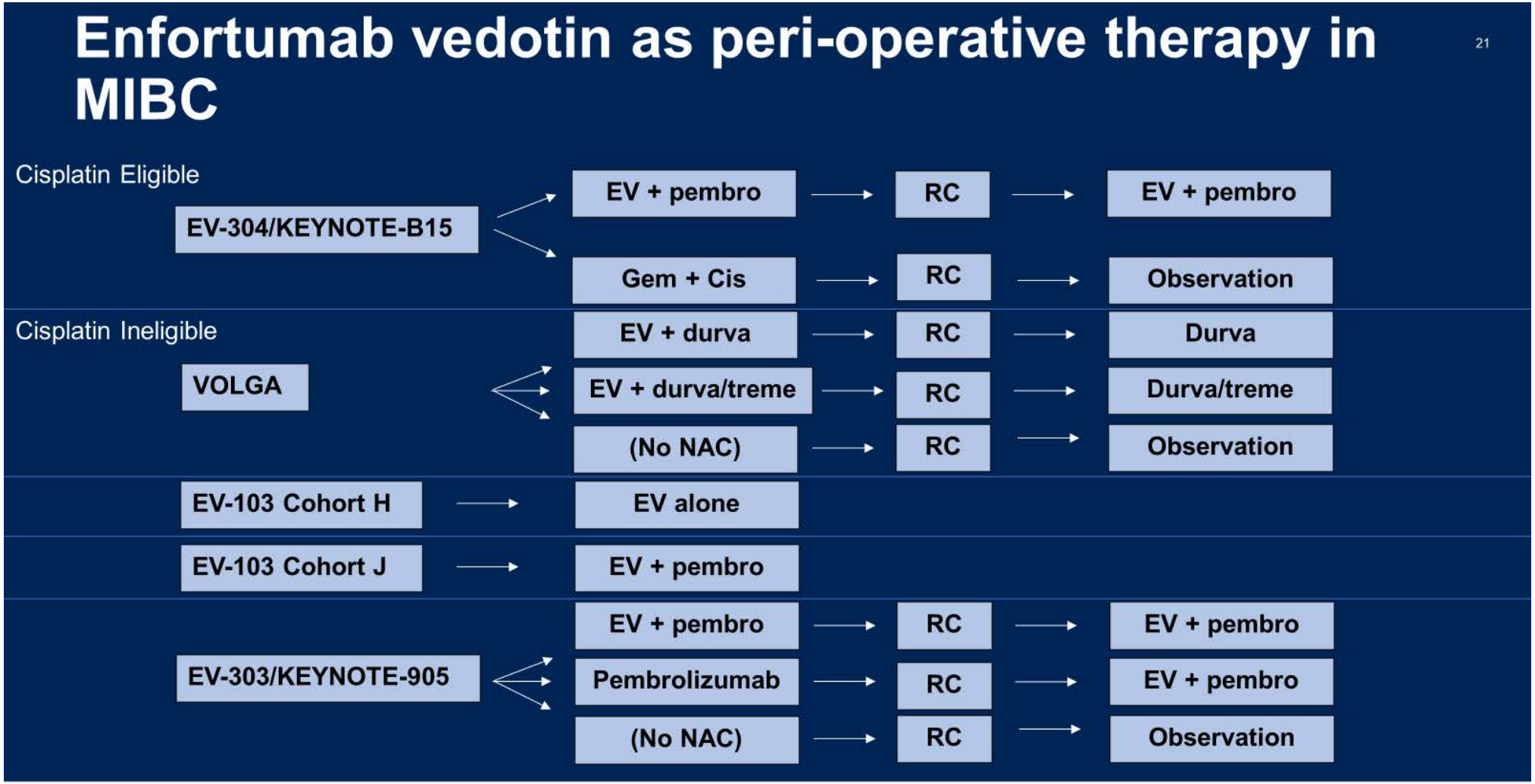
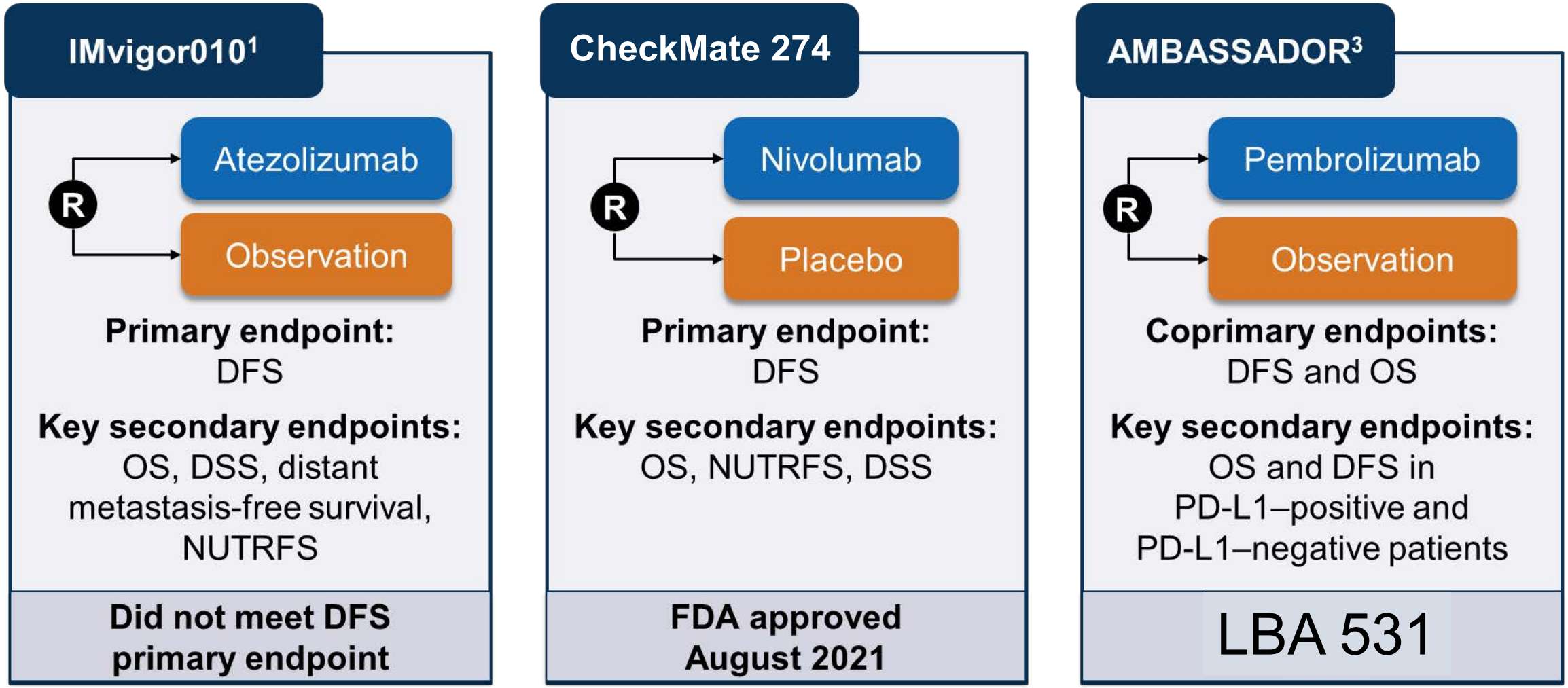
Trial	n	Immunotherapy	Chemotherapy	Primary Outcome	Adjuvant?
NIAGARA	1050	Durvalumab	Gemcitabine + Cisplatin	Co: pCR + EFS	Yes – durva arm only
KEYNOTE-866	790	Pembrolizumab	Gemcitabine + Cisplatin	Co: pCR + EFS	Yes – pembro arm only
ENERGIZE	976	Nivolumab *or* Nivolumab + IDO1-inhibitor linrodostat	Gemcitabine + Cisplatin	Co: pCR + EFS	Yes – nivo arms only

ICI plus EV



Adjuvant trials with PD-1/L1 inhibitors



https://clinicaltrials.gov/ct2/show/NCT02450331.
https://clinicaltrials.gov/ct2/show/NCT02632409.
https://clinicaltrials.gov/ct2/show/NCT03244384.

CheckMate 274

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

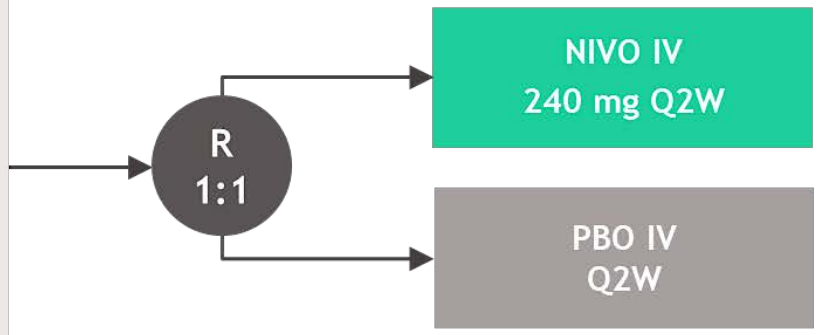
N = 709

Key inclusion 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

Minimum[c]/median (range)[d] follow-up, months:

ITT population: 31.6/36.1 (0.0-75.3)
All randomized with PD-L1 ≥ 1%: 32.1/37.1 (0.0-75.3)
MIBC population: 31.6/34.5 (0.0-75.3)
MIBC and PD-L1 ≥ 1%: 32.1/36.7 (0.0-75.3)

Database lock, October 20, 2022

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[e]
Exploratory endpoints included: DMFS, PFS2, and safety

[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 immunohistochemistry assay. [c]Defined as time from clinical cutoff date to last patient's randomization date. [d]Defined as time between randomization date and last known date alive (for patients who are alive) or death. [e]OS will be assessed at a future database lock. OS and DSS data are not presented.
DSS, disease-specific survival; ITT, intent-to-treat; IV, intravenous; OS, overall survival; PD-L1, programmed death ligand 1; PFS2, second progression-free survival; Q2W, every 2 weeks; R, randomized.

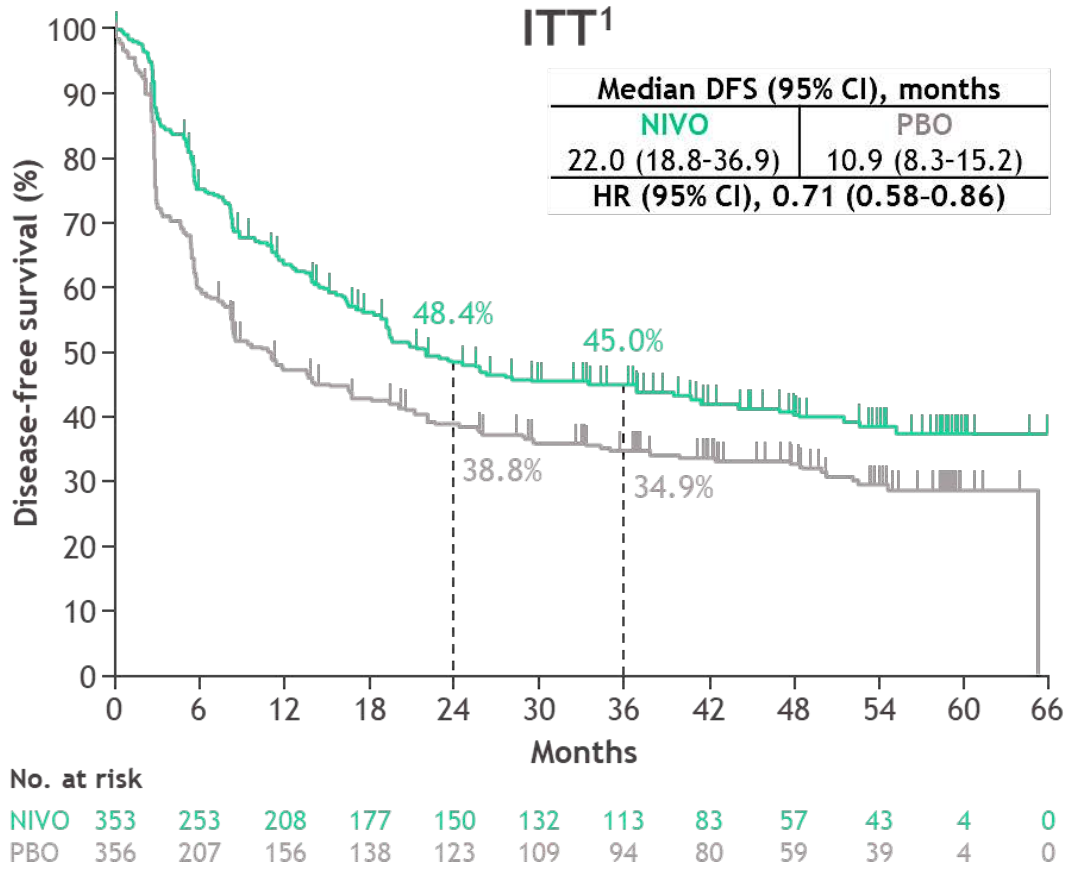
Baseline characteristics

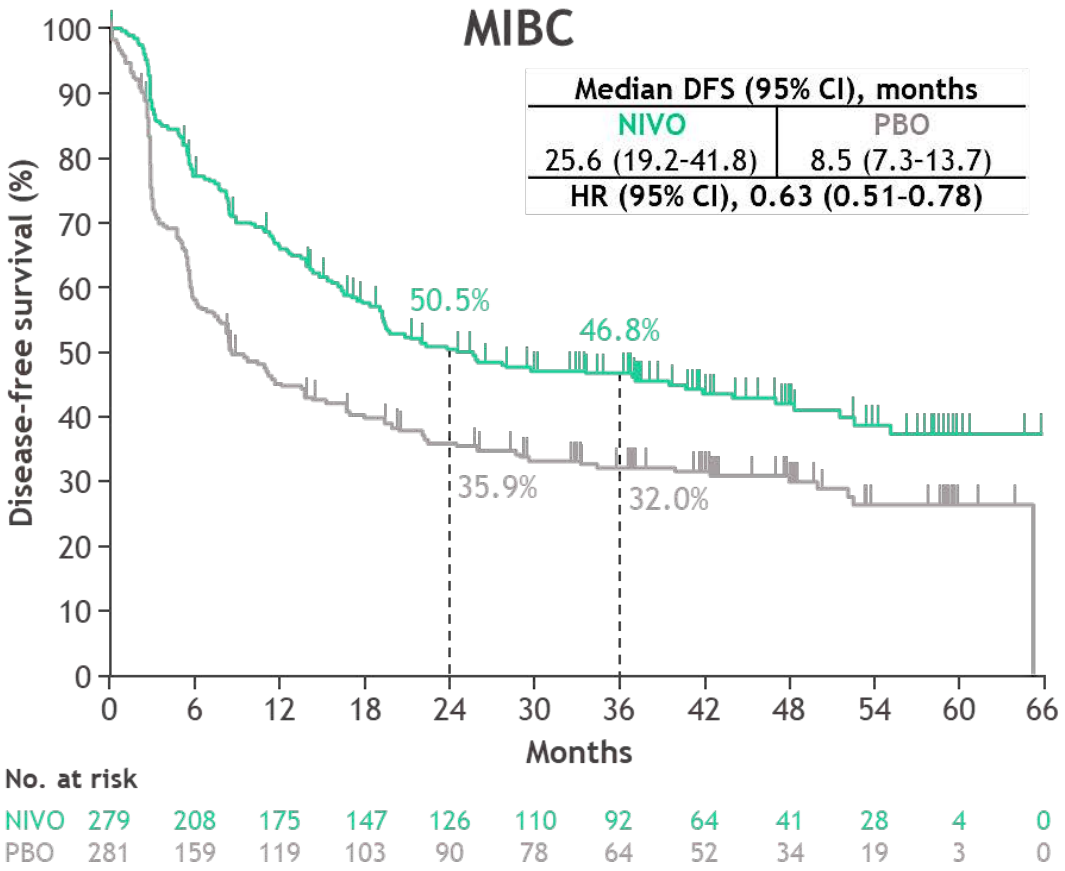
	ITT[1]		MIBC[2]	
	NIVO (N = 353)	PBO (N = 356)	NIVO (n = 279)	PBO (n = 281)
Mean age (range), years	65.3 (30-92)	65.9 (42-88)	64.8 (37-83)	65.7 (42-88)
Male, %	75	77	78	79
Race or ethnic group, %				
White	75	76	83	82
Asian	23	21	14	15
Black	1	1	< 1	1
Other	2	1	3	2
Unreported	0	< 1	0	< 1
ECOG PS,[a] %				
0	63	62	63	58
1	35	35	35	39
2	2	3	2	3
Tumor origin at initial diagnosis, %				
Urinary bladder	79	79	100	100
Renal pelvis	12	15	0	0
Ureter	8	6	0	0
Tumor PD-L1 expression ≥ 1% as recorded at randomization, %	40[b]	40[b]	40[c]	41[c]
Prior neoadjuvant cisplatin, %	43	44	51	51
Pathologic T stage at resection, %				
pTX	1	0	2	0
pT0	1	2	2	2
pTis	1	1	1	1
pT1	4	4	3	5
pT2	18	18	20	23
pT3	58	57	52	49
pT4a	16	17	19	20
Not reported	< 1	< 1	< 1	< 1
Nodal status at resection, %				
N+	47	47	53	55
N0/x with < 10 nodes removed	27	28	17	16
N0 with ≥ 10 nodes removed	26	25	30	28
Not reported	< 1	< 1	< 1	< 1

[a]Not reported for 1 patient in the PBO arm. [b]By interactive voice response system. [c]By clinical source.
ECOG PS, Eastern Cooperative Oncology Group performance status.
1. Bajorin DF, et al. *N Engl J Med* 2021;384:2102-2114. 2. Witjes JA, et al. Poster presentation at ASCO 2022. Abstract 4585.

Disease-free survival

- Continued DFS benefit was observed with NIVO versus PBO both in the ITT and MIBC populations



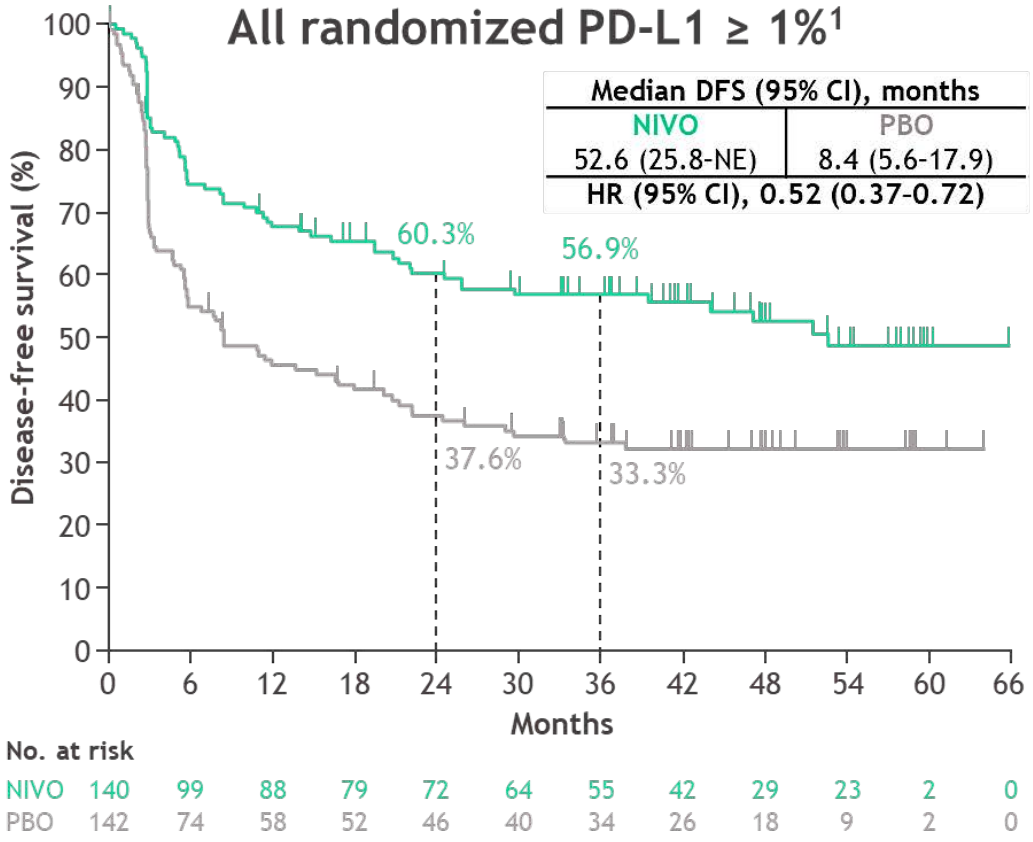


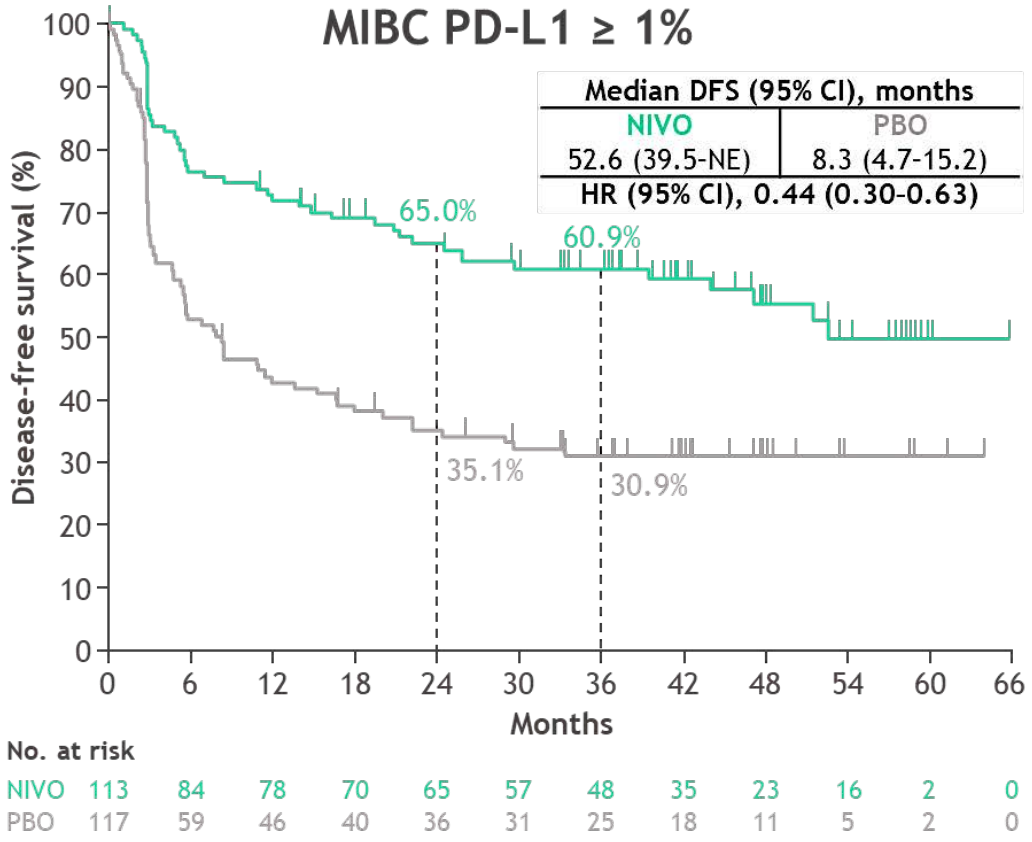
Minimum follow-up in both the ITT and MIBC populations, 31.6 months. DFS was defined as the time between the date of randomization and the date of first recurrence (local urothelial tract, local non-urothelial tract, or distant) or death (of any cause), whichever occurs first. CI, confidence interval; HR, hazard ratio.

1. Galsky MD, et al. Oral presentation at ASCO GU 2023. Abstract LBA443.

Disease-free survival

- Continued DFS benefit with NIVO versus PBO was observed both in all randomized patients with PD-L1 ≥ 1% and in patients with MIBC and PD-L1 ≥ 1%



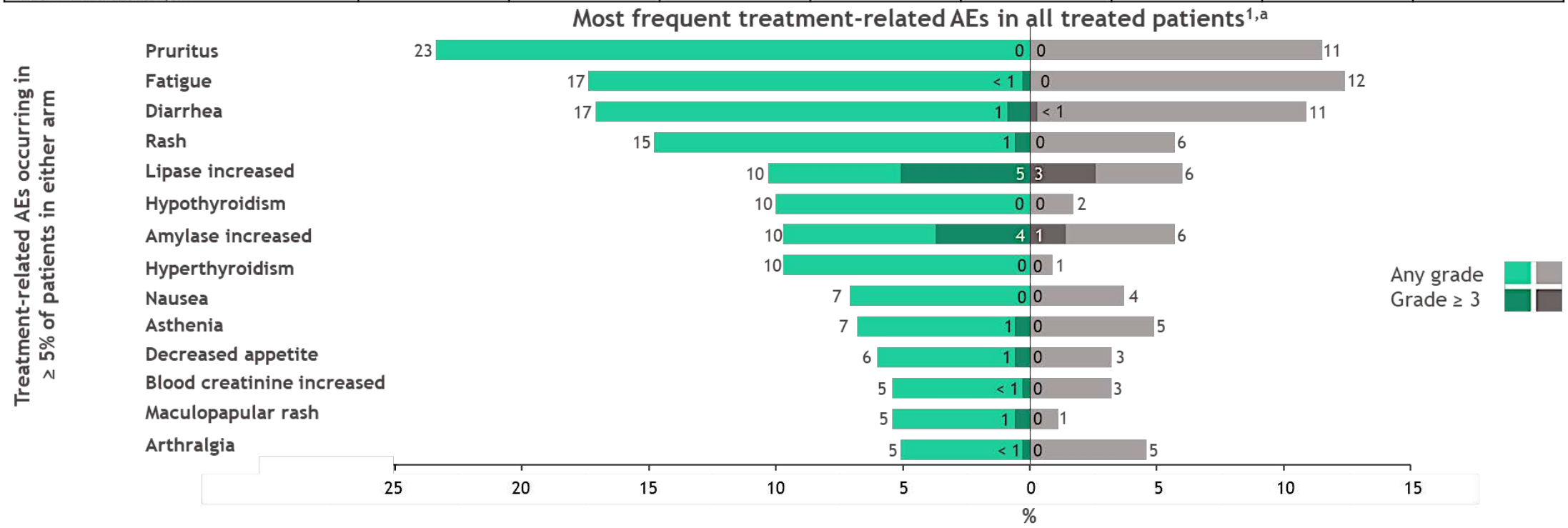


Minimum follow-up in both the ITT and MIBC populations, 31.6 months. DFS was defined as the time between the date of randomization and the date of first recurrence (local urothelial tract, local non-urothelial tract, or distant) or death (of any cause), whichever occurs first. NE, not estimable.

1. Galsky MD, et al. Oral presentation at ASCO GU 2023. Abstract LBA443.

Safety

	All treated patients[1]				All treated patients with MIBC			
	NIVO (n = 351)		PBO (n = 348)		NIVO (n = 277)		PBO (n = 275)	
	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3
Treatment-related AEs, %	79	18	56	7	80	17	56	6
Treatment-related AEs leading to discontinuation, %	14	7	2	1	15	7	2	1



There were 3 treatment-related deaths in the NIVO arm in the ITT population (2 instances of pneumonitis and 1 instance of bowel perforation). [a]Includes events reported between the first dose and 30 days after the last dose of NIVO or PBO in both the ITT and MIBC populations. Minimum follow-up in both the ITT and MIBC populations, 31.6 months. AE, adverse event.

1. Galsky MD, et al. Oral presentation at ASCO GU 2023. Abstract LBA443.

A031501 AMBASSADOR: Study Design

Phase 3 randomized, open label, multicenter study of adjuvant pembrolizumab vs observation in patients with high-risk muscle-invasive urothelial carcinoma (MIUC)

NCT03244384

Key Eligibility

- Muscle-invasive urothelial carcinoma: bladder, urethra, renal pelvis, ureter
- Post-radical surgery (cystectomy, nephrectomy, nephroureterectomy, or ureterectomy) ≥ 4 but ≤ 16 weeks
- Post-neoadjuvant chemotherapy and ≥ pT2 and/or N+/+margins

OR

- cisplatin-ineligible or refusing and ≥ pT3 or pN+/+margins

Stratify

- PD-L1 status*
- Neoadjuvant chemotherapy yes/no
- Pathologic stage:
  - pT2/3/4aN0
  - pT4aN0
  - pT4bNx/N1-3
  - +surgical margins

N=739

R 1:1

Pembrolizumab 200 mg q3W 1 year (18 cycles)

Observation

Dual Primary Endpoints

- **Disease-free survival**
- **Overall survival**

Key Secondary Endpoints
- DFS/OS PD-L1 +/-
- Safety

Correlative Endpoints
- DFS/OS ctDNA +/-
- DFS/OS immune gene signatures
- DFS/OS tumor molecular subtype
- DFS/OS TCR clonality
- QOL

*PD-L1 status was tested centrally and defined using the combined positive score: percentage of PD-L1-positive tumor cells and infiltrating immune cells relative to the total number of tumor cells. PD-L1 positive = CPS ≥ 10%, Dako PD-L1 immunohistochemistry 22C3 pharmDx assay. DFS: disease-free survival (defined as new MIUC, metastatic disease, or death without recurrence); OS: overall survival

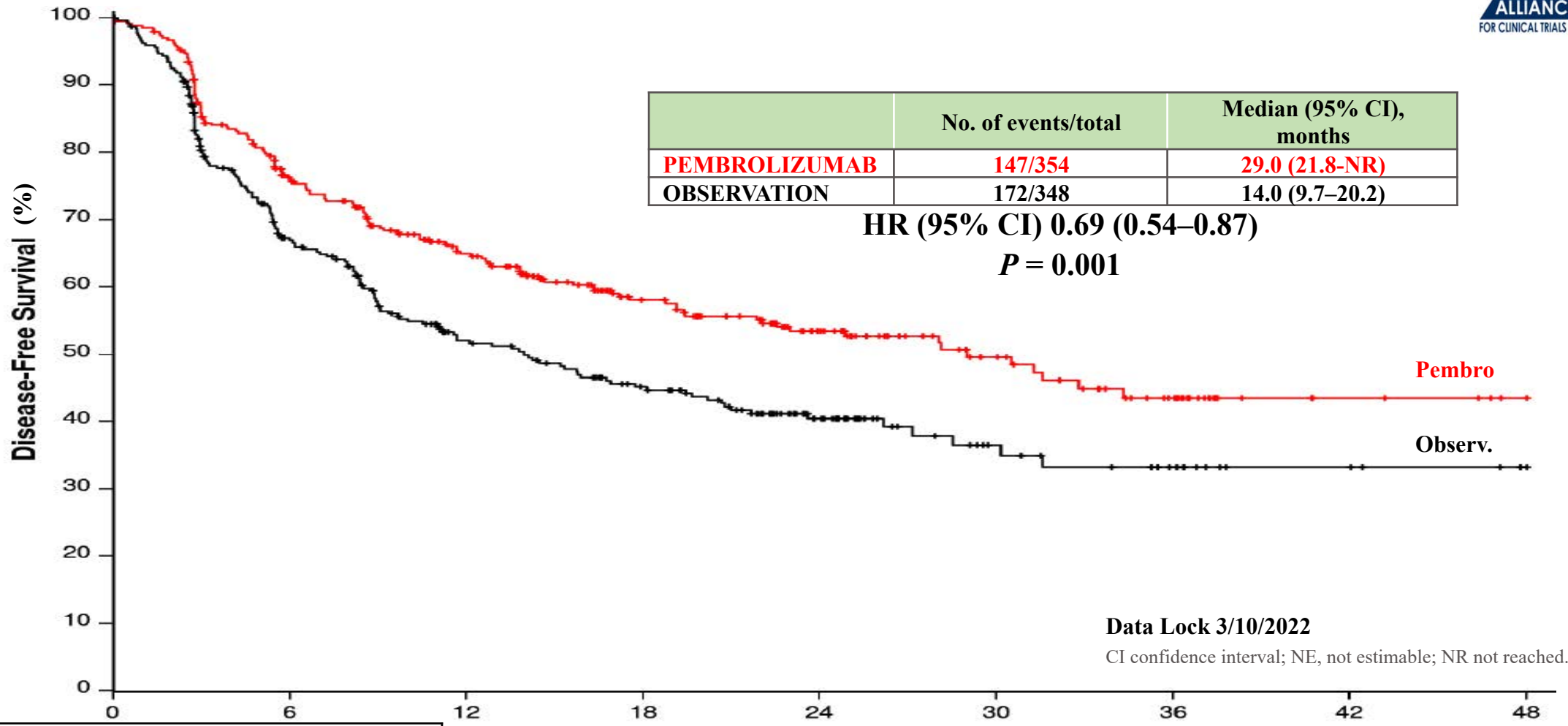
PRESENTED BY: Andrea B. Apolo, MD @apolo_andrea

A031501 AMBASSADOR: Disease-Free Survival

	No. of events/total	Median (95% CI), months
PEMBROLIZUMAB	147/354	29.0 (21.8-NR)
OBSERVATION	172/348	14.0 (9.7–20.2)

HR (95% CI) 0.69 (0.54–0.87)

***P* = 0.001**



Data Lock 3/10/2022

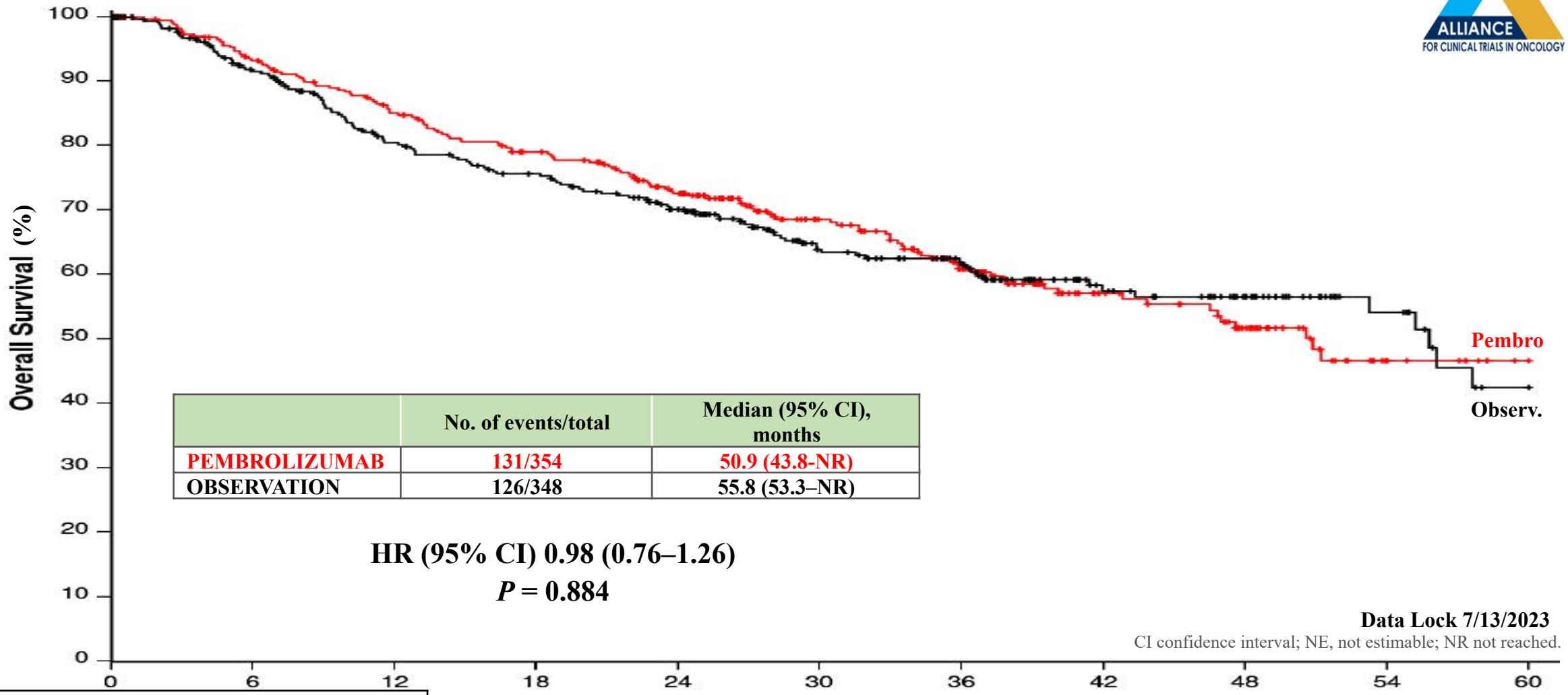
CI confidence interval; NE, not estimable; NR not reached.

Median follow-up (range) 22.3 months (0.03-48.9)

Patients-at-Risk

Pembro	354	238	178	123	80	45	26	6	2
Observ.	348	192	125	97	53	23	13	6	1

A031501 AMBASSADOR: Overall Survival (interim)



	No. of events/total	Median (95% CI), months
PEMBROLIZUMAB	131/354	50.9 (43.8-NR)
OBSERVATION	126/348	55.8 (53.3–NR)

HR (95% CI) 0.98 (0.76–1.26)
***P* = 0.884**

Data Lock 7/13/2023

CI confidence interval; NE, not estimable; NR not reached.

Median follow-up (range) 36.9 months (0-63.9)

Patients-at-Risk

Pembro	354	313	280	253	218	152	115	69	50	17	10
Observ.	348	296	249	227	195	139	117	65	45	23	12

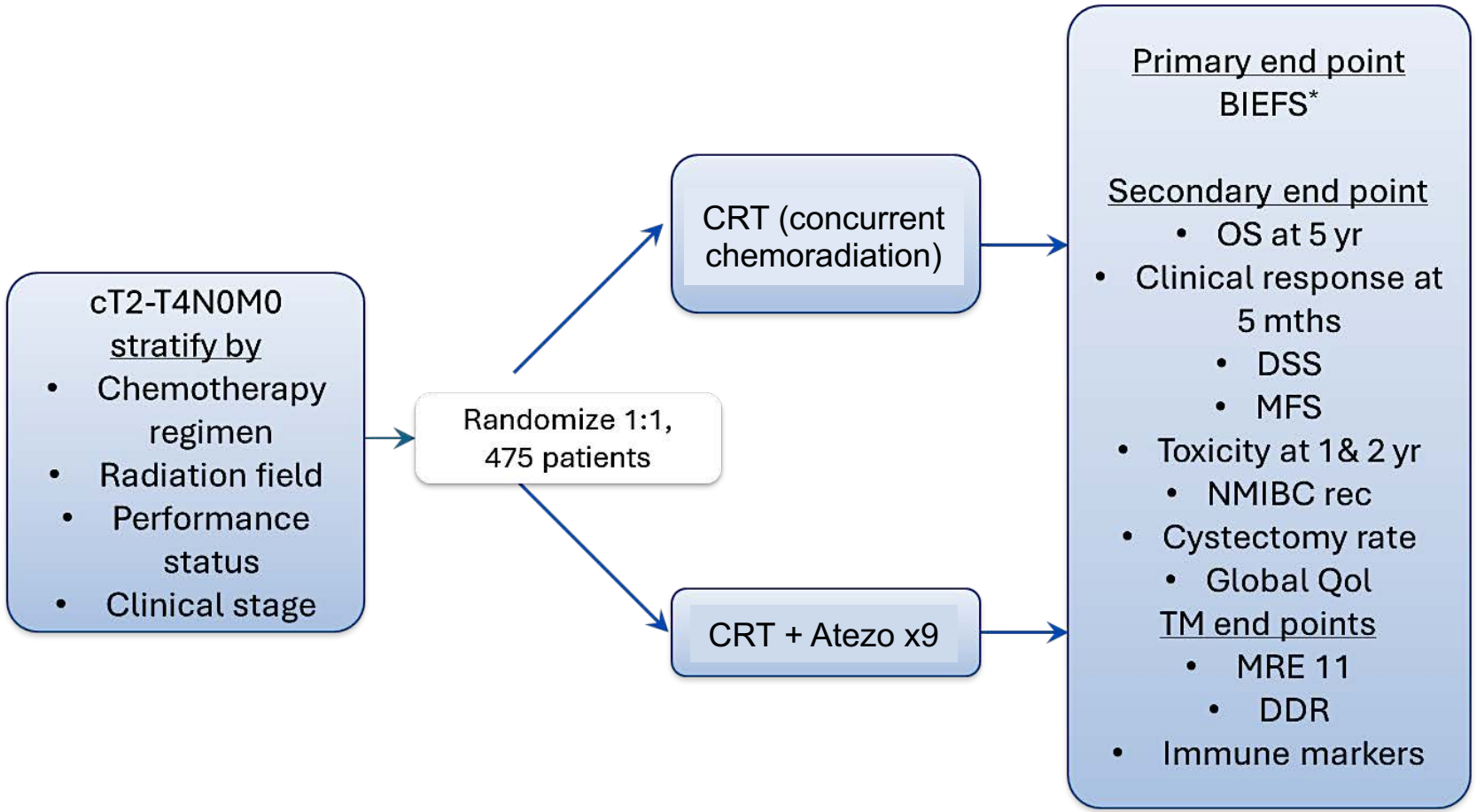
PRESENTED BY: Andrea B. Apolo, MD

@apolo_andrea

A031501 AMBASSADOR: Safety Summary

All AEs (regardless of attribution)		Pembrolizumab N=345		Observation N=343
Adverse Events (any)		**N (%)**		**N (%)**
Grade 3	**Grade ≥3 167 (48.4)**	133 (38.6%)	**Grade ≥3 109 (31.8)**	80 (23.3%)
Grade 4		17 (4.9%)		13 (3.8%)
Grade 5		17 (4.9%)		16 (4.7%)
Hematologic Adverse Events				
Grade 3		19 (5.5%)		9 (2.6%)
Grade 4		3 (0.9%)		0 (0.0%)
Grade 5		0 (0.0%)		0 (0.0%)
Non-Hematologic Adverse Events				
Grade 3		130 (37.7%)		78 (22.7%)
Grade 4		16 (4.6%)		13 (3.8%)
Grade 5		17 (4.9%)		16 (4.7%)

Phase III trial of concurrent chemoradiation with or without atezolizumab for localized MIBC: SWOG/NRG Intergroup Trial (S1806) (NCT03775265)



*BIEFS (bladder intact event free survival) includes: muscle invasive recurrence in the bladder, regional pelvic soft tissue or nodal recurrence, distant metastases, bladder cancer or toxicity related death or cystectomy

SWOG

c/o Himanshu Nagar

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

Conclusion

- Pembrolizumab monotherapy is a treatment option for patients with high-risk BCG-unresponsive NMIBC
- Additional studies are needed prior to the incorporation of ICIs into neoadjuvant treatment of patients with MIBC
- Adjuvant ICI is a standard of care in patients with high-risk MIBC
- Ongoing phase 3 clinical trials with ICI in combination with chemotherapy, immunotherapy, and chemoradiation may change the treatment landscape for patients with nonmetastatic UC

MODULE 2: Other Novel Strategies Under Investigation for Nonmetastatic UBC – Dr O'Donnell

Consulting Faculty Questions

Perspectives on bladder preservation and the evolution of systemic therapies for patients with MIBC

Neil Love, MD

Elizabeth R Plimack, MD, MS

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

Elizabeth R Plimack, MD, MS

What novel approaches to neoadjuvant therapy do you find particularly promising?

As neoadjuvant systemic therapy improves, can we identify more patients who can avoid cystectomy? What is your experience with bladder-sparing strategies in MIBC?

Consulting Faculty Questions

Pembrolizumab as treatment for BCG-unresponsive, high-risk NMIBC; intravesical drug delivery systems for MIBC

Neil Love, MD

Terence Friedlander, MD

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

Terence Friedlander, MD

What are the unique challenges associated with cystectomy in elderly patients with comorbidities?

Do you believe novel intravesical approaches such as TAR-200 and TAR-210 will provide meaningful improvements in outcomes over current standard therapies for patients with NMIBC and MIBC?

How are these strategies tolerated, and how do you anticipate they will be used in the future?

RTP
RESEARCH
TO PRACTICE

Please describe the last patient in your practice with localized UBC (muscle invasive or not muscle invasive) who was enrolled on a clinical trial.

	Age	Clinical trial	Assigned Tx arm (if applicable)	Response	Tolerability
 Dr Milowsky	78 years	Alliance A031803	N/A	Pending	Probable IO-related arthritis
 Dr O'Donnell	71 years	KN-905/EV-303	Awaiting assignment	Pending	Pending
 Dr Rosenberg	77 years	EV monotherapy for upper tract tumors	N/A	Pending	Similar to expected
 Dr Siefker-Radtke	65 years	Neoadjuvant chemo with IO	IO	Still free of disease	—
 Dr Yu	69 years	Neoadjuvant variant trial with MVAC/pembro	N/A	Tx ongoing	Tx ongoing
 Dr Friedlander	65 years	EV-304/B15	EV + pembro	Pending	Pending
 Dr Plimack	70 years	RETAIN-2	N/A	Tx ongoing	Tx ongoing

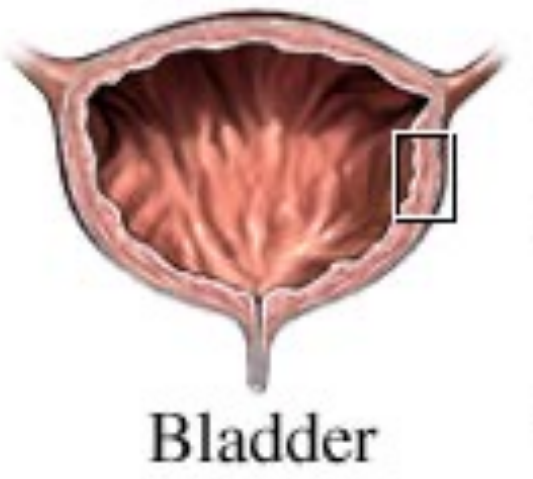
EV = enfortumab vedotin; MVAC = methotrexate/vinblastine/doxorubicin/cisplatin; pembro = pembrolizumab

Based on your personal clinical experience and/or knowledge of available data, what is your global perspective on the overall efficacy and tolerability of the TAR-200 delivery system?

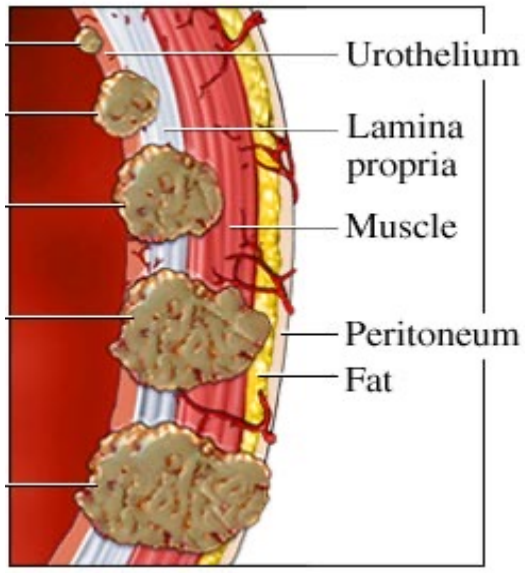
 Dr Milowsky	Exciting approach to intravesical therapy with activity in BCG-unresponsive disease and more limited but provocative data in the neoadjuvant MIBC setting
 Dr O'Donnell	No personal experience yet but looks very favorable based on the literature
 Dr Rosenberg	Seems quite active but not sure how effective it will be controlling invasive disease to prevent metastasis (it's not systemic therapy, which is a real issue for MIBC)
 Dr Siefker-Radtke	Very promising options under development!
 Dr Yu	It looks promising — I have not used it myself yet
 Dr Friedlander	Very encouraging – effective and fairly well tolerated therapy for some patients with an MIBC; Mechanistically it makes sense to expose the tumor to longer durations of chemotherapy.
 Dr Plimack	Very tolerable, seems effective, long-term outcomes not disclosed yet and will be key

RTP RESEARCH TO PRACTICE

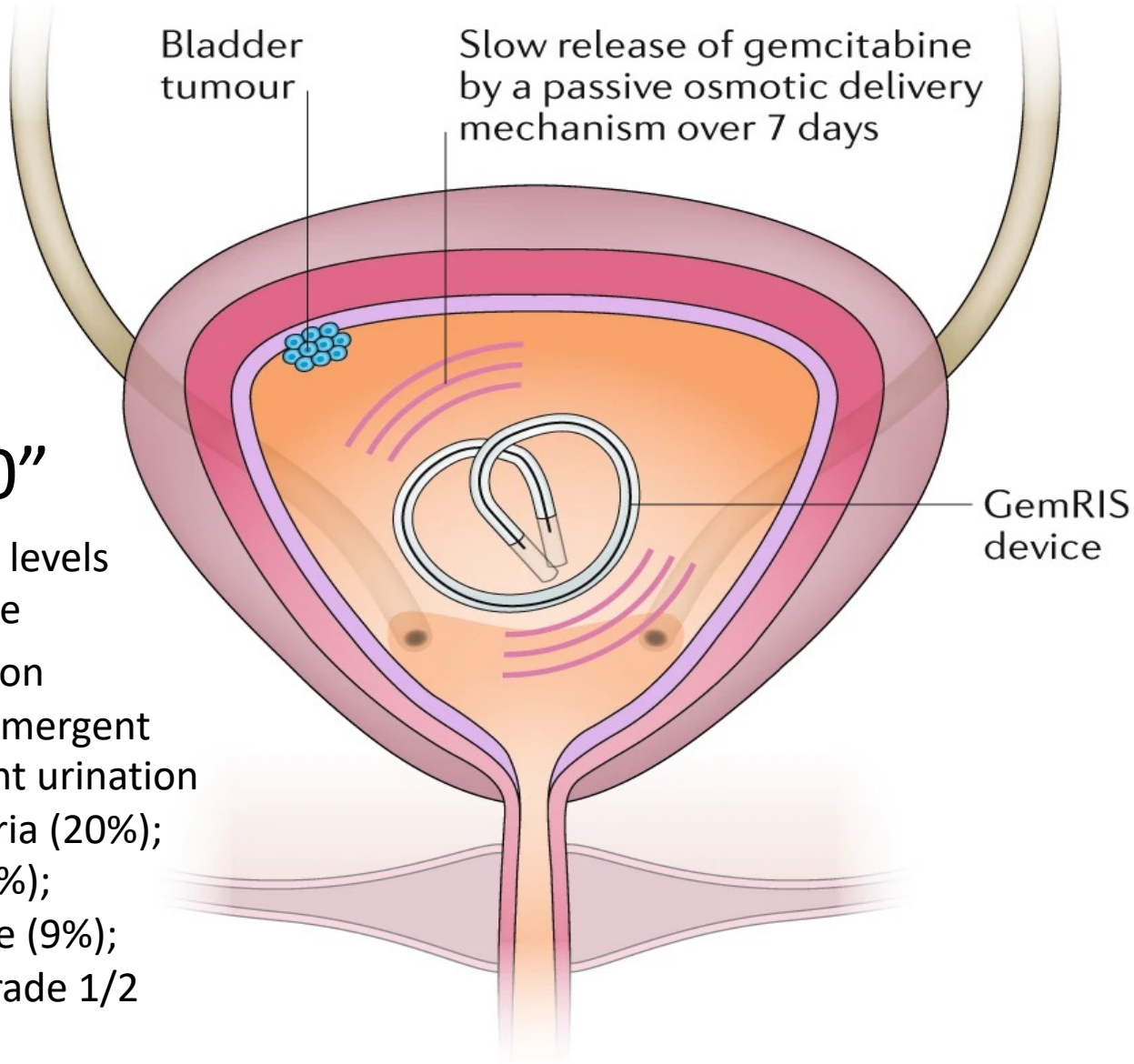
Other Novel Strategies Under Investigation for Nonmetastatic Urothelial Bladder Cancer (UBC)



Peter H. O'Donnell, M.D.
Section of Hematology/Oncology
Genitourinary Oncology Program
Committee on Clinical Pharmacology
and Pharmacogenomics
The University of Chicago



Intravesical Depot Delivery System

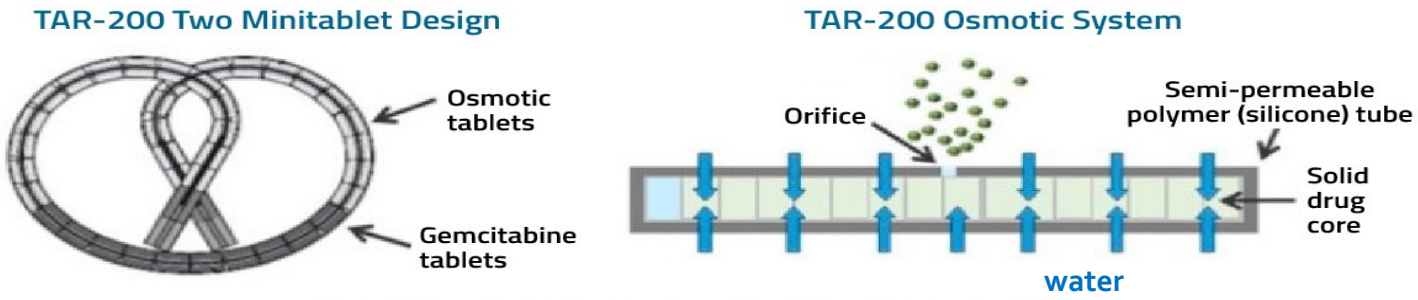


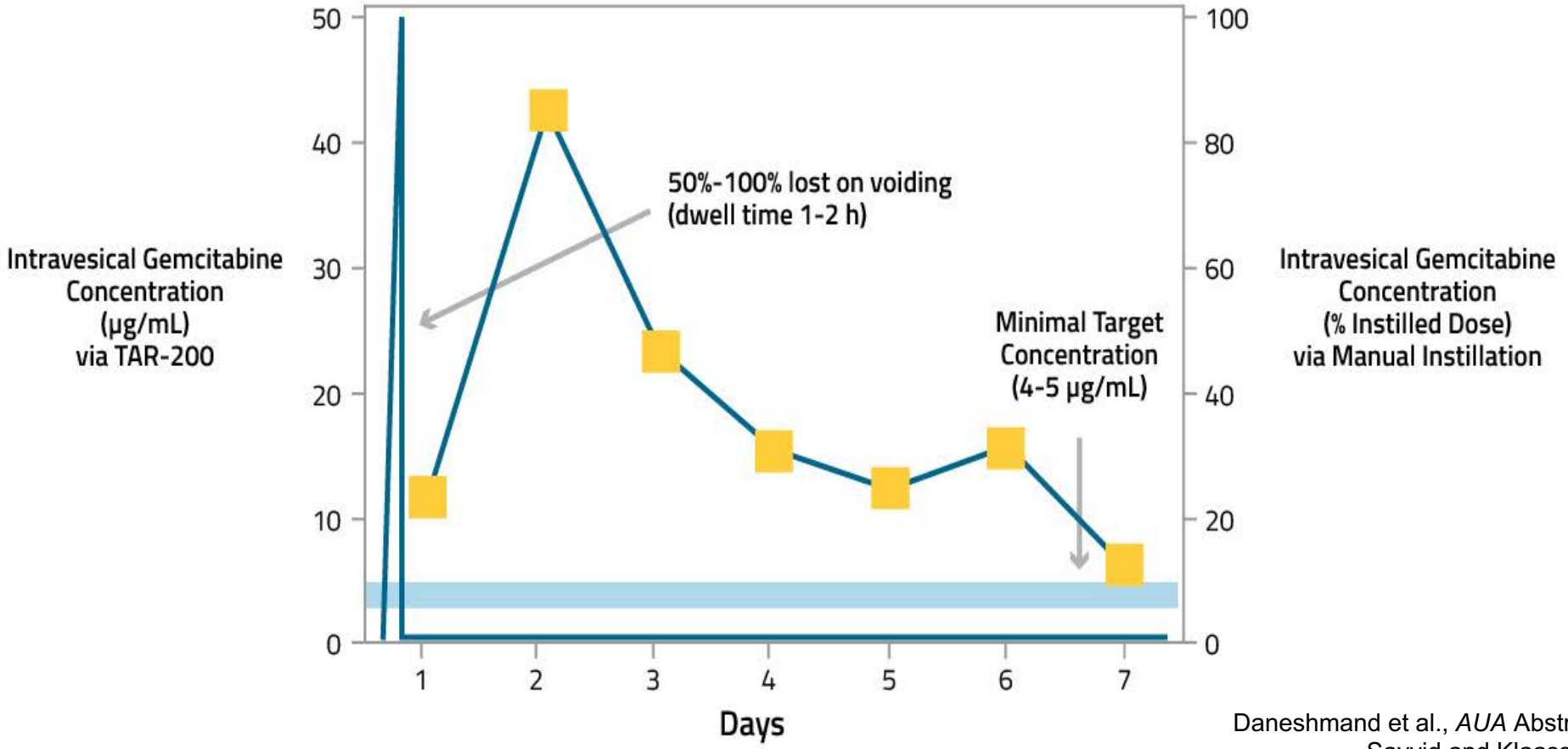
"TAR-200"

- Plasma gem levels undetectable
- Most common treatment-emergent AEs: frequent urination (22%); dysuria (20%); urgency (18%); incontinence (9%); almost all grade 1/2

Tan and Kelly, *Nat Rev Urol* (2018)
Daneshmand et al., *Urol Oncol* (2022)
Necchi et al., *ESMO* Abstract LBA105 (2023)

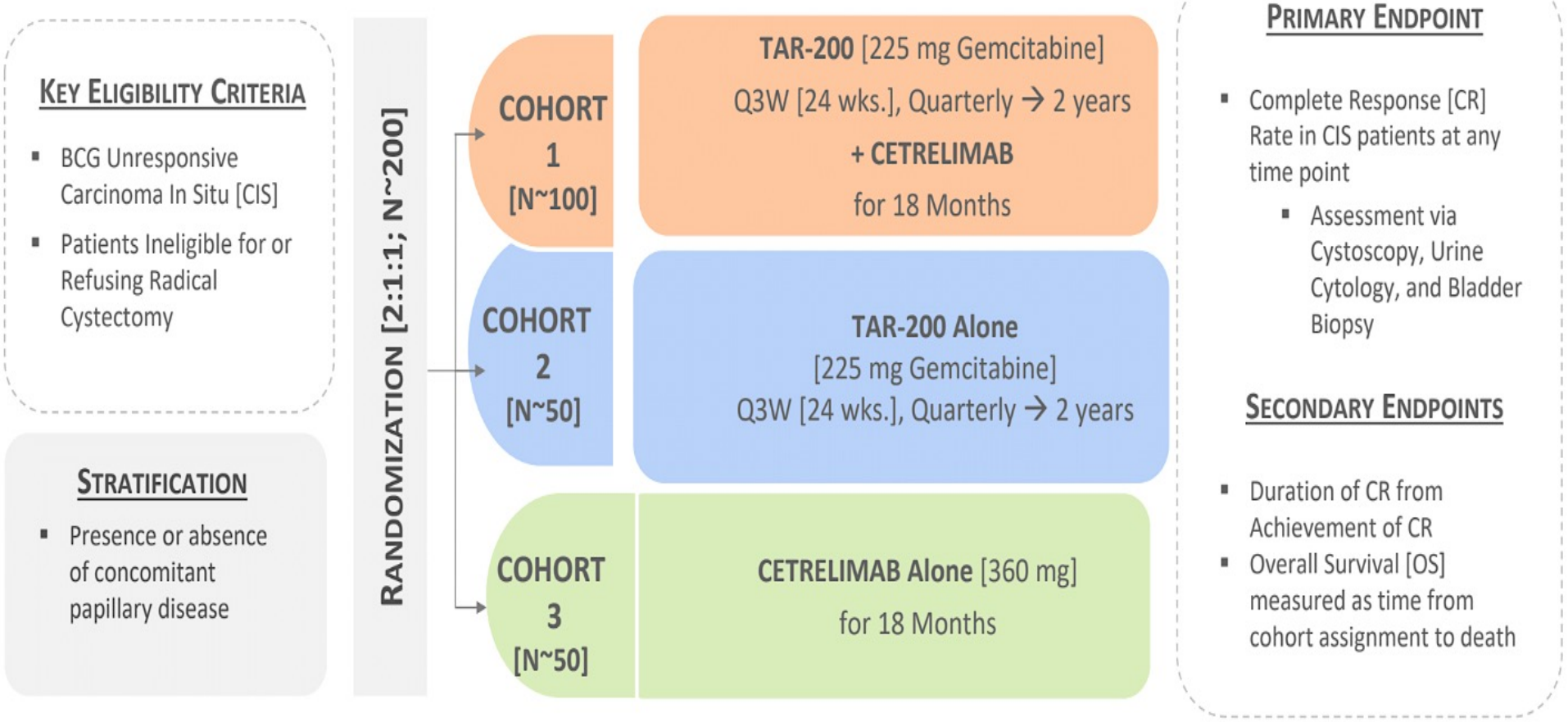
Intravesical Drug Levels





Daneshmand et al., *AUA* Abstract LBA02-03 (2023)
Sayyid and Klaassen, UroToday (2023)

SunRISe-1: TAR-200 in NMIBC

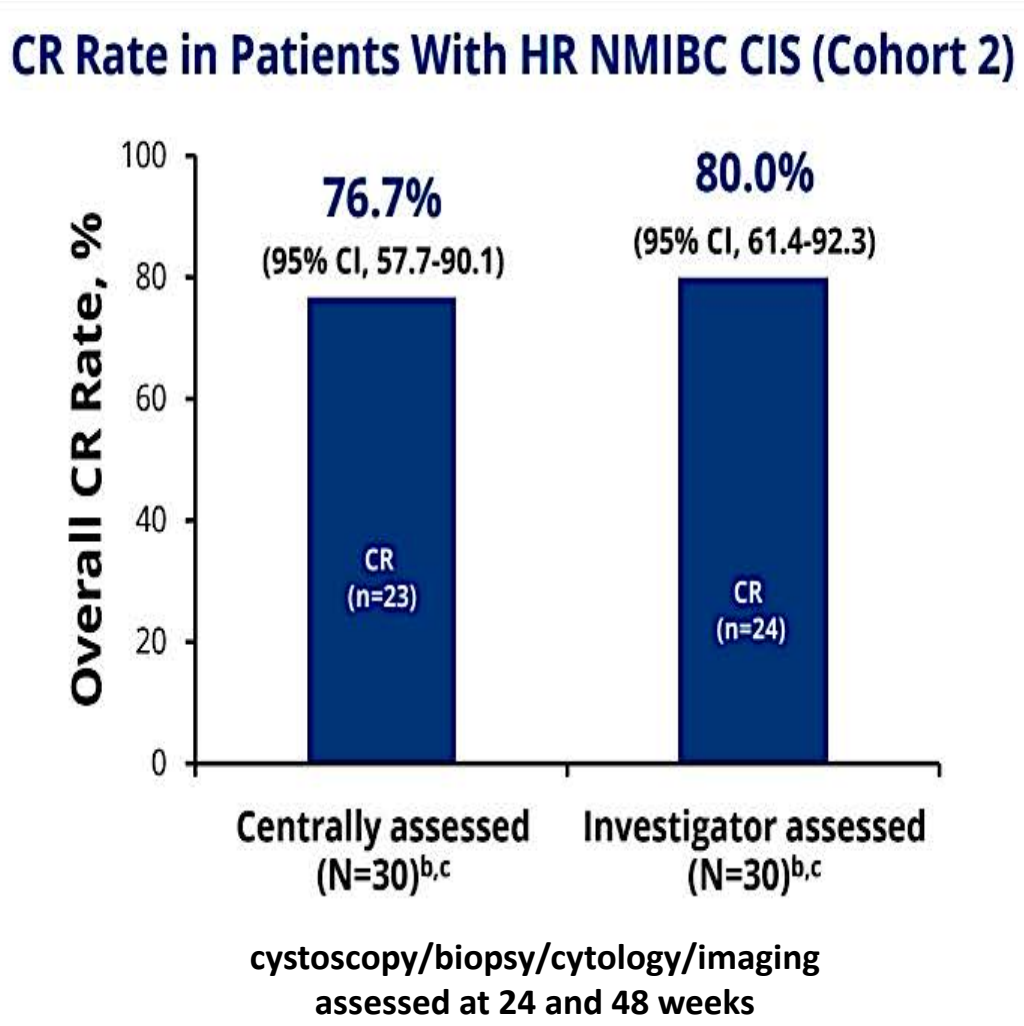


Historical benchmarks for 12-month CR rates:

- **Pembrolizumab (19%)**
- **Atezolizumab (15%)**
- **Nadofaragene firadenovec (23%)**

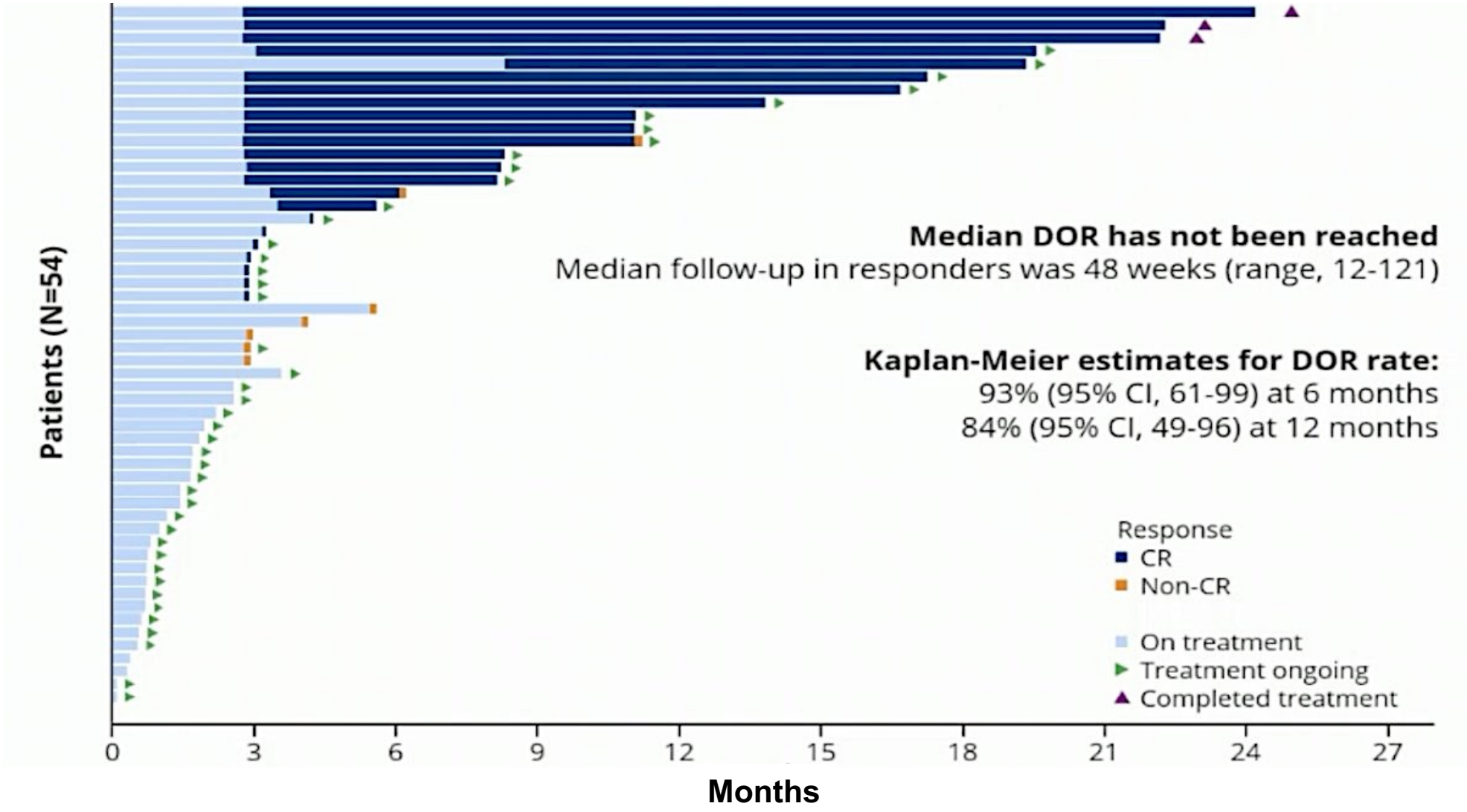
TAR-200 Intravesical Results

Characteristics	TAR-200 (N=54)
ECOG performance status 0, %	96.3
Tumor stage, %	
CIS only	66.7
CIS + papillary disease	33.3
Total doses of prior BCG, n, median (range)	12 (7-42)
Time from last BCG to CIS diagnosis, months, median (range)	3.0 (0.2-22.4)[a]
Reason for not receiving radical cystectomy, %	
Declined	94.4
Ineligible	5.6



Necchi et al., *ESMO* Abstract LBA105 (2023)

Duration of Response – TAR-200



Necchi et al., *ESMO* Abstract LBA105 (2023)

SunRISe-3: TAR-200 +/- Cetrelimab vs BCG

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)

Age ≥18 years

Eastern Cooperative Oncology Group performance status 0, 1, or 2

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 (225 mg gemcitabine Q3W [induction phase] and Q12W [maintenance phase]) + cetrelimab

Group C (n≈350)
TAR-200 (225 mg gemcitabine Q3W [induction phase] and Q12W [maintenance phase])

Group B (n≈350)
BCG (QW for 6 weeks [induction] and QW for 3 weeks at Weeks 12, 24, 48, 72, and 96 [maintenance])

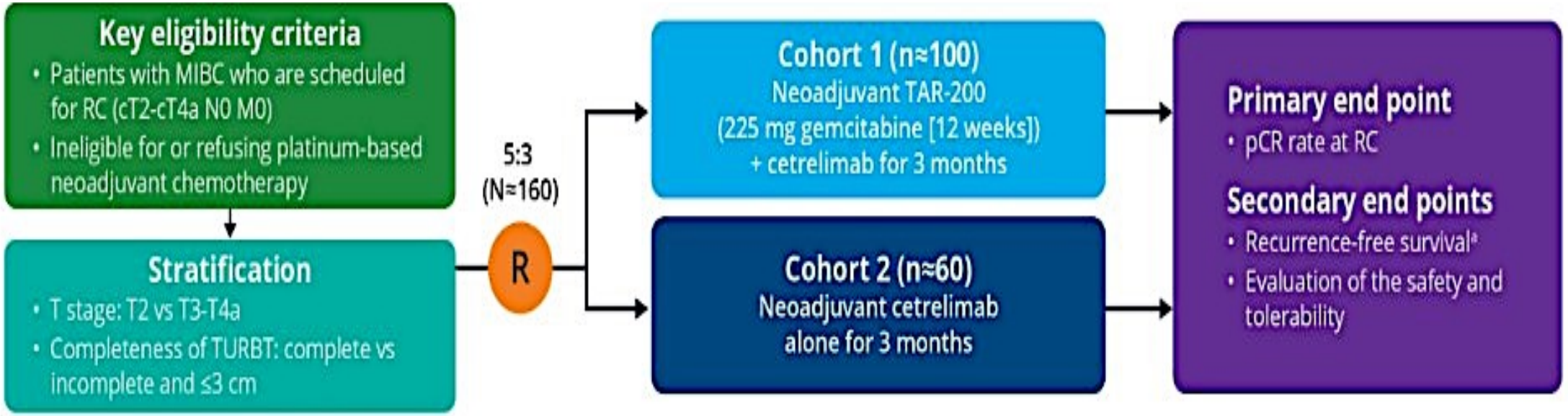
Primary end point — EFS
Time from randomization to first occurrence of HR disease, progression,[a] or any-cause death, whichever occurs first[b]

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

Necchi et al., *ESMO* Abstract 2407TiP (2023)

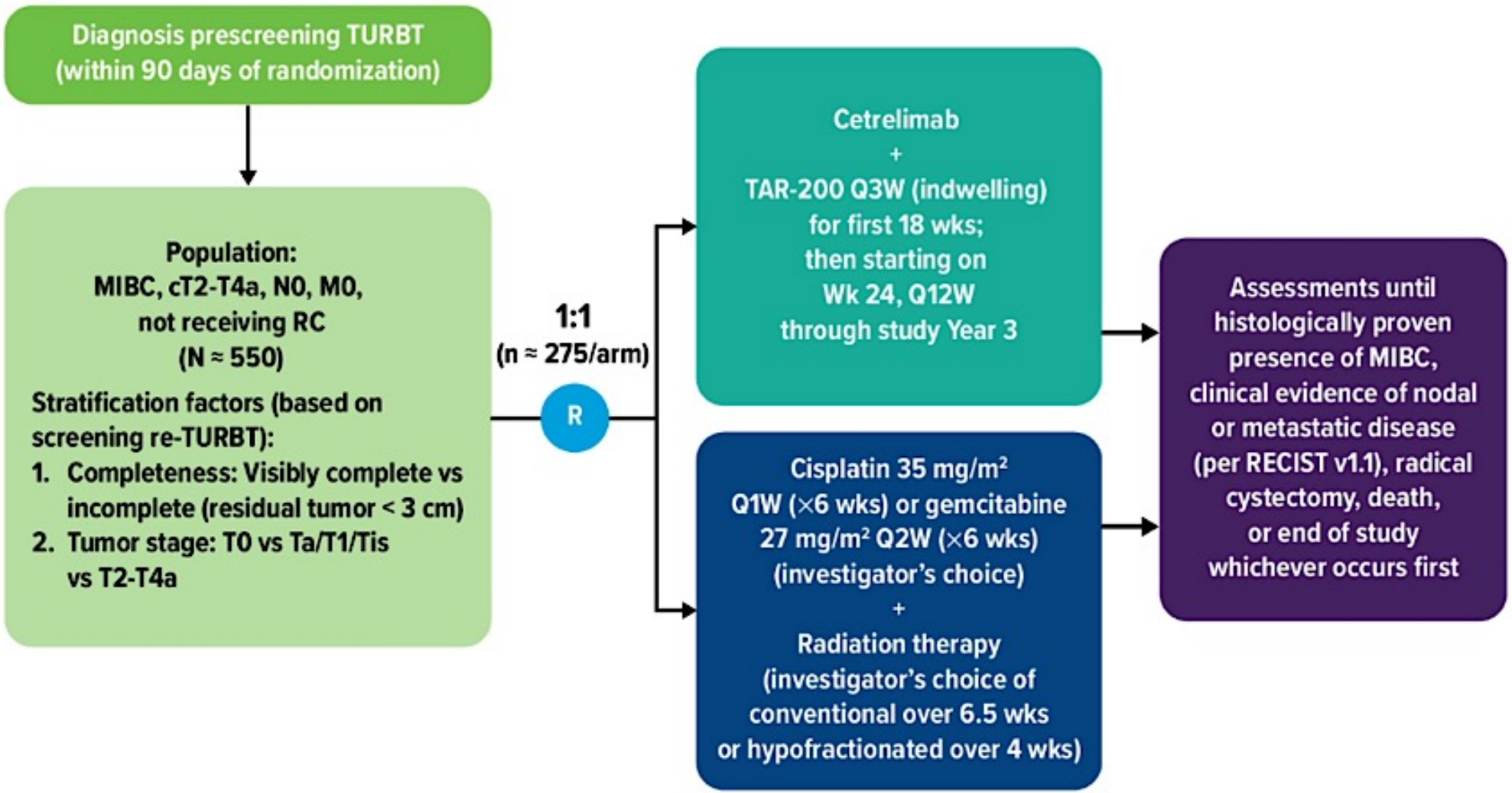
TAR-200 + Cetrelimab vs Cetrelimab Alone as Neoadjuvant Therapy in MIBC



pCR, pathologic complete response; TURBT, transurethral resection of bladder tumor.
[a]Per Response Evaluation Criteria In Solid Tumors 1.1 or histologic evidence.

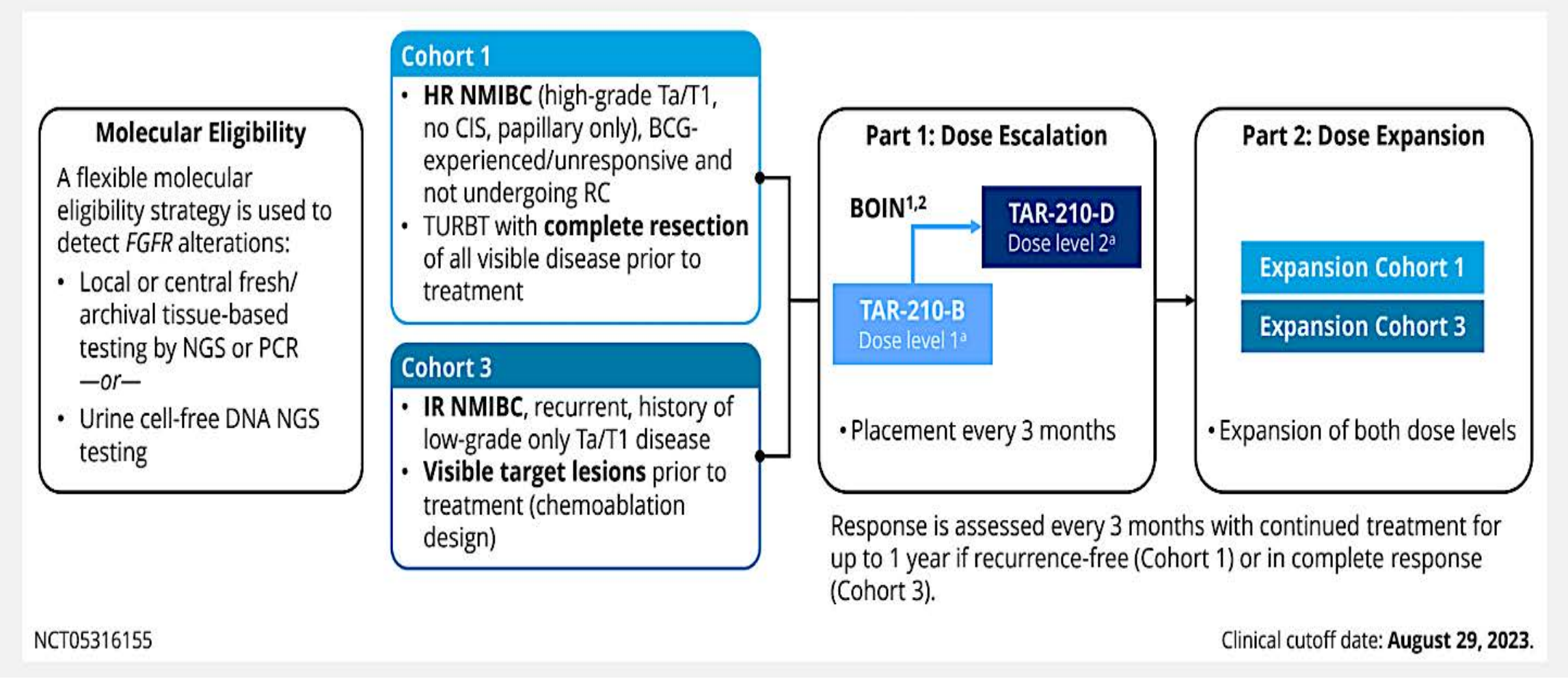
Psutka et al., *GU ASCO* Abstract TPS584 (2023)

TAR-200 + Cetrelimab vs ChemoRT in MIBC



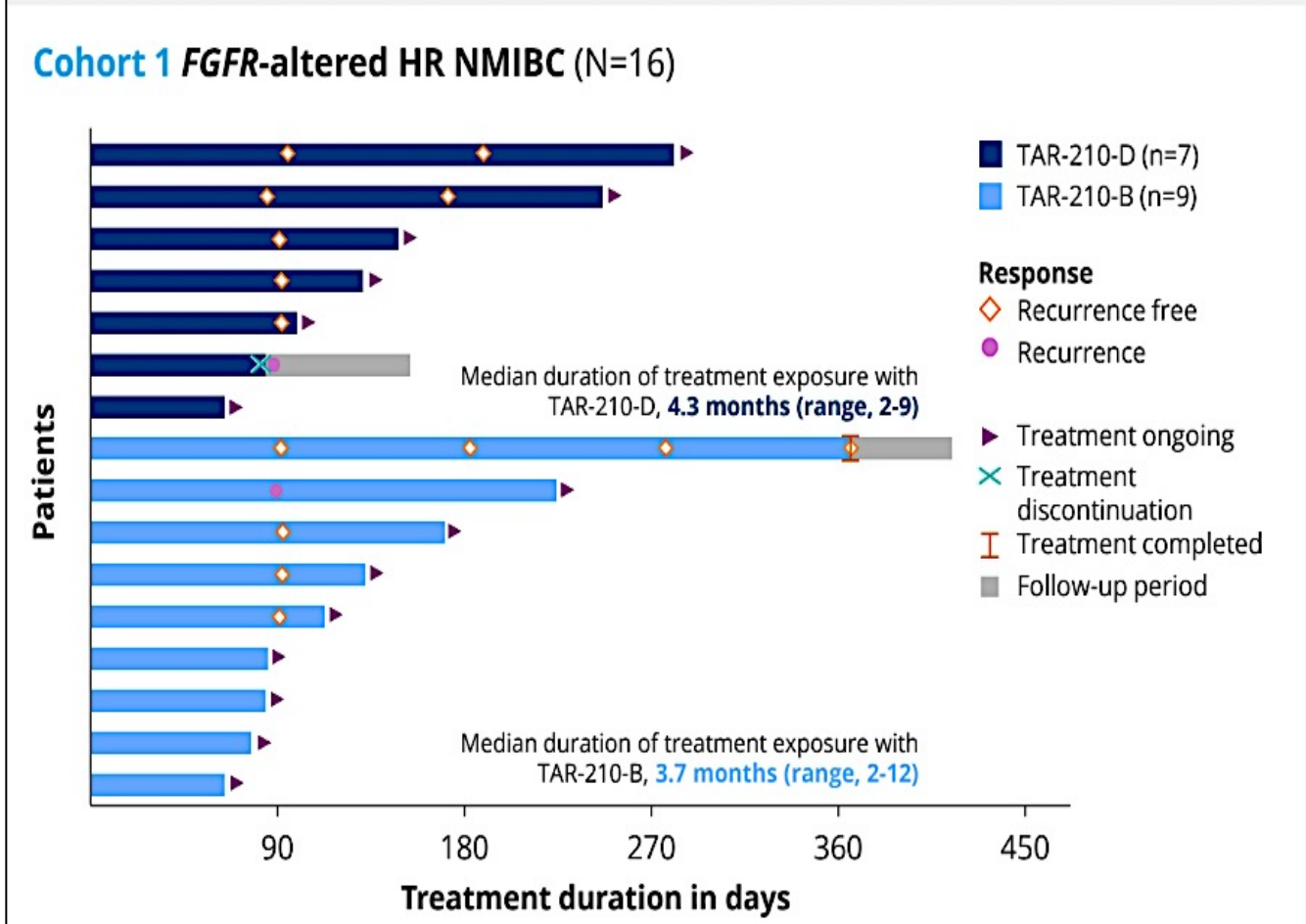
Williams et al., *ASCO* Abstract TPS4586 (2021)

TAR-210: Erdafitinib Intravesical Delivery System in FGFR-Altered NMIBC



Vilaseca et al., *ESMO* Abstract LBA104 (2023)

TAR-210: Erdafitinib-RIS Results (NMIBC)



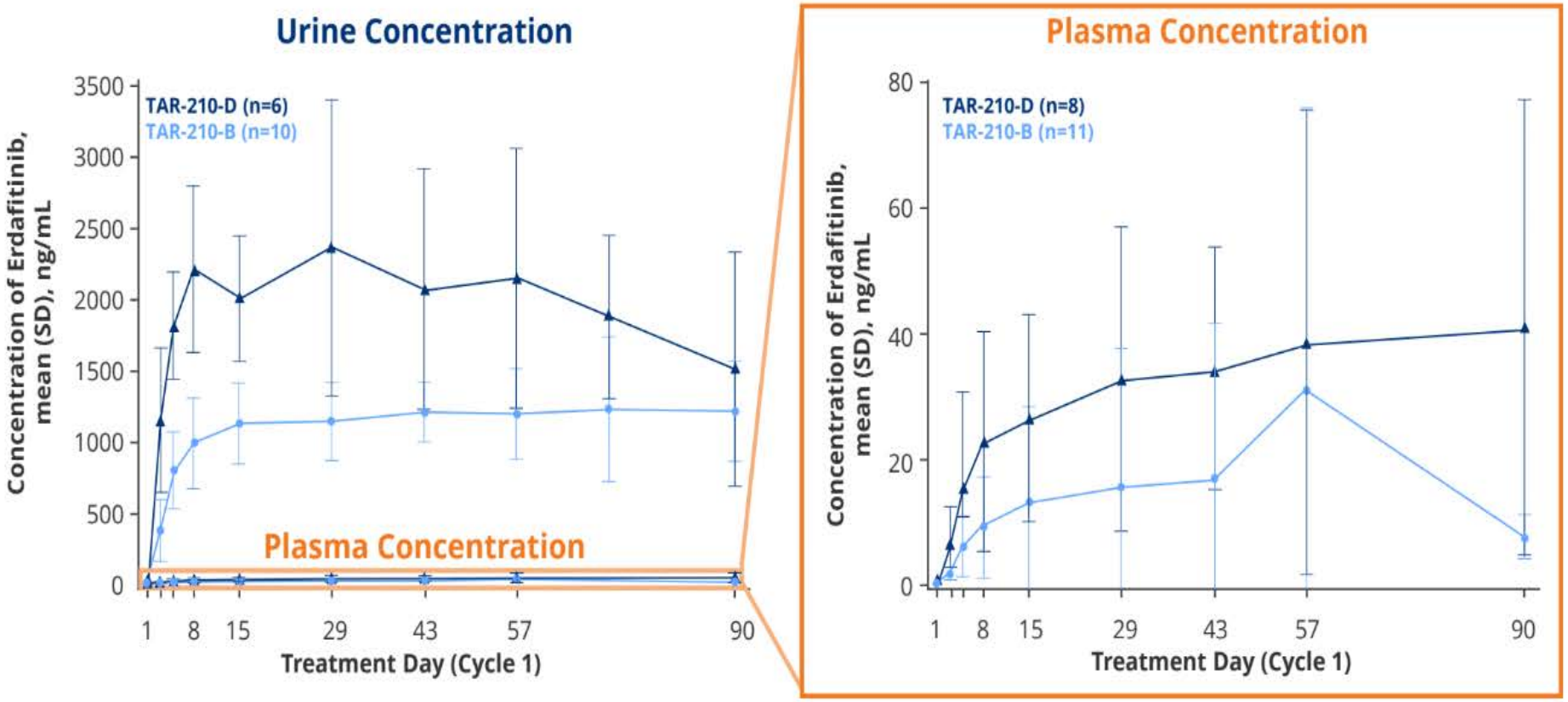
- Patient characteristics (N=16):
  - Median age was 73.5 years (range, 62-90)
  - 75% were male
  - 75% and 25% had tumor stage Ta and T1, respectively
  - 44% had multiple tumors
  - 100% had prior BCG
- In 11 patients with a response assessment, 9 were recurrence free (**recurrence-free rate, 82%**)
  - First response assessment was at 3 months
- Median recurrence-free survival was NE (95% CI, 2.96 months-NE)

CI, confidence interval; NE, non-estimable.

9

Vilaseca et al., *ESMO* Abstract LBA104 (2023)

Sustained Urinary Erdafitinib Release Over 90 Days, with Low Systemic Exposure



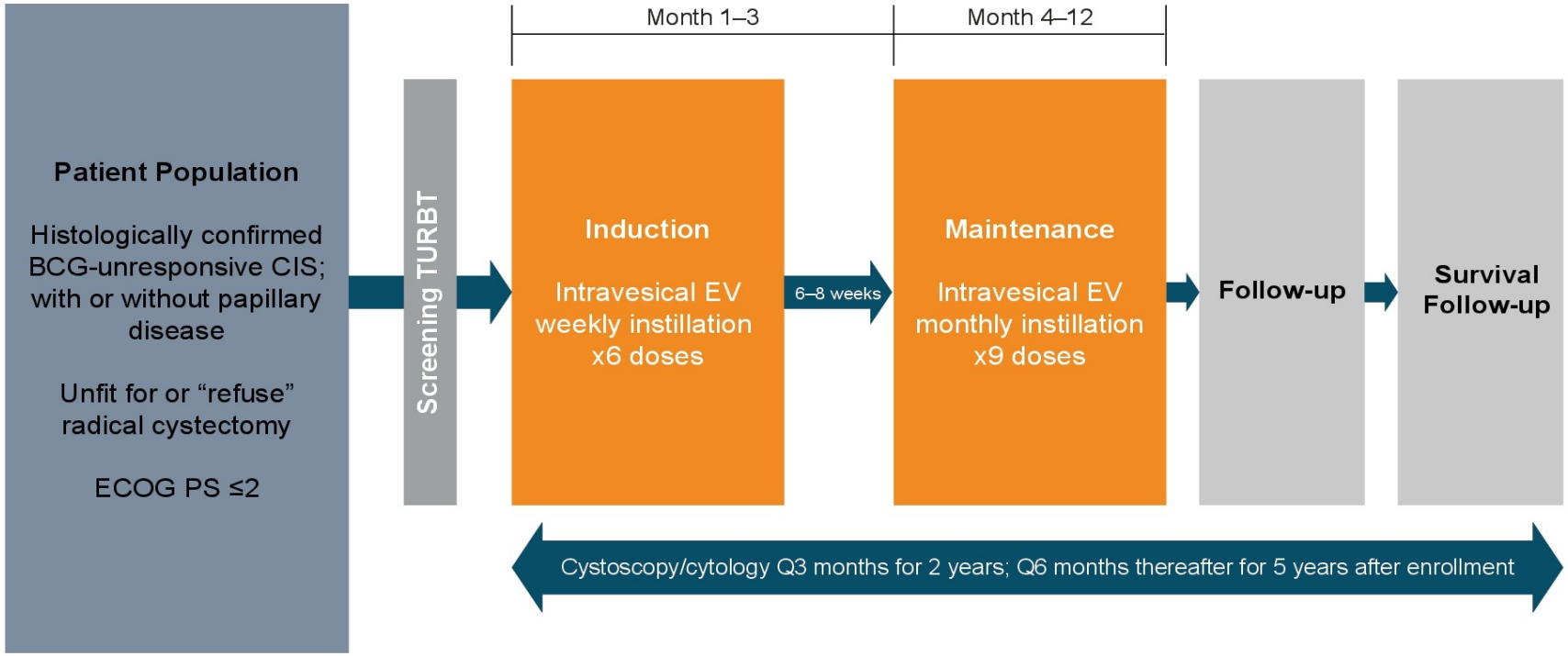
- **>50 x lower mean [plasma] than oral erdafitinib 9mg daily**
- **No hyperphosphatemia**

Vilaseca et al., *ESMO* Abstract LBA104 (2023)

Intravesical Enfortumab Vedotin

EV-104 Study Design

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



- The study treatment regimen will include an induction phase where patients will receive intravesical enfortumab vedotin weekly for 6 weeks followed by monthly maintenance for a total of 9 additional enfortumab vedotin doses

Kamat et al., *GU ASCO* Abstract TPS582 (2023)

Select Ongoing Trials Evaluating Other Novel Therapies for Patients with High-Risk NMIBC

Trial	Phase	n	Population	Intervention
NCT05704244	III	24	BCG unresponsive	• Nadofaragene firadenovec
CREST NCT04165317	III	1,070	BCG naïve, BCG unresponsive	• Sasanlimab • Sasanlimab + BCG • BCG
QUILT-3.032 NCT03022825	II/III	190	BCG unresponsive	• N-803 (interleukin-15 superagonist complex) + BCG • N-803
TRUCE-04 NCT05495724	II	176	HER2 overexpressing	• Tislelizumab + disitamab vedotin
ADAPT-BLADDER NCT03317158	I/II	55	BCG unresponsive, BCG relapsing, BCG naïve	• Durvalumab • Durvalumab + BCG or radiation therapy or gemcitabine or tremelimumab
NCT04706598	I/II	56	BCG unresponsive	• Camrelizumab
NCT05843448	I	30	BCG unresponsive/intolerant	• PD-L1/IDO peptide vaccine + pembrolizumab IV

BCG = Bacillus Calmette-Guérin

Hannouneh ZA et al. *Cancer Med* 2023;12(24):21944-68.

Summary

- Novel delivery systems and intravesical use of traditionally-systemic agents show promise in early-stage bladder cancer
- TAR-200 granted FDA breakthrough therapy designation in BCG-unresponsive high-risk NMIBC (Dec 2023)
- Combination strategies being explored
- Delay progression / need for cystectomy?

MODULE 3: Front-Line Treatment for Metastatic UBC (mUBC) – Dr Rosenberg

RTP
RESEARCH
TO PRACTICE

Consulting Faculty Questions

Enfortumab vedotin (EV) with pembrolizumab as first-line treatment for metastatic urothelial bladder cancer (UBC); management of rash and neuropathy associated with EV

Neil Love, MD

Elizabeth R Plimack, MD, MS

Terence Friedlander, MD

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

Elizabeth R Plimack, MD, MS

Are you using enfortumab vedotin/pembrolizumab as first-line therapy for mUBC regardless of platinum eligibility?

Terence Friedlander, MD

What has been your experience with the tolerability of enfortumab vedotin/pembrolizumab?

How do you manage common side effects (eg, rash, peripheral neuropathy) with this combination?

RTP
RESEARCH
TO PRACTICE

Consulting Faculty Questions

Autoimmune contraindications to immunotherapy

Neil Love, MD

Terence Friedlander, MD

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

Terence Friedlander, MD

Which autoimmune conditions do you believe constitute an absolute contraindication to treatment with an immune checkpoint inhibitor?

How do you think through the use of these agents in patients with autoimmune diseases or those who have undergone solid organ transplant?

RTP
RESEARCH
TO PRACTICE

Please describe the last patient in your practice who received enfortumab vedotin/pembrolizumab as first-line treatment for metastatic UBC.

	Age	PD-L1 status	Benefit derived	Side effects
 Dr Milowsky	73 years	Unknown	Some	Rash, Grade 1 neuropathy
 Dr O'Donnell	65 years	Unknown	Too early to determine	Faring well
 Dr Rosenberg	65 years	Unknown	A great deal	Neuropathy, fatigue, dysgeusia
 Dr Siefker-Radtke	65 years	Unknown	A great deal	Neuropathy
 Dr Yu	72 years	Unknown	A great deal	Peripheral neuropathy, dry skin
 Dr Friedlander	72 years	Positive	A great deal	Neuropathy, colitis
 Dr Plimack	86 years	Unknown	A great deal	Pruritus/dry skin, fatigue

In general, what is your preferred first-line treatment regimen for an 80-year-old patient with metastatic UBC who has received no prior systemic therapy and is not a candidate for cisplatin? Does PD-L1 level affect your decision-making?

	Preferred first-line regimen	PD-L1 affect decision-making?
 Dr Milowsky	Enfortumab vedotin/pembrolizumab	No
 Dr O'Donnell	Enfortumab vedotin/pembrolizumab	No
 Dr Rosenberg	Enfortumab vedotin/pembrolizumab	No
 Dr Siefker-Radtke	Enfortumab vedotin/pembrolizumab	No
 Dr Yu	Enfortumab vedotin/pembrolizumab	No
 Dr Friedlander	Enfortumab vedotin/pembrolizumab	No
 Dr Plimack	Enfortumab vedotin/pembrolizumab	No

In general, what is your preferred first-line treatment regimen for an 80-year-old patient with metastatic UBC who has received no prior systemic therapy and is not a candidate for cisplatin or carboplatin? Does PD-L1 level affect your decision-making?

	Preferred first-line regimen	PD-L1 affect decision-making?
 Dr Milowsky	Enfortumab vedotin/pembrolizumab	No
 Dr O'Donnell	Pembrolizumab	Yes
 Dr Rosenberg	Pembrolizumab	Yes
 Dr Siefker-Radtke	Enfortumab vedotin/pembrolizumab	No
 Dr Yu	Enfortumab vedotin/pembrolizumab	No
 Dr Friedlander	Pembrolizumab	Yes, slightly
 Dr Plimack	Atezolizumab	No

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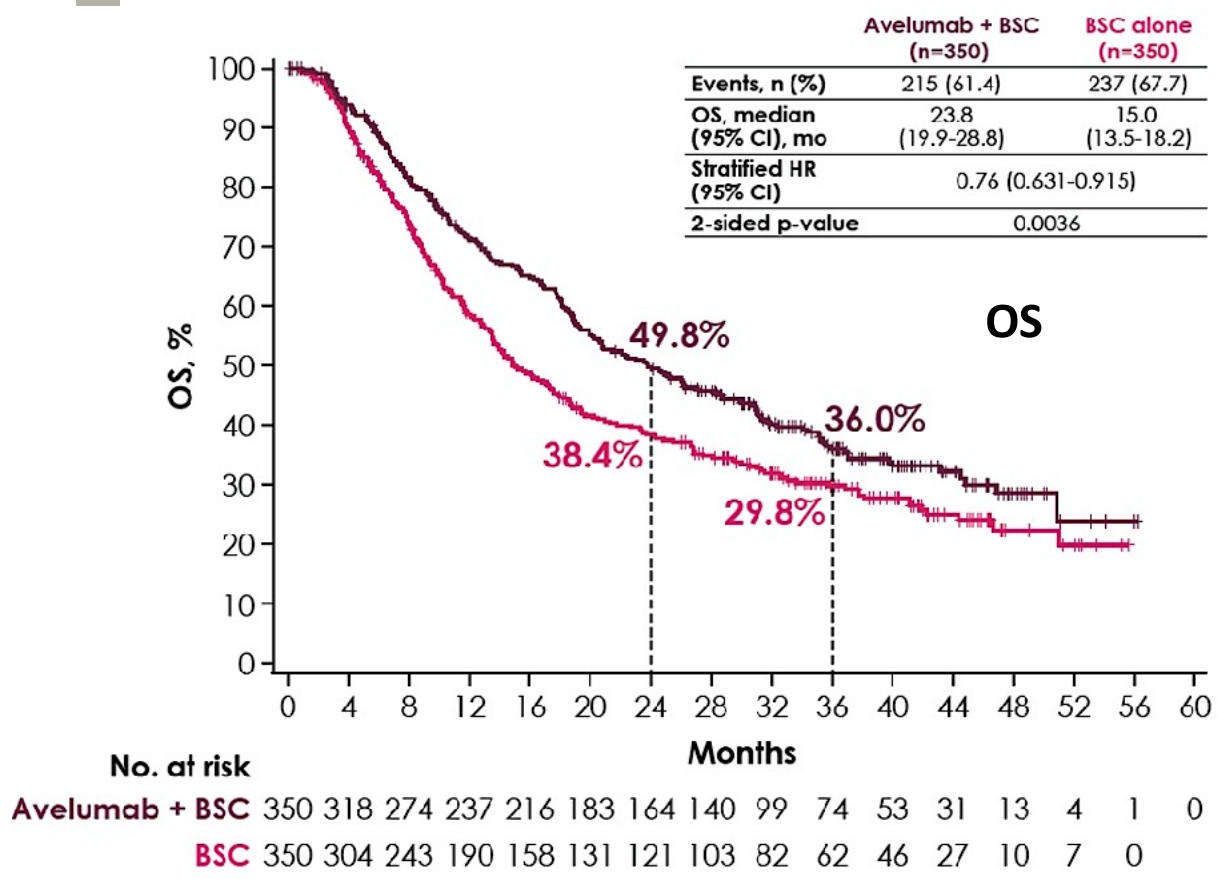
First-line and maintenance therapy for metastatic urothelial cancer

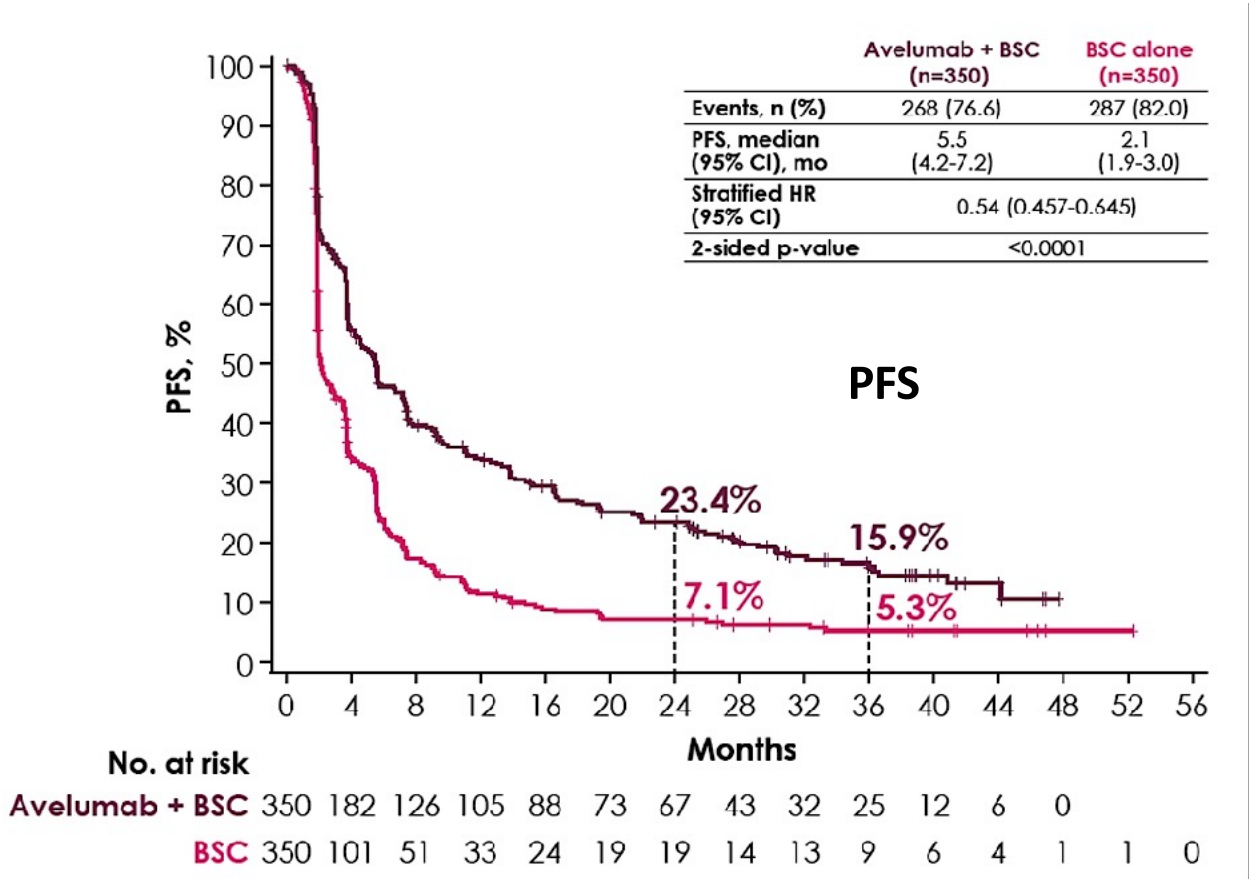
Jonathan Rosenberg, MD
Chief, Genitourinary Oncology Service
Enno Ercklentz Chair
Department of Medicine
Memorial Sloan Kettering Cancer Center
Professor of Medicine
Weill Cornell Medical College

Treatment Landscape of metastatic UC

- Enfortumab vedotin and pembrolizumab approved for metastatic UC
- Platinum based chemotherapy is no longer the default option for metastatic UC patients
  - Role of avelumab maintenance is reduced in this new paradigm
- Patients who are not felt to be candidates for cytotoxic agents may receive pembrolizumab monotherapy

JAVELIN Bladder100 trial: Longer term follow-up (≥ 2 years) confirms initial data





Powles, et al. J Clin Oncol 40, 2022 (suppl 6; abstr 487)

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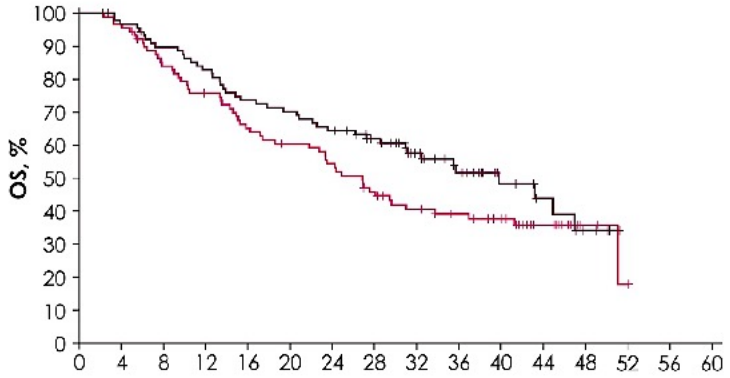
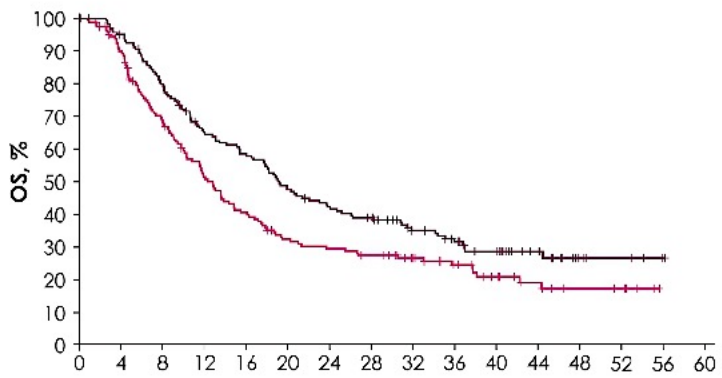
JAVELIN Bladder100 trial: Overall, outcomes favor avelumab no matter prior chemo response

Complete response



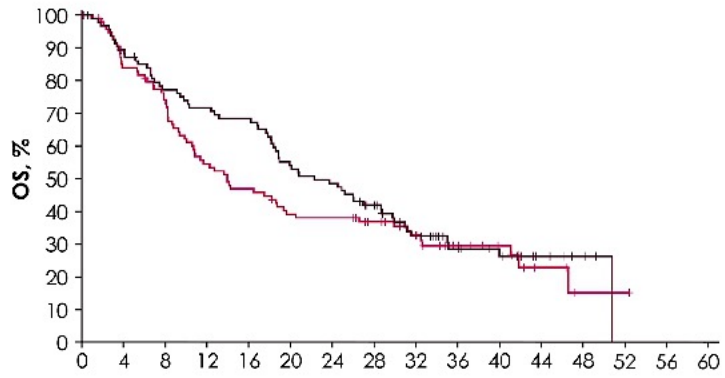
No. at risk														
Avelumab + BSC	90	85	78	72	64	61	56	47	34	24	14	9	4	0
BSC	89	86	72	64	55	50	45	37	30	26	21	13	3	1	0

Partial response



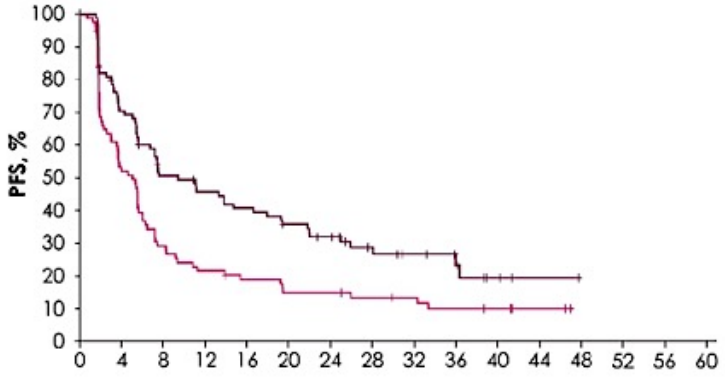
No. at risk															
Avelumab + BSC	163	151	126	100	90	73	64	58	42	35	27	16	6	4	1	0
BSC	163	140	103	76	60	46	42	37	29	22	15	10	6	5	0

Stable disease



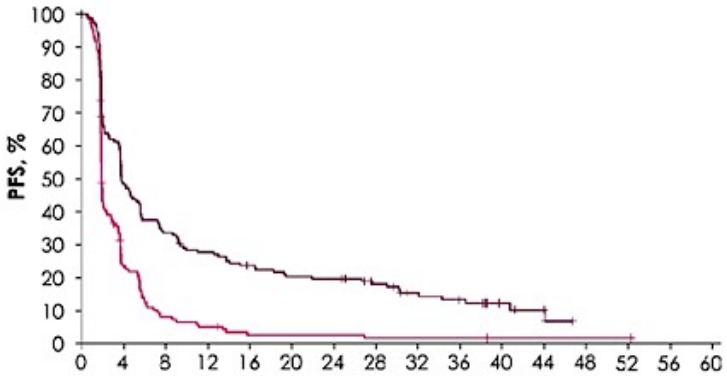
No. at risk														
Avelumab + BSC	97	82	70	65	62	49	44	35	23	15	12	6	3	0
BSC	98	78	68	50	43	35	34	29	23	14	10	4	1	1	0

Complete response



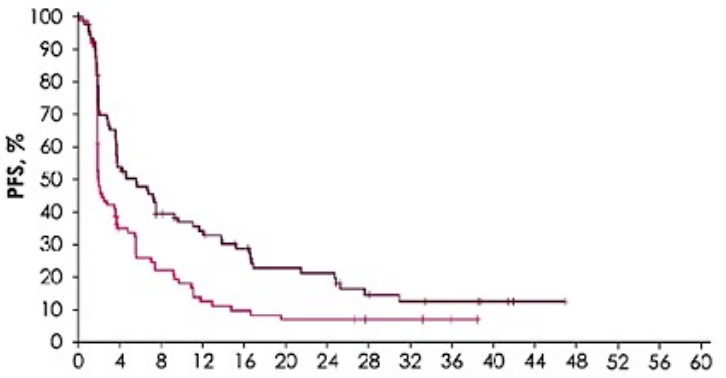
No. at risk													
Avelumab + BSC	90	61	42	37	33	28	24	14	11	7	3	1	0
BSC	89	42	23	17	14	11	11	9	8	6	5	3	0

Partial response



No. at risk															
Avelumab + BSC	163	75	52	42	35	30	29	21	15	13	6	4	0		
BSC	163	32	11	7	3	3	3	2	2	2	1	1	1	1	0

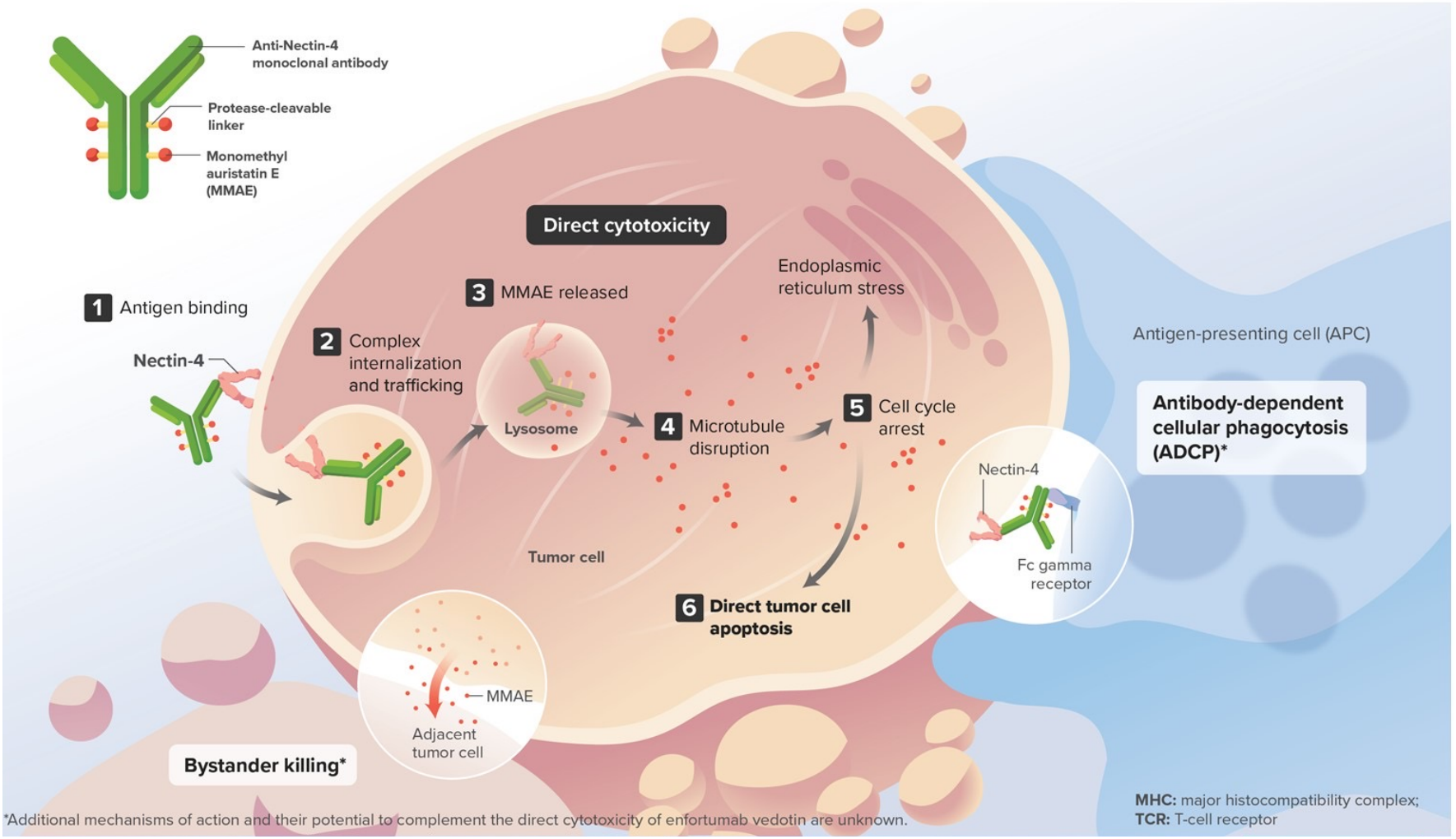
Stable disease



No. at risk													
Avelumab + BSC	97	46	32	26	20	15	14	8	6	5	3	1	0
BSC	98	27	17	9	7	5	5	3	3	1	0

Sridhar et al. ASCO 2022

Metastatic UC: ADC Therapy with enfortumab vedotin



Targets Nectin-4 which is highly expressed in urothelial cancers

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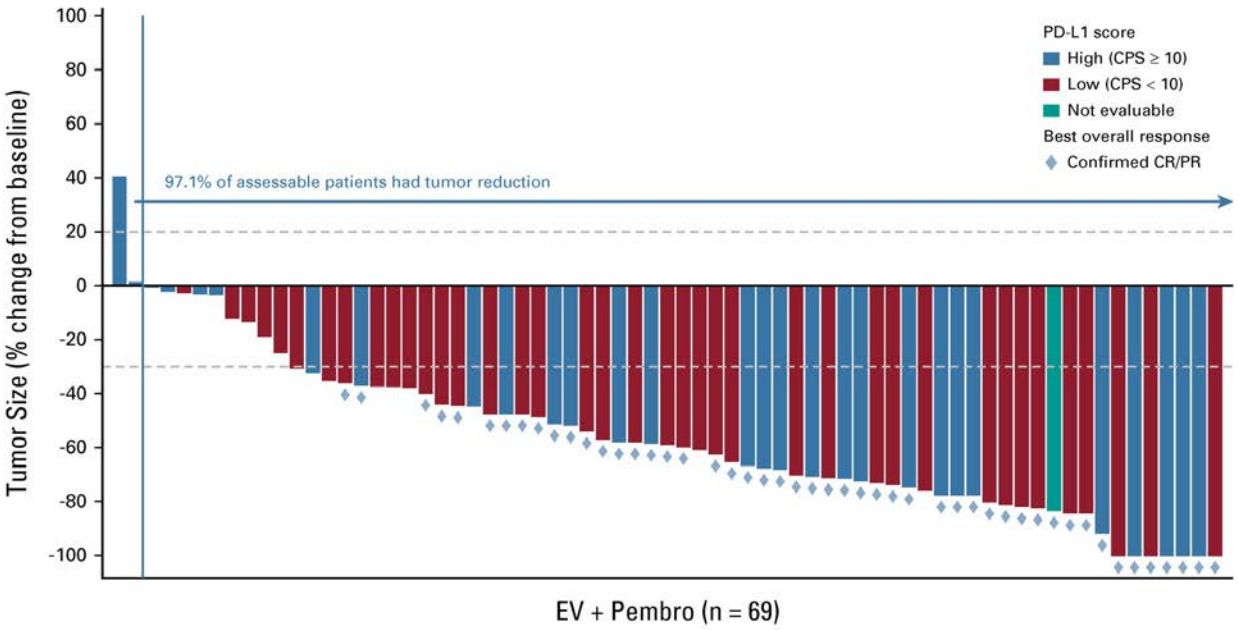
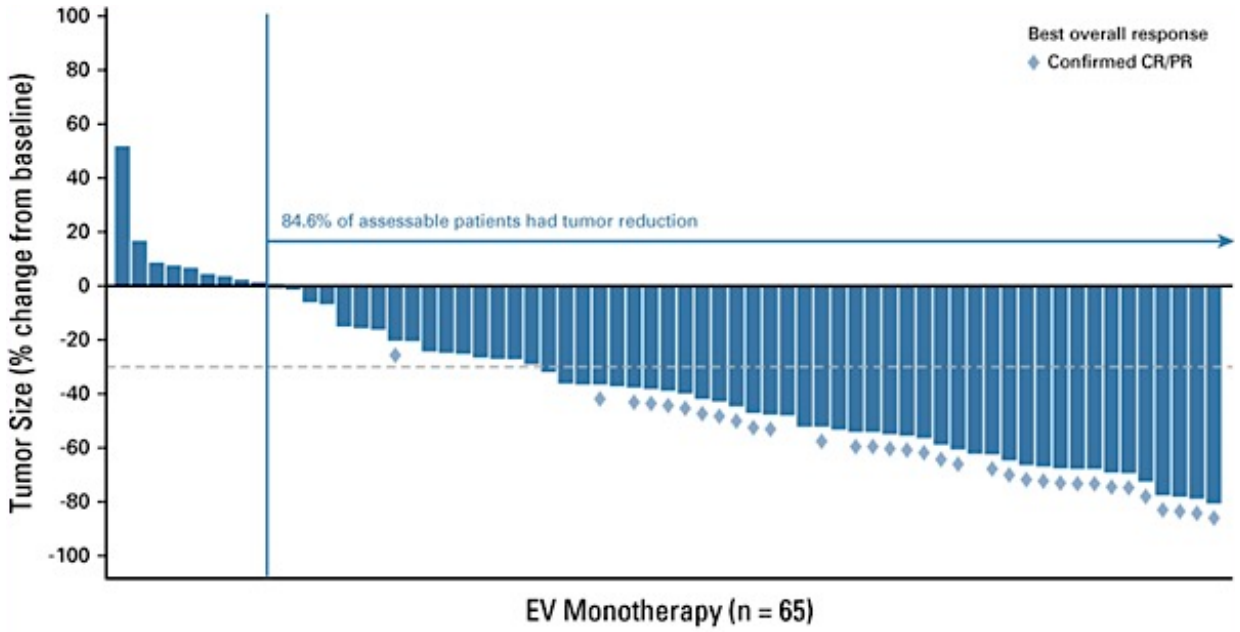
EV-103 Cohort K: EV +/- pembrolizumab





- EV/Pembro activity independent of PD-L1 status
  - 27/44 (61.4%) cORR in CPS<10
  - 21/31 (67.7%) cORR in CPS≥10

	EV+Pembro (N=76)	EV Monotherapy (N=73)
Confirmed ORR (95% CI)	**64.5% (52.7-75.1)**	**45.2% (33.5-57.3)**
Complete response	10.5%	4.1%
Partial Response	53.9%	41.1%
Progressive Disease	7.9%	9.6%
Not evaluable or no assessment	5.3%	10.9%

O'Donnell et al. *JCO* 2023 41(25):4107-4117.

EV-302/KEYNOTE-A39 (NCT04223856)

Patient population

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

N=886

R 1:1

EV + Pembrolizumab
No maximum treatment cycles for EV, maximum 35 cycles for P

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

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

Dual primary endpoints:

- **PFS by BICR**
- **OS**

Select secondary endpoints:

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

Stratification factors: cisplatin eligibility (eligible/ineligible), PD-L1 expression (high/low), liver metastases (present/absent)

•Cisplatin eligibility and assignment/dosing of cisplatin vs carboplatin were protocol-defined; patients received 3-week cycles of EV (1.25 mg/kg; IV) on Days 1 and 8 and P (200 mg; IV) on Day 1

Statistical plan for analysis: the first planned analysis was performed after approximately 526 PFS (final) and 356 OS events (interim); if OS was positive at interim, the OS interim analysis was considered final

Adapted from Powles et al. ESMO 2023 LBA6

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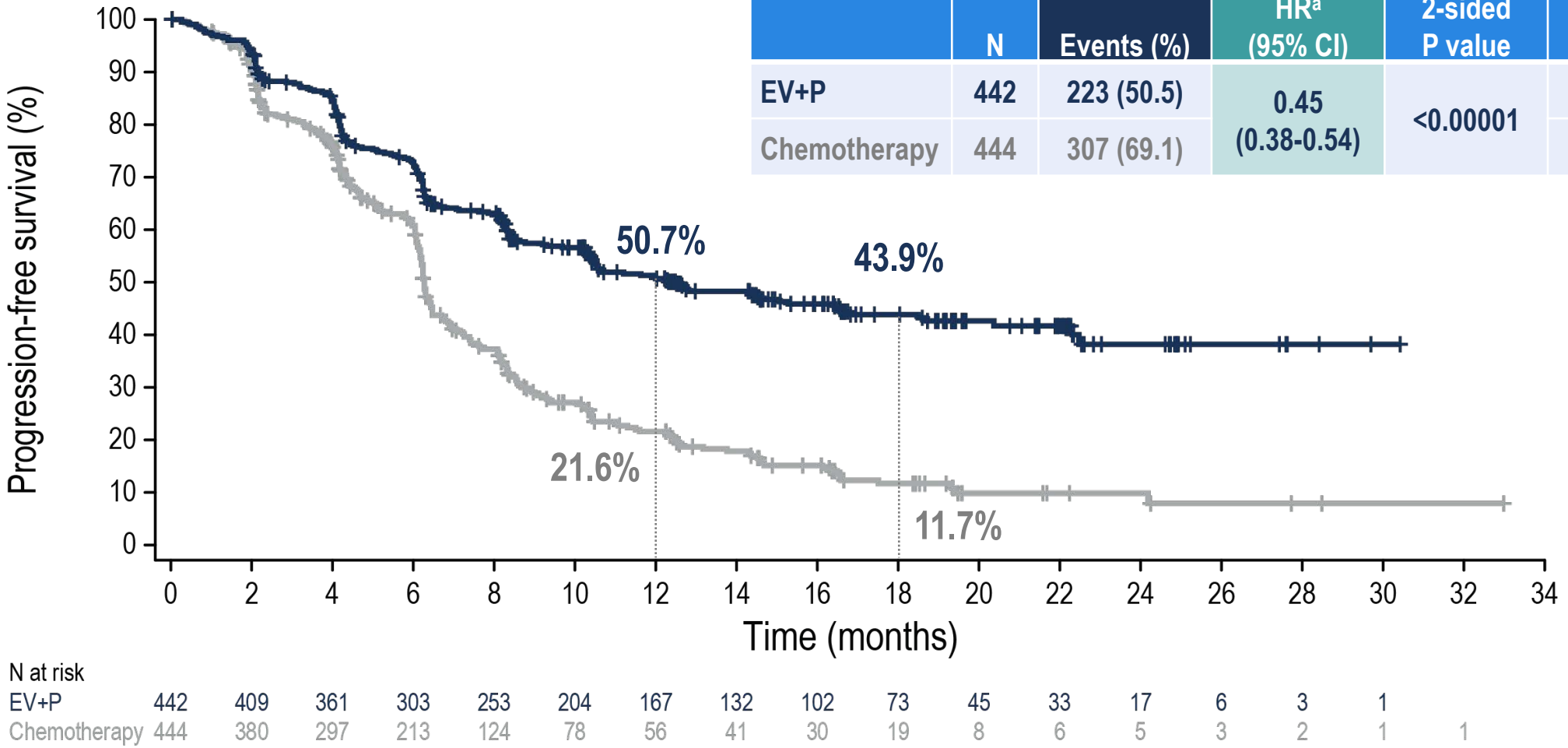
EV-302: Progression-Free Survival per BICR

Risk of progression or death was reduced by 55% in patients who received EV+P

	N	Events (%)	HR[a] (95% CI)	2-sided P value	mPFS (95% CI), months
EV+P	442	223 (50.5)	0.45 (0.38-0.54)	<0.00001	12.5 (10.4-16.6)
Chemotherapy	444	307 (69.1)			6.3 (6.2-6.5)



Adapted from Powles et al. ESMO 2023 LBA6

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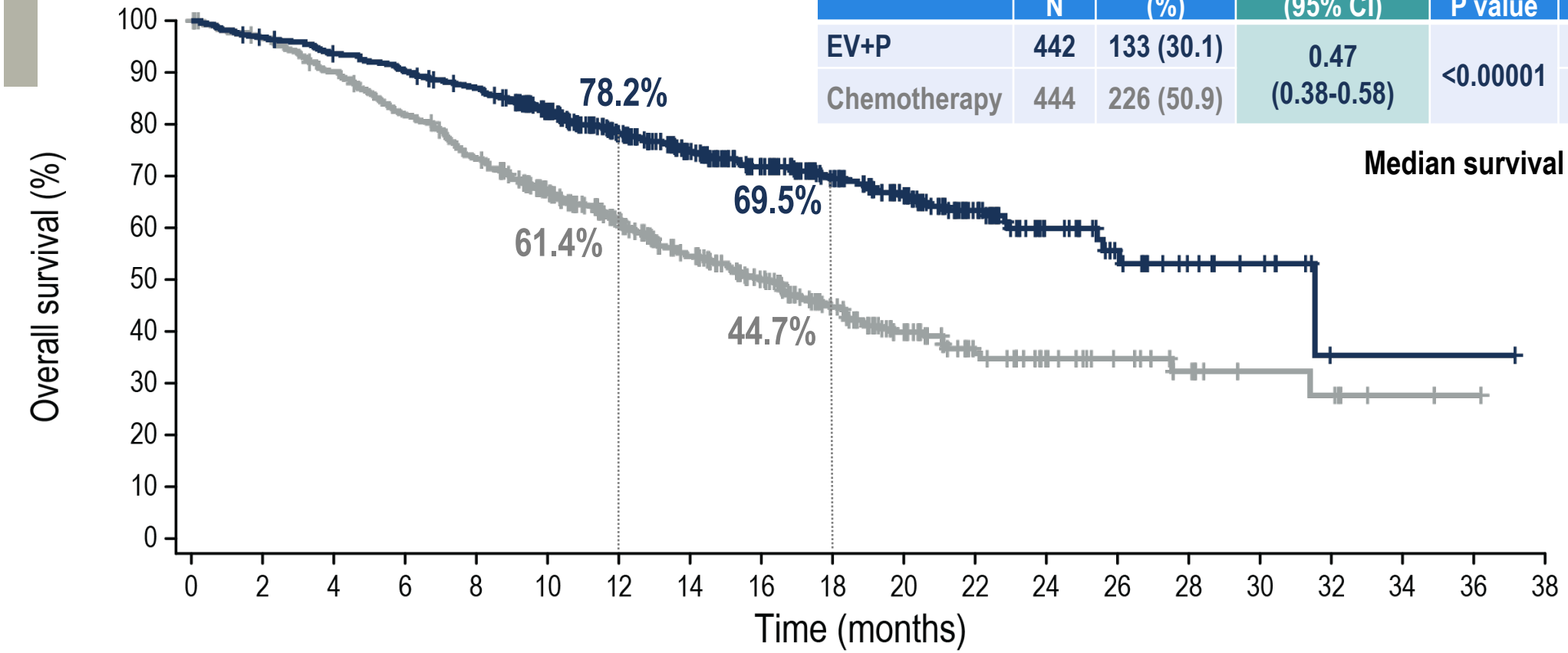
EV-302: Overall Survival

Risk of death was reduced by 53% in patients who received EV+P

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

Median survival follow-up: 17.2 months



N at risk

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

Adapted from Powles et al. ESMO 2023 LBA6

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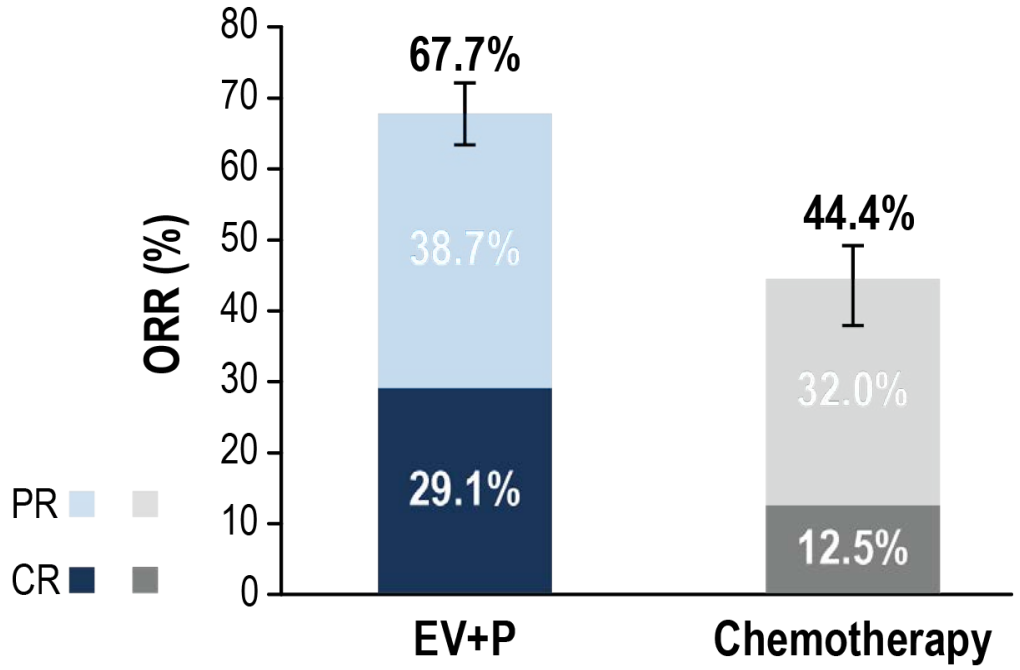
EV-302: Confirmed Overall Response per BICR

Significant improvement in objective response rate was observed with EV+P



	EV+P (N=437)	Chemotherapy (N=441)
Confirmed ORR, n (%) (95% CI)	**296 (67.7) (63.1-72.1)**	**196 (44.4) (39.7-49.2)**
2-sided P value	<0.00001	
Best overall response[a], n (%)		
Complete response	127 (29.1)	55 (12.5)
Partial response	169 (38.7)	141 (32.0)
Stable disease	82 (18.8)	149 (33.8)
Progressive disease	38 (8.7)	60 (13.6)
Not evaluable/No assessment[b]	21 (4.8)	36 (8.2)
Median DOR (95% CI)	NR (20.2, NR)	7.0 (6.2, 10.2)

EV+P ORR is remarkably consistent across studies

Adapted from Powles et al. ESMO 2023 LBA6

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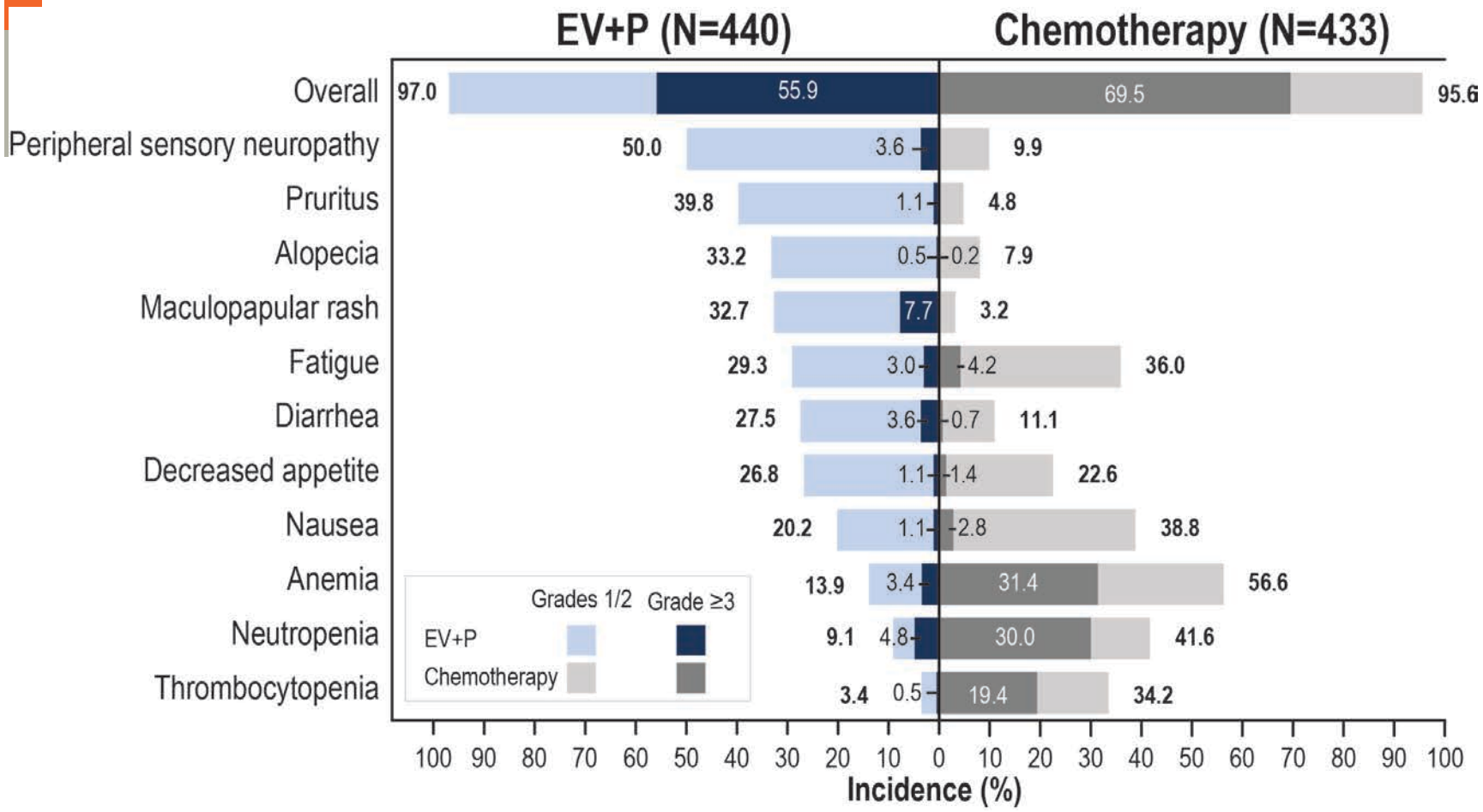
EV-302: Treatment-Related Adverse Events

Grade ≥3 events were 56% in EV+P and 70% in chemotherapy



Serious TRAEs:

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

TRAEs leading to death (per investigator):

EV+P: 4 (0.9%)

- Asthenia
- Diarrhea
- Immune-mediated lung disease
- Multiple organ dysfunction syndrome

Chemotherapy: 4 (0.9%)

- Febrile neutropenia
- Myocardial infarction
- Neutropenic sepsis
- Sepsis

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

Adapted from Powles et al. ESMO 2023 LBA6

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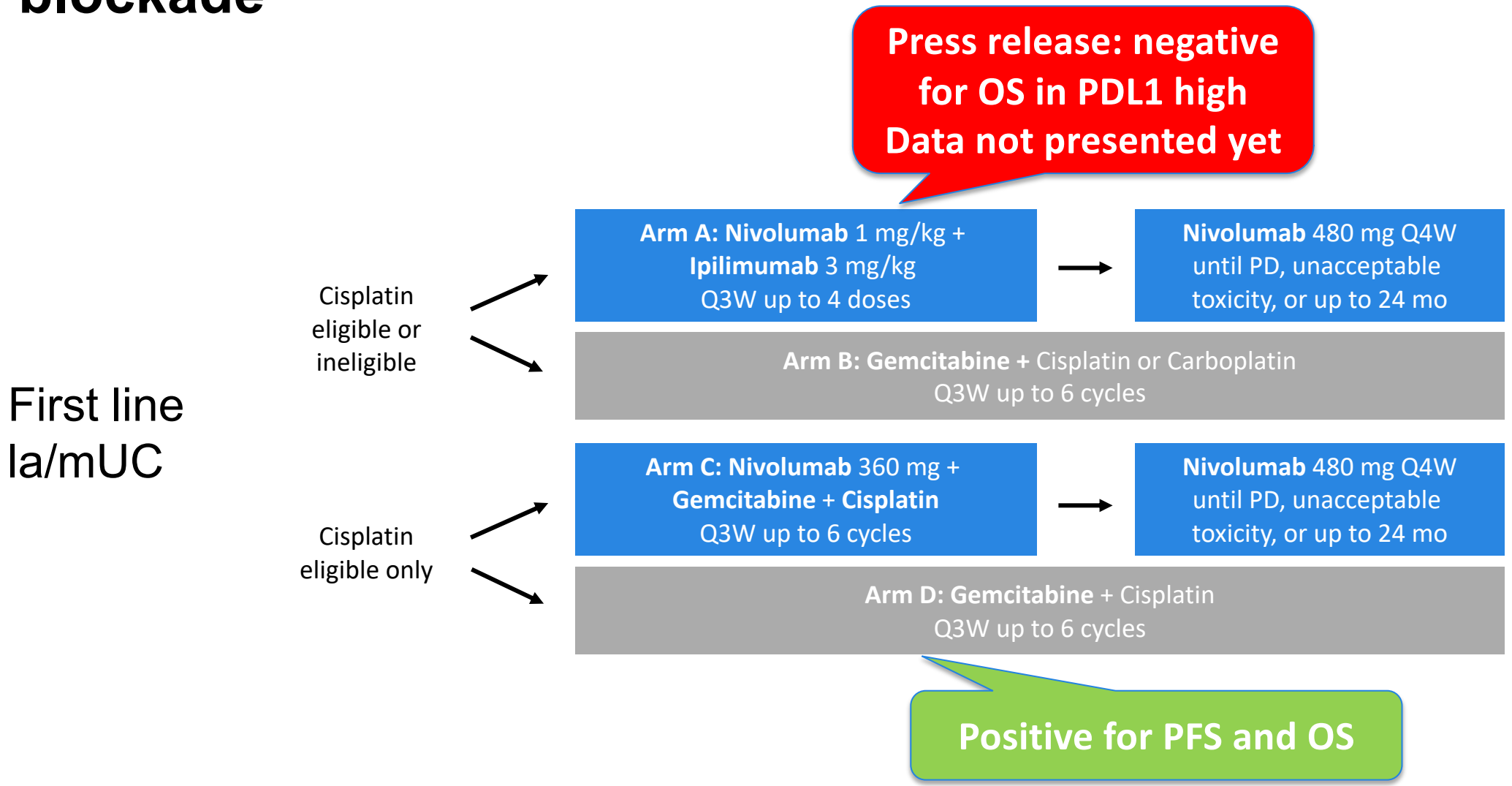
EV-302: Conclusions

- Risk of progression or death reduced by 55% with EV+P
- Risk of death reduced by 53% with EV+P
  - Median OS 31.5 months with EV+P
- All patient subsets seemed to benefit
- Confirmed ORR was 67.7% and 44.4% in the EV+P and chemo arms, respectively
- Transformative data
  - Will replace chemotherapy for most patients with mUC
  - Availability will be limited for some time in certain regions

CheckMate901: two phase 3 trials of immune checkpoint blockade



Galsky. ASCO 2018. Abstr TPS539. NCT03036098.

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CheckMate 901: Study design

Does Nivolumab improve outcomes when added to gemcitabine-cisplatin?

Key inclusion criteria

- Age ≥ 18 years
- Previously untreated unresectable or mUC involving the renal pelvis, ureter, bladder, or urethra
- Cisplatin eligible
- ECOG PS of 0-1

Stratification factors:
- Tumor PD-L1 expression (≥ 1% vs < 1%)
- Liver metastases (yes vs no)

R

Combination phase

N = 304

NIVO 360 mg on D1
+ **Gemcitabine** 1000 mg/m^2 on D1/D8
+ **Cisplatin** 70 mg/m^2 on D1
Q3W (up to 6 cycles)[b]

N = 304

Gemcitabine 1000 mg/m^2 on D1/D8
+ **Cisplatin** 70 mg/m^2 on D1
Q3W (up to 6 cycles)[b]

3 weeks

Monotherapy phase

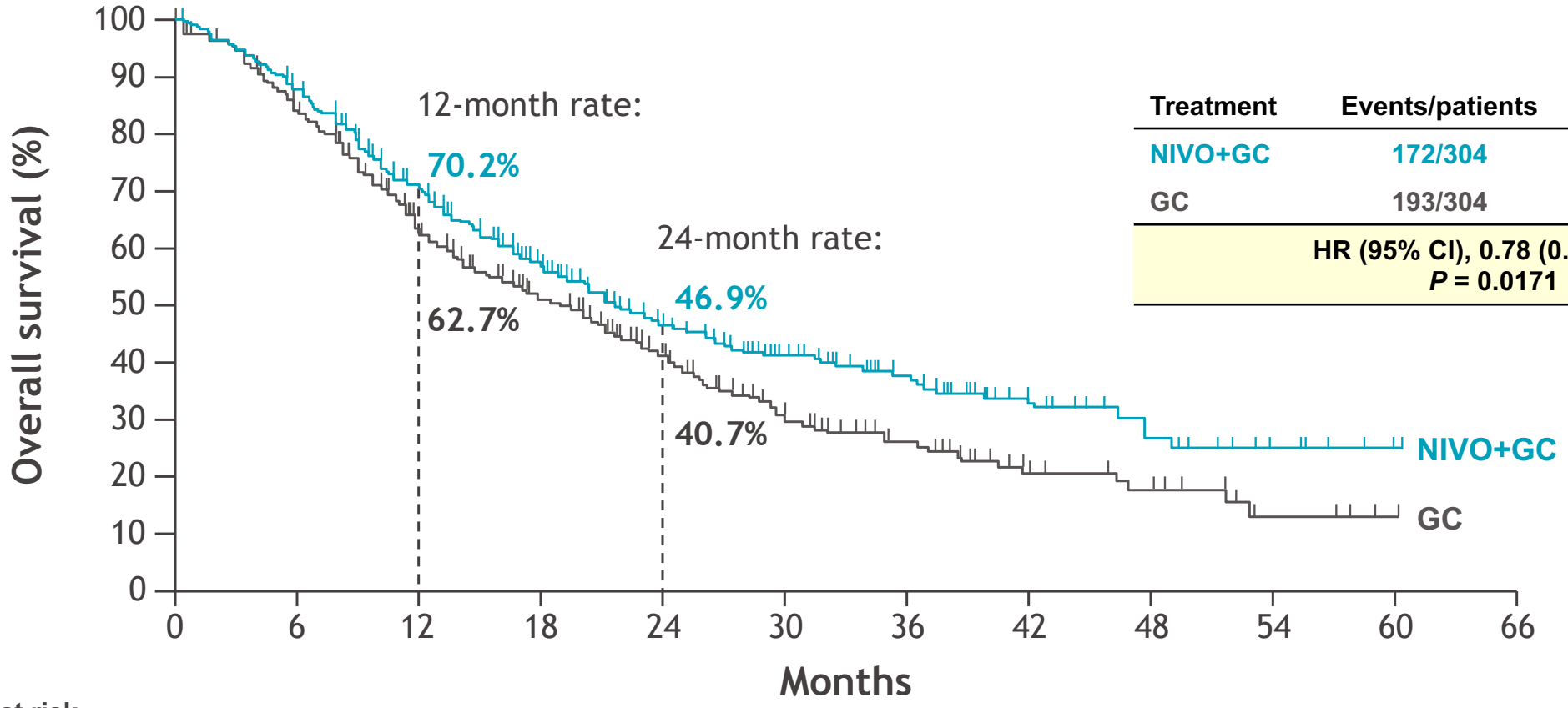
NIVO 480 mg Q4W
(until progression, unacceptable toxicity, withdrawal, or up to 24 months[c])

Median (range) study follow-up, 33.6 (7.4–62.4) months

Primary endpoints: OS, PFS per BICR
Key secondary endpoints: OS and PFS by PD-L1 ≥ 1%,[d] HRQoL
Key exploratory endpoints: ORR per BICR, safety

Adapted from M van der Heijden; ESMO LBA7 2023

CheckMate 901: OS (primary endpoint)



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

Adapted from M van der Heijden; ESMO LBA7 2023

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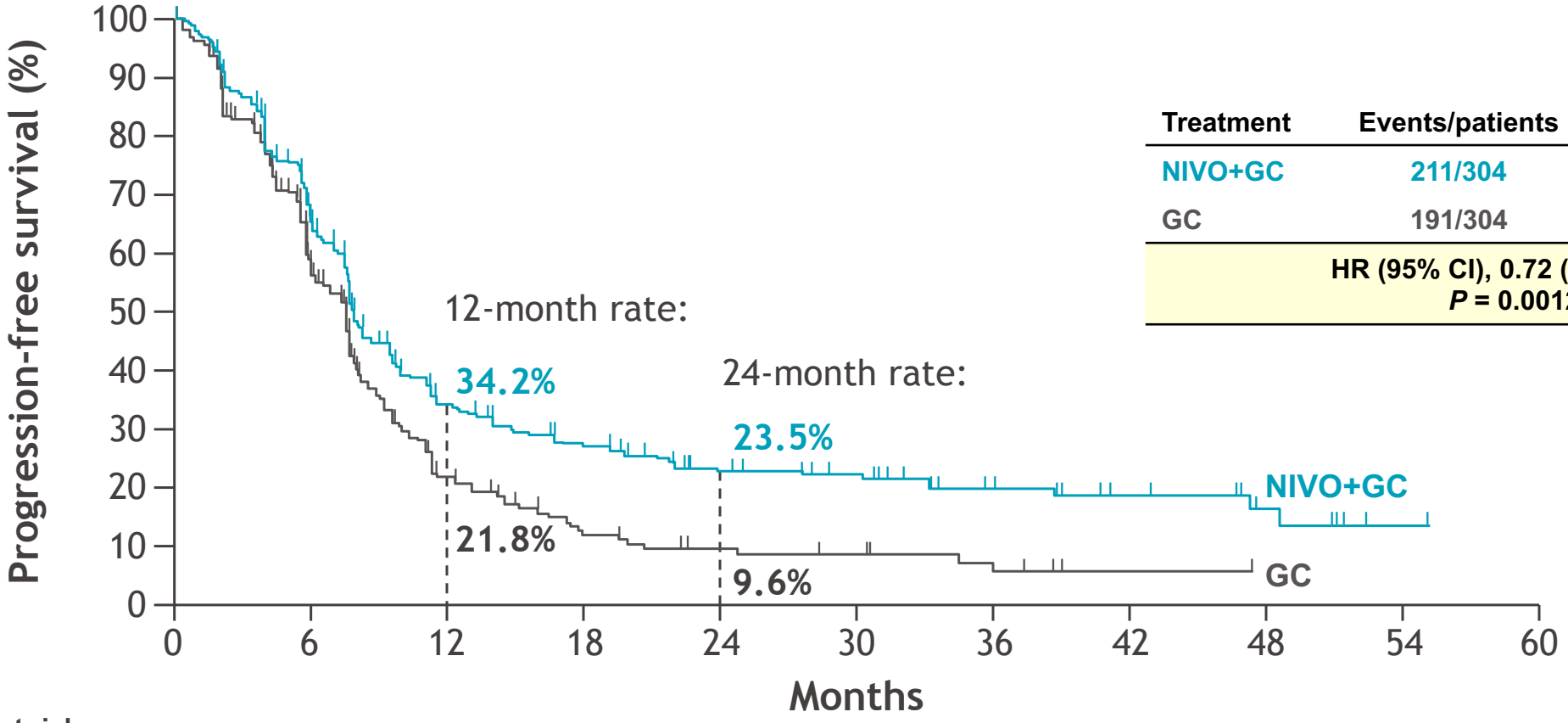
CheckMate 901: PFS per BICR (primary endpoint)



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		

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

Adapted from M van der Heijden; ESMO LBA7 2023

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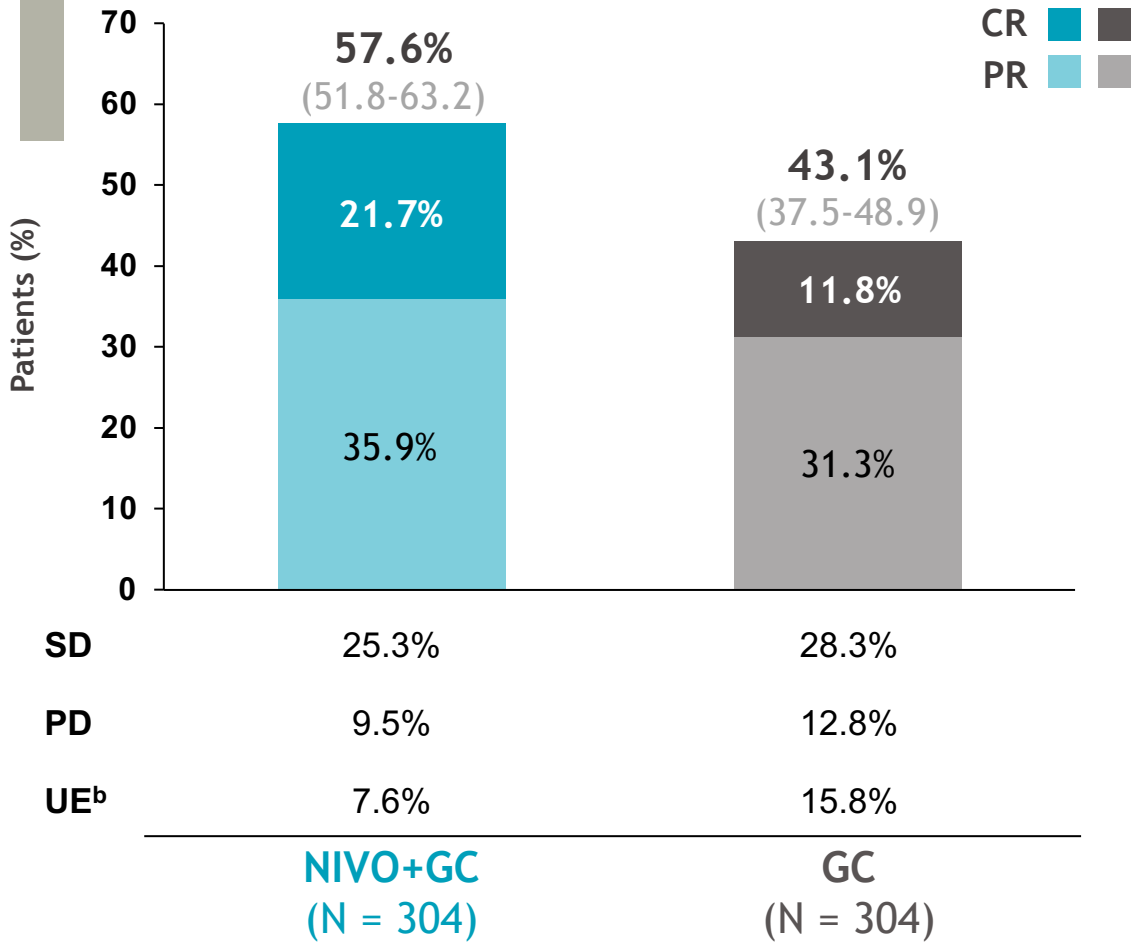
CheckMate 901: Objective response outcomes

ORR (95% CI) and BOR per BICR[a]



Time to and duration of responses

Any objective response[c]	NIVO+GC (n = 175)	GC (n = 131)
Median TTR (Q1-Q3), months	2.1 (2.0–2.3)	2.1 (2.0–2.2)
Median DoR (95% CI), months	9.5 (7.6–15.1)	7.3 (5.7–8.9)

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

Nivolumab associated with higher ORR, CR rate, and longer DOR

Adapted from M van der Heijden; ESMO LBA 2023

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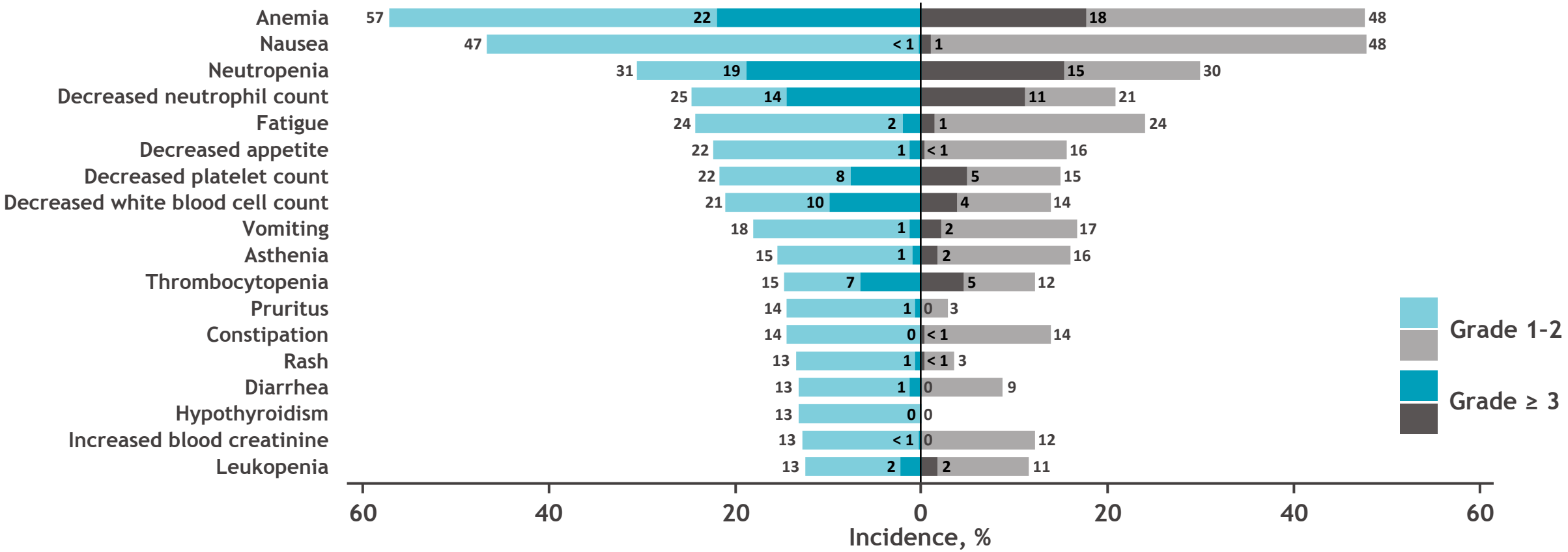
CheckMate 901: Treatment-related AEs in all treated patients

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



Adapted from M van der Heijden; ESMO LBA 2023

Modest increase in grade ≥3 toxicity

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CheckMate 901: Nivolumab + GC

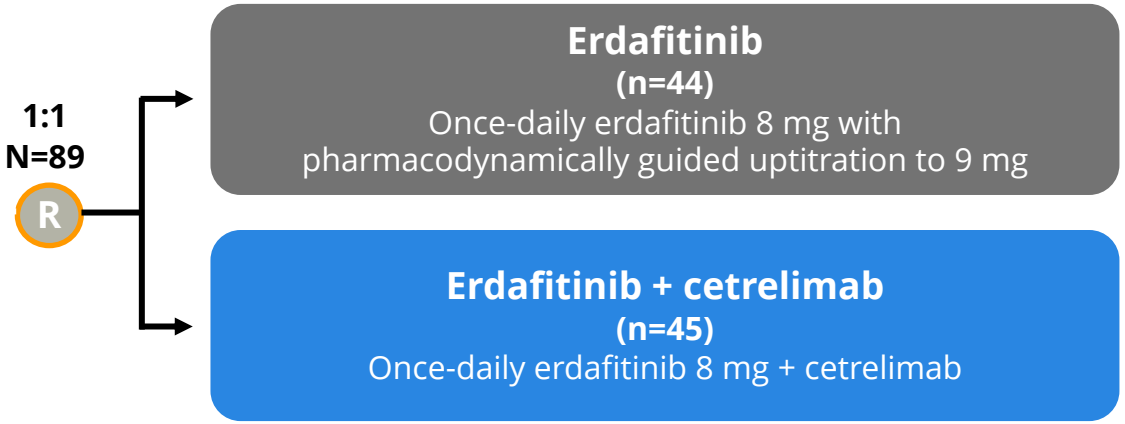
- Higher ORR, DOR and CR rate with addition of nivolumab compared to gem/cis
- Significantly longer PFS and OS
- First study where chemotherapy + checkpoint inhibitor improved outcomes in mUC
- Cisplatin and immunotherapy may have advantages over carboplatin-based combinations
- Is this better than avelumab maintenance strategy?
  - All patients get a checkpoint inhibitor, rather than only those who benefit

NORSE Phase 2 Study Design: 1st line cisplatin ineligible mUC with FGFR3 alterations

Key eligibility criteria

- Age ≥18 years
- mUC diagnosis
- Ineligible for cisplatin[b]
- Select *FGFR* alterations (mutation/fusion)[c]
- Measurable disease
- No prior systemic therapy for mUC

Patients with any PD-L1 status could be enrolled



Primary end points

- ORR
- Safety

Secondary end points

- DCR
- DOR
- Time to response
- PFS
- OS

- Molecular eligibility was determined by central or local testing; a total of 1430 patients underwent central molecular screening[c]

Non-comparative phase II study

2/3 were CPS <10

Siefker-Radtke et al. J Clin Oncol 41, 2023 (suppl 16; abstr 4504)

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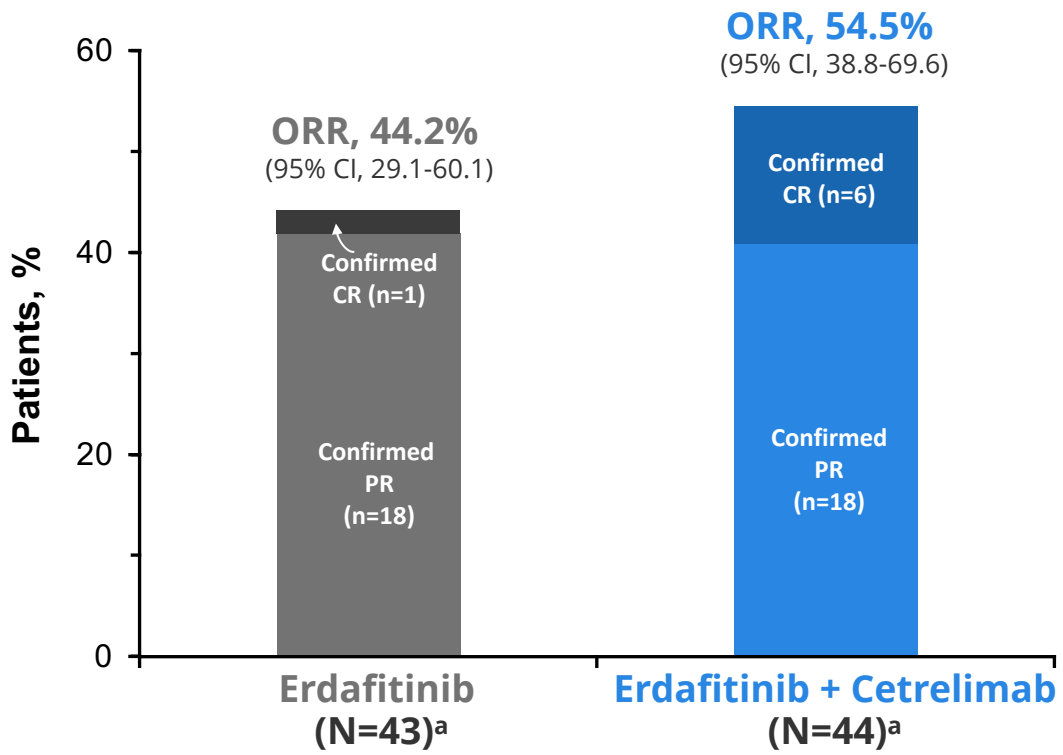
NORSE: ORR of 44% and 55% Was Observed With Erdafitinib and Erdafitinib Plus Cetrelimab, Respectively



Responses are investigator assessed.

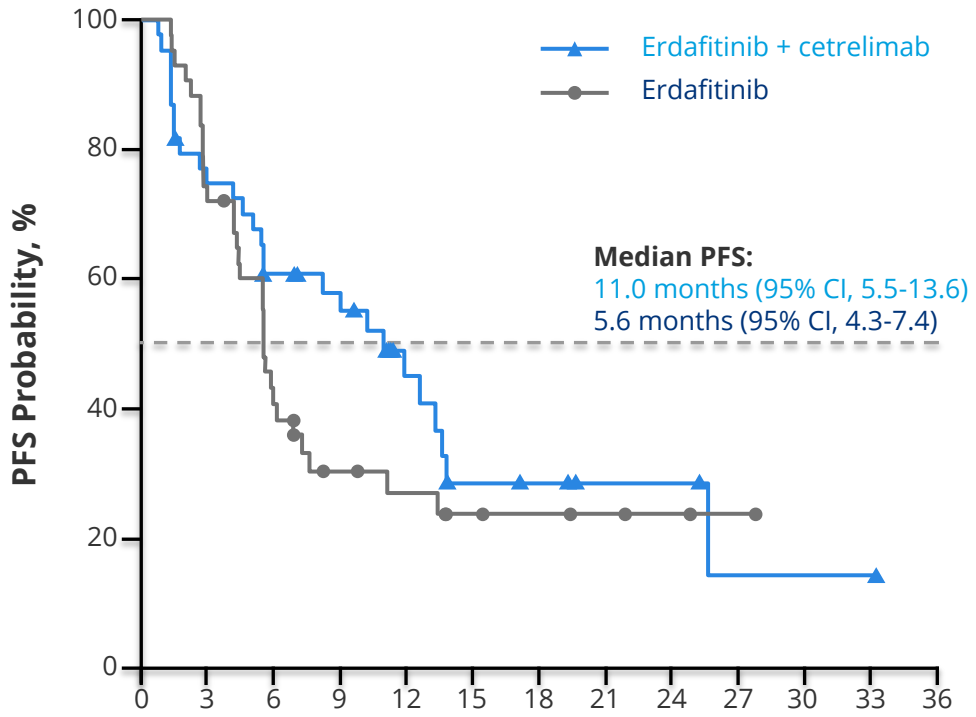
- ORR with erdafitinib monotherapy was consistent with previous results in *FGFR*-altered mUC, and responses were durable
- ORR >50% was observed with combination therapy, with a durable DOR
  - For patients with a CR in the combination arm (n=6), median DOR was not reached
- In patients with a CPS <10, ORR was 46.4% in monotherapy and 50.0% in the combination arm
  - Data are limited in patients with PD-L1 high status (CPS ≥10)

	Erdafitinib (N=43)	Erdafitinib + Cetrelimab (N=44)
DCR, median (95% CI), %	**88.4 (74.9-96.1)**	**79.5 (64.7-90.2)**
DOR, median (95% CI), months	**9.72 (4.6-NE)**	**11.10 (8.8-NE)**

Siefker-Radtke et al. J Clin Oncol 41, 2023 (suppl 16; abstr 4504)

NORSE: Longer PFS and OS provocative with combination therapy

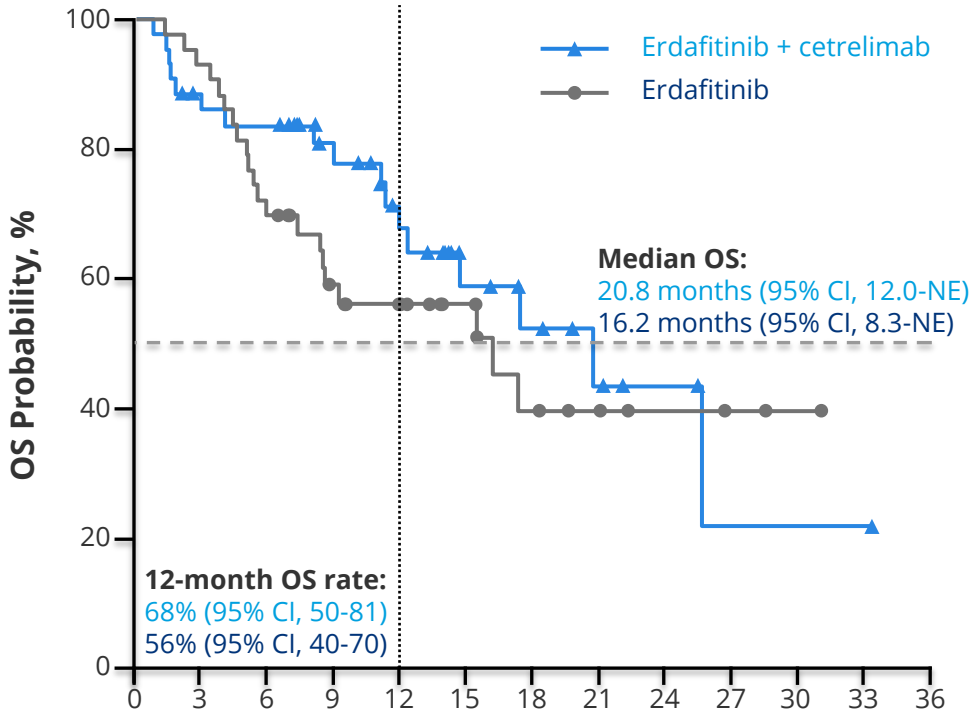
Progression-free Survival



Patients at risk

Erdafitinib + cetrelimab	44	32	25	21	11	6	5	3	3	1	0	0	0
Erdafitinib	43	32	17	10	8	5	4	3	2	1	0	0	0

Overall Survival



Patients at risk

Erdafitinib + cetrelimab	44	36	35	27	19	11	8	5	3	1	1	1	0
Erdafitinib	43	40	30	21	17	12	7	5	3	2	1	0	0

Siefker-Radtke et al. J Clin Oncol 41, 2023 (suppl 16; abstr 4504)

Memorial Sloan Kettering Cancer Center

First-line therapy for la/mUC is changing finally!

- EV/pembro is now standard for metastatic UC patients in US
  - EV-302 comparing to platinum-based chemotherapy is positive for PFS/OS (OS EV/P 31.5mo vs GP 16.1mo)
- Addition of nivolumab to gem/cis improves PFS and OS (OS NGC 21.7mo vs GC 18.9mo)
  - GC+N will be a first-line option for patients and likely used more frequently outside US where EV/P is not as readily available
- Pembrolizumab monotherapy for frail patients
- Avelumab maintenance checkpoint blockade following response to initial platinum-based chemotherapy remains a standard of care today
  - As landscape evolves and CPI is started at initial therapy for metastatic disease, its role will diminish
- Combinations of IO+FGFR3i remain investigational
- Key unanswered question: what is the best treatment for recurrences after adjuvant CPI?

MODULE 4: Emerging Role of HER2-Targeted Therapy for mUBC – Dr Yu

RTP
RESEARCH
TO PRACTICE

Consulting Faculty Questions

Perspectives from the breast cancer experience: HER2 testing and durability of responses with trastuzumab deruxtecan (T-DXd)

Neil Love, MD

Priyanka Sharma, MD

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

Priyanka Sharma, MD

What is your approach to HER2 testing in mUBC?

What is the appropriate threshold for the use of HER2-targeted therapy?

Assuming you could access both T-DXd and disitamab vedotin, how would you integrate these agents into the treatment algorithm for mUBC?

RTP
RESEARCH
TO PRACTICE

Consulting Faculty Questions

Perspectives from the breast cancer experience: Identification and management of T-DXd-associated side effects

Neil Love, MD

Priyanka Sharma, MD

RTP
RESEARCH
TO PRACTICE

QUESTIONS FOR THE FACULTY

Priyanka Sharma, MD

What is your approach to the prevention and management of T-DXd-associated nausea and vomiting?

How do you screen for ILD in patients receiving T-DXd?

What is your experience with T-DXd and disitamab vedotin, and have you observed clinically meaningful responses to these agents?

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Please describe a patient in your practice with HER2-positive metastatic UBC who received trastuzumab deruxtecan (T-DXd).

	Age	Tx received	Benefit derived	Side effects
 Dr Milowsky	N/A	N/A	N/A	N/A
 Dr O'Donnell	65 years	T-DXd	Not much	Well tolerated
 Dr Rosenberg	78 years	T-DXd	A great deal	Mild fatigue
 Dr Siefker-Radtke	65 years	T-DXd	A great deal	Don't know — treated in Phase I
 Dr Yu	58 years	T-DXd + nivolumab	Some	None
 Dr Friedlander	68 years	T-DXd	Not much	Fatigue, asthenia, alopecia, lower blood counts, mild nausea
 Dr Plimack	No personal experience			

Have you offered or would you offer HER2-targeted therapy to your patients with HER2-positive metastatic UBC outside of a protocol setting?

 Dr Milowsky	I have, trastuzumab deruxtecan
 Dr O'Donnell	I have, trastuzumab deruxtecan
 Dr Rosenberg	I have, trastuzumab deruxtecan
 Dr Siefker-Radtke	I have not but would for the right patient
 Dr Yu	I have, trastuzumab deruxtecan (FDA approved in other diseases and accessible off label); disitamab vedotin (wish list)
 Dr Friedlander	I have, trastuzumab deruxtecan
 Dr Plimack	I have not and would not

Should HER2 testing be ordered for patients with metastatic UBC?

 Dr Milowsky	Yes
 Dr O'Donnell	Yes
 Dr Rosenberg	Yes
 Dr Siefker-Radtke	Yes
 Dr Yu	Yes
 Dr Friedlander	Yes
 Dr Plimack	Yes

RTP
RESEARCH
TO PRACTICE

Regulatory and reimbursement issues aside, in which line of therapy would you generally offer targeted treatment to a patient with HER2-positive metastatic UBC?

 Dr Milowsky	Third line and beyond
 Dr O'Donnell	Beyond third line
 Dr Rosenberg	Third line
 Dr Siefker-Radtke	Third line
 Dr Yu	Beyond third line
 Dr Friedlander	Third line
 Dr Plimack	Third line and beyond

Based on your personal clinical experience and/or knowledge of available data, for each of the following agents please estimate the chance that a patient will experience toxicity during treatment that will require withholding administration. What is the primary toxicity patients experience that leads to withholding this drug?

	Trastuzumab deruxtecan		Disitamab vedotin	
	Chance of withholding	Primary toxicity	Chance of withholding	Primary toxicity
 Dr Milowsky	30%-40%	Pneumonitis/ neutropenia	40%-50%	Neuropathy
 Dr O'Donnell	30%	GI issues	80%	Neuropathy
 Dr Rosenberg	20%	Fatigue	40%	Fatigue
 Dr Siefker-Radtke	—	—	100%	Neuropathy
 Dr Yu	Low	Pneumonitis	Medium	Fatigue
 Dr Friedlander	50%	Myelosuppression	70%	Neuropathy
 Dr Plimack	No personal experience			

FRED HUTCH / UNIVERSITY OF WASHINGTON / SEATTLE CHILDREN'S

CANCER CONSORTIUM

Emerging Role of HER2-Targeted Therapy in Metastatic Urothelial Bladder Cancer

2024 ASCO GU: Urothelial Bladder Cancer Symposium

January 26, 2024

Evan Y. Yu, M.D.
Section Head, Medical Oncology, Clinical Research Division
Medical Director, Clinical Research Support
Fred Hutchinson Cancer Center
Professor of Medicine, Division of Hematology & Oncology
University of Washington, Seattle, WA

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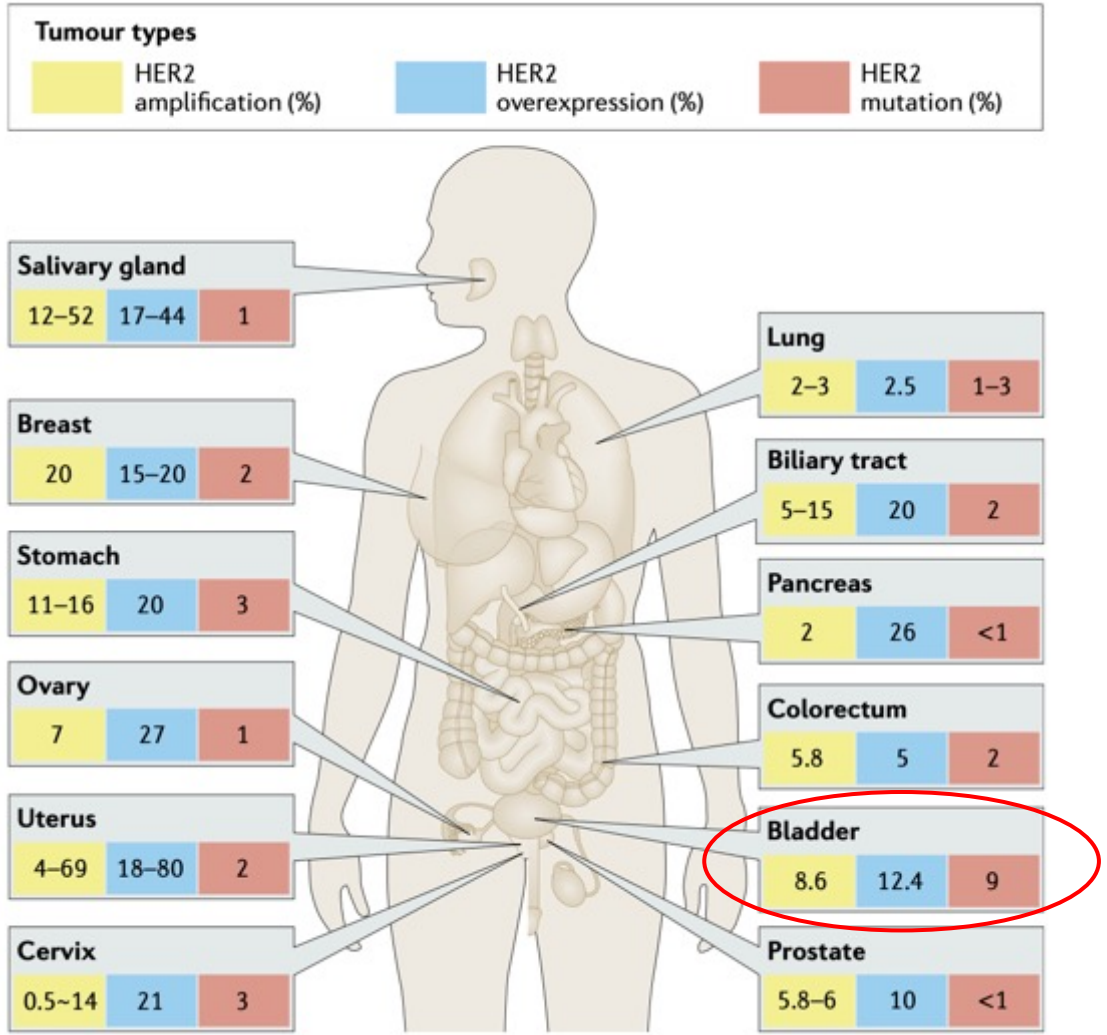
Discussion Topics

- HER2 expression in urothelial bladder cancer
- Antibody drug conjugates (ADCs) e.g. trastuzumab deruxtecan and disitamab vedotin
- Monotherapy
- Combination therapy with ADCs and checkpoint inhibitors

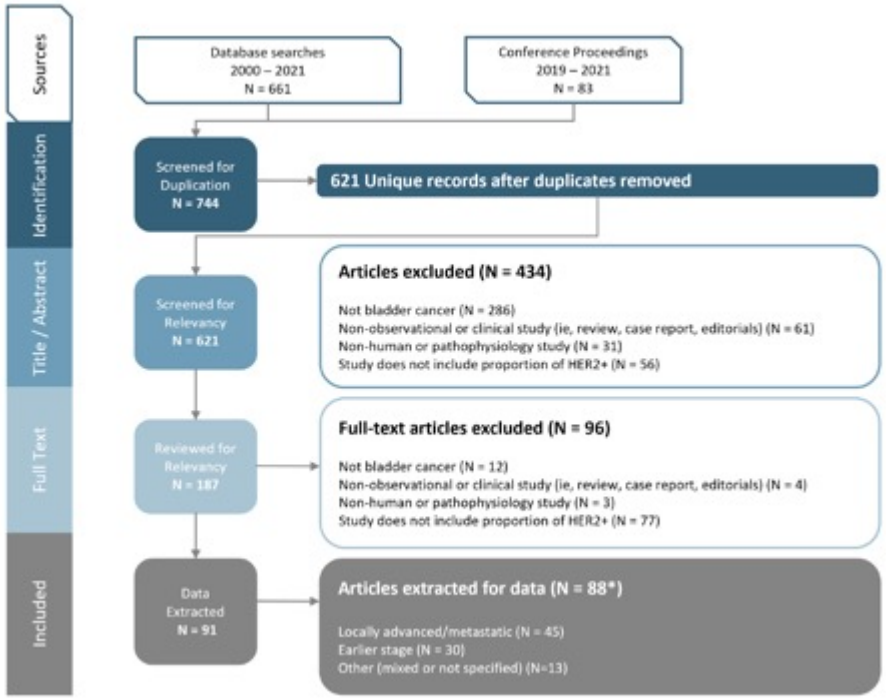
HER2 as a Cancer Specific Target



Oh DY, Bang YJ. Nat Rev Clin Oncol 2020; 17:33-48.

HER2 Expression in Locally Advanced/Metastatic Urothelial Bladder Cancer (LA/mUC)

- HER2 IHC not typically assessed as part of standard clinical care
- No standardized criteria for defining HER2 expression
- Systemic Literature Review of reported HER2 status in LA/mUC



- A significant proportion of patients with LA/mUC have tumors with HER2 expression based on pre-defined criteria
- **HER2+** (IHC 3+ OR IHC 2+ / ISH+): **12.3% weighted avg** (6 studies, N=971 pts)
- **HER2 low** (IHC 2+/ISH- OR IHC 1+): **47.9% weighted avg** (4 studies, N=275 pts)

Data on slide courtesy of Vadim Koshkin from:
Scherrer E, et al. Front Oncol 2022.

HER2 Expression in Primary Urothelial Bladder Cancer Resection Samples Using Standardized Laboratory Methods

- HER2 expression in n=362 surgical UC samples using a standardized protocol
- Samples were commercially sourced, paraffin-embedded primary UC resections evaluated by trained readers for HER2 expression
- Methods:
  - HER2/neu (4B5) Rabbit Monoclonal Primary Antibody IHC assay used
  - For HER2 gene amplification, used HER2 Dual ISH DNA Probe Cocktail that detects both *ERBB2* and its residing chromosome (17). HER2 gene amplification defined by HER2/Chr17 ratio ≥2.0
  - HER2 IHC staining scored based on an established algorithm for gastric cancer

HER2 Status	N	Percentage of samples (95% CI)
HER2+ and HER2-low	160	44.2% (39.2%–49.3%)
HER2+/overexpression	57	15.7% (12.4%–19.9%)
HER2-low	103	28.5% (24.1%–33.3%)
HER2-zero	202	55.8% (50.7%–60.8%)

		N (row %)		
Stage	N	HER2+	HER2-low	HER2-zero
Stage I	7	1 (14)	0	6 (86)
Stage II	133	17 (13)	46 (35)	70 (53)
Stage III	192	37 (19)	50 (26)	102 (55)
Stage IV	30	2 (7)	7 (23)	21 (70)
All	362	57 (16)	103 (28)	202 (56)

a Stage information as supplied by the tissue vendor. Staging may have been based on clinical information or on tissue samples different from those included in the current study

Koshkin VS, et al. J Clin Oncol 41, 2023 (suppl 6; abstr 556).

Disappointing Early Results with HER2 Targeted Therapy in Urothelial Bladder Cancer

Trastuzumab, Paclitaxel, Carboplatin, and Gemcitabine in Advanced Human Epidermal Growth Factor Receptor-2/*neu*–Positive Urothelial Carcinoma: Results of a Multicenter Phase II National Cancer Institute Trial

Maha H.A. Hussain, Gary R. MacVicar, Daniel P. Petrylak, Rodney L. Dunn, Ulka Vaishampayan, Primo N. Lara Jr, Gurkamal S. Chatta, David M. Nanus, L. Michael Glode, Donald L. Trump, Helen Chen, and David C. Smith

- Her2/neu overexpression selected by IHC, gene amplification or elevated serum levels
- 31/44 (70%) ORR[1]
- 22.7% with grade 1-3 cardiotoxicity

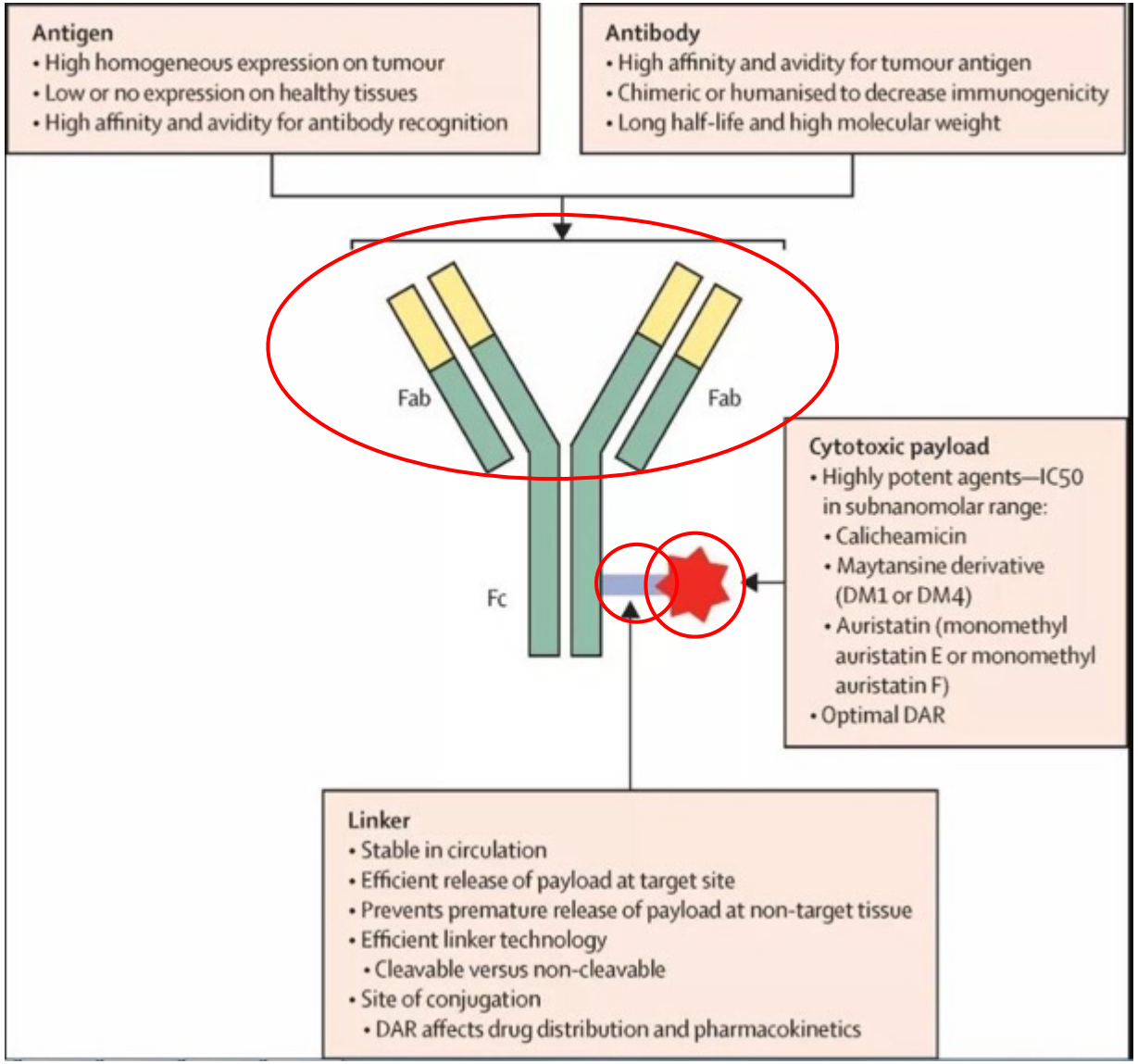
- 3/9 (33%) ORR with HER2 amplified urothelial carcinoma in a trastuzumab/pertuzumab basket trial[2]

- Other HER2 targeted drugs tested in bladder cancer[3]
  - DN24-02
  - Lapatinib
  - Afatinib

- 2 ADC basket trials with Ado-trastuzumab emtansine (T-DM1) and bladder cancer cohorts
  - KAMELEON (NCT02999672) – HER2 overexpression
  - MSKCCC (NCT02675829) – HER amplified or mutated

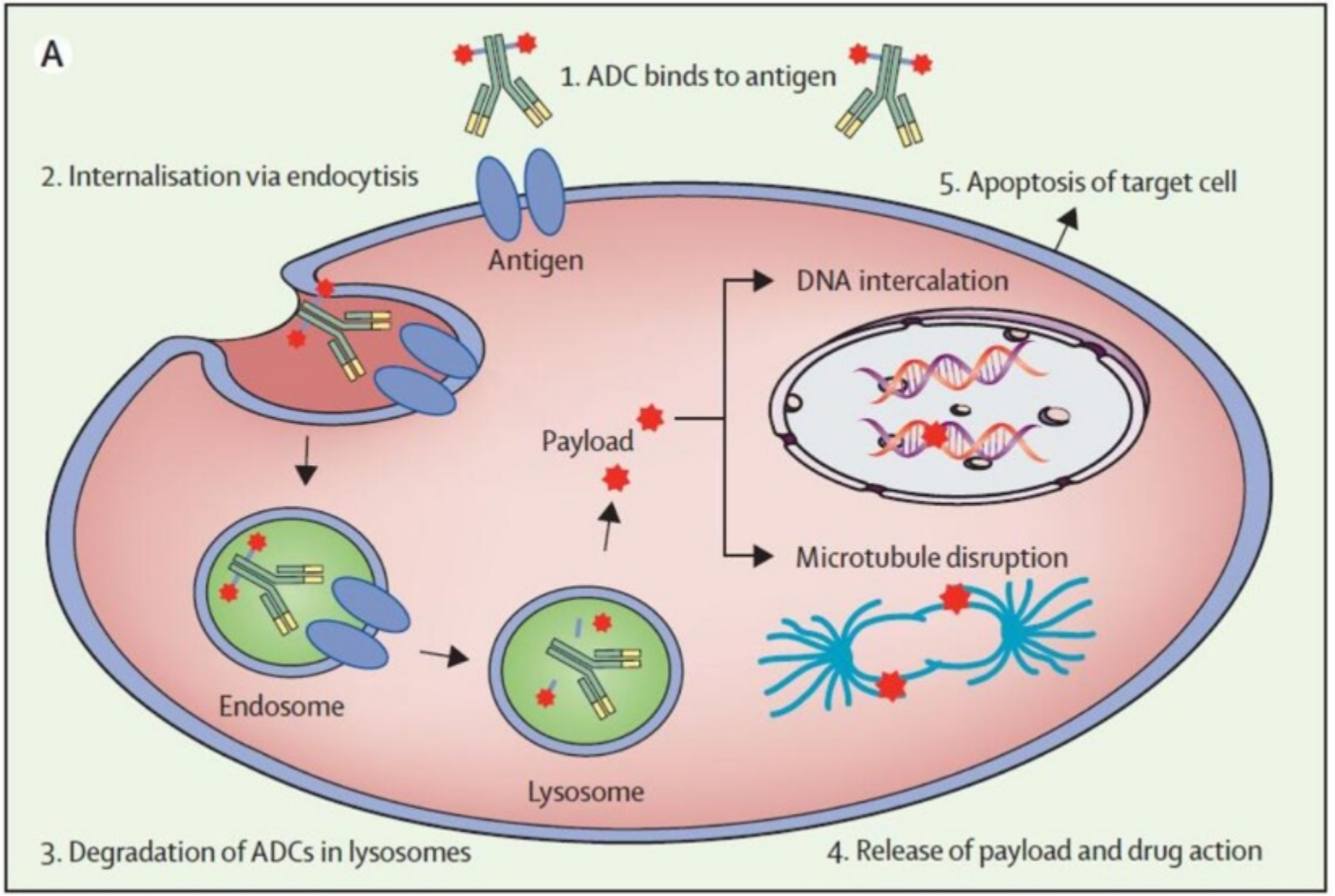
1. Hussain MH, et al. *J Clin Oncol* 2007; 25:2218-24.
2. Bryce AH, et al. *J Clin Oncol* 35, 2017 (suppl 6S; abstr 348)
3. Koshkin V, et al. *Bladder Cancer* 2019; 5:1-12

General Design Elements for an Antibody Drug Conjugate (ADC)



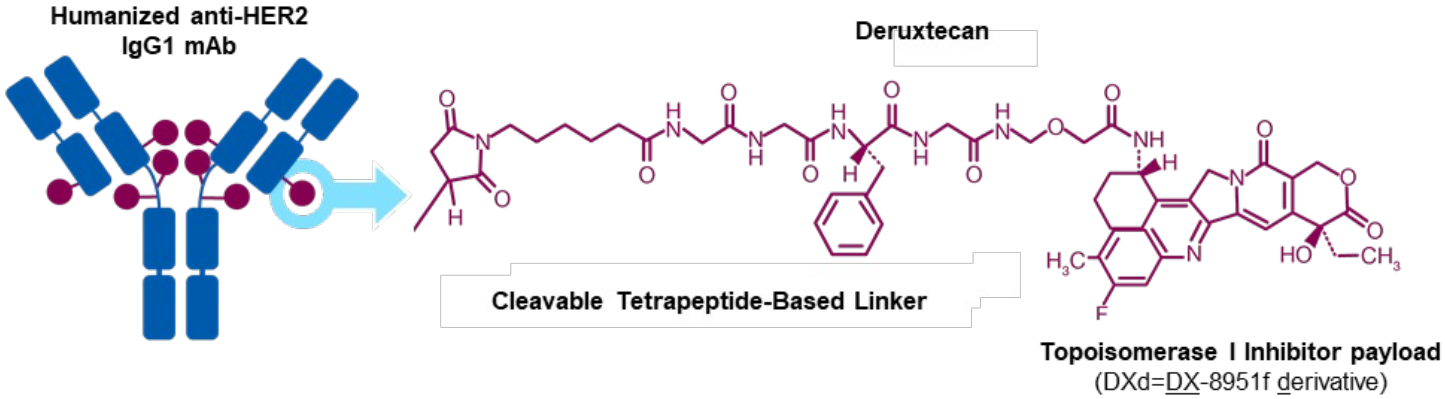
Chau CH, et al. Lancet 2019; 394:793-804

ADC Mechanism of Action



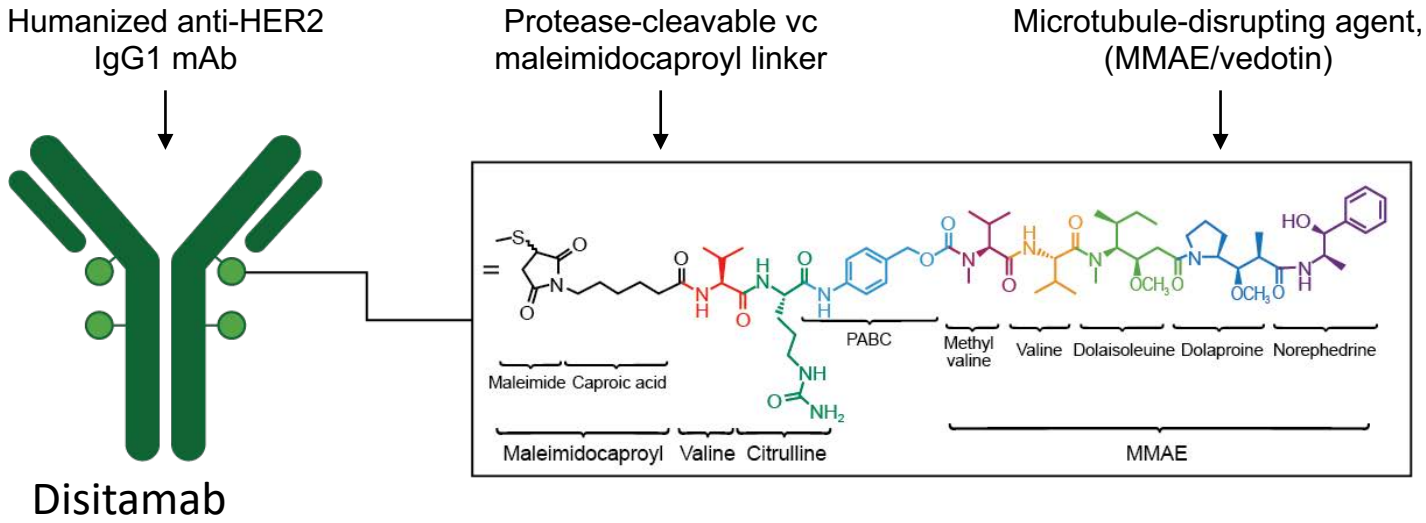
Chau CH, et al. Lancet 2019; 394:793-804

Trastuzumab Deruxtecan and Disitamab Vedotin



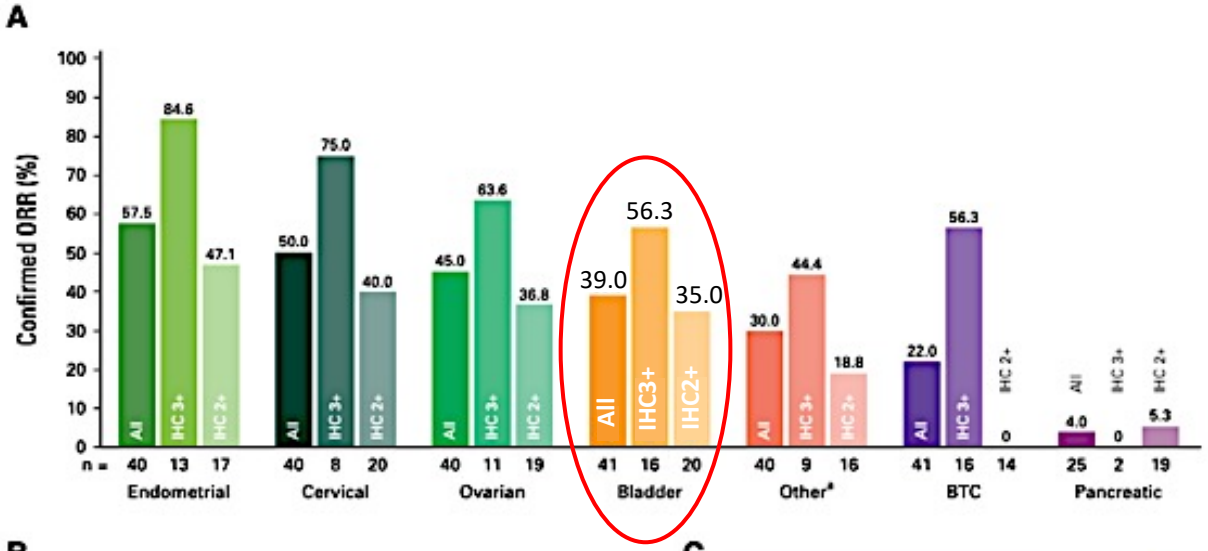
Conjugation chemistry
The tetrapeptide-based cleavable linker is connected to the humanized anti-HER2 IgG1 monoclonal antibody, with the same amino acid sequence as trastuzumab

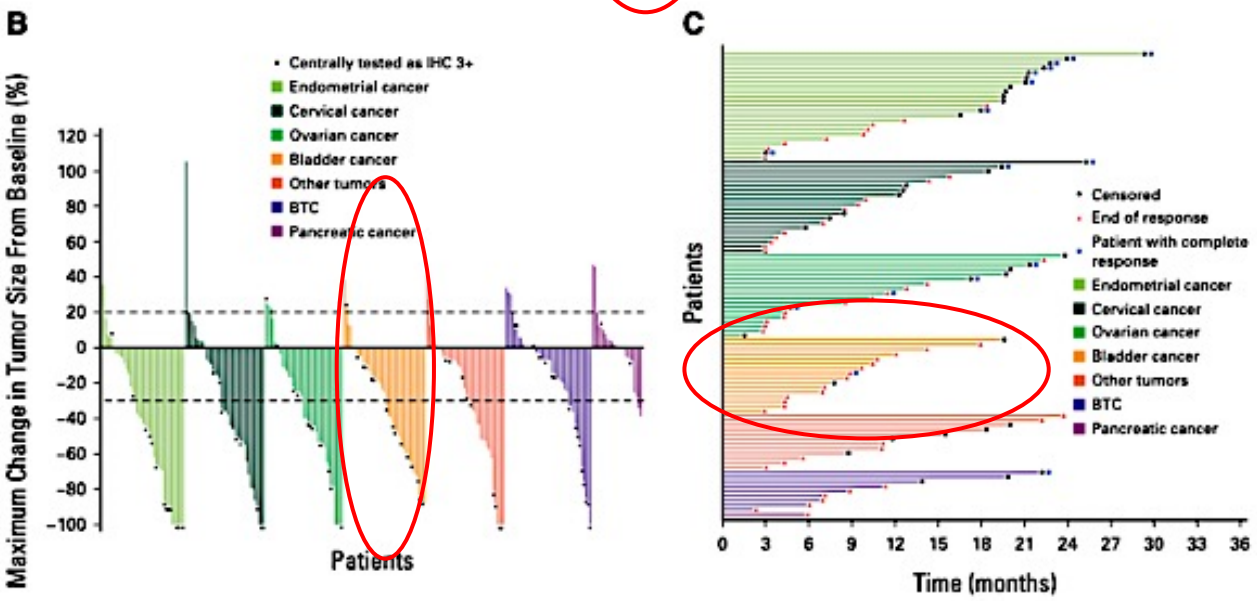
Trastuzumab Deruxtecan

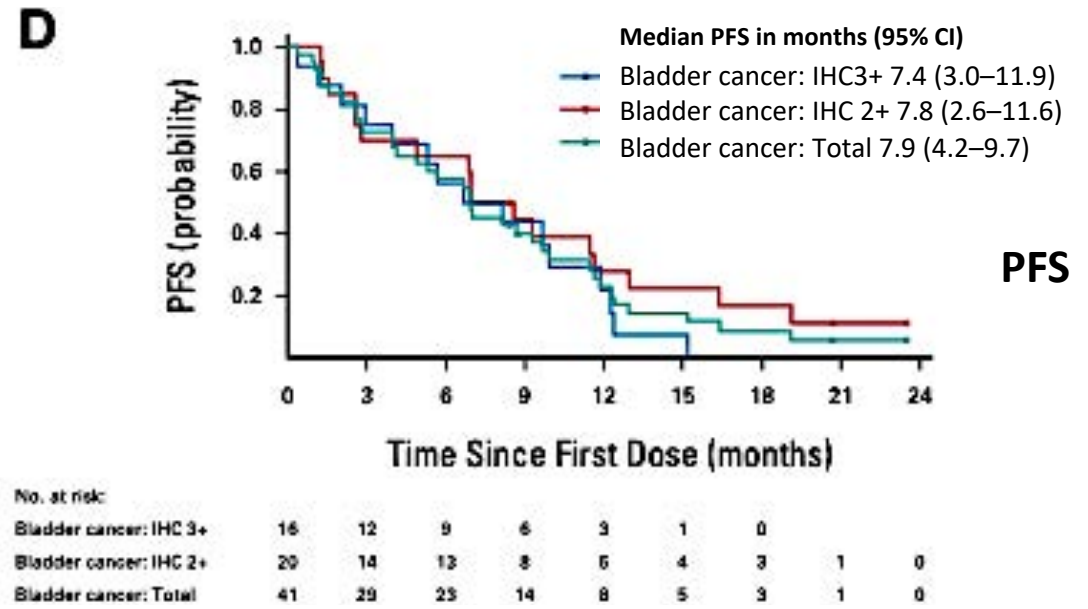


Disitamab vedotin

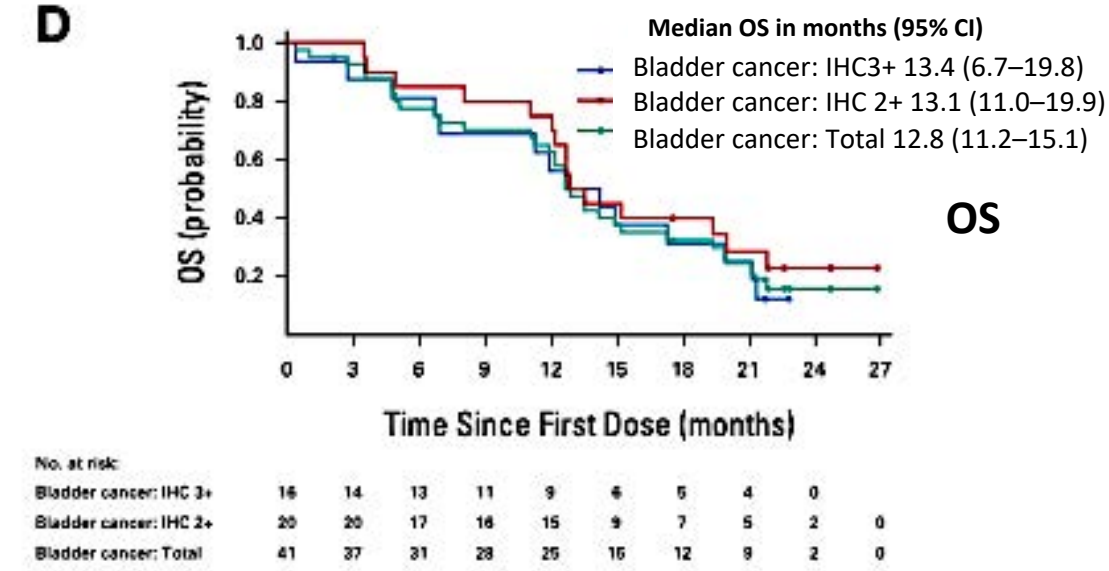
Trastuzumab Deruxtecan Monotherapy from DESTINY-PanTumor02 Phase 2 trial







PFS



OS

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

Trastuzumab Deruxtecan Monotherapy from DESTINY-PanTumor01 Phase 2 trial – Focus on mUC Patients with HER2 Mutations

- Patients with advanced solid tumors harboring prespecified HER2 mutations
- Progressed on previous systemic therapy
- Trastuzumab Deruxtecan 5.4 mg/kg q3w

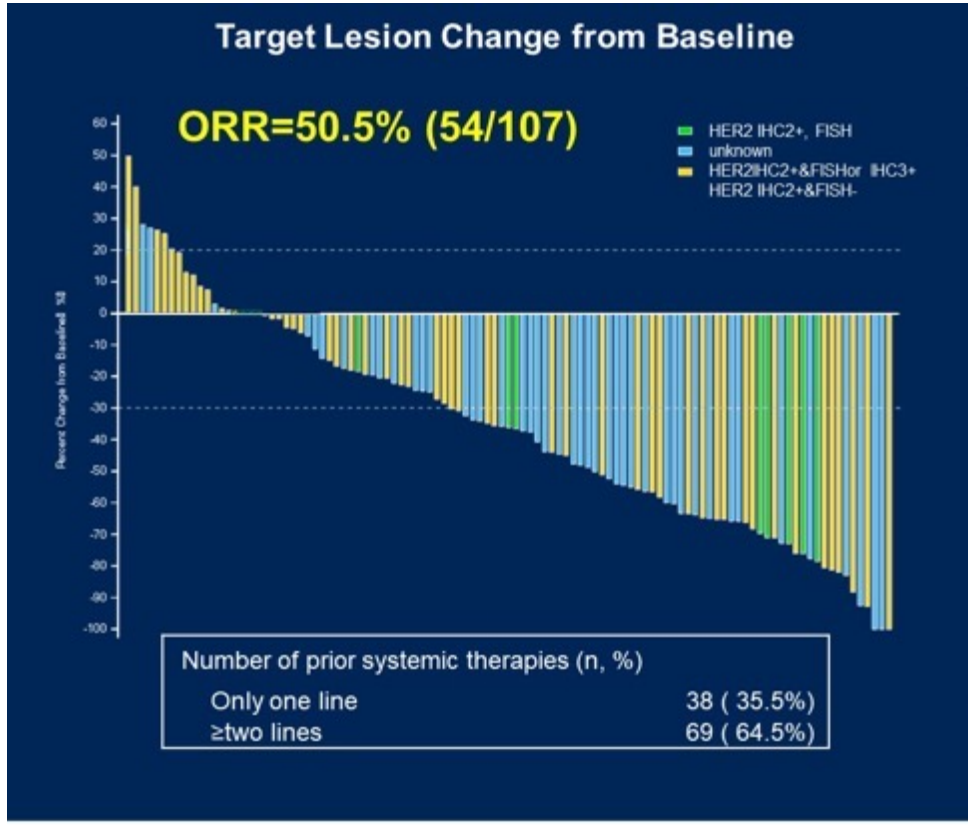
Table: 654O

	N	ORR by ICR	
		n	%
All pts	102	30	29.4
Tumor type			
Breast	20	10	50.0
Colorectal	20	4	20.0
Biliary tract	19	2	10.5
Esophageal/esophagogastric	11	1	9.1
Urothelial	7	2	28.6
Salivary gland/head and neck AC	6	4	66.7
Small intestinal AC	5	0	-
Cervical	3	2	66.7
Endometrial	2	2	100
Other neuroendocrine	2	1	50.0
Pancreatic	2	0	-
AC of unknown primary	1	1	100
Extramammary Paget's disease	1	1	100
Melanoma	1	0	0
Ovarian	1	0	0
Urachal	1	0	0
***HER2*m domain**[a]			
Tyrosine kinase[b]	52	19	36.5
Extracellular[c]	34	10	29.4
Transmembrane/juxtamembrane[d]	17	1	5.9

Li BT, et al. Ann Oncol 2023; 34 (suppl 2):S459-S460.

Disitamab Vedotin (RC48) Monotherapy

Activity in HER2 2-3+



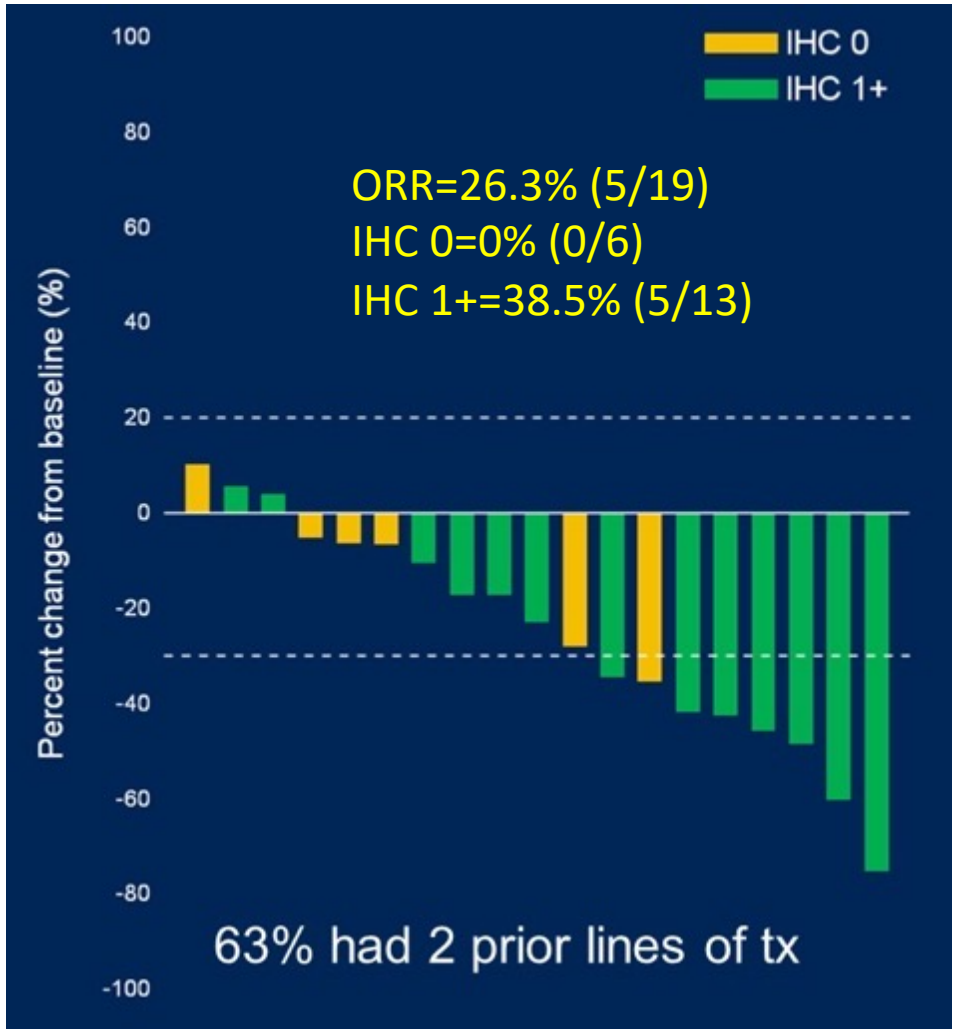
ORR

IHC2+FISH+ or IHC3+ (n=45) = 62.2%

IHC2+FISH- (n=53) = 39.6%

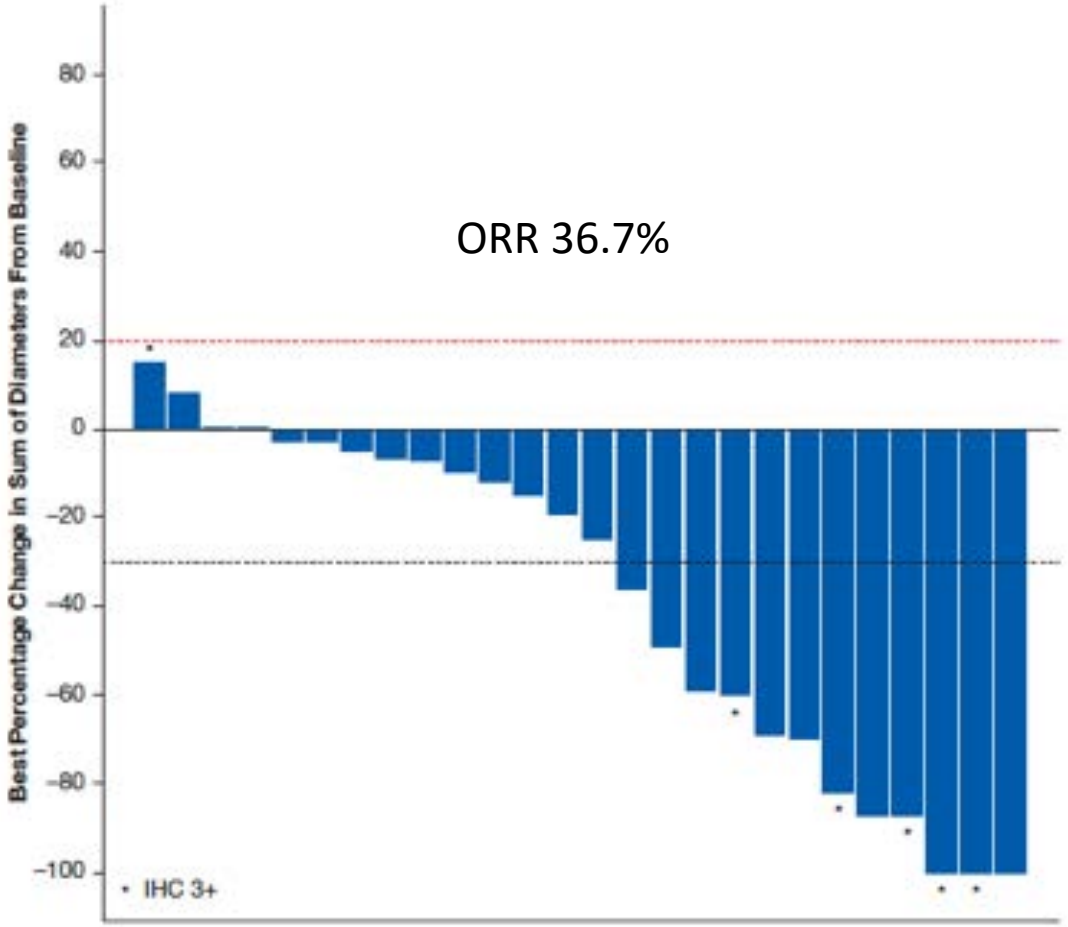
Sheng X, et al. J Clin Oncol 40, no. 16_suppl (June 1, 2022) 4518-4518.
Sheng X, et al. J Clin Oncol; epub November 21, 2023.

Activity in HER2 1+



Xu H, et al. J Clin Oncol 40, no. 16_suppl (June 1, 2022) 4519-4519.

Trastuzumab Deruxtecan Combination with Nivolumab Trial Schema

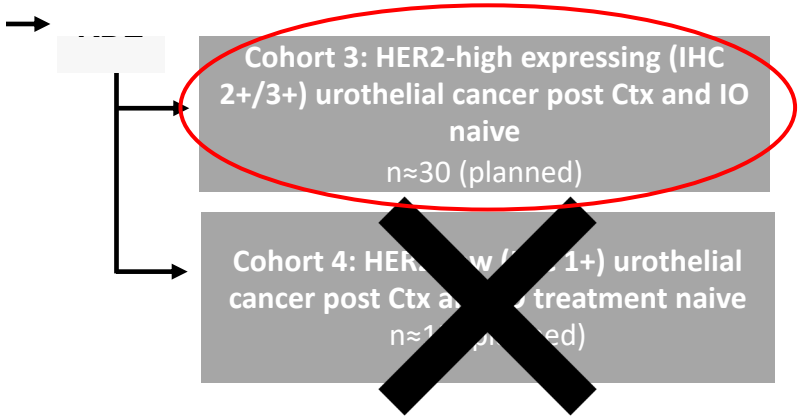


ORR 36.7%

Cohort 3 IHC 3+/2+ (n = 30) (part 2: T-DXd 5.4 mg/kg and nivolumab 360 mg) Best (minimum) percentage change					
n	Mean	SD	Median	Min	Max
26	−37.8	38.52	−22.0	−100	15

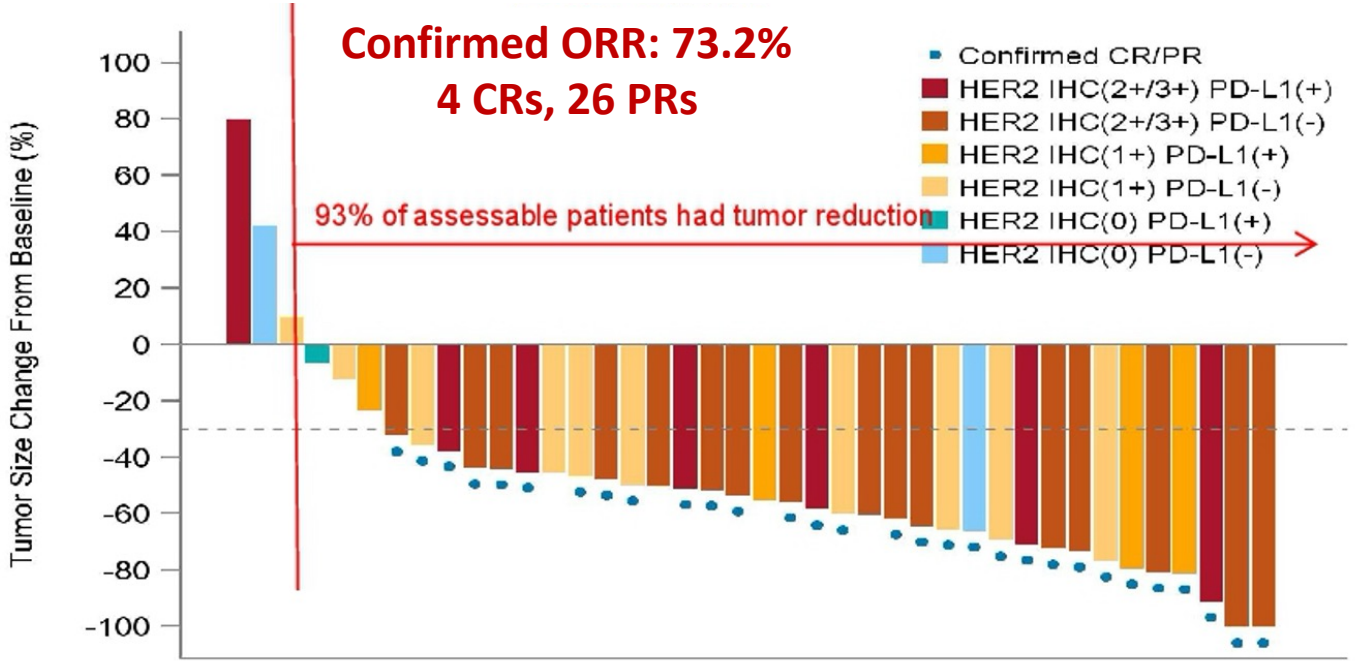
*In cohort 3, 4 patients did not have best percentage change available, of whom 2 were IHC 3+.
The line at 20% indicates progressive disease, and the line at −30% indicates a partial response.

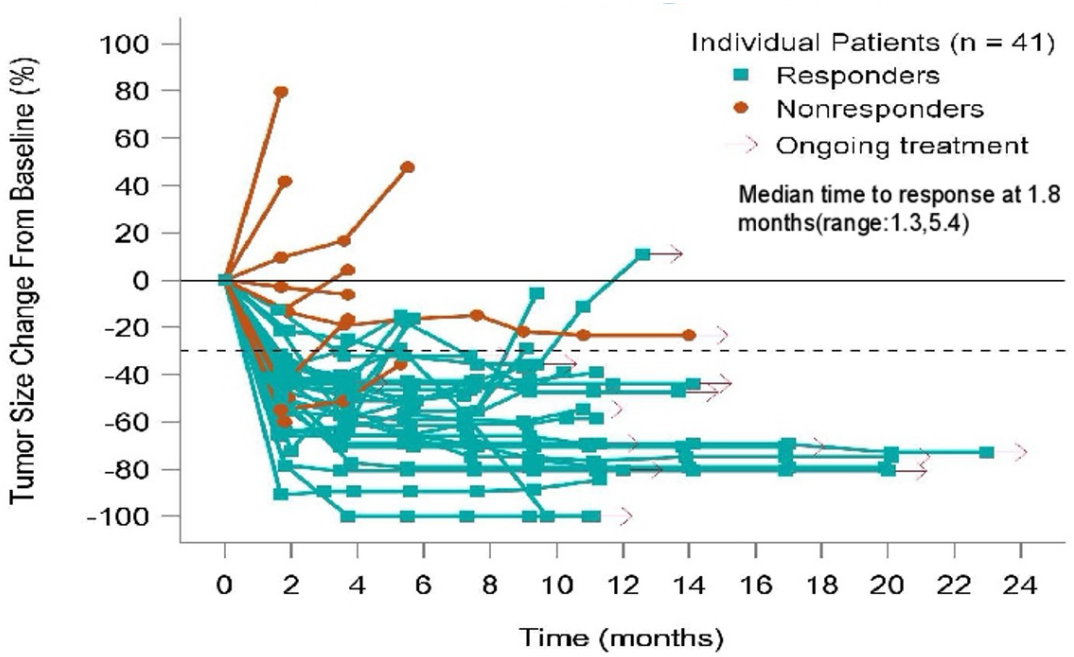
Part 2: Dose Expansion



Galsky MD, et al. J Clin Oncol 40, no.6_suppl (Feb 20, 2022) 438-438.

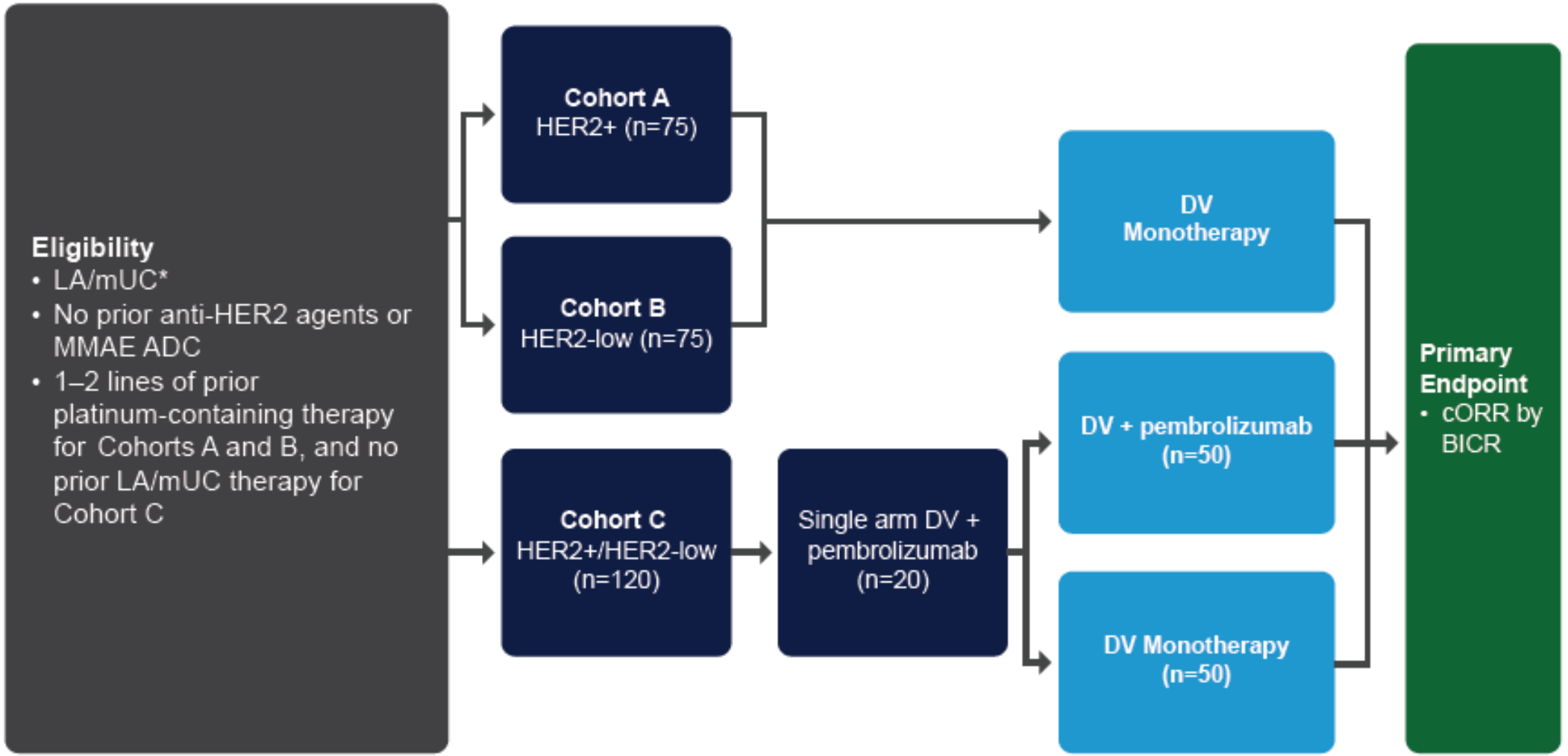
Disitamab Vedotin and Toripalimab





Sheng X et al. ASCO 2023;Abstract 4566.

Disitamab Vedotin Bladder Cancer Phase 2 Trial Design



ADC: antibody-drug conjugate; **BICR:** blinded independent central review; **cORR:** confirmed objective response rate; **DV:** disitamab vedotin; **HER2:** human epidermal growth factor receptor 2; **LA/mUC:** locally advanced unresectable or metastatic urothelial carcinoma; **MMAE:** monomethyl auristatin E

*Histologically-confirmed, including UC originating from the renal pelvis, ureters, bladder, or urethra

Disitamab Vedotin Bladder Cancer Randomized Phase 3 Trial Design

An Open-label, Randomized, Controlled Phase 3 Study of Disitamab Vedotin in Combination with Pembrolizumab Versus Chemotherapy in Subjects with Previously Untreated Locally Advanced or Metastatic Urothelial Carcinoma that Expresses HER2 (IHC 1+ and Greater)

Eligibility:
- LA/mUC
- Previously untreated
- Eligible for platinum
- Central lab HER2 status ≥ IHC 1+

(n=700)

R
1:1

DV + Pembrolizumab
*Treatment until progression

Stratification Factors:
- Cisplatin eligibility
- Presence of liver metastasis
- HER2 status
- Intent of avelumab maintenance use

Cisplatin/Carboplatin + Gemcitabine
X 4-6 cycles, maintenance therapy as clinically appropriate

* DV 1.5 mg/kg Q2W until disease progression and pembrolizumab 400 mg Q6W for up to 18 cycles

Dual-Primary Endpoints
- **PFS by BICR**
- **OS**

289 sites in 30 countries globally

- US, Canada, LATAM, EU, Israel, Turkey, APAC
- Competitive enrollment – No site/country cap
- Estimated enrollment start & end date
  - FPI: Q3 2023
  - LPI: Q1 2026

NCT05911295

Maintenance therapy in the 1L setting as clinically appropriate and locally approved is allowed.
Avelumab will not be provided by sponsor.

Take Home Points

- HER2 expression is not uncommon for urothelial bladder cancer
- Antibody drug conjugates offer an exciting technology that recently has shown clinical efficacy in many cancers, including bladder cancer
- HER2 is being revisited as a promising drug target for patients with urothelial bladder cancer
- A couple examples of promising ADCs for bladder cancer that target HER2 include trastuzumab deruxtecan and disitamab vedotin, both as monotherapy and in combination with checkpoint inhibitors

MODULE 5: Selection and Sequencing of Therapy for Relapsed/Refractory mUBC – Dr Siefker-Radtke

Consulting Faculty Questions

Selection and sequencing of therapies for relapsed/refractory metastatic UBC; potential integration of erdafitinib for patients with metastatic UBC and FGFR alterations

Neil Love, MD

Elizabeth R Plimack, MD, MS

RTP RESEARCH TO PRACTICE

QUESTIONS FOR THE FACULTY

Elizabeth R Plimack, MD, MS

How do you generally sequence enfortumab vedotin, erdafitinib and sacituzumab govitecan for patients who are eligible to receive all 3 agents?

How do you generally screen for ocular toxicities in patients with mUBC receiving erdafitinib? How often do you recommend consultation with an ophthalmologist? How do you approach the management of ocular AEs?

Consulting Faculty Questions

Efficacy and tolerability of erdafitinib

Neil Love, MD

Terence Friedlander, MD

RTP RESEARCH TO PRACTICE

QUESTIONS FOR THE FACULTY

Terence Friedlander, MD

What other common toxicities (eg, rash, nail changes, hand-foot syndrome, stomatitis) have been reported with erdafitinib, and how do you manage each of these?

How much of an advantage is the oral route of administration of erdafitinib for patients in your practice?

Please describe the last patient in your practice who received erdafitinib for metastatic UBC. What side effects, if any, did the patient experience? How much benefit, if any, did the patient derive from treatment?

	Age	Side effects	Benefit derived
 Dr Milowsky	77 years	PPE, nail disorders, diarrhea, stomatitis, decreased appetite, weight loss	A great deal
 Dr O'Donnell	60 years	Mouth sores, skin toxicity, nail disorders, failure to thrive	None
 Dr Rosenberg	72 years	Dysgeusia, paronychia, nail loss, rash, mucositis	A great deal
 Dr Siefker-Radtke	83 years	None so far	A great deal
 Dr Yu	58 years	Fatigue, hand-foot syndrome, nail dystrophy	Not much
 Dr Friedlander	71 years	Hand-foot syndrome, asthenia/fatigue, CSR	Some
 Dr Plimack	72 years	CSR, paronychia, fatigue, cytopenias	Not much

PPE = Palmar-plantar erythrodysesthesia; CSR = central serous retinopathy

What would you generally recommend as third-line therapy for a 65-year-old patient with FGFR-mutated metastatic UBC whose disease had progressed on first-line pembrolizumab and second-line enfortumab vedotin?

 Dr Milowsky	Erdafitinib
 Dr O'Donnell	Erdafitinib
 Dr Rosenberg	Erdafitinib
 Dr Siefker-Radtke	Erdafitinib
 Dr Yu	Erdafitinib
 Dr Friedlander	Erdafitinib
 Dr Plimack	Erdafitinib

Is it reasonable to refer patients about to receive enfortumab vedotin or erdafitinib to an optometrist rather than an ophthalmologist prior to commencing therapy?

 Dr Milowsky	Yes
 Dr O'Donnell	No
 Dr Rosenberg	I'm not sure
 Dr Siefker-Radtke	No
 Dr Yu	I'm not sure
 Dr Friedlander	Yes
 Dr Plimack	Yes

RTP RESEARCH TO PRACTICE

How would you generally sequence erdafitinib, enfortumab vedotin and sacituzumab govitecan for a patient with metastatic UBC who is eligible to receive all 3?

 Dr Milowsky	Enfortumab vedotin → erdafitinib → sacituzumab govitecan
 Dr O'Donnell	Enfortumab vedotin → sacituzumab govitecan → erdafitinib
 Dr Rosenberg	Enfortumab vedotin → erdafitinib → sacituzumab govitecan
 Dr Siefker-Radtke	Enfortumab vedotin → erdafitinib → sacituzumab govitecan
 Dr Yu	Enfortumab vedotin → erdafitinib → sacituzumab govitecan
 Dr Friedlander	Enfortumab vedotin → erdafitinib → sacituzumab govitecan
 Dr Plimack	Enfortumab vedotin → erdafitinib → sacituzumab govitecan

RTP RESEARCH TO PRACTICE

In general, when you administer erdafitinib, do you preemptively prescribe a steroid mouthwash for the prevention of treatment-related stomatitis?

 Dr Milowsky	No
 Dr O'Donnell	No
 Dr Rosenberg	No
 Dr Siefker-Radtke	No
 Dr Yu	No
 Dr Friedlander	Yes
 Dr Plimack	No

RTP RESEARCH TO PRACTICE

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Selection and Sequencing: Optimizing Therapy for Relapsed/Refractory Metastatic Urothelial Cancer

Arlene Siefker-Radtke, MD
Professor
Department of Genitourinary Medical Oncology

CHOOSING A GOOD TARGET

Easily reproducible

- Anyone can do it
- CLIA certification
- Not open to interpretation/everyone agrees
- Does not fluctuate or change

Predicts response or benefit!

Front-line Treatment Metastatic Urothelial Cancer

Cisplatin eligible

- Enfortumab Vedotin + Pembrolizumab (category 1, new 2023)
- DDMVAC/GC (category 1)
- Gemcitabine and cisplatin + Nivolumab (category 1, new 2023)

Cisplatin ineligible

- Enfortumab Vedotin + Pembrolizumab (category 1, new 2023)
- Gemcitabine and carboplatin
- Atezolizumab or pembrolizumab
  - Those not eligible for any chemotherapy regardless of PDL1 expression

Maintenance (in first response to platinum)

- Avelumab
  - Consider maintenance avelumab for patients with CR/PR, or SD with platinum-based chemotherapy (category 1)

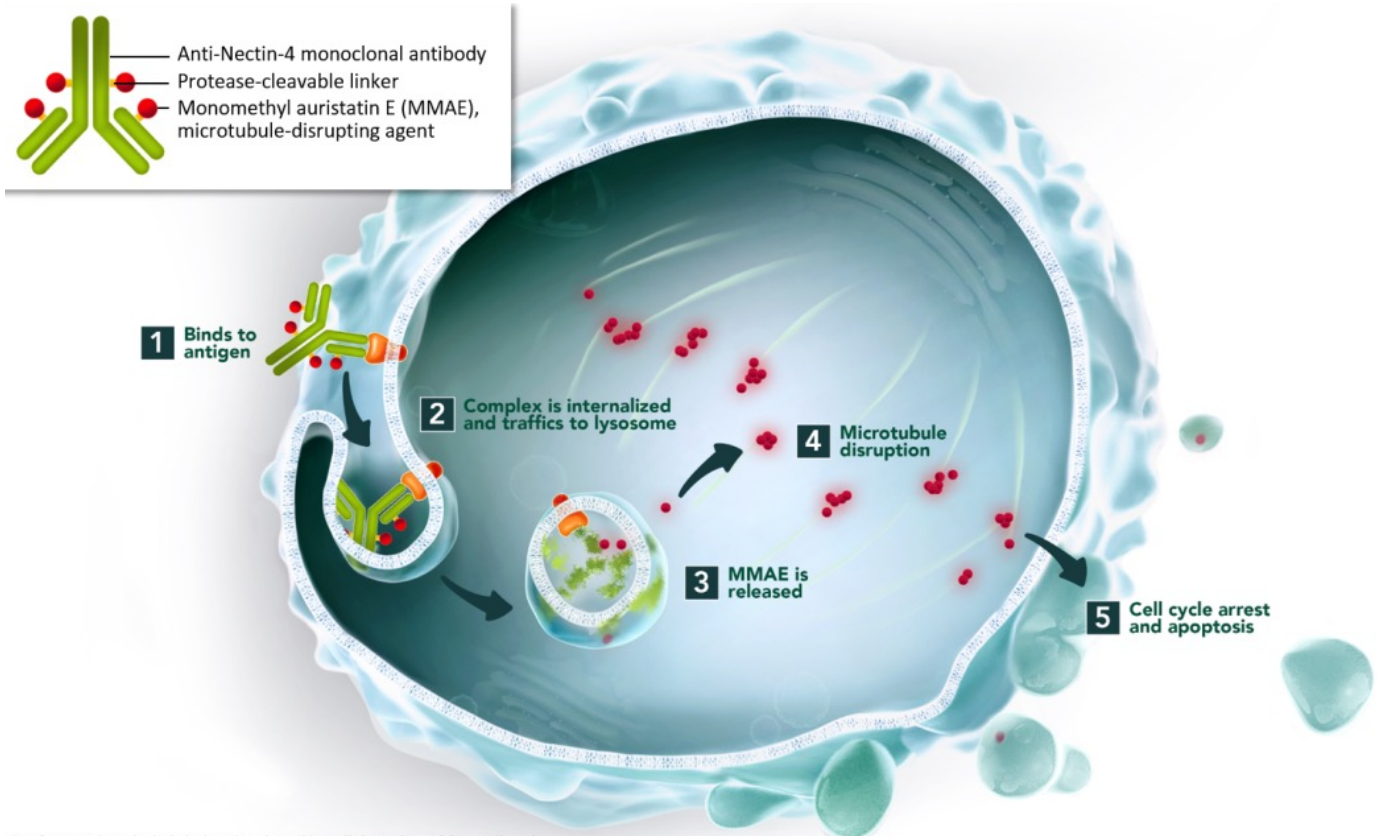

Previously Treated,
Metastatic Urothelial Cancer

Previously Treated/mUC: Basic Concepts

- Includes those who progress within 12 months of neoadjuvant or adjuvant chemotherapy
- If you've given it before, don't give it again
- No data on the role of additional immunotherapy (for or against)
- Look for mutations
- Limited information on sequencing
  - Erdafitinib
- Decisions often based upon toxicity


Enfortumab Vedotin:
The First Antibody Drug Conjugate in mUC

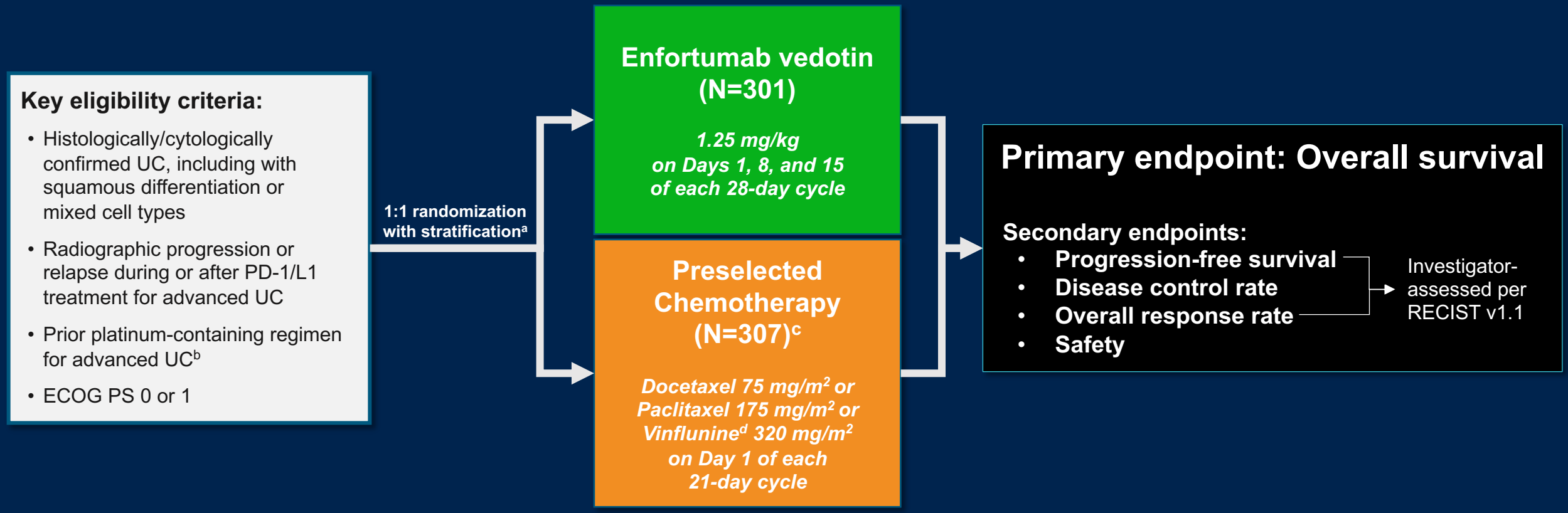
Enfortumab Vedotin



- Fully humanized monoclonal antibody targeting Nectin-4
- Nectin-4
  - A transmembrane cell adhesion molecule
  - Expressed in 83% of mUC patient samples
- “Payload” is auristatin-E, a microtubule disrupting agent
- Antibody is conjugated by a protease cleavable linker

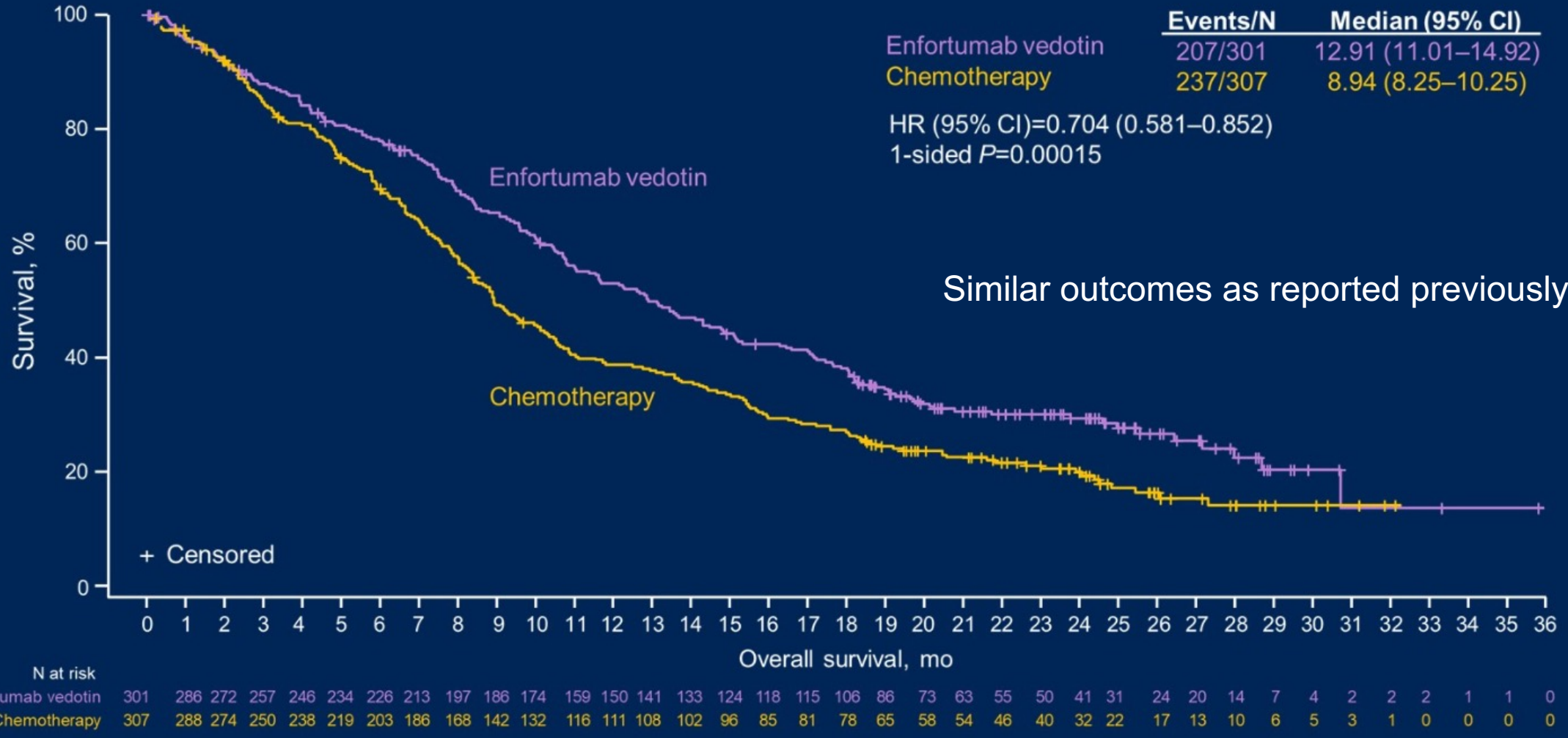
Abstract 393

EV-301 Open-Label Phase 3 Trial Design



[a]Stratification variables were ECOG performance status (0 or 1), regions of the world (United States, western Europe, or rest of world), liver metastasis (yes or no).
[b]If used in the adjuvant/neoadjuvant setting, progression must be within 12 months of completion.
[c]Investigator selected prior to randomization.
[d]In countries where approved; overall proportion of patients receiving vinflunine capped at 35%.
Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; PD-1/L1, programmed cell death protein-1/programmed death-ligand 1; RECIST, Response Evaluation Criteria in Solid Tumors; UC, advanced urothelial carcinoma.

Overall Survival



	Events/N	Median (95% CI)
Enfortumab vedotin	207/301	12.91 (11.01–14.92)
Chemotherapy	237/307	8.94 (8.25–10.25)

HR (95% CI)=0.704 (0.581–0.852)
1-sided *P*=0.00015

Similar outcomes as reported previously!

Data shown for intention-to-treat population.
HR, hazard ratio.

Data cutoff date: July 30, 2021

Adverse Events of Special Interest[a] (Safety Population)

Treatment-related adverse event, n (%)	Enfortumab vedotin (N=296)						Chemotherapy (N=291)					
		Grade						Grade				
	Any	1	2	3	4	5	Any	1	2	3	4	5
Rash	133 (44.9)	41 (13.9)	48 (16.2)	43 (14.5)	1 (0.3)	NR	28 (9.6)	21 (7.2)	6 (2.1)	1 (0.3)	0	NR
Severe cutaneous adverse reaction	60 (20.3)	20 (6.8)	25 (8.4)	14 (4.7)	1 (0.3)	NR	22 (7.6)	12 (4.1)	8 (2.7)	2 (0.7)	0	NR
Peripheral neuropathy	142 (48.0)	36 (12.2)	84 (28.4)	22 (7.4)	NR	NR	92 (31.6)	43 (14.8)	41 (14.1)	8 (2.7)	NR	NR
Peripheral neuropathy sensory events	135 (45.6)	35 (11.8)	82 (27.7)	18 (6.1)	NR	NR	89 (30.6)	42 (14.4)	39 (13.4)	8 (2.7)	NR	NR
Peripheral neuropathy motor events	23 (7.8)	6 (2.0)	11 (3.7)	6 (2.0)	NR	NR	7 (2.4)	5 (1.7)	2 (0.7)	0	NR	NR
Dry eye	48 (16.2)	34 (11.5)	12 (4.1)	2 (0.7)	NR	NR	9 (3.1)	6 (2.1)	2 (0.7)	1 (0.3)	NR	NR
Blurred vision	13 (4.4)	11 (3.7)	2 (0.7)	0	NR	NR	6 (2.1)	5 (1.7)	0	1 (0.3)	NR	NR
Corneal disorders	2 (0.7)	2 (0.7)	NR	NR	NR	NR	0	0	NR	NR	NR	NR
Infusion-related reaction	27 (9.1)	12 (4.1)	11 (3.7)	4 (1.4)	NR	NR	14 (4.8)	7 (2.4)	7(2.4)	0	NR	NR
Systemic infusion-related reaction event	24 (8.1)	11 (3.7)	9 (3.0)	4 (1.4)	NR	NR	9 (3.1)	4 (1.4)	5 (1.7)	0	NR	NR
Local infusion-related reaction event	4 (1.4)	2 (0.7)	2 (0.7)	0	NR	NR	7 (2.4)	5 (1.7)	2 (0.7)	0	NR	NR
Infusion-site reaction	2 (0.7)	0	2 (0.7)	0	NR	NR	5 (1.7)	4 (1.4)	1 (0.3)	0	NR	NR
Extravasation-site reaction	4 (1.4)	2 (0.7)	2 (0.7)	0	NR	NR	4 (1.4)	2 (0.7)	2 (0.7)	0	NR	NR
Hyperglycemia	20 (6.8)	3 (1.0)	4 (1.4)	12 (4.1)	0	1 (0.3)	1 (0.3)	0	1 (0.3)	0	0	0

MedDRA, Medical Dictionary for Regulatory Activities; NR, not reported.

[a]Adverse events of special interest to enfortumab vedotin. Events represent listings by preferred term and are sponsor-specific query/customized medical queries or standard MedDRA queries. Order of adverse events is as it appears in the Supplementary Appendix to the EV-301 primary publication (Powles, et al. *N Engl J Med.* 2021;384:1125-1135).

Data cutoff date: July 30, 2021

Adverse Events of Special Interest[a] (Safety Population)

Treatment-related adverse event, n (%)	Enfortumab vedotin (N=296)						Chemotherapy (N=291)					
	Any	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Rash	133 (44.9)	41 (13.9)	48 (16.2)	43 (14.5)	1 (0.3)	NR	28 (9.6)	21 (7.2)	6 (2.1)	1 (0.3)	0	NR
Severe cutaneous adverse reaction										2 (0.7)	0	NR
Peripheral neuropathy										8 (2.7)	NR	NR
Peripheral neuropathy sensory events										8 (2.7)	NR	NR
Peripheral neuropathy motor events										0	NR	NR
Dry eye										1 (0.3)	NR	NR
Blurred vision										1 (0.3)	NR	NR
Corneal disorders										NR	NR	NR
Infusion-related reaction										0	NR	NR
Systemic infusion-related reaction event										0	NR	NR
Local infusion-related reaction event										0	NR	NR
Infusion-site reaction										0	NR	NR
Extravasation-site reaction	4 (1.4)	2 (0.7)	2 (0.7)	0	NR	NR	4 (1.4)	2 (0.7)	2 (0.7)	0	NR	NR
Hyperglycemia	20 (6.8)	3 (1.0)	4 (1.4)	12 (4.1)	0	1 (0.3)	1 (0.3)	0	1 (0.3)	0	0	0

WARNING: SERIOUS SKIN REACTIONS

See full prescribing information for complete boxed warning.

- **Enfortumab vedotin can cause severe and fatal cutaneous adverse reactions, including Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN).**
- **Immediately withhold enfortumab vedotin and consider referral for specialized care for suspected SJS or TEN or severe skin reactions.**
- **Permanently discontinue enfortumab vedotin in patients with confirmed SJS or TEN; or Grade 4 or recurrent Grade 3 skin reactions. (2.2), (5.1) (6.1)**

MedDRA, Medical Dictionary for Regulatory Activities; NR, not reported.

[a]Adverse events of special interest to enfortumab vedotin. Events represent listings by preferred term and are sponsor-specific query/customized medical queries or standard MedDRA queries. Order of adverse events is as it appears in the Supplementary Appendix to the EV-301 primary publication (Powles, et al. *N Engl J Med.* 2021;384:1125-1135).

Data cutoff date: July 30, 2021

Metabolism of Enfortumab Vedotin

- Metabolite MMAE
  - 17% recovered in feces over 1 week period
  - 6% recovered in urine over 1 week period
- Dose reduction
  - Renal impairment: No differences in AUC for mild-moderate-severe
    - No significant dose reductions
    - Effect on end-stage renal disease/dialysis is unknown
  - Liver impairment: Mild hepatic impairment 48% AUC increase in MMAE
    - Mild hepatic impairment: bilirubin 1-1.5 x ULN with NL AST and ALT or bilirubin ≤ ULN and AST > ULN
    - Frequency of ≥ Grade 3 adverse reactions and deaths in moderate (Child-Pugh B) or severe (Child-Pugh C)
- AVOID use in moderate-severe hepatic impairment

FDA package insert 12/2023

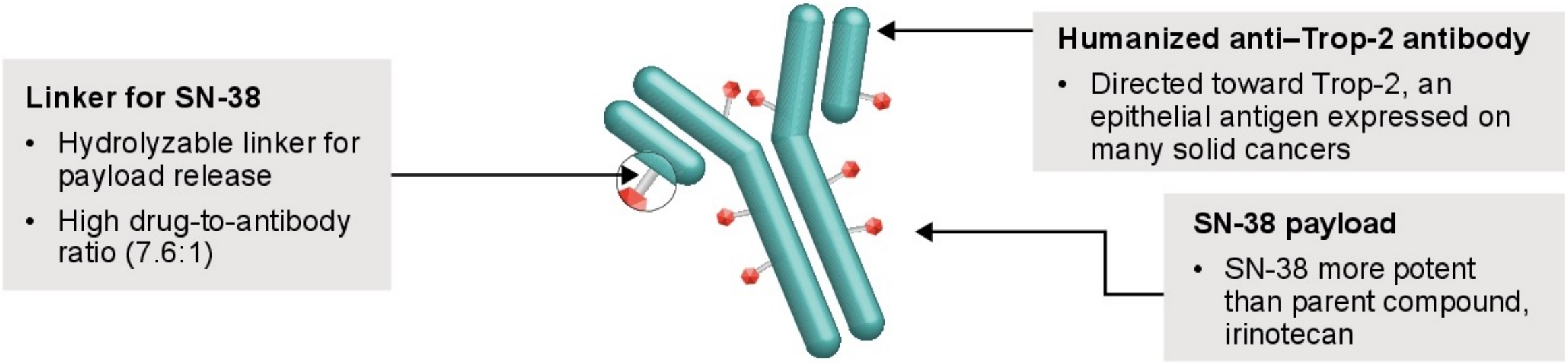
Monitoring Caveats

- Grade 3-4 hyperglycemia increase in greater BMI and higher HgbA1C
  - HgbA1C ≥ 8 excluded
- HOLD for:
  - Glucose > 250 mg/dL
    - Could be a sign of impaired clearance of MMAE
    - Mechanism unknown
    - ~~Personal hypothesis: impaired glycogen storage as a sign of saturation of liver metabolism~~
    - New Hypothesis: potent tubule stabilization resulting in decreased glucose transport and muscle weakness resulting in decreased glucose utilization and even rhabdomyolysis
  - Peeling skin or bullous skin lesions
    - May have more diffuse rash preceding this
  - Grade 3 diarrhea

FDA package insert 12/2023


Sacituzumab Govitecan:
The Second Antibody Drug Conjugate in mUC

Sacituzumab Govitecan (SG)



- Humanized monoclonal antibody targeting Trop-2 expression
- Trop-2
  - Epithelial antigen expressed on many solid cancers
  - Expressed in ~ 83% of mUC patient samples; testing for expression not necessary
- “Payload” is SN-38, the active metabolite of irinotecan, inhibiting topoisomerase 1
- Payload is conjugated by a hydrolyzable linker

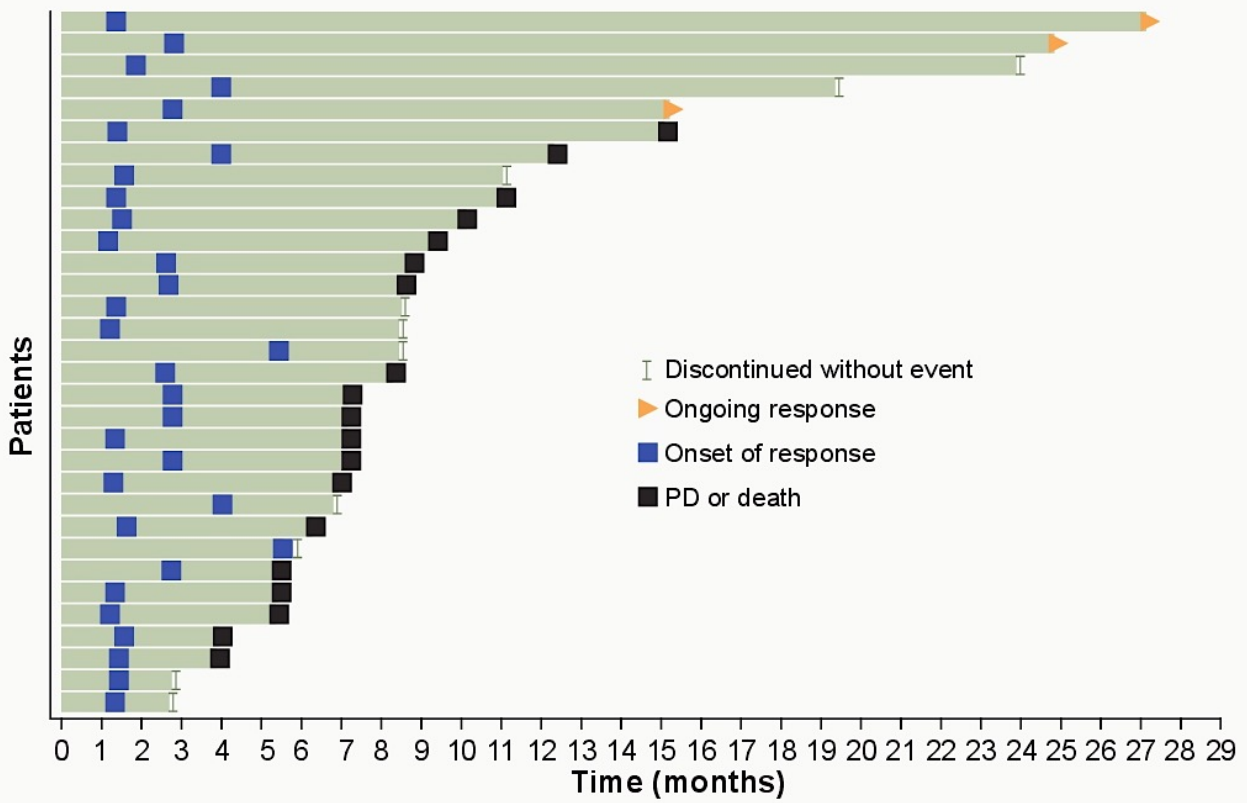
TROPHY-U-01 Cohort 1: Phase II Study of Sacituzumab Govitecan for mUC That Progressed After Platinum Chemotherapy and a Checkpoint Inhibitor

Table 1. Best Overall Response Rates

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

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

Figure 4. Objective Response From Start of Treatment to Progression



Tagawa ST et al. Genitourinary Cancers Symposium 2023;Abstract 526.

TROPHY-U-01 Cohort 1: Phase II Study of Sacituzumab Govitecan for mUC That Progressed After Platinum Chemotherapy and a Checkpoint Inhibitor (cont.)

Figure 6. Progression-Free Survival

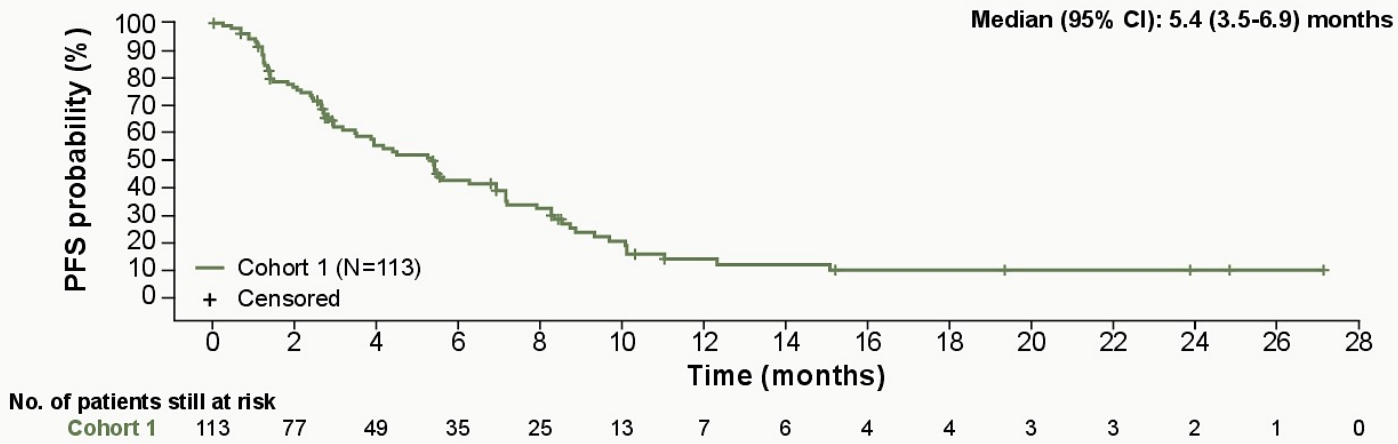
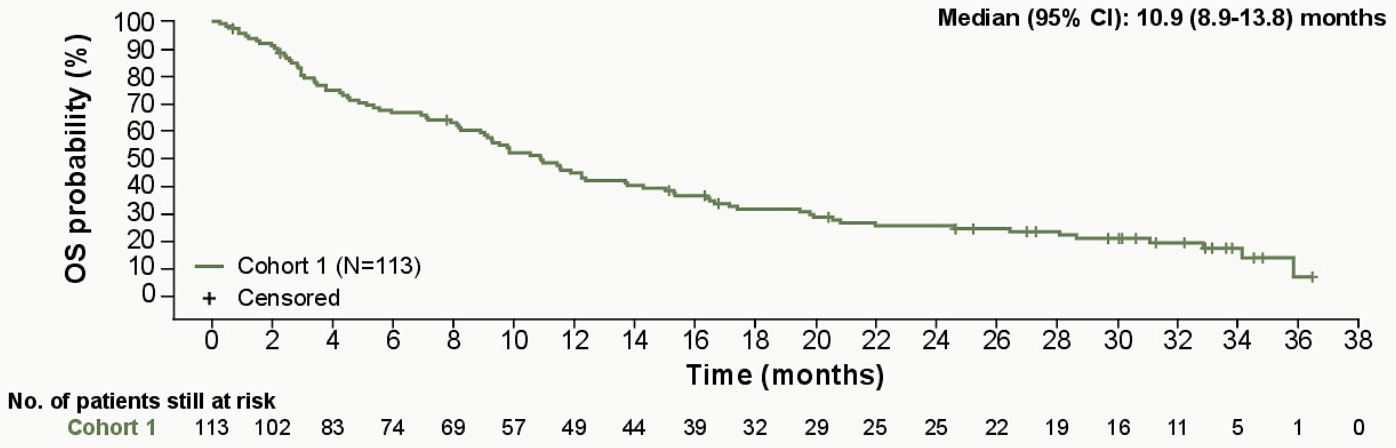


Figure 7. Overall Survival



Tagawa ST et al. Genitourinary Cancers Symposium 2023;Abstract 526.

TROPHY-U-01 Cohort 1: Phase II Study of Sacituzumab Govitecan for mUC That Progressed After Platinum Chemotherapy and a Checkpoint Inhibitor (cont.)

Table 2. Most Common Grade ≥3 Treatment-Related Adverse Events

	Cohort 1 (N=113)		
Most Common Grade ≥3 TRAEs[a]	All Grades, n (%)	Grade 3, n (%)	Grade 4, n (%)
Neutropenia	53 (47)	25 (22)	14 (12)
Leukopenia	29 (26)	14 (12)	6 (5)
Anemia	38 (34)	16 (14)	0
Diarrhea	73 (65)	10 (9)	1 (1)
Febrile neutropenia	11 (10)	8 (7)	3 (3)

[a]Grade ≥3 TRAEs that occurred in ≥10% of patients.
TRAE, treatment-related adverse events.

Tagawa ST et al. Genitourinary Cancers Symposium 2023;Abstract 526.


Erdafitinib:
The First Biomarker Targeted Therapy in mUC

Phase 3 THOR Study: Erdafitinib Versus Chemotherapy of Choice in Patients With Advanced Urothelial Cancer and Select *FGFR* Aberrations

Cohort 1

Key eligibility criteria

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

1:1
N=266[b]
R

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

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

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

Primary end point:
- OS

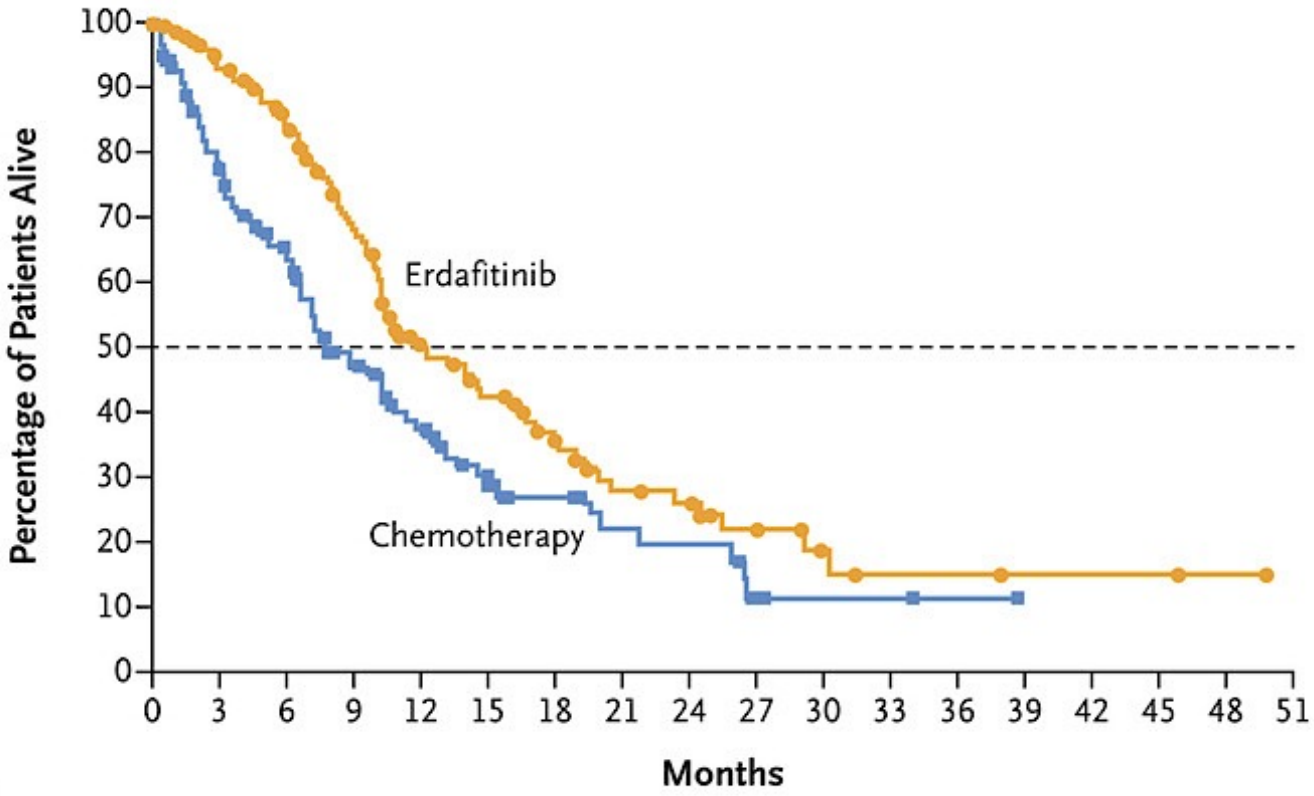
Key secondary end points:
- PFS
- ORR
- Safety

NCT03390504

Loriot Y et al. ASCO 2023; Abstract LBA4619.

[a]Molecular eligibility can be confirmed using either central or local historical *FGFR* test results (Qiagen assay). If a patient was enrolled based on local historical testing, a tissue sample must still be submitted at the time of enrollment for retrospective confirmation (by central lab) of *FGFR* status. Tumors must have ≥1 of the following translocations: *FGFR2-BICC1*, *FGFR2-CASP7*, *FGFR3-TACC3_V1*, *FGFR3-TACC3_V3*, *FGFR3-BAIAP2L1*; or 1 of the following *FGFR3* gene mutations: R248C, S249C, G370C, Y373C.
[b]Number of patients randomized at the time of the interim analysis (data cutoff January 15, 2023).
ECOG PS, Eastern Cooperative Oncology Group performance status; FGFR, fibroblast growth factor receptor; *FGFR3/2alt*, *FGFR3/2* alterations; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; Q3W, every 3 weeks; tx, treatment; UC, urothelial cancer.

Overall Survival.



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

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

No. at Risk
(no. with censored data)

Erdafitinib	136	117	97	74	46	35	25	17	15	9	5	3	3	2	2	2	1	0
	(0)	(10)	(20)	(25)	(35)	(39)	(44)	(47)	(48)	(52)	(55)	(56)	(56)	(57)	(57)	(57)	(58)	(59)
Chemotherapy	130	87	66	43	30	18	13	9	8	3	2	2	1	0	0	0	0	0
	(0)	(17)	(25)	(30)	(35)	(41)	(45)	(47)	(47)	(49)	(50)	(50)	(51)	(52)	(52)	(52)	(52)	(52)

Y Loriot et al. N Engl J Med 2023. DOI: 10.1056/NEJMoa2308849

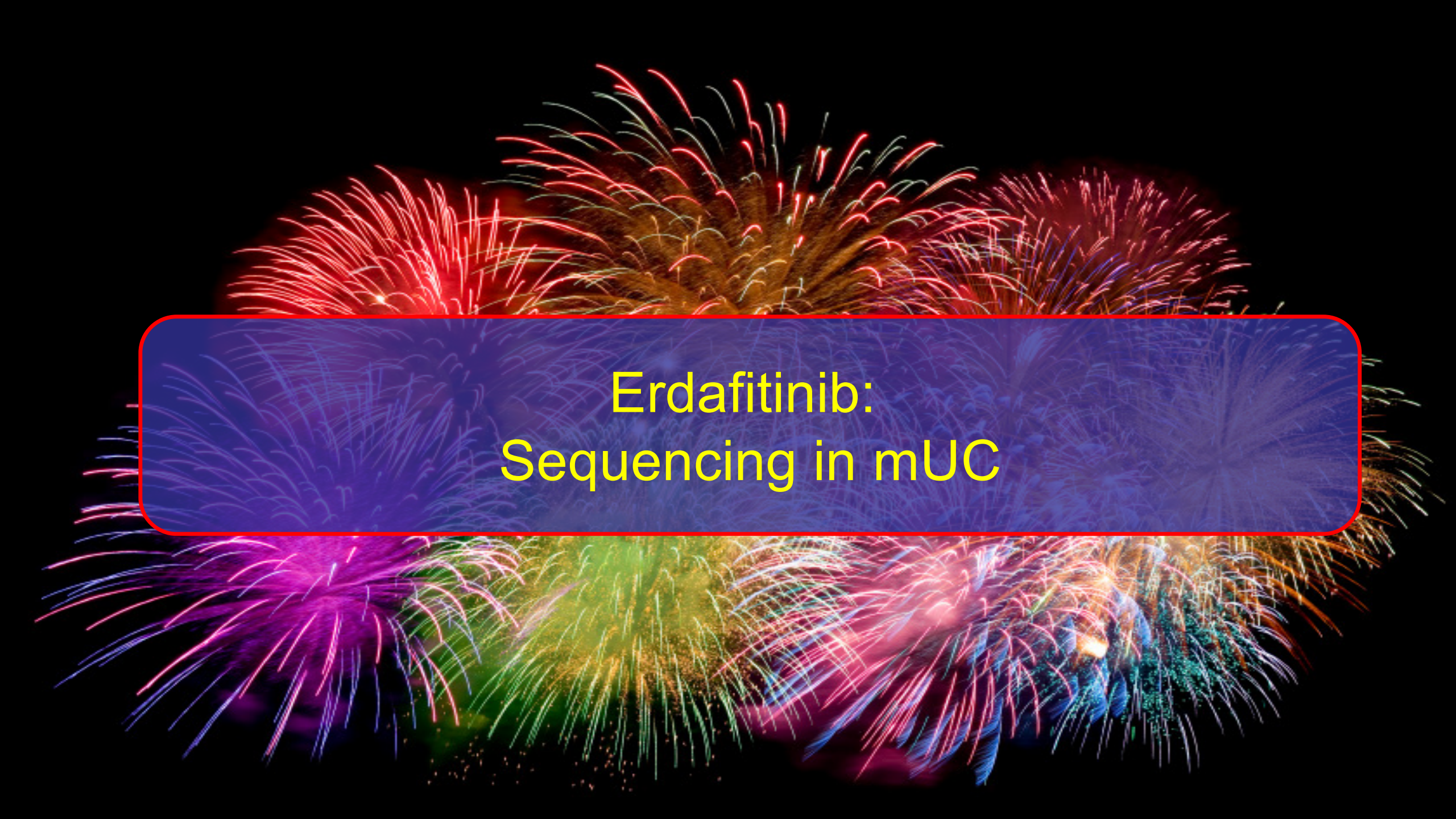
The NEW ENGLAND JOURNAL of MEDICINE

The Safety Profiles Were Consistent With the Known Profiles of Erdafitinib and Chemotherapy (2/2)

Patients with AEs of interest, n (%)	Erdafitinib (n=135)		Chemotherapy (n=112)	
	Any grade	Grade 3-4	Any grade	Grade 3-4
Nail disorders[a]	90 (66.7)	15 (11.1)	6 (5.4)	0
Skin disorders[b]	74 (54.8)	16 (11.9)	14 (12.5)	0
Eye disorders (excluding central serous retinopathy)[c]	57 (42.2)	3 (2.2)	6 (5.4)	0
Central serous retinopathy[d]	23 (17.0)	3 (2.2)	0	0

Loriot Y et al. ASCO 2023; Abstract LBA4619.

[a]Nail disorders: nail bed bleeding, nail discoloration, nail disorder, nail dystrophy, nail ridging, nail toxicity, onychalgia, onychoclasis, onycholysis, paronychia, onychomadesis.
[b]Skin disorders: blister, dry skin, erythema, hyperkeratosis, palmar erythema, palmar-plantar erythrodysesthesia syndrome, plantar erythema, rash, rash erythematous, rash generalized, rash macular, rash maculo-papular, skin atrophy, skin exfoliation, skin fissures, skin lesion, skin ulcer, toxic skin eruption, xeroderma.
[c]Eye disorders (excluding central serous retinopathy): blepharitis, cataract, cataract subcapsular, conjunctival hemorrhage, conjunctival hyperemia, conjunctival irritation, corneal erosion, corneal infiltrates, dry eye, eye inflammation, eye irritation, eye pain, foreign body sensation in eyes, keratitis, lacrimation increased, night blindness, ocular hyperemia, photophobia, vision blurred, visual acuity reduced, visual impairment, xanthopsia, xerophthalmia, chorioretinitis, conjunctivitis, ulcerative keratitis.
[d]Central serous retinopathy: retinal detachment, vitreous detachment, retinal edema, retinopathy, chorioretinopathy, detachment of retinal pigment epithelium, detachment of macular retinal pigment epithelium, macular detachment, serous retinal detachment, subretinal fluid, retinal thickening, chorioretinitis, serous retinopathy, maculopathy, choroidal effusion.
AE, adverse event.


Erdafitinib:
Sequencing in mUC

Phase 3 THOR Study: Erdafitinib Versus Pembrolizumab in Patients With Metastatic Urothelial Carcinoma and Select *FGFR* Alterations

Cohort 2

Key eligibility criteria

- Age ≥18 years
- Metastatic or unresectable UC
- Confirmed disease progression on 1 prior tx
- Naive to anti–PD-(L)1 tx
- Select *FGFR3/2alt* (mutation/fusion)[a]
- ECOG PS 0-2

1:1
N=351[b]
R

Erdafitinib
(n=175)
Once-daily erdafitinib 8 mg with pharmacodynamically guided uptitration to 9 mg

Pembrolizumab
(n=176)
200 mg once every 3 weeks

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

Primary end point
- OS

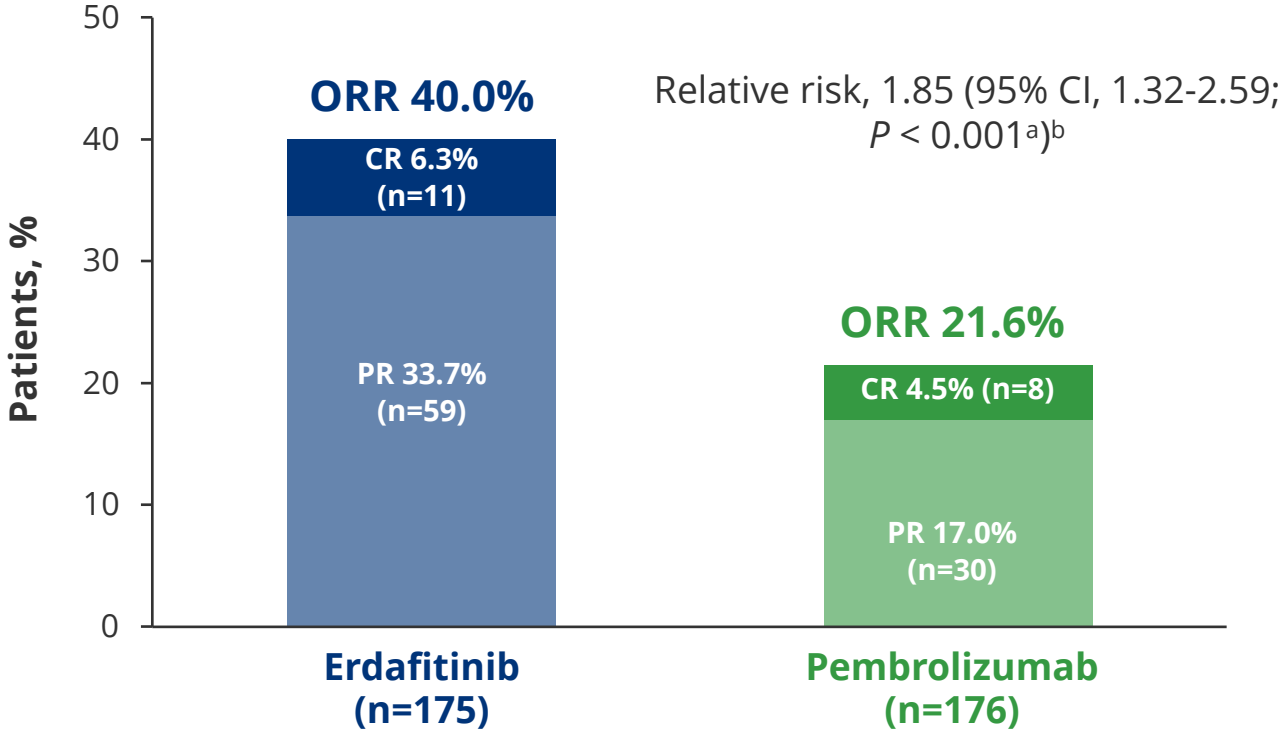
Secondary end points
- PFS
- ORR
- Safety

NCT03390504

Siefker-Radtke AO et al. *Ann Oncol* 2024;35(1):107-117.

[a]Molecular eligibility was confirmed using either central or local historical *FGFR* test results (Qiagen assay). If a patient was enrolled based on local historical testing, a tissue sample must still be submitted at the time of enrollment for retrospective confirmation (by central lab) of *FGFR* status. Tumors must have ≥1 of the following translocations: *FGFR2-BICC1*, *FGFR2-CASP7*, *FGFR3-TACC3_V1*, *FGFR3-TACC3_V3*, *FGFR3-BAIAP2L1*; or 1 of the following *FGFR3* gene mutations: R248C, S249C, G370C, Y373C.
[b]Number of patients randomized at the time of the interim analysis (data cutoff January 15, 2023).
ECOG PS, Eastern Cooperative Oncology Group performance status; *FGFR3/2alt*, *FGFR3/2* alterations; ORR, overall response rate; PFS, progression-free survival; R, randomization; tx, treatment; UC, urothelial cancer.

ORR: 40.0% With Erdafitinib and 21.6% With Pembrolizumab

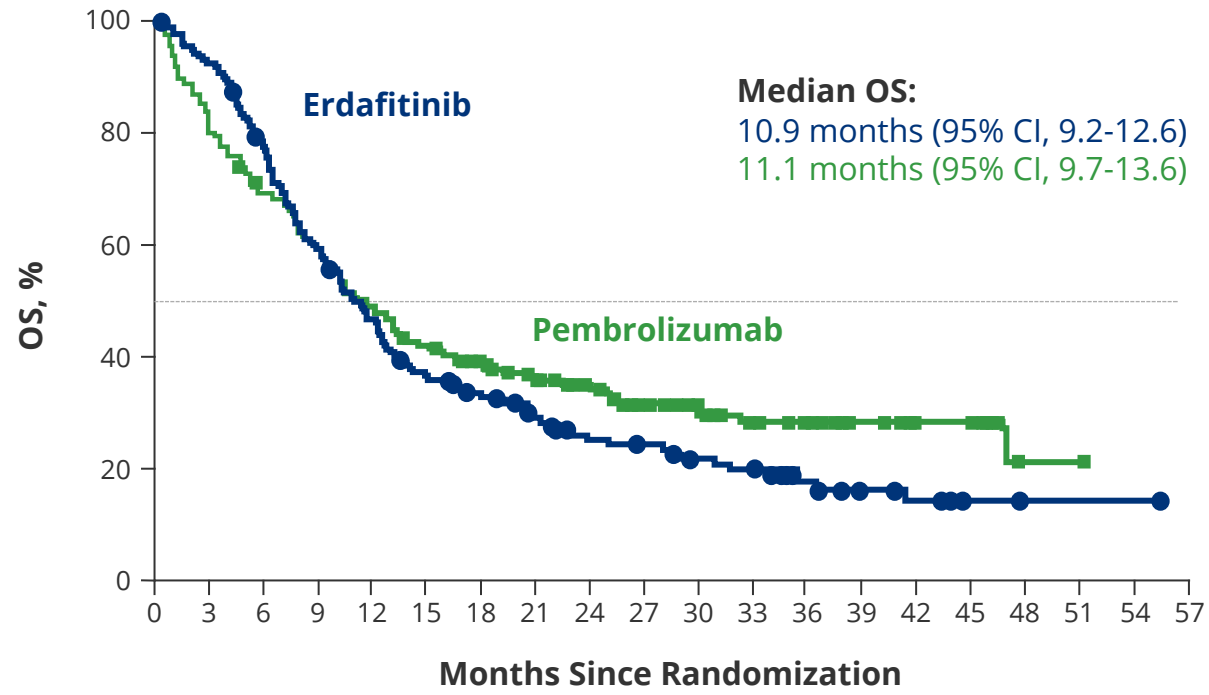


- ORR was 40.0% (95% CI, 32.7-47.7) for erdafitinib and 21.6% (95% CI,15.8-28.4) for pembrolizumab
- Median DOR was 4.3 months (95% CI, 3.7-6.9) for erdafitinib and 14.4 months (95% CI, 7.4-27.8) for pembrolizumab

Siefker-Radtke AO et al. *Ann Oncol* 2024;35(1):107-117.

CR, complete response; DOR, duration of response; PR, partial response.
[a]Nominal *P* value, due to primary end point not being met; [b]Relative risk, 95% CI, and *P* value are estimated using Cochran-Mantel-Haenszel procedure with ECOG PS (0 or 1 vs 2) as stratification factor.

No Significant Difference Was Found in Overall Survival Between Erdafitinib and Pembrolizumab



- The primary end point was not met
- Median OS was 10.9 months (95% CI, 9.2-12.6) for erdafitinib and 11.1 months (95% CI, 9.7-13.6) for pembrolizumab
  - HR, 1.18 (95% CI, 0.9-1.5; *P* = 0.18)

Siefker-Radtke AO et al. *Ann Oncol* 2024;35(1):107-117.

Previously Treated/mUC: Options

- Checkpoint inhibitors
  - Pembrolizumab, Avelumab, or Nivolumab (pick-one!)
- Antibody-Drug Conjugates
  - Enfortumab Vedotin
  - Sacituzumab Govitecan
- Mutation driven
  - Erdafitinib
    - After immunotherapy, unless need for cytoreductive therapy: visceral crisis

Previously Treated/mUC: Options

- Checkpoint inhibitors
  - Pembrolizumab, Avelumab, or Nivolumab (pick-one!)
- Antibody-Drug Conjugates
  - Enfortumab Vedotin
  - Sacituzumab Govitecan
- Mutation driven
  - Erdafitinib
- Do we need to give platinum???

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

Part 2 of a 2-Part CME Symposium Series Held in Conjunction with the 2024 ASCO Genitourinary Cancers Symposium

Friday, January 26, 2024

7:00 PM – 9:00 PM PT (10:00 PM – 12:00 AM ET)

Faculty

Matthew Milowsky, MD, FASCO

Peter H O'Donnell, MD

Jonathan E Rosenberg, MD

Arlene Siefker-Radtke, MD

Moderator

Evan Y Yu, MD

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Thank you for joining us!
Your feedback is very important to us.

Please complete the survey currently up on Zoom for those attending virtually. The survey will remain open up to 5 minutes after the meeting ends.

How to Obtain CME Credit

In-person attendees: Please refer to the program syllabus for the CME credit link or QR code. You may also use the iPads available in the meeting room to complete the course evaluation.

Online/Zoom attendees: The CME credit link is posted in the chat room.

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