Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse

A Complimentary NCPD Symposium Series Held During the 51st Annual ONS Congress

Non-Muscle-Invasive and Muscle-Invasive Bladder Cancer

Thursday, May 14, 2026

6:00 PM – 7:30 PM

Faculty

Alexandra Drakaki, MD, PhD
Krisztina Emodi, NP-C, MPH, CNS
Margarita Huober, MS, AGNP-C, AOCNP

Moderator

Terence Friedlander, MD

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Zuckerberg San Francisco General Hospital
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San Francisco, California

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Dr Drakaki — Disclosures

Advisory Committees	AstraZeneca Pharmaceuticals LP, Bristol Myers Squibb, Daiichi Sankyo Inc, Janssen Biotech Inc, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Pfizer Inc
Consulting Agreements	AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Pfizer Inc
Contracted Research	Acrivon Therapeutics, Adcentrx Therapeutics, Allogene Therapeutics, Arcus Biosciences, AstraZeneca Pharmaceuticals LP, Daiichi Sankyo Inc, Genentech, a member of the Roche Group, Infinity Pharmaceuticals Inc, Kite, A Gilead Company, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Pfizer Inc
Data and Safety Monitoring Boards/Committees	Nektar Therapeutics
Speakers Bureaus	AstraZeneca Pharmaceuticals LP
Stock OPTIONS — Private Companies	Athos Therapeutics
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Ms Emodi — Disclosures

No relevant financial relationships to disclose.

Ms Huober — Disclosures

No relevant financial relationships to disclose.

Dr Friedlander — Disclosures

Advisory Committees	Aadi Bioscience, AbbVie Inc, Adaptimmune, Aktis Oncology, Astellas, Bicycle Therapeutics, Bristol Myers Squibb, Gilead Sciences Inc, Merck, Pfizer Inc, Samsung Bioepis
Consulting Agreements	Astellas, EMD Serono Inc, Genentech, a member of the Roche Group
Contracted Research	AbbVie Inc, Bicycle Therapeutics, Flare Therapeutics, Genentech, a member of the Roche Group, Johnson & Johnson, Pfizer Inc

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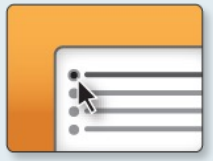
Clinicians in the Meeting Room

Networked iPads are available.

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



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

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

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

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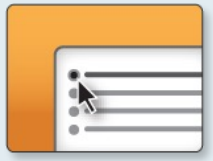
Clinicians Attending via Zoom

Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

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

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

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About the Enduring Program

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

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RTP RESEARCH TO PRACTICE ONCOLOGY NURSING UPDATE WITH NEIL LOVE, MD

NONMELANOMA SKIN CANCERS
Check out our recent program with Dr Nikhil I Khushalni from Moffitt Cancer Center in Tampa, Florida. Published May 7, 2026.

Overview of nonmelanoma skin cancers (12 min)

Systemic therapy for nonmelanoma skin cancers (8 min)

Immune checkpoint inhibitors for special patient populations (12 min)

Hedgehog inhibitors for basal cell carcinoma (6 min)

New developments in therapy for nonmelanoma skin cancers (5 min)

CASE: A man in his early 70s with cutaneous squamous cell carcinoma receives cemiplimab (8 min)

CASE: A man in his mid 70s with a history of basal cell carcinoma presents with disease of the ocular surface and receives immunotherapy (6 min)

CASE: A man in his early 70s with recurrent metastatic basal cell carcinoma receives vismodegib followed by cemiplimab on disease progression (6 min)

Subscribe to our Oncology Nursing Update podcast

Feedback (Please!)

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“Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse”
Eighteenth Annual RTP-ONS NCPD Symposium Series

Wednesday May 13	**Antibody-Drug Conjugates** 11:15 AM – 12:45 PM CT
	Ovarian Cancer 6:00 PM – 7:30 PM CT
Thursday May 14	**Immunotherapeutic Approaches for Endometrial Cancer** 6:00 AM – 7:30 AM CT
	Prostate Cancer 12:15 PM – 1:45 PM CT
	Non-Muscle-Invasive and Muscle-Invasive Bladder Cancer 6:00 PM – 7:30 PM CT
Friday May 15	**Pancreatic Cancer** 6:00 AM – 7:30 AM CT
	Targeting the PI3K/AKT/mTOR Pathway in HR-Positive Metastatic BC 12:15 PM – 1:45 PM CT
	Non-Hodgkin Lymphoma and Chronic Lymphocytic Leukemia 6:00 PM – 8:00 PM CT
Saturday May 16	**CDK4/6 Inhibitors for HR-Positive Breast Cancer** 6:00 AM – 7:30 AM CT
	Relapsed/Refractory Multiple Myeloma 12:15 PM – 1:45 PM CT
	Oral SERDs for Breast Cancer 6:00 PM – 7:30 PM CT

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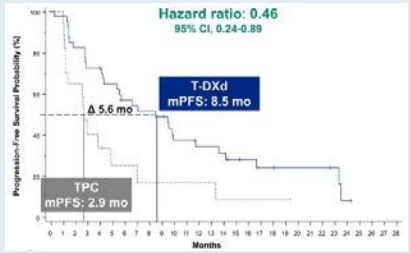
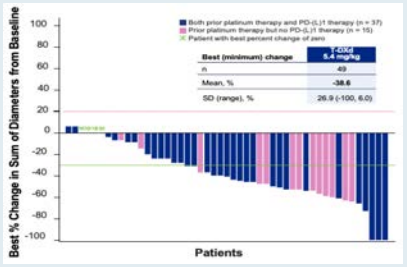
Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse

New Agents, Therapies and Regimens

- When should it be used, for whom and why?
- How to prevent and manage side effects: dose holds and reductions
  - Kaplan Meier curves — HR and absolute benefit



  - Waterfall plots



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RTP RESEARCH TO PRACTICE

Agenda

Introduction: Basic Biology of Nonmetastatic Urothelial Bladder Cancer (UBC)

Module 1: Systemic Therapy for Cisplatin-Eligible Patients with Muscle-Invasive Bladder Cancer (MIBC)

Module 2: Evolving Approach to Systemic Therapy for Cisplatin-Ineligible Patients with MIBC

Module 3: Immune Checkpoint Inhibitors in Non-Muscle-Invasive Bladder Cancer

Module 4: Novel Intravesical Therapies for Nonmetastatic UBC

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Introduction: Basic Biology of Nonmetastatic Urothelial Bladder Cancer (UBC)

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Module 3: Immune Checkpoint Inhibitors in Non-Muscle-Invasive Bladder Cancer

Module 4: Novel Intravesical Therapies for Nonmetastatic UBC

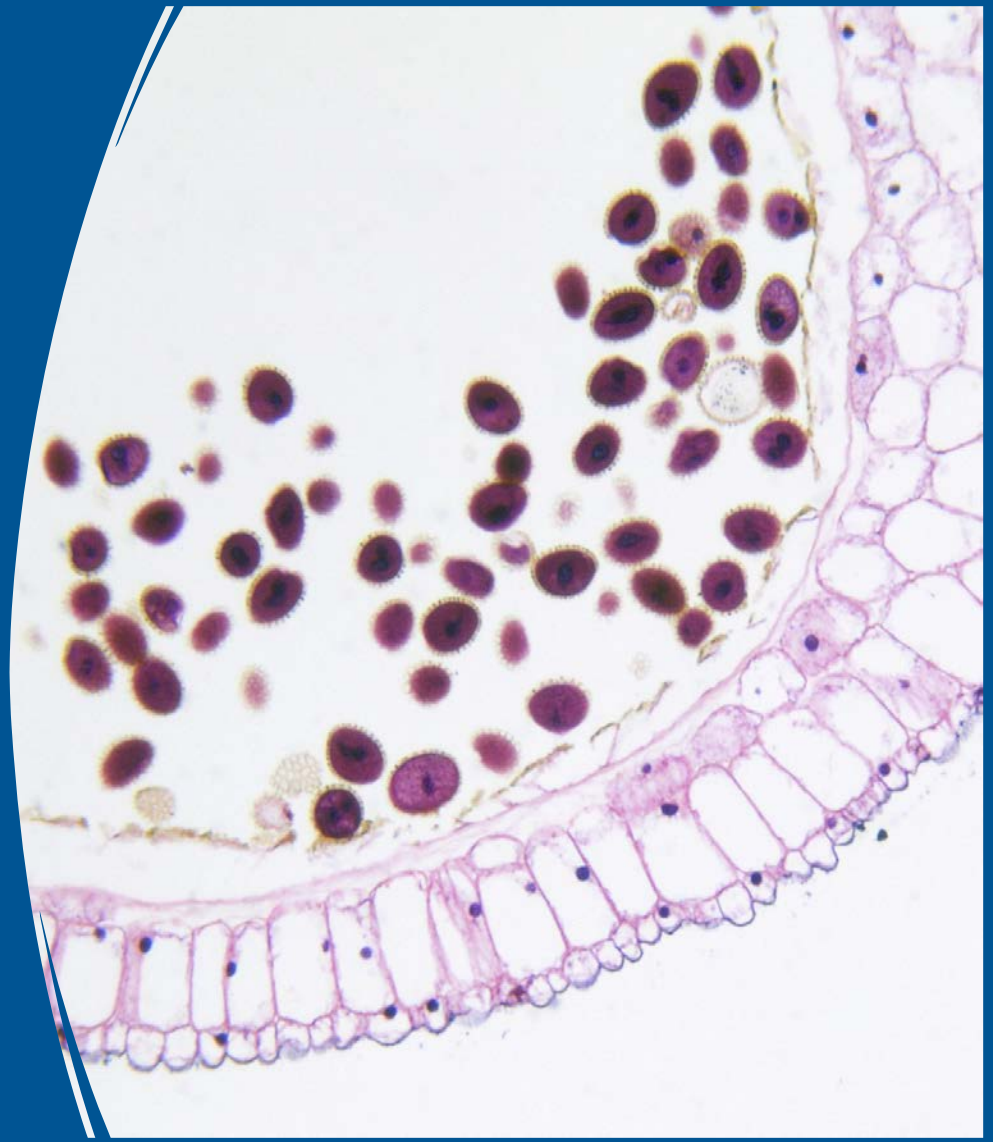
Basic Biology of Nonmetastatic Urothelial Bladder Cancer (UBC)

Krisztina Emodi NP-C, MPH, CNS

Nurse Practitioner III

UCSF GU Surgical Oncology

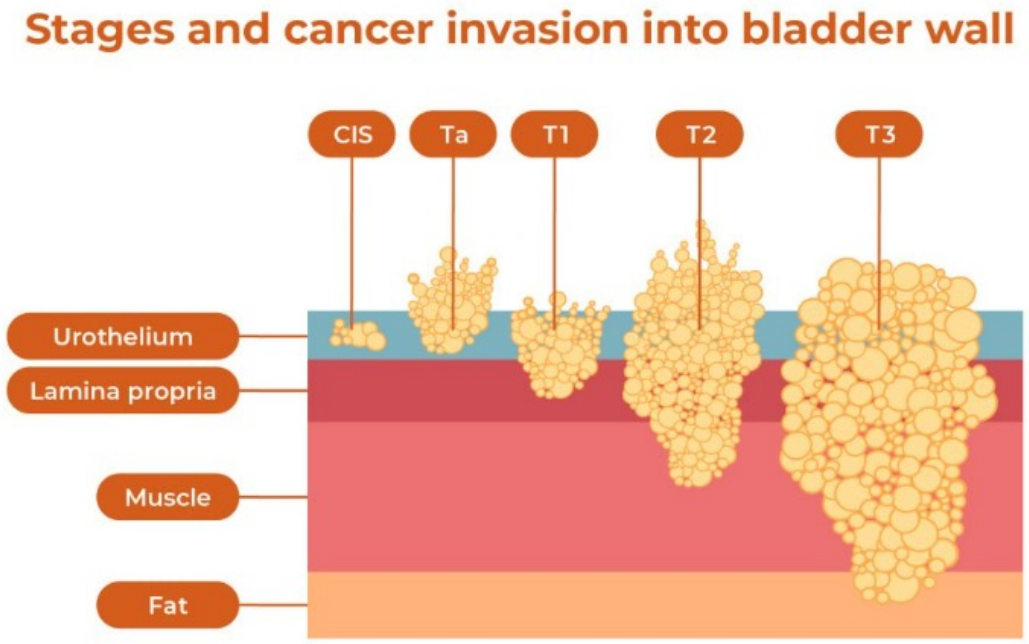
Bladder Cancer Survivorship Program Lead

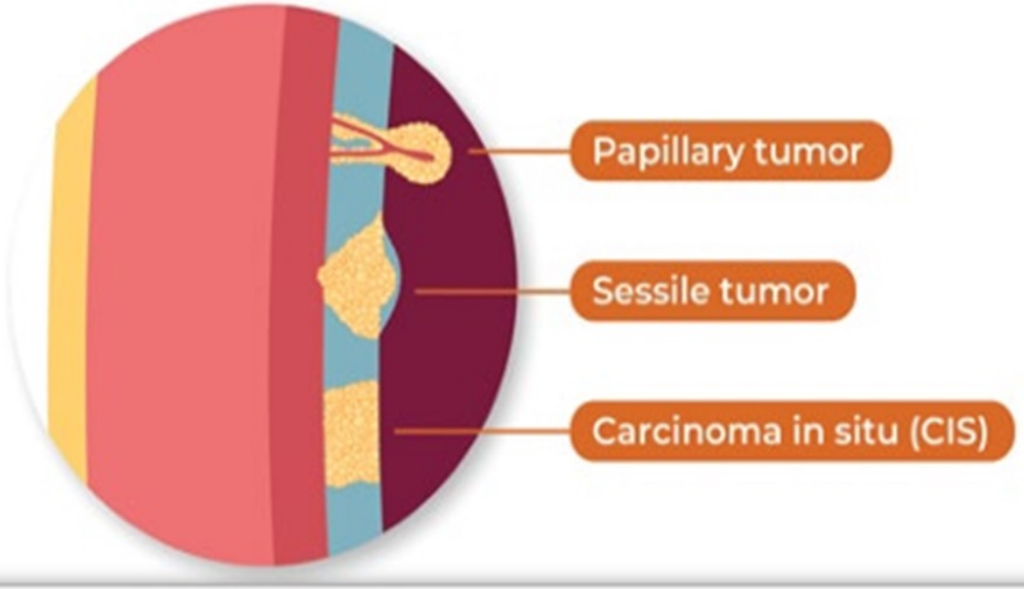


Agenda

- **Staging of nonmetastatic UBC; difference between non-muscle-invasive bladder cancer (NMIBC) and muscle-invasive bladder cancer (MIBC)**
- **Role of various treatment strategies that have historically been employed in nonmetastatic UBC**
- **Educating patients regarding expectations surrounding radical cystectomy**
- **Criteria used to determine platinum eligibility in patients with MIBC**
- **Case study**

Bladder Cancer Staging





The Urothelium:
-basal cells
-intermediate cells
-umbrella cells.
The urothelium is the most impermeable of all human epithelia

AUA guidelines for risk stratification

Low Risk	Intermediate Risk	High Risk
LG[a] solitary Ta ≤ 3cm	Recurrence within 1 year, LG Ta	HG T1
PUNLMP[b]	Solitary LG Ta > 3cm	Any recurrent, HG Ta
	LG Ta, multifocal	HG Ta, >3cm (or multifocal)
	HG[c] Ta, ≤ 3cm	Any CIS[d]
	LG T1	Any BCG failure in HG patient
		Any variant histology
		Any LVI[e]
		Any HG prostatic urethral involvement

[a]LG = low grade; [b]PUNLMP = papillary urothelial neoplasm of low malignant potential; [c]HG = high grade; [d]CIS=carcinoma in situ; [e]LVI = lymphovascular invasion

Diagnostic Tests (Cystoscopy, Cytology, CTU)

- **Initial evaluation:** Office cystoscopy for hematuria or symptoms
- **Limitations:** WL cystoscopy may miss tumors; CIS can resemble normal or inflamed mucosa

- **Next step:** CTU, OR biopsy/resection for diagnosis and treatment (TURBT)
- **Cytology:** detects malignant cells in urine
- Low sensitivity for low-grade tumors (true +)

Case Presentation

Patient Case: NMIBC

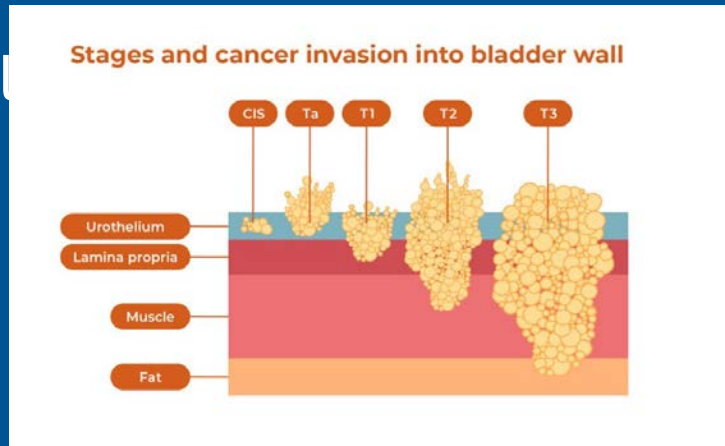
- **He is a 54 yo male who initially presented for evaluation of gross hematuria on 11/29/2022. Former smoker, quit in 2000s, no work or chemical exposures.**
- **PMH: former smoker (quit 2000s), anxiety, childhood asthma, claustrophobia, HLD, IBS, allergies**
- **Meds: finasteride, semaglutide**
- **All: NKDA**
- **Mother with hx of bladder cancer**
- **Widowed and lost husband d/t leukemia. Now raising 12-yo twins alone**

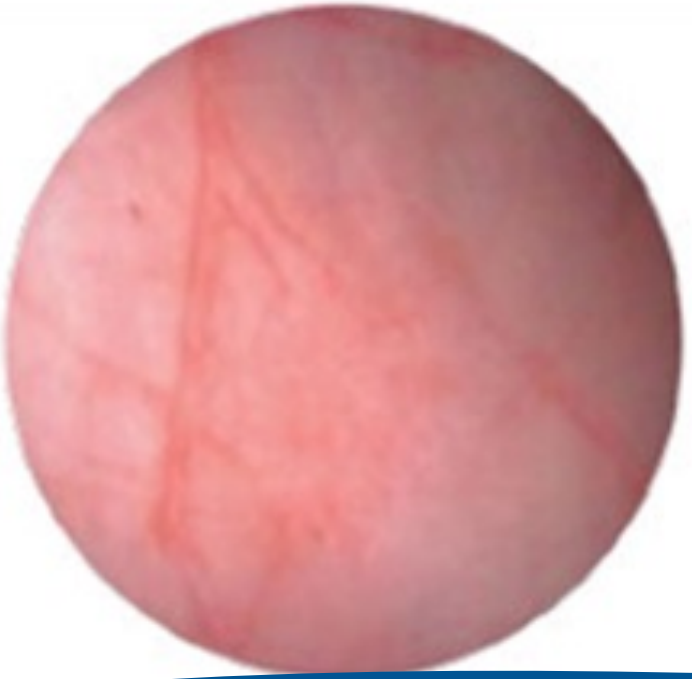
Transurethral resection of the bladder tumor (TURBT)

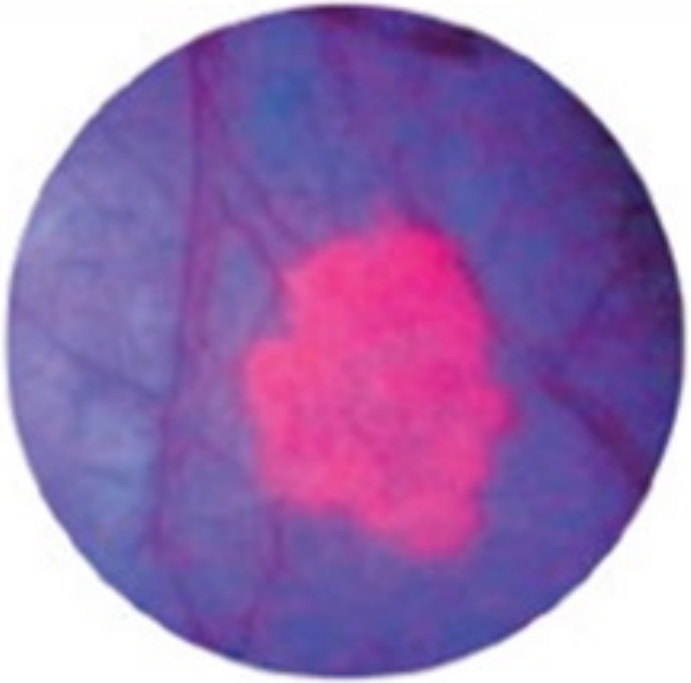
- Cytology on 11/29/22 was AUC (PARIS III, classified from I-IV)
- 12/22/22: CTU: 2.8 cm bladder mass at left wall. No hydronephrosis, renal masses or filling defects. L renal cyst 1 cm.
- Cysto Findings: no bladder stones, no foreign bodies, no diverticula, no active bleeding. At left bladder dome, one ~2 cm bladder tumor with wide-based stalk. Adjacent 0.5 cm papillary tumor.

- TURBT: 1/10/22 TURBT #1
- - bladder tumor #1: HG T1 UC, muscle present uninvol
- - bladder tumor #2: HG UC
- - bladder tumor #3: HG Ta

High risk NMIBC







3/1/2023, the patient underwent a re-resection TURBT per guidelines for T1 with blue light and urethral dilation at UCSF to confirm stage + maximal TUR

Findings: Tight proximal penile urethral stricture, NED

BCG: The Gold Standard to treat HG NMIBC

- BCG with a maintenance protocol
  - BCG is administered as a 6-week induction 3-6 weeks after TUR
  - Followed by 3-week maintenance boosters at 3, 6, 12, 18, 24, 30 and 36 months. Strict cystoscopic and upper tract surveillance must be maintained throughout this period.

- BCG induction – six treatments, once a week for six weeks
- BCG maintenance – three treatments, once a week for three weeks
- 1 year program: at 3, 6, 12 months after induction treatment.
- 3 year program: at 3, 6, 12, 18, 24, 30, and 36 months after induction treatment.
- Cystoscopy schedule – your provider will need to see you in clinic every 3-6 months for surveillance cystoscopies.

BCG Journey: Induction to Maintenance

BCG #1-6 3/23/2023-4/26/2023
BCG #7-9 with catheter in place: 7/5/2023-7/19/2023
BCG #10-12 (3/20/24-3/27/24)
BCG #13-15 (10/8/24-10/29/24)
BCG #16-18 (4/11/25-4/25/25)
BCG # 19-21 (July to Nov 2025)
5 mm L bladder wall lesion on Cystoscopy Jan 2026
OR/TURBT HG T1 into LP
CTU irregular mural thickening and urothelial hyperenhancement of the left lateral bladder wall

What is next after BCG unresponsive HG T1?

Treatment options for BCG-unresponsive high-grade T1 disease

-Pembrolizumab systemic immunotherapy with approximately 20% response rate at 1 year, generally reserved for older patients who cannot tolerate additional intravesical therapy

-Nadofaragene firadenovec-vncg gene-based viral vector therapy administered every 3 months with approximately 40-50% complete response rate at one year for papillary disease, but high-grade recurrence-free survival at 5 years is only 33% in the TA/T1 cohort

-Nogapendekin alfa inbakicept-pmln, which is the preferred bladder preservation option given the patient's prior good response to BCG (QUILT-3.032 Study)

58% (n=28) ≥12 months; 40% (n=19) ≥24 months

Radical Cystectomy as Definitive Treatment

- High-grade T1 recurrence after BCG is one of the situations where bladder preservation carries significant risk of disease progression. It offers a 95% cure rate
- If MIBC patients usually get NAC
- Pre-op RC pathway, needs high volume cancer center
  - Complex surgeries w/ high readmission rates
  - Pre op materials include 22 page PDF document created by RN team
  - Ostomy practice kits, video x 30 min
  - Pre op meeting w/ NP x 60 min individually or in group visit
- March 27, 2026- Radical Cystectomy w/ Neobladder, final pathology HG papillary tumor, pTaN0, no invasion

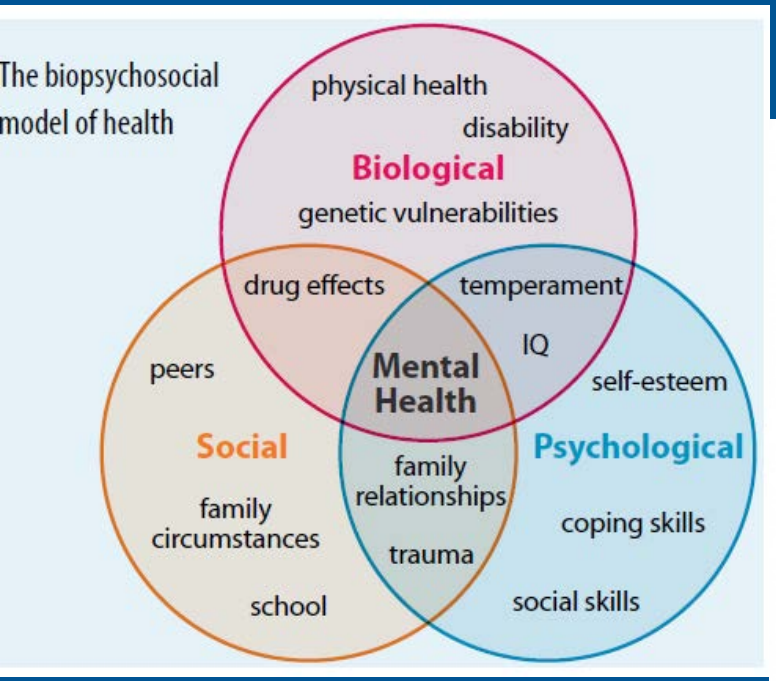
Criteria used to Determine Platinum Eligibility in Patients with MIBC

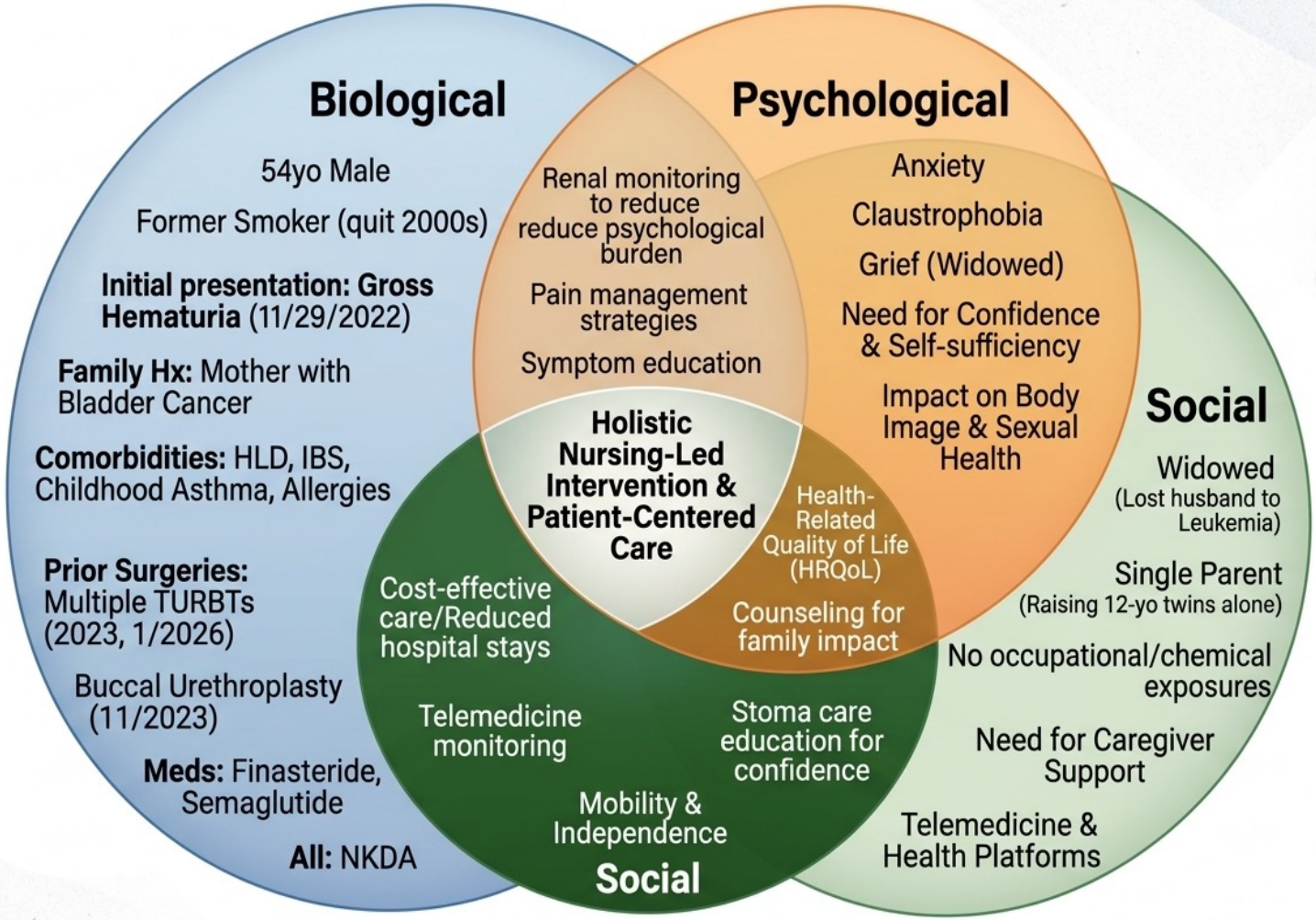
Cisplatin Eligibility

- **GUMO uses the Galsky criteria (widely used in urothelial cancer to answer the question if a patient can get cisplatin therapy, typically gemcitabine/cisplatin or ddMVAC)**
- **A patient is considered cisplatin-ineligible if they have any one of the following:**
  - **Poor performance status**
  - **ECOG performance status ≥ 2**
  - **Renal dysfunction**

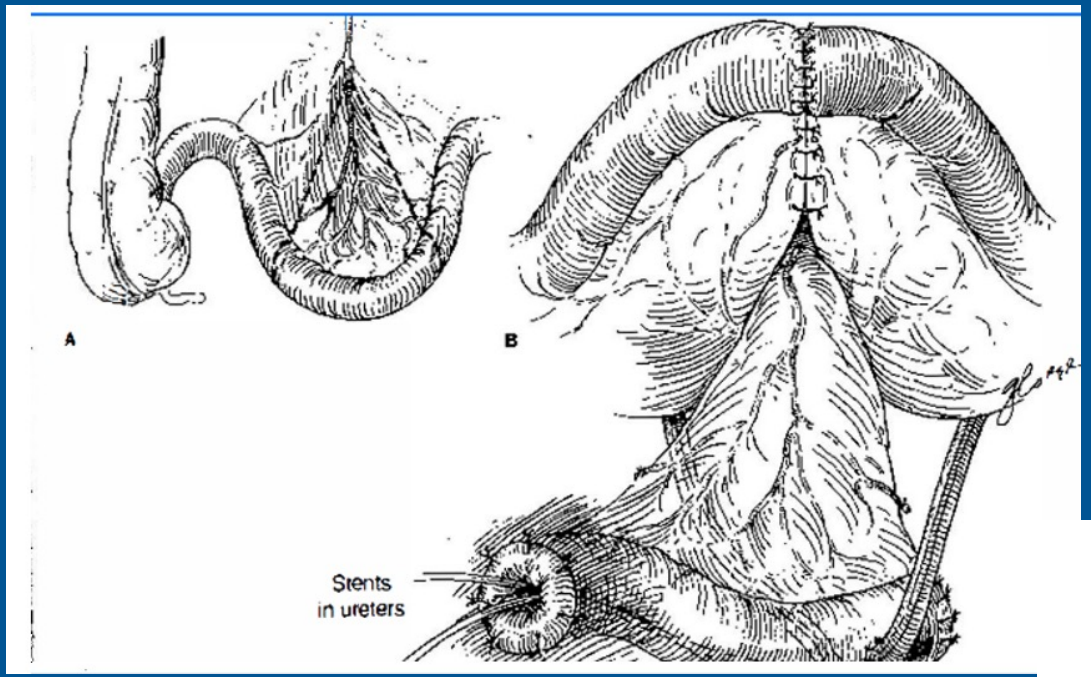
    Creatinine clearance < 60 mL/min

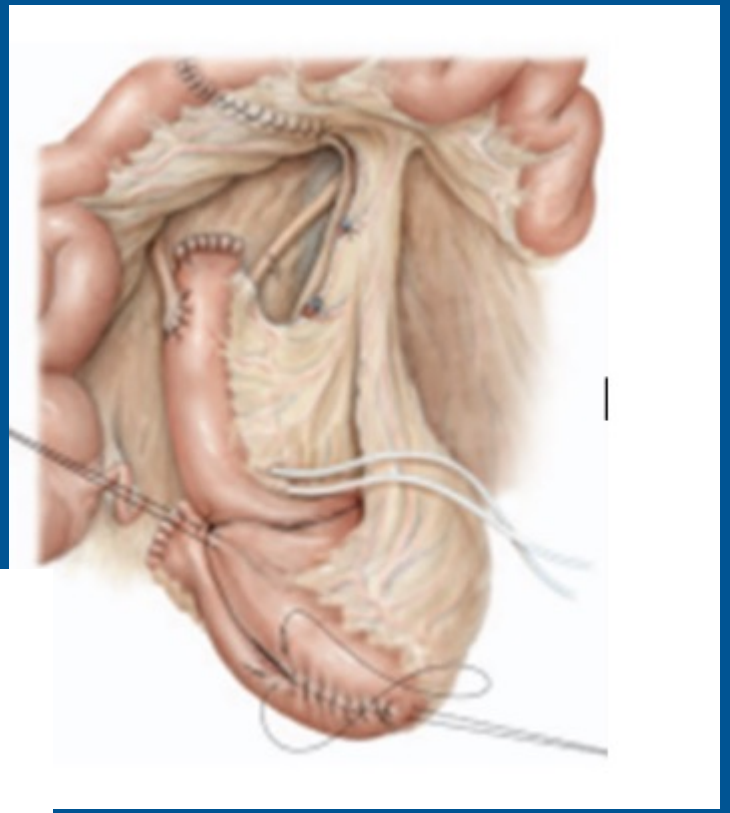
    Hearing loss
  - **Grade ≥ 2 audiometric hearing loss (clinically significant hearing impairment)**
  - **Neuropathy**
  - **Grade ≥ 2 peripheral neuropathy**

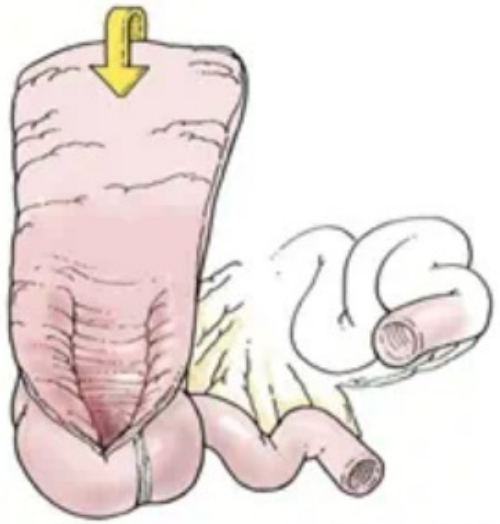

The biopsychosocial model of health
physical health
disability
Biological
genetic vulnerabilities
drug effects
temperament
IQ
peers
Mental Health
self-esteem
Social
Psychological
family relationships
family circumstances
coping skills
trauma
school
social skills


Biological
54yo Male
Former Smoker (quit 2000s)
Initial presentation: Gross Hematuria (11/29/2022)
Family Hx: Mother with Bladder Cancer
Comorbidities: HLD, IBS, Childhood Asthma, Allergies
Prior Surgeries: Multiple TURBTs (2023, 1/2026)
Buccal Urethroplasty (11/2023)
Meds: Finasteride, Semaglutide
All: NKDA
Psychological
Renal monitoring to reduce reduce psychological burden
Pain management strategies
Symptom education
Anxiety
Claustrophobia
Grief (Widowed)
Need for Confidence & Self-sufficiency
Impact on Body Image & Sexual Health
Holistic Nursing-Led Intervention & Patient-Centered Care
Health-Related Quality of Life (HRQoL)
Counseling for family impact
Social
Widowed
(Lost husband to Leukemia)
Single Parent
(Raising 12-yo twins alone)
No occupational/chemical exposures
Need for Caregiver Support
Telemedicine & Health Platforms
Cost-effective care/Reduced hospital stays
Telemedicine monitoring
Stoma care education for confidence
Mobility & Independence
Social

Urinary Diversion Options







Efficacy of Nursing-Led Interventions in Bladder Cancer Care

- Specialized nursing care is more efficacious and cost-effective than usual care, primarily by reducing complications and hospital length of stay (LOS) + readmissions post RC
- High-level urological nursing catches complications before they become costly emergencies
- Stoma Care post op and long term/WOCN
- Long term survivorship care/holistic approach w/ biopsychosocial model
- Sexual health/support groups led by RNs/SW
- Continence/pelvic floor
- Improvement in QoL

Algaisi et al, Medicina 2026 PMID: 41597472

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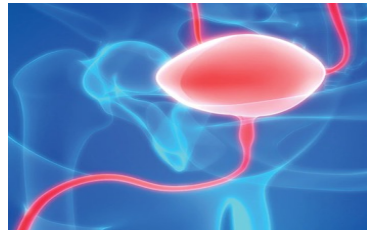
Perioperative Systemic Therapy for Cisplatin-**Eligible** Patients with MIBC

Alexandra Drakaki, MD, PhD
Associate Professor of Medicine, Hematology/Oncology and Urology
Medical Director of the Genitourinary Oncology Program
Leader of the Genitourinary Research Program
University of California, Los Angeles
05/14/2026



Management of T2-T4a N0M0 Urothelial Bladder Cancer

Cisplatin Eligible?

YES

Neoadjuvant Therapy

- DDMVAC with growth factor support for 3–6 cycles
- Gemcitabine + cisplatin + durvalumab
  NIAGARA – FDA Approved, March 2025
- Enfortumab vedotin + pembro **EV-304**

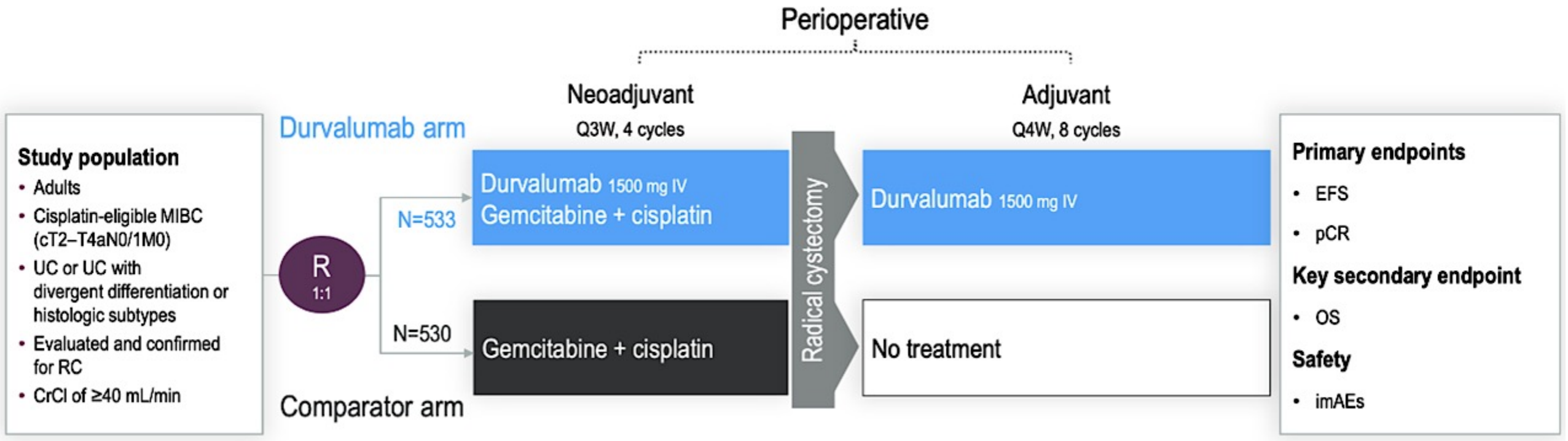
NO

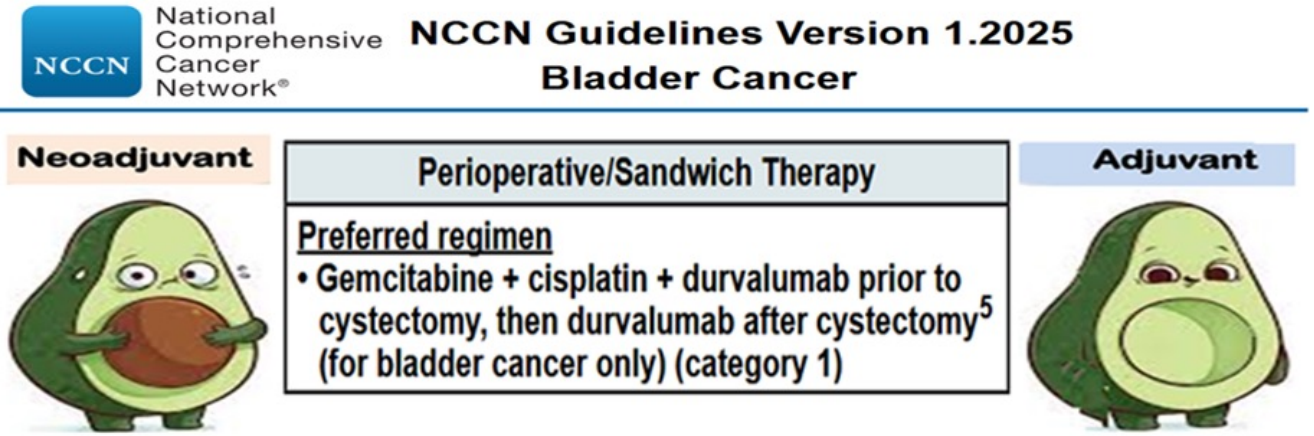
Neoadjuvant Therapy

- Enfortumab vedotin + pembro
  EV-303 – FDA Approved, November 2025

Radical Cystectomy

NIAGARA was the first global Phase 3 study to evaluate a perioperative IO, durvalumab, combined with NAC in cisplatin-eligible patients with MIBC

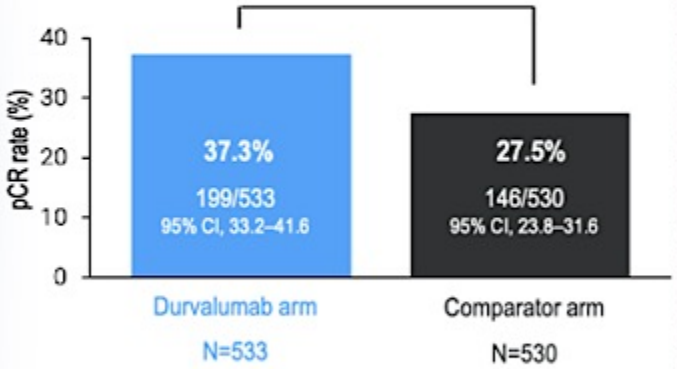




Perioperative durvalumab provided a 10% improvement in pCR rate and statistically significant and clinically meaningful EFS and OS for patients with cisplatin-eligible MIBC

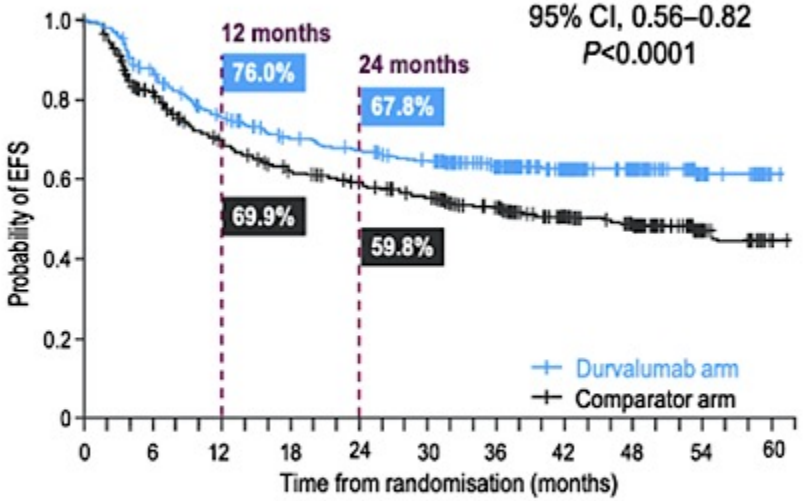
pCR (ITT)

OR, 1.60
95% CI, 1.23–2.08
Nominal P=0.0005[a]



EFS

HR, 0.68
95% CI, 0.56–0.82
P<0.0001



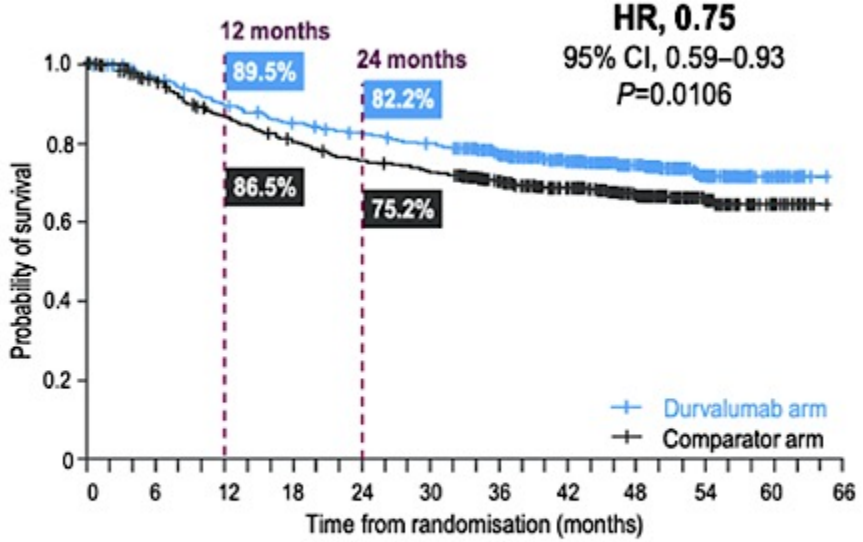
No. of patients at risk

D arm	533	454	386	348	330	312	255	180	115	32	1
C arm	530	416	343	300	281	259	214	159	94	24	2

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

OS

HR, 0.75
95% CI, 0.59–0.93
P=0.0106



No. of patients at risk

D arm	533	505	468	440	423	408	349	271	182	96	21	0
C arm	530	490	438	402	378	363	311	239	174	90	21	0

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

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

Median follow-up: 42.3 months

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

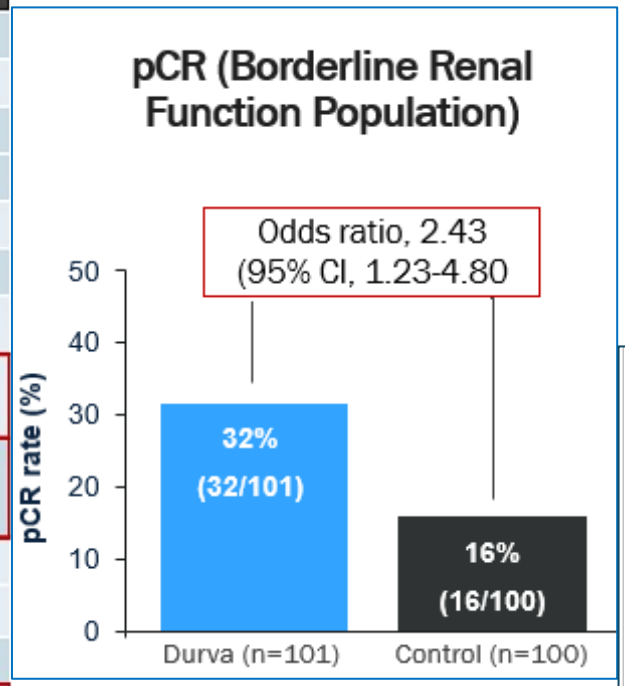
Median follow-up: 42.3 months

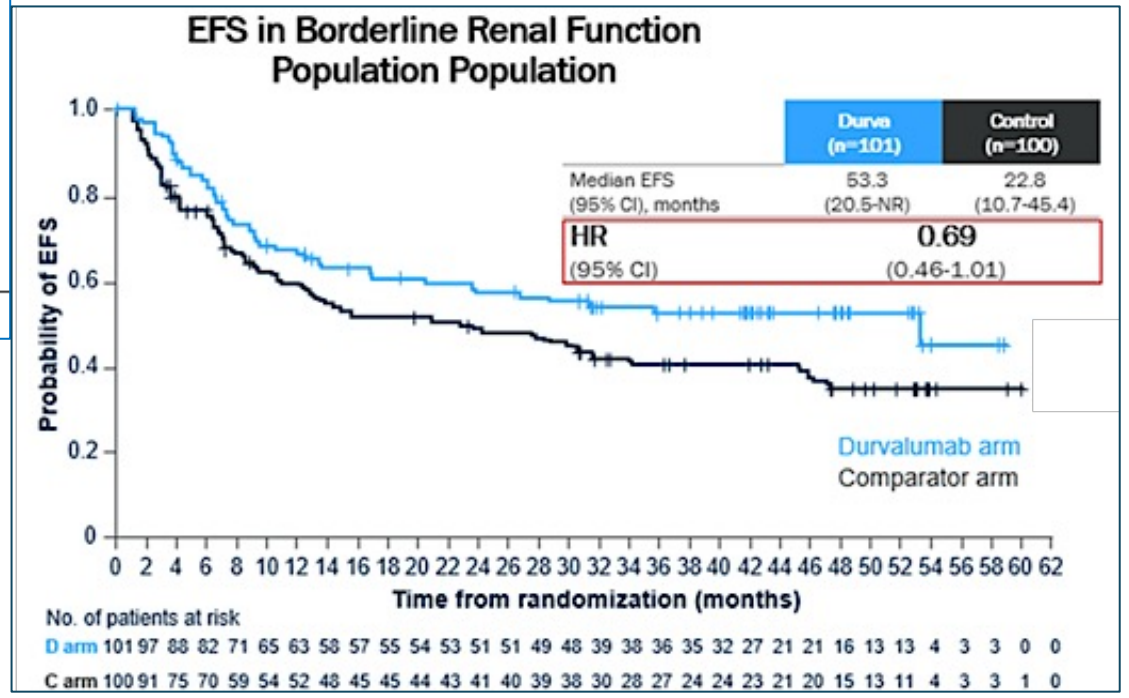
BARCELONA 2024 ESMO

Powles T et al. ESMO 2024;Abstract LBA5; Meeks JJ et al. AUA 2025; Abstract PD39-09.

NIAGARA: pCR and EFS in Borderline Renal Function (CrCl ≥40 to <60 mL/min)

Characteristics, %		Durva (n=533)	Control (n=530)
Median age (range), years		65 (34-84)	66 (32-83)
Male		82	82
Race	White	66	68
	Asian	29	27
ECOG PS	0/1	78/22	78/22
Current or former smoker		71	75
Renal function	CrCl ≥60 mL/min	81	81
	CrCl ≥40 to <60 mL/min	19	19
Tumor stage	T2N0/>T2N0	40/60	40/60
PD-L1 expression	High	73	73
	Low/negative	27	27
Histology	UC	86	83
	Divergent differentiation	14	17
Regional lymph nodes	N0/N1	95/5	94/6





Meeks JJ et al. AUA 2025; Abstract PD39-09.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 14, 2024 VOL. 391 NO. 19

Perioperative Durvalumab with Neoadjuvant Chemotherapy in Operable Bladder Cancer

NIAGARA Investigators

FDA U.S. FOOD & DRUG ADMINISTRATION

March 28, 2025

FDA approves durvalumab for muscle invasive bladder cancer

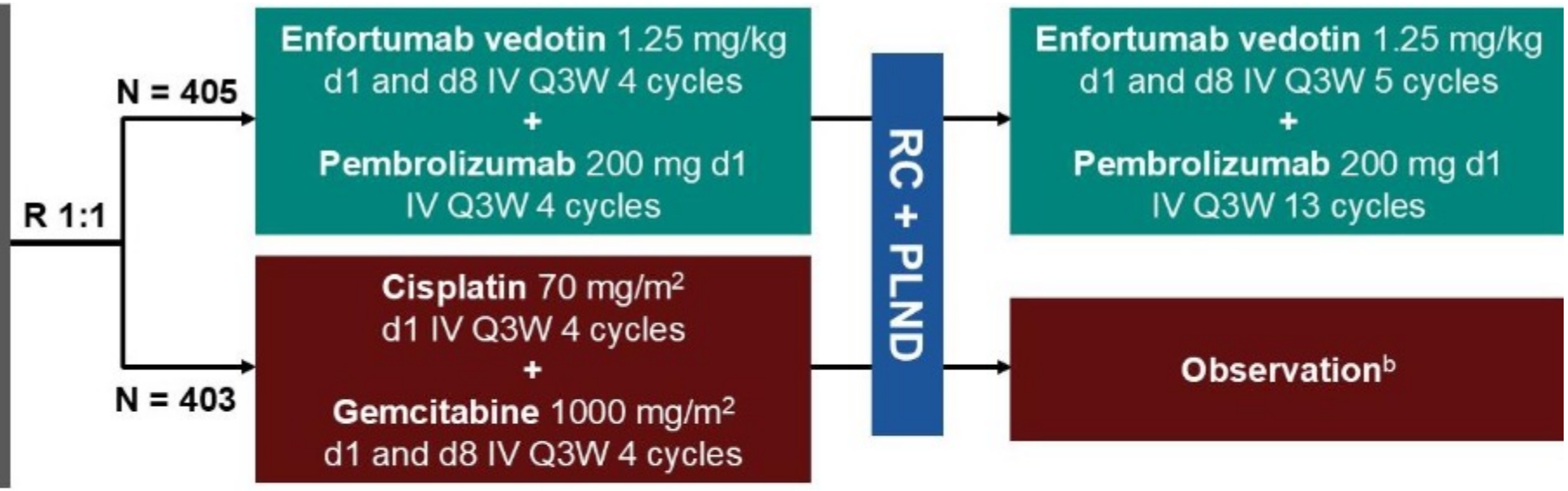
KEYNOTE-B15/EV-304: Trial Design

Key Eligibility Criteria

- Adults with MIBC
- Clinical stage T2-T4aN0M0 or T1-T4aN1M0 by central assessment
- Urothelial histology ≥50%
- Eligible for RC + PLND
- Did not meet any Galsky criteria for cisplatin ineligibility
- ECOG PS 0-1

Stratification Factors

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

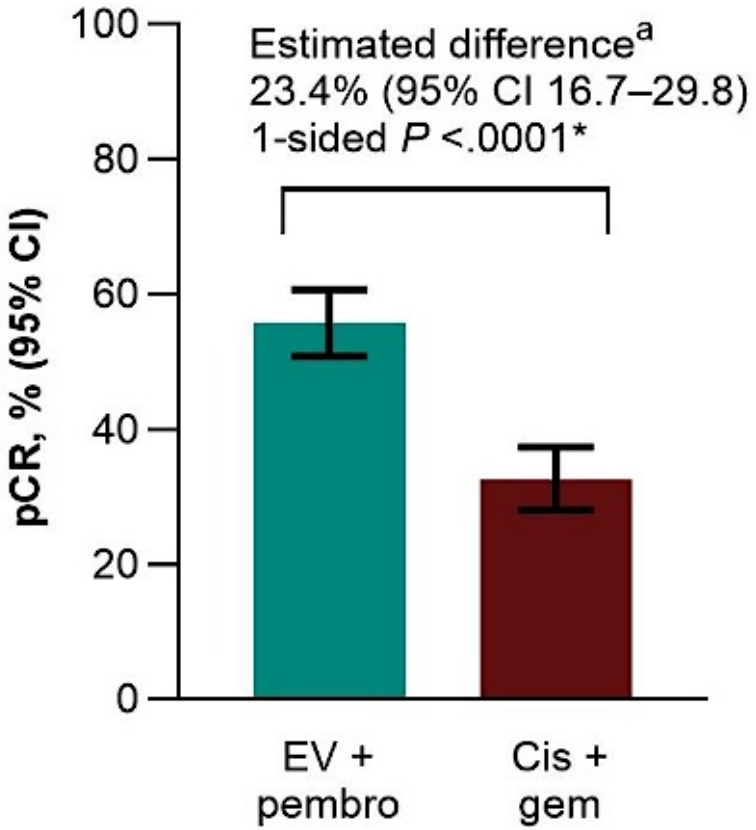


Primary endpoint: Event-free survival (EFS) by BICR

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

Other secondary endpoints include: Safety

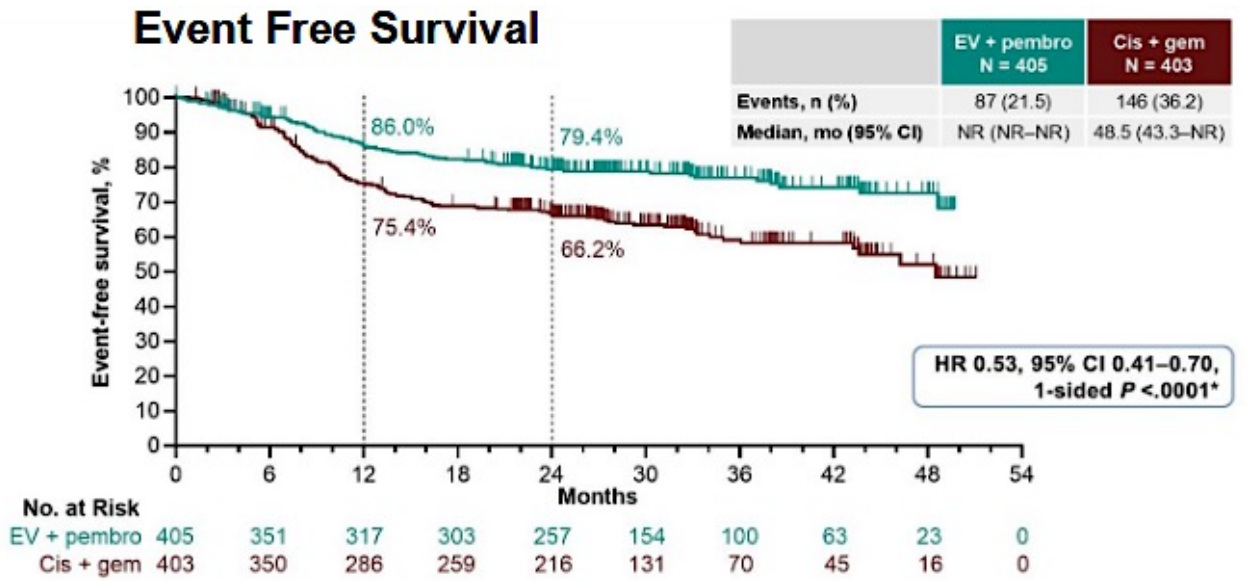
KEYNOTE-B15/EV-304: Primary Results

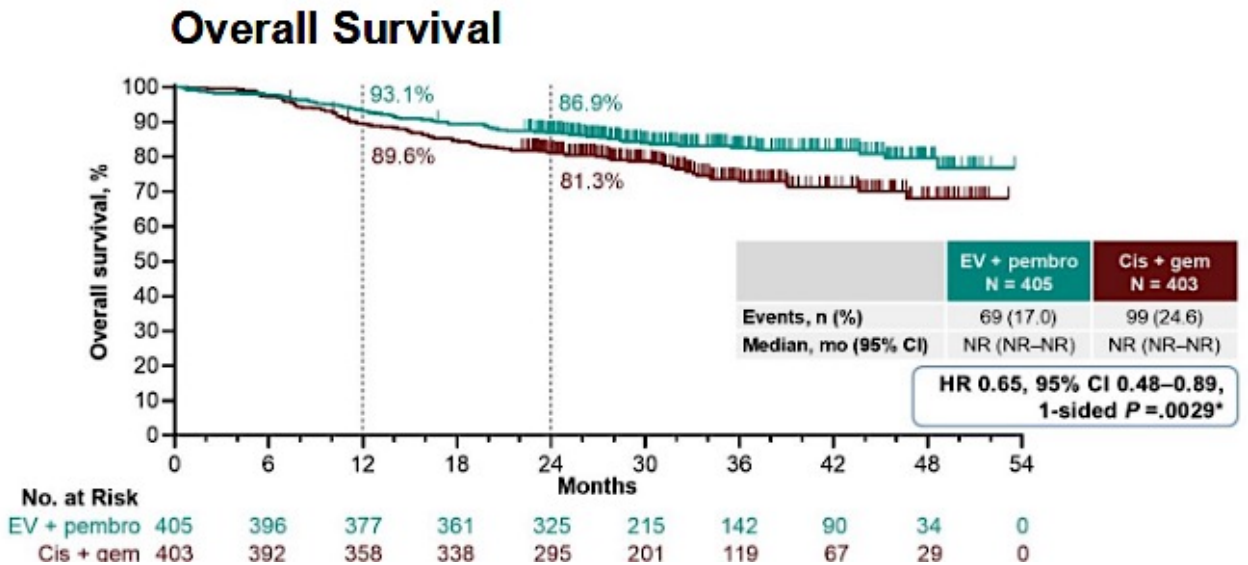


pCR: 55.8%, 95% CI 50.8–60.7

EFS: HR 0.53, 95% CI 0.41–0.70

OS: HR 0.65, 95% CI 0.48–0.89





KEYNOTE B15/EV304 : Patient Characteristics & Safety

Characteristics, %		EV + Pembro (n=405)	Observation (n=403)
Median age (range), years		66 (35-83)	66 (37-85)
≥65 years		61	61
Male		81	81
ECOG PS	0/1	78/22	77/23
Renal function	CrCl ≥90 mL/min	37	39
	CrCl ≥60 to <90 mL/min	62	61
	CrCl ≥30 to <60 mL/min	1	0.5
PD-L1	CPS ≥10	58	57
	CPS <10	42	43
Tumor stage	T2N0	20	19
	T3/T4aN0	72	73
	T1-4aN1	8	8
Pure urothelial carcinoma histology		91	88

Safety n (%)	EV + Pembro (n=403)	GemCis (n=396)
Discontinuation in neoadjuvant phase	101 (25.1)	61 (15.4)
Discontinuation in adjuvant phase	75/262 (28.6)	NA
Grade ≥3 TEAEs	305 (75.7)	266 (67.2)
Grade 5 TEAEs	17 (4.2)[a]	11 (2.8)
Median (range) cycles neoadjuvant	EV: 4 (1-4); Pembro: 4 (1-4)	Gem: 4 (1-4) Cis: 4 (1-4)
Median (range) cycles adjuvant	EV: 5 (1-5); Pembro: 13 (1-13)	NA

~50% of patients in the EV + Pembro arm did not complete the entire 9 cycles of EV and 17 cycles of Pembro

Conclusions

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2026
Bladder Cancer

NCCN Guidelines Index
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Discussion

PRINCIPLES OF SYSTEMIC THERAPY[a]

Neoadjuvant Chemotherapy
Preferred • DDMVAC (dose-dense Methotrexate, Vinblastine, Doxorubicin, and Cisplatin) with growth factor support for 3–6 cycles[1,2] **Useful in certain circumstances** • Cisplatin/Gemcitabine for 4 cycles[3,4]

Perioperative/Sandwich Therapy
Preferred • Cisplatin/Gemcitabine + Durvalumab for 4 cycles prior to cystectomy, then Durvalumab for 8 cycles after cystectomy[5] (for bladder cancer only) (category 1)

Adjuvant Therapy	
No previous platinum-based neoadjuvant therapy (pT3, pT4a, pN+)	**Previous platinum-based neoadjuvant therapy (ypT2–ypT4a or ypN+)**
Preferred • DDMVAC with growth factor support for 3–6 cycles[1,2] **Other recommended** • Nivolumab (category 1)[7] • Cisplatin/Gemcitabine for 4 cycles[3,4] • Pembrolizumab[8]	**Preferred** • Nivolumab[7] (category 1) **Other recommended** • Pembrolizumab[8]

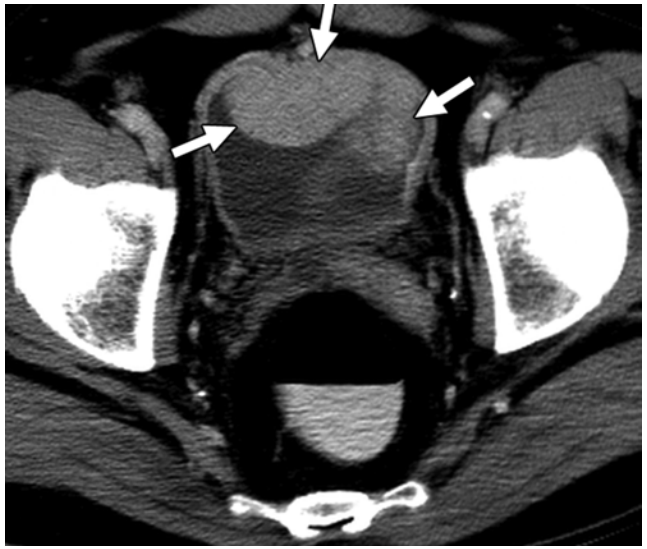
Case Presentation

48-year-old female with new diagnosis of Muscle Invasive Bladder Cancer

History of Present Illness:

48-year-old female is seen in urology clinic for stress incontinence. She has been having chronic UTIs since she started being sexually active in her early 20s, however more recently is having dysuria and irregular bleeding that is felt to be due to being perimenopausal. She has 4 children, two pairs of twins, age 20 and 16. Both deliveries were normal but prolonged and the second was an assisted vaginal delivery. She is having pelvic floor weakening and therefore stress incontinence. Given her recent complaints of intermittent hematuria, she was seen by her Ob/Gyn who did not identify any abnormalities during the exam and therefore referred to Urology for urodynamic studies and cystoscopy to evaluate the intermittent hematuria.

Patient underwent CT chest/abdomen/pelvis that revealed the tumor mass but no metastatic disease



Patient had TURBT with maximum resection of the tumor.
Pathology was consistent with High Grade Urothelial carcinoma, with micropapillary features, invasion into the muscularis propria and perivesical fat.
Given new diagnosis of T3N0M0, she was referred to medical oncology for evaluation and management.

Past Medical History:

Gestational Diabetes, osteopenia

Past Surgical History:

None

Family History:

Mother: Ovarian Cancer, Father:Stroke, Brother: Prostate Cancer on active surveillance

Social History:

Works as a kindergarten teacher, does not smoke or drink, exercises 5 days a week and is vegan

Current Medications:

Calcium and Vitamin D, Multivitamin

- She wants to be as aggressive as possible given her young age and her young kids and is asking about combination therapies.

Treatment Approach:

Given that she was very healthy otherwise, she was offered full dose Cisplatin/Gemcitabine/Durvalumab in the neoadjuvant setting. Underwent radical cystectomy with lymph node dissection and total abdominal hysterectomy and bilateral salpingo-oophorectomy with ileal conduit. Her pathology revealed yT1N0M0 with CIS and negative margins. She completed the 8 cycles of adjuvant durvalumab and currently is cancer free.

Discussion Questions

For which patients with MIBC are you prioritizing the use of perioperative durvalumab?

If perioperative pembrolizumab/enfortumab vedotin were to receive FDA approval for cisplatin-eligible patients with MIBC, how would you choose between these strategies? How would their individual side-effect profiles affect this decision?

Tolerability with the Use of Immune Checkpoint Inhibitors in Urothelial Bladder Cancer

Margarita Huober, AGNP, AOCNP

Stanford Health Care

MECHANISM OF ACTION: PD-1 / PD-L1 CHECKPOINT

PD-1: Receptor on T cells → "off switch"

PD-L1: On tumor cells → turns T cells OFF

Tumors use this to escape the immune system

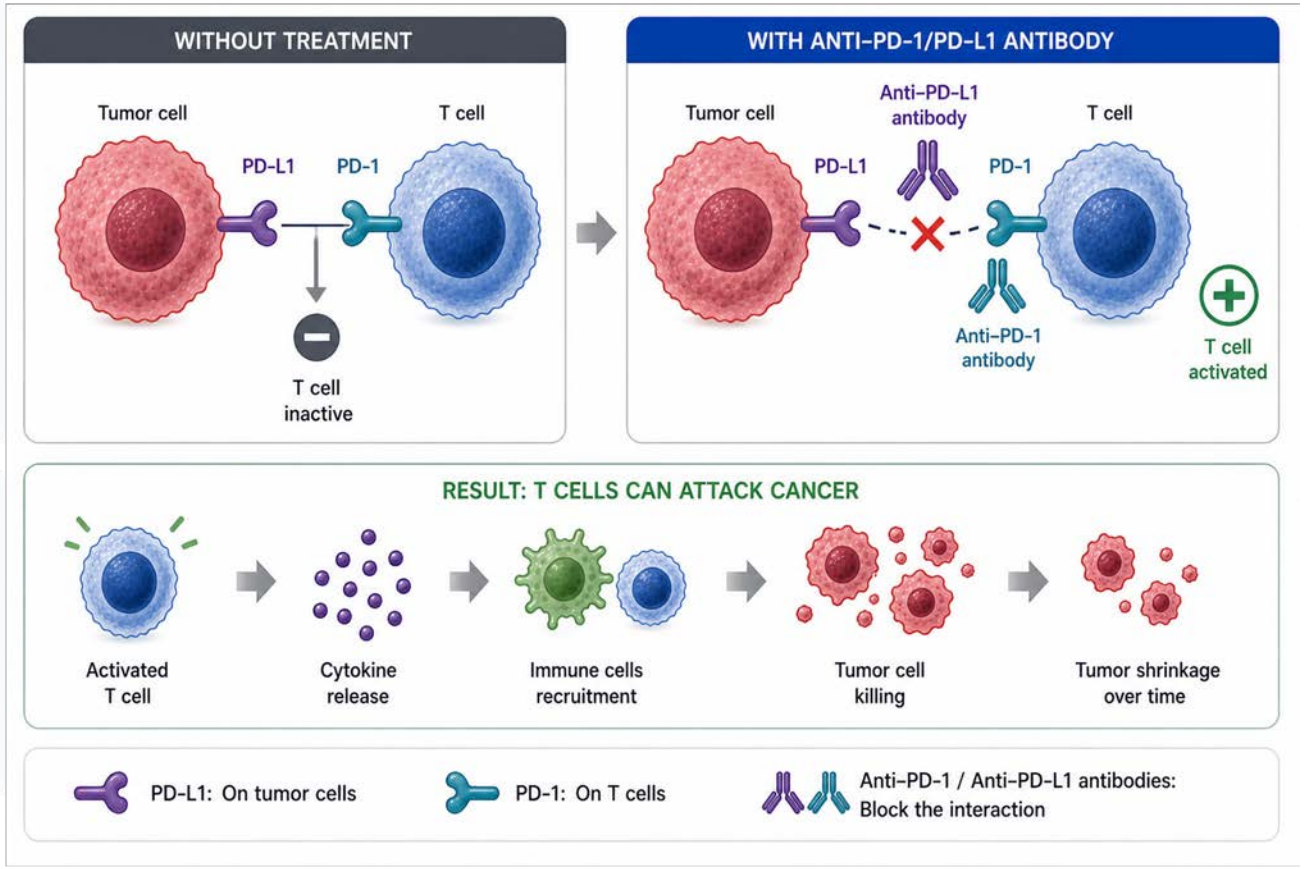
Drugs block PD-1 / PD-L1 interaction

→ T cells turn back ON and attack cancer

BLADDER CANCER AGENTS:

Anti–PD-1: Pembrolizumab, Nivolumab

Anti–PD-L1: Avelumab, Durvalumab



Atezolizumab UC indication withdrawn 2021

PD-1: programmed cell death 1; PD-L1: programmed cell death ligand 1; ICI: immune checkpoint inhibitor

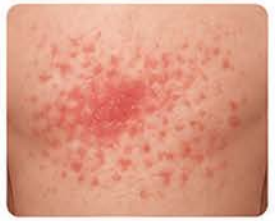
TIMING OF IMMUNE-RELATED ADVERSE EVENTS (irAEs)

WITH PD-1/PD-L1 INHIBITORS IN UROTHELIAL CARCINOMA

irAEs can occur at any time – Most occur within the first 6 months

1–2 WEEKS
Earliest

CUTANEOUS
(Most common early)



- Rash
- Pruritus (itching)
- Vitiligo

Incidence:
~22–24% (any grade)

~4–6 WEEKS
(Early)

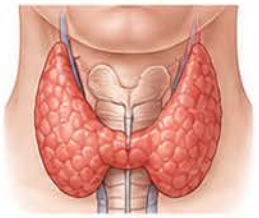
CARDIAC
(High risk – early)

- Myocarditis
  (Median onset ~28–34 days)

Incidence:
~1%
(often severe, life-threatening)

4–12 WEEKS

ENDOCRINE
(Common)



- Hypothyroidism (most common)
- Hyperthyroidism
- Adrenal insufficiency
- Type 1 DM / DKA

Incidence:
Hypothyroidism ~6–20%
Hyperthyroidism ~2–3%
(others ~1%)

~4–12 WEEKS

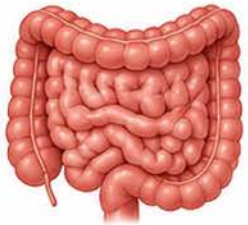
HEPATIC

- Transaminitis
- Hepatitis

Incidence:
~1–3%

6–8 WEEKS

GASTROINTESTINAL



- Diarrhea
- Colitis
- Abdominal pain

Incidence:
Diarrhea ~17–21%
Colitis ~1–2%

2–3 MONTHS

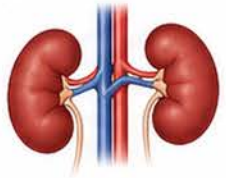
PULMONARY

- Pneumonitis (leading cause of immune-related death)
- Dyspnea, cough

Incidence:
~2%

≥3 MONTHS
Any time

RENAL



- Nephritis
- AKI

Incidence:
~2%

Most irAEs occur within the first 6 months

Myocarditis can occur early (~4–6 weeks) and can be rapidly fatal – High index of suspicion is critical

irAEs can affect any organ system at any time

Early recognition, prompt reporting, and management improve outcomes

irAEs may be associated with better treatment response in UC

Most irAEs develop within 6 months (only ~3% after 1 year), but continued vigilance is essential throughout therapy and follow-up.

Schneider BJ et al. **J Clin Oncol.** 2021;39(36):4073-4126. Postow MA, et al. **N Engl J Med.** 2018;378(2):158-168. Daetwyler E, et al. **J Immunother Cancer.** 2024;12(1):e007409.

MONITORING FOR IMMUNE-RELATED ADVERSE EVENTS

BASELINE (BEFORE C1)

- Labs: CBC, CMP
- Endocrine: TSH, free T4, AM Cortisol, ACTH
- History: Screen for Autoimmune History (Risk vs. Contraindication)

EVERY CYCLE

- Labs: CBC, CMP, TSH (6–12 wk)
- Symptom Check: Fatigue, Rash, GI, Cough, Joint Pain, Vision, Numbness, Polyuria
- *Ask directly — patients underreport mild symptoms*

Red Flag Labs: Act Immediately

- Trop/BNP ↑ → Myocarditis workup
- AST/ALT >5x ULN → Hold ICI, start steroids
- Cr Rise >1.5x → Nephritis workup

ICI: immune checkpoint inhibitor; ULN: upper limit of normal

Schneider BJ et al. **J Clin Oncol.** 2021;39(36):4073-4126. Brahmer JR, et al. **J Immunother Cancer.** 2021;9(6):e002435. Postow MA, et al. **N Engl J Med.** 2018;378(2):158-168. Chan KK, Bass AR. **BMJ.** 2020;369:m736. Daetwyler E, et al. **J Immunother Cancer.** 2024;12(1):e007409.

IRAE MANAGEMENT — GRADES 1 & 2

GRADE 1 (MILD)

CONTINUE ICI

- Maintain ICI + close clinical monitoring
- Symptomatic treatment only (topicals, etc.)

⚠ **EXCEPTIONS: Myocarditis, Guillain-Barré, or Myasthenia → Hold/Discontinue even at Grade 1**

GRADE 2 (MODERATE)

HOLD ICI

- Oral Prednisone 0.5–1 mg/kg/day
- Prompt subspecialty referral
- Taper steroids slowly over 4+ weeks

Endocrinopathies: Hormone replacement, NOT steroids

irAE: immune-related adverse event; ICI: immune checkpoint inhibitor

Schneider BJ et al. **J Clin Oncol.** 2021;39(36):4073-4126. Brahmer JR, et al. **J Immunother Cancer.** 2021;9(6):e002435. Postow MA, et al. **N Engl J Med.** 2018;378(2):158-168. Puzanov I, et al. **J Immunother Cancer.** 2017;5(1):95.

IRAE MANAGEMENT — GRADES 3 & 4

GRADE 3 (SEVERE)

HOLD / DISCONTINUE

- IV Methylprednisolone 1–2 mg/kg/day
- Consider permanent ICI discontinuation
- Refractory at 48–72h: Add 2nd line (Infliximab, etc.)

Hospitalization often required for IV management

GRADE 4 (LIFE-THREATENING)

PERMANENT DISCONTINUE

- IV Pulse Steroids ± Critical Care (ICU)

Stable Endocrinopathies on replacement: may continue ICI

irAE: immune-related adverse event

Schneider BJ et al. **J Clin Oncol.** 2021;39(36):4073-4126. Brahmer JR, et al. **J Immunother Cancer.** 2021;9(6):e002435. Postow MA, et al. **N Engl J Med.** 2018;378(2):158-168. Puzanov I, et al. **J Immunother Cancer.** 2017;5(1):95.

PROMPT REPORTING CHANGES OUTCOMES

THE CLINICAL IMPACT

- Pneumonitis: #1 cause of immune-related death; early steroids improve outcomes
- **Myocarditis**: Early aggressive treatment ↓ mortality from ~50% to <15%
- Colitis: Rapid intervention reduces perforation risk and surgical needs
- Hepatitis: Early (G2) = Hold & Monitor; Late (G3) = Prolonged Steroid Tapers

THE "BIG 5" SYMPTOMS

- **New shortness of breath or cough** → Pneumonitis
- **Chest pain, palpitations, or swelling** → Myocarditis
- **Severe diarrhea (≥4 stools/day above baseline)** → Colitis
- **Yellowing of skin/eyes or dark urine** → Hepatitis
- **Polyuria/polydipsia, severe headache, vision changes, or fatigue** → Endocrinopathy

irAE: immune-related adverse event; G: grades 1-4 (1=mild, 2=moderate, 3=severe, 4=life-threatening)

Schneider BJ et al. **J Clin Oncol.** 2021;39(36):4073-4126. Brahmer JR, et al. **J Immunother Cancer.** 2021;9(6):e002435. Postow MA, et al. **N Engl J Med.** 2018;378(2):158-168. Puzanov I, et al. **J Immunother Cancer.** 2017;5(1):95.

FINAL TAKEAWAYS: IRAE MANAGEMENT

Detect Early

Any organ can be affected at any time

Monitor Always

Baseline labs + assessment every cycle

Act Fast

Treat Myocarditis/ Neurological IRAE aggressively

Taper Safely

Reduce steroids slowly (≥4–6 wks)

Endocrinopathy = Hormones, NOT steroids

irAE: Immune-Related Adverse Event; **Neuro:** Neurological toxicity

CASE PRESENTATION:

IMMUNOTHERAPY — RESPONSE & TOXICITY

CASE STUDY: MEET THE PATIENT

SOCIAL & FAMILY SUPPORT

DS lives with his wife. His daughter is a nurse and calls the clinic frequently for updates regarding his status.

CLINICAL HISTORY

- DS, 71: Retired long-haul trucker; former smoker (40 pk-yr)
- PMH: Hypertension and mild COPD
- Status: Cisplatin-ineligible (CrCl 47 mL/min)

DIAGNOSIS & TREATMENT PLAN

- Diagnosis: High-grade urothelial carcinoma, cT3bN0M0 (MIBC)
- Treatment Plan: 3 cycles of perioperative EV + pembrolizumab → radical cystectomy

CrCl: creatinine clearance; **EV:** enfortumab vedotin; **MIBC:** muscle-invasive bladder cancer; **PMH:** past medical history

CASE STUDY: THE PHONE CALL (C2, D14)

DS’s daughter calls the infusion clinic:

"He can barely keep his eyes open — his eyelids are drooping."

"He's having trouble swallowing his pills and choked on water at dinner."

"He says his legs feel heavy and he can't get up from the couch."

HIGH ALERT

"He also mentioned some chest tightness but says it's probably heartburn."

DIAGNOSIS — TRIPLE M SYNDROME

DS was directed to the Emergency Department immediately for urgent evaluation

Myocarditis

Heart Muscle Attack

(Troponin Elevated)

Myositis

Muscle Inflammation

(CK Elevated, Weakness)

Myasthenia

Nerve-Muscle Block

(Ptosis, Dysphagia)

Clinical Urgency: **Fatal within days if not caught early. Mortality ~25–40%.**

CK: Creatine Kinase

TREATMENT — WHAT HAPPENED NEXT

- **IMMEDIATE ACTIONS**
  Pembrolizumab permanently **discontinued**
  High-dose IV steroids (Methylprednisolone pulse dose)
- **EARLY ESCALATION**
  Within 48 hrs: Added IVIG (myasthenia component)
- **ICU CARE REQUIRED**
  Telemetry | Respiratory monitoring | Serial labs (CK, troponin)

🔑 Do not wait for steroids alone to work; Start aggressive, combination immunosuppression early

IVIG: Intravenous Immunoglobulin

OUTCOME & TAKEAWAYS

PATIENT STATUS
Stabilized in ICU → Transferred to floor

THERAPY UPDATE
Pembro discontinued; Completed with EV alone

FINAL RESULT
Cystectomy → Pathologic Complete Response (pT0)

REMEMBER "TRIPLE M SYNDROME"

PTOSIS + DYSPHAGIA + WEAKNESS + CHEST SYMPTOMS = EMERGENCY

Do not wait — escalate immediately. **Triple M** can progress rapidly to respiratory failure

PROACTIVE SCREENING

Ask directly during every assessment. Do not rely on patient self-reporting.

- Droopy eyelids
- Trouble swallowing
- New weakness
- Chest discomfort

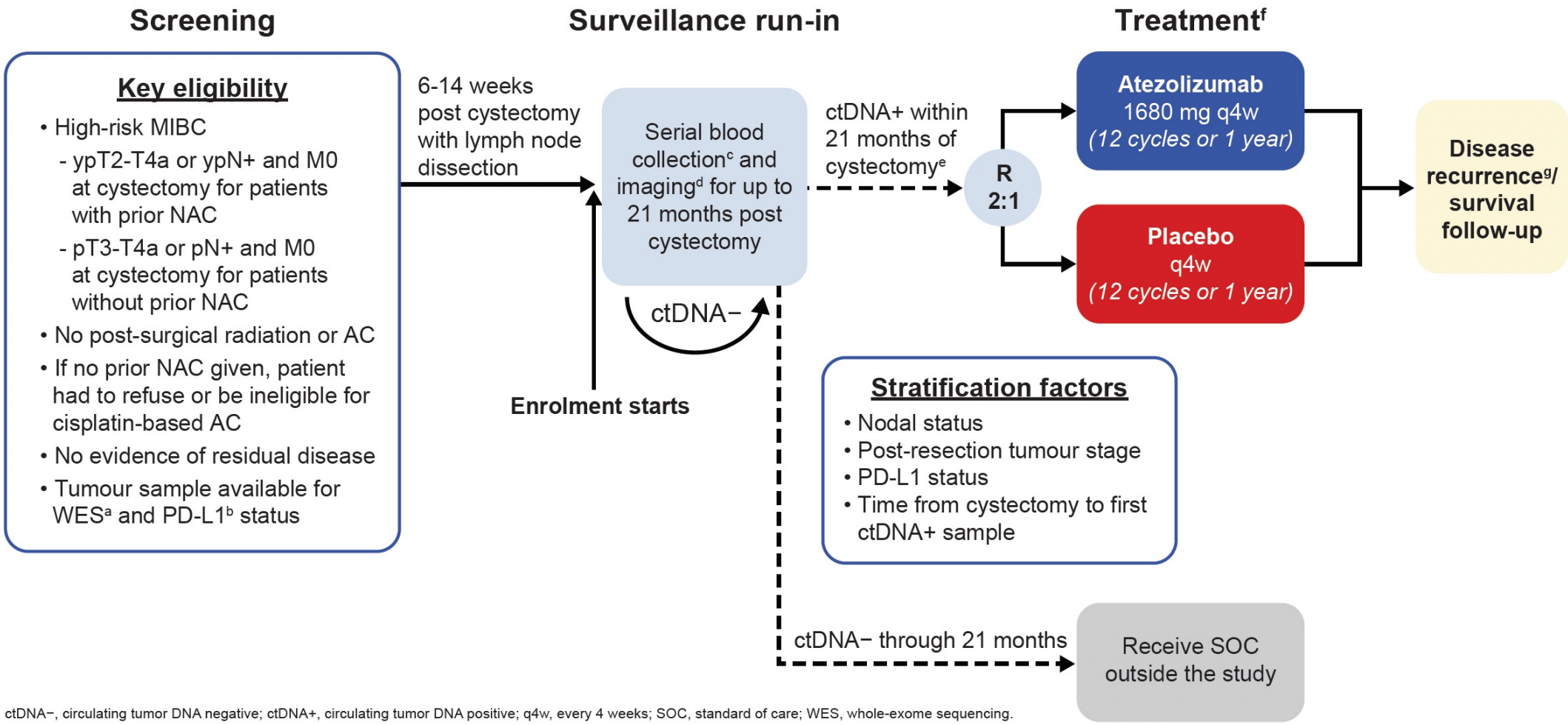
EV: enfortumab vedotin; **Triple M:** Myocarditis, Myositis, Myasthenia

Discussion Questions

If a patient with nonmetastatic UBC were to ask you the likelihood that they will experience an immune-related adverse event (irAE) while receiving an anti-PD-1/PD-L1 antibody, how would you respond? What about an irreversible irAE? What about a severe or life-threatening event?

Potential Role of ctDNA in Nonmetastatic UBC

IMvigor011 Study Design



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

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

[b] Per the VENTANA SP142 IHC assay.

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

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

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

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

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

Powles et al. ESMO 2021;Abstract 716TiP.

Abstract LBA8

IMvigor011: a Phase 3 trial of circulating tumour (ct)DNA-guided adjuvant atezolizumab vs placebo in muscle-invasive bladder cancer

Thomas Powles[1], Ariel G. Kann[2], Daniel Castellano[3], Marine Gross-Goupil[4], Hiroyuki Nishiyama[5], Sergio Bracarda[6], Jørgen Bjerggaard Jensen[7], Shusuan Jiang[8], Ja Hyeon Ku[9], Marco Maruzzo[10], Dingwei Ye[11], Rafael Morales-Barrera[12], Oscar Reig Torras[13], Andrea Necchi[14,15], Wei Zou[16], Zoe June Assaf[16], Jacqueline Vuky[16], Elizabeth E. Steinberg[16], Joaquim Bellmunt[17], Jürgen E. Gschwend[18]

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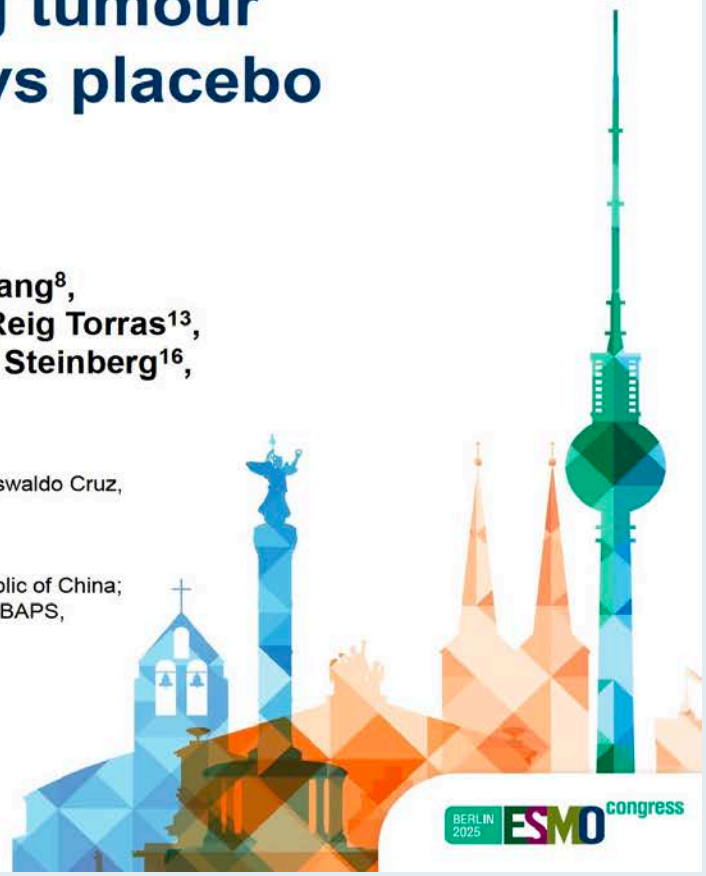
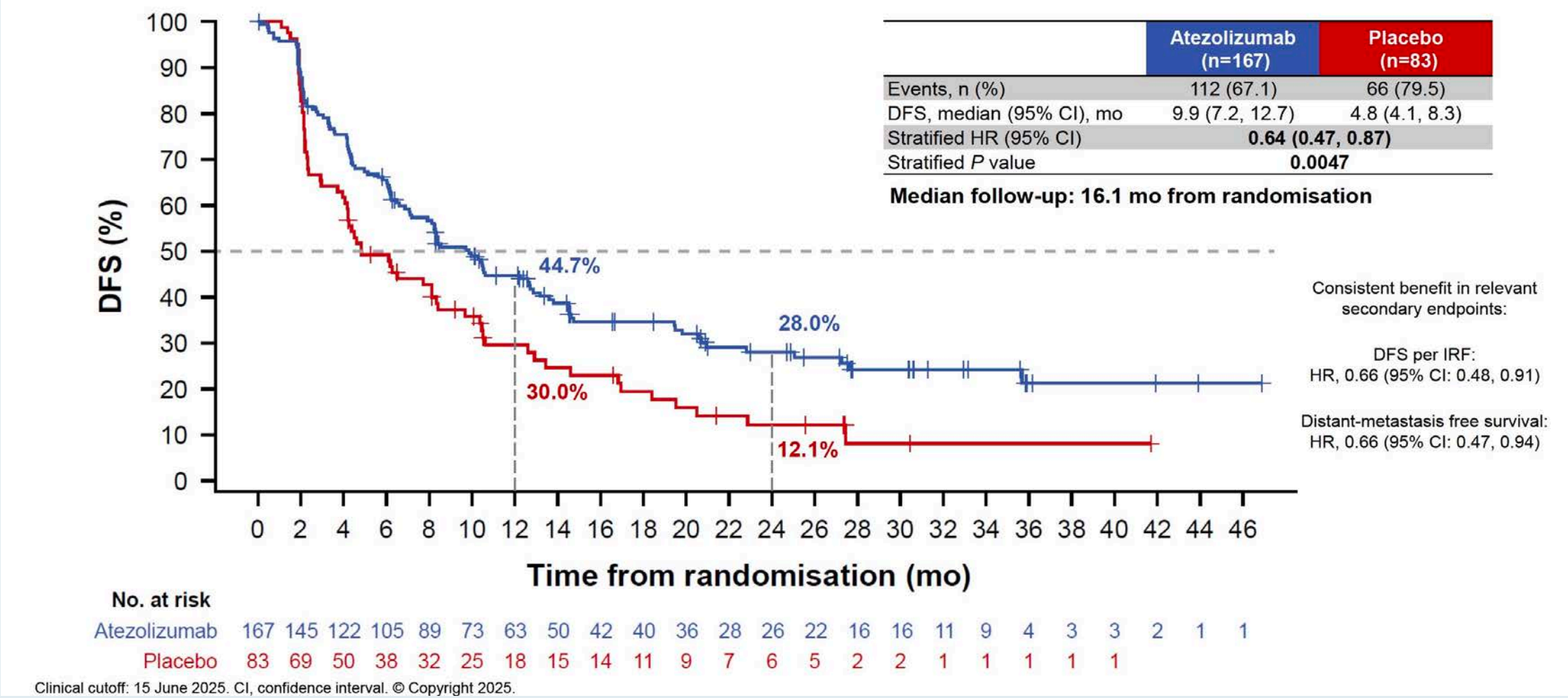


Presented by: Thomas Powles, MBBS, MRCP, MD

Phase III IMvigor011: Investigator-Assessed Disease-Free Survival for Patients Whose Disease Tested ctDNA Positive



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

Median follow-up: 16.1 mo from randomisation

Consistent benefit in relevant secondary endpoints:

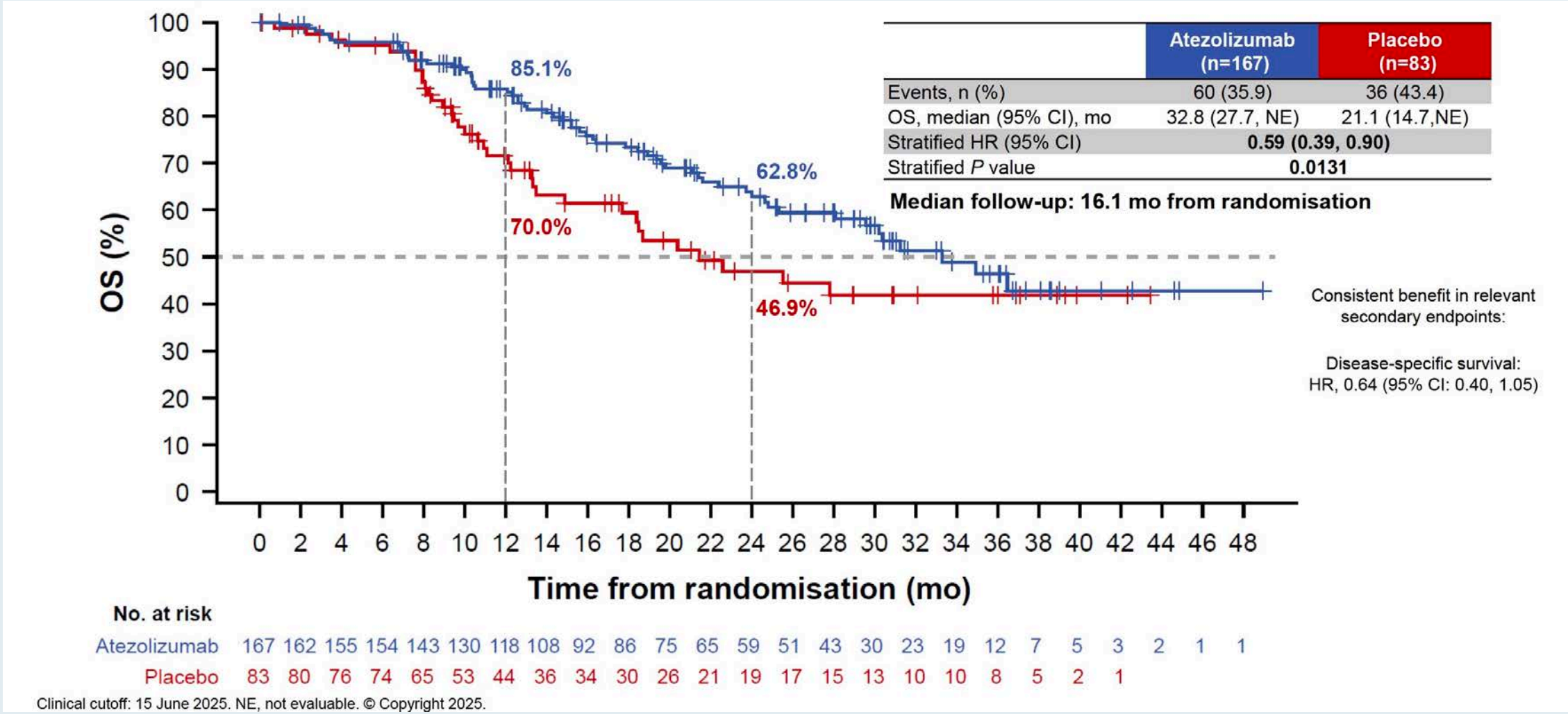
DFS per IRF:
HR, 0.66 (95% CI: 0.48, 0.91)

Distant-metastasis free survival:
HR, 0.66 (95% CI: 0.47, 0.94)

Clinical cutoff: 15 June 2025. CI, confidence interval.

Powles T et al. ESMO 2025;Abstract LBA8.

Phase III IMvigor011: OS for Patients Whose Disease Tested ctDNA Positive



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

Median follow-up: 16.1 mo from randomisation

Consistent benefit in relevant secondary endpoints:

Disease-specific survival:
HR, 0.64 (95% CI: 0.40, 1.05)

Clinical cutoff: 15 June 2025. NE, not evaluable.

Powles T et al. ESMO 2025;Abstract LBA8.

Phase III IMvigor011: Authors' Conclusions

- Adjuvant atezolizumab demonstrated statistically significant DFS and OS improvements vs placebo in patients with MIBC identified as ctDNA+ through serial MRD testing
  - Clinical benefit with atezolizumab was generally consistent across key subgroups, including patients excluded from prior adjuvant trials (e.g. those with pT2N0 disease), which suggests that ctDNA status enhances risk determination beyond classical surgical pathological staging
  - Similar efficacy was observed in patients with ctDNA+ status at baseline and those who converted to ctDNA+ status with repeated testing
- Patients who persistently tested ctDNA− had low risk of recurrence and death
- The atezolizumab safety profile was tolerable, with no new findings
- **These findings indicate that serial ctDNA monitoring can identify patients with MIBC who benefit from adjuvant atezolizumab while sparing patients who persistently test ctDNA− from unnecessary treatment**

MRD = molecular residual disease

Powles T et al. ESMO 2025;Abstract LBA8.

Discussion Questions

Do you believe ctDNA will be used to inform treatment decision-making for patients with nonmetastatic UBC in routine practice in the near future? How so?

Are you using ctDNA analysis in your own practice today? What role might oncology nurses play in identifying patients for whom ctDNA analysis might be appropriate and helping them understand their test results?

Agenda

Introduction: Basic Biology of Nonmetastatic Urothelial Bladder Cancer (UBC)

Module 1: Systemic Therapy for Cisplatin-Eligible Patients with Muscle-Invasive Bladder Cancer (MIBC)

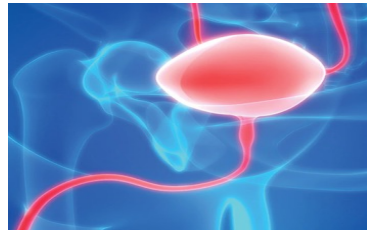
Module 2: Evolving Approach to Systemic Therapy for Cisplatin-Ineligible Patients with MIBC

Module 3: Immune Checkpoint Inhibitors in Non-Muscle-Invasive Bladder Cancer

Module 4: Novel Intravesical Therapies for Nonmetastatic UBC

Perioperative Systemic Therapy for Cisplatin-**Ineligible** Patients with MIBC

Alexandra Drakaki, MD, PhD
Associate Professor of Medicine, Hematology/Oncology and Urology
Medical Director of the Genitourinary Oncology Program
Leader of the Genitourinary Research Program
University of California, Los Angeles
05/14/2026



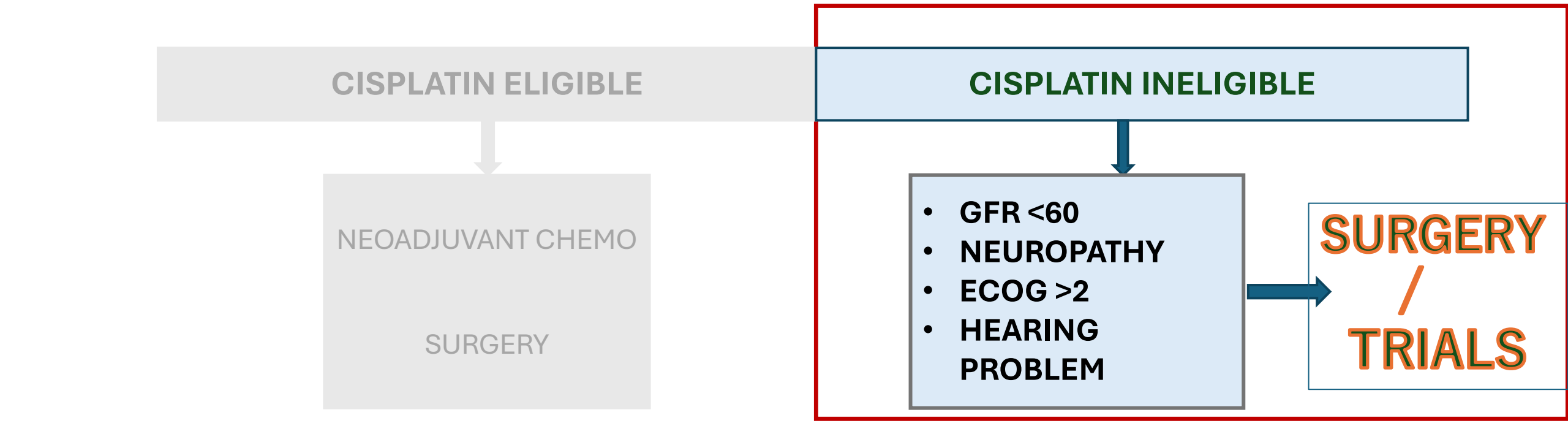
How to think in bladder cancer

JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

Guideline on Muscle-Invasive and Metastatic Bladder Cancer (European Association of Urology Guideline): American Society of Clinical Oncology Clinical Practice Guideline Endorsement

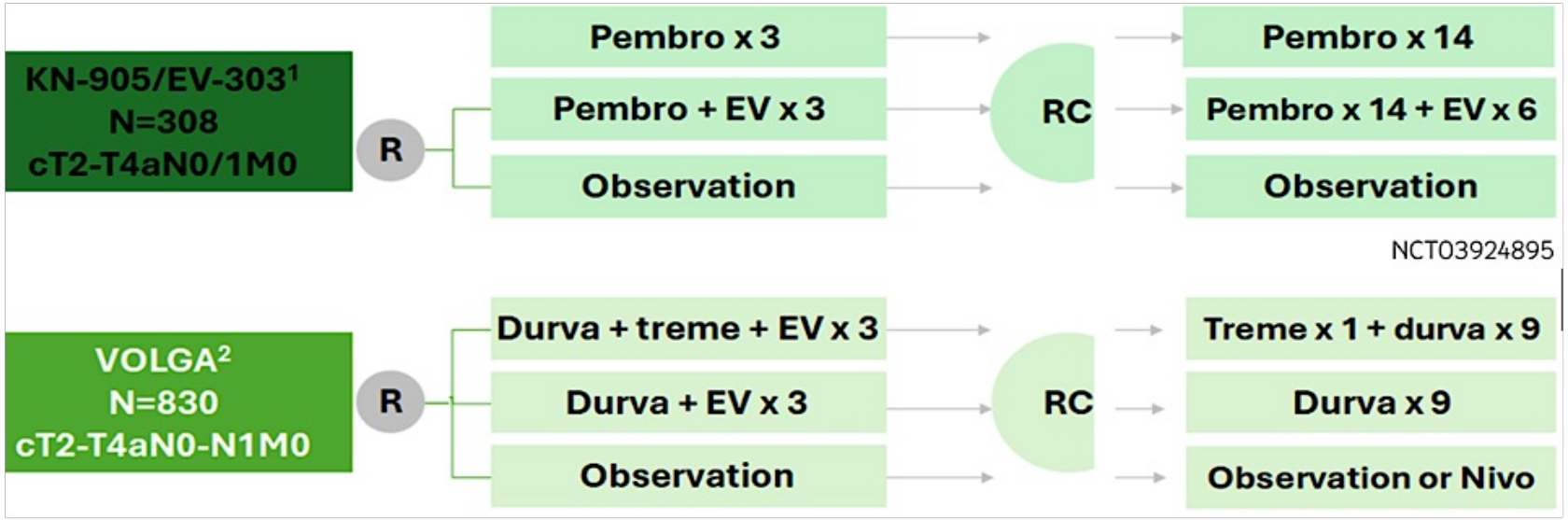
JUNE 1, 2016

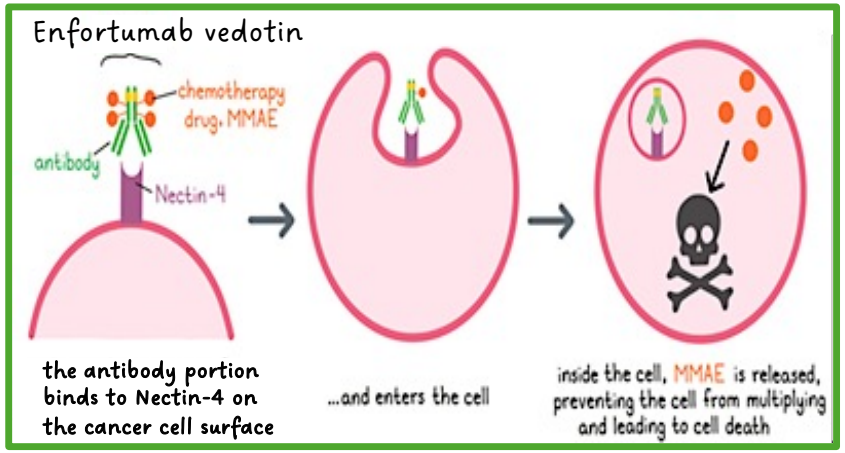


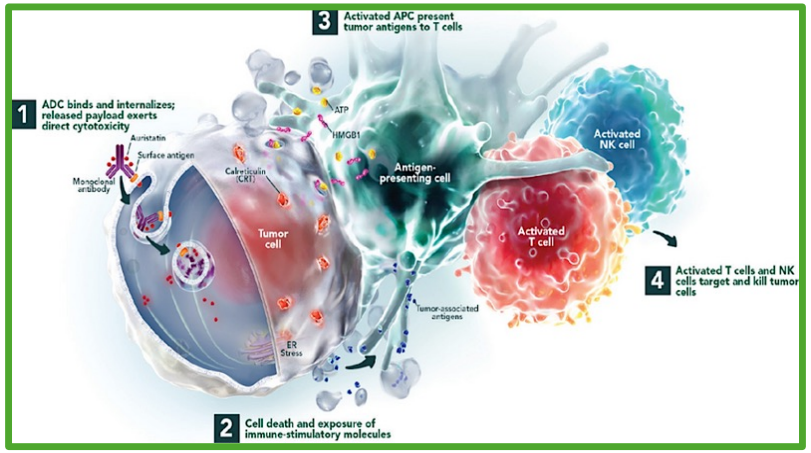
Neoadjuvant

Perioperative Phase 3 Studies in Cis-Ineligible MIBC

Adjuvant







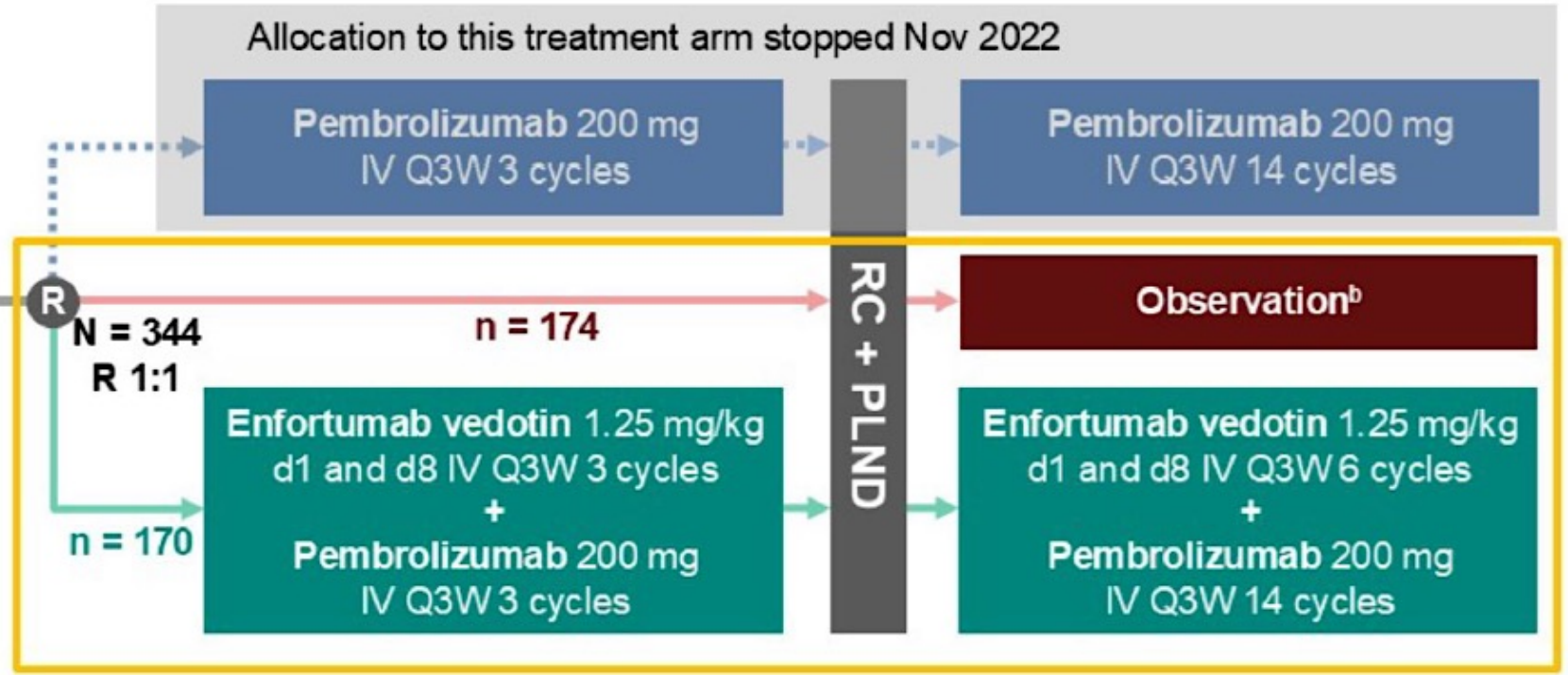
KEYNOTE-905/EV-303: Trial Design

Key Eligibility Criteria

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

Stratification Factors

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



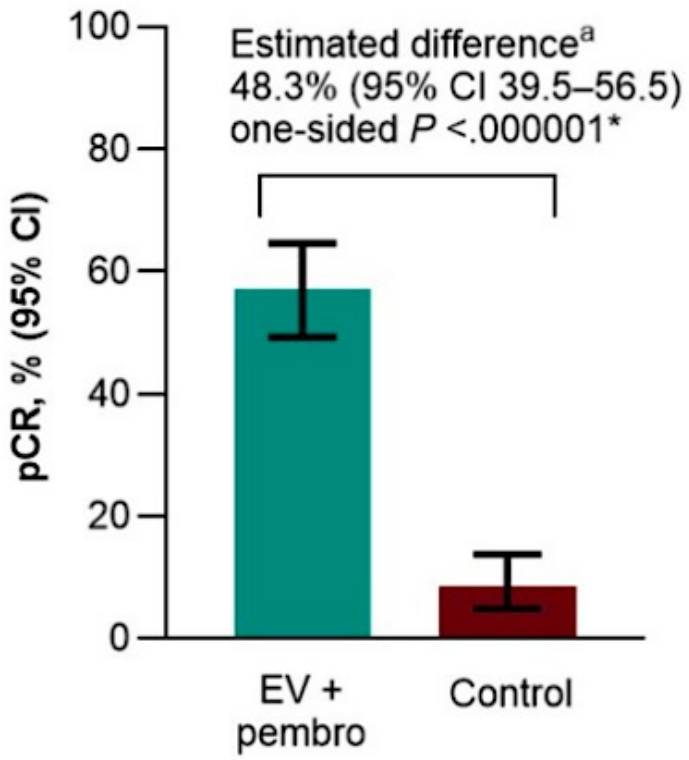
Primary endpoint: Event-free survival (EFS) by BICR
Key secondary endpoints: OS and pathological complete response (pCR; pT0N0, i.e. absence of viable tumor in examined tissue from surgery) by central pathologist review
Other secondary endpoints include: Safety
Exploratory endpoints include: EFS by pCR status

KEYNOTE 905/EV303: Patient Characteristics

Characteristics, %		EV + Pembro (n=170)	Observation (n=174)
Median age (range), years		74 (47-87)	72.5 (46-87)
≥65 to <75 years/≥75 years		37/46	44/39
Male (%)		81	75
ECOG PS (%)	0/1/2	60/28/12	55/31/15
Renal Function (%)	CrCl ≥60 mL/min	40	41
	CrCl ≥30 to <60 mL/min	60	58
	CrCl <30 mL/min	0	1
PD-L1 CPS ≥10		47	48
Cisplatin eligibility (%)	Ineligible	84	80
	Eligible but declining	17	20
Tumor Stage (%)	T2N0	18	18
	T3/T4aNO	78	76
	T1-4aN1	4	6
Pure urothelial carcinoma histology (%)		89	92

Christof Vulsteke, ESMO 2025; *N Engl J Med* 2026;394(13):1257-69.

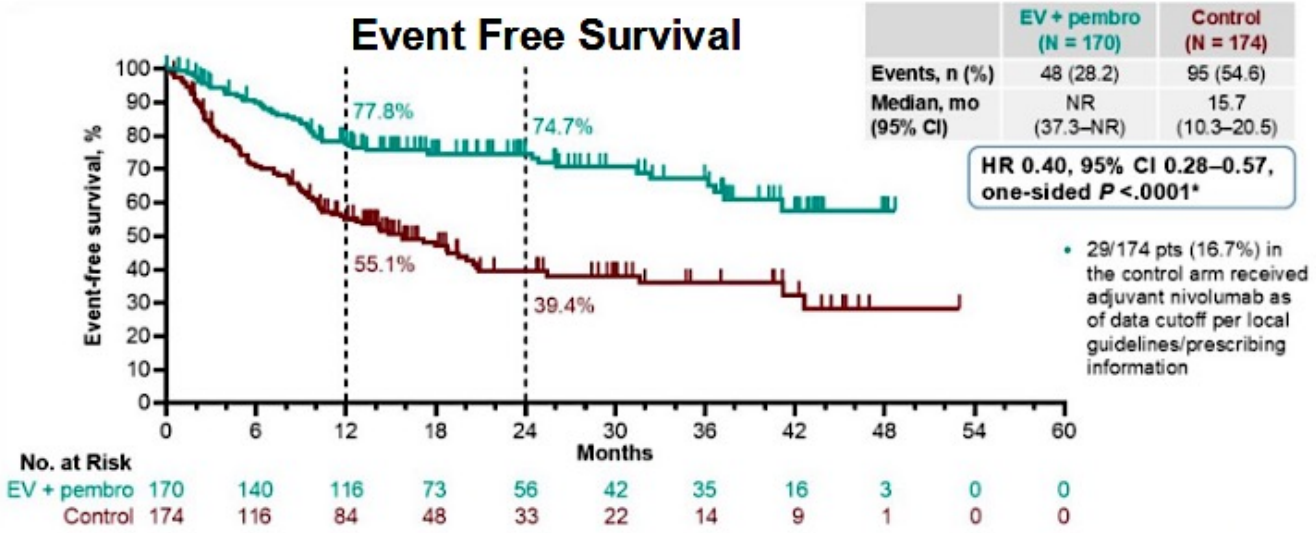
KEYNOTE-905/EV-303: Primary Results



pCR: 57.1%, 95% CI 49.3–64.6

EFS: HR 0.50, 95% CI 0.33–0.74

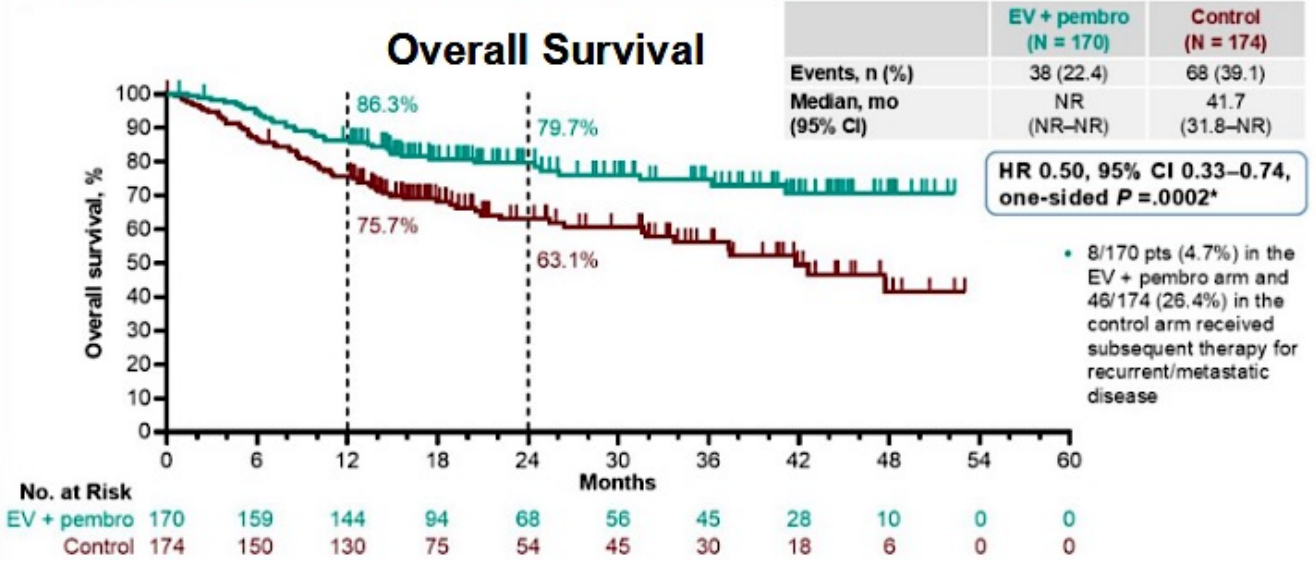
OS: HR 0.40, 95% CI 0.28–0.57



	EV + pembro (N = 170)	Control (N = 174)
Events, n (%)	48 (28.2)	95 (54.6)
Median, mo (95% CI)	NR (37.3–NR)	15.7 (10.3–20.5)

HR 0.40, 95% CI 0.28–0.57, one-sided *P* <.0001*

- 29/174 pts (16.7%) in the control arm received adjuvant nivolumab as of data cutoff per local guidelines/prescribing information



	EV + pembro (N = 170)	Control (N = 174)
Events, n (%)	38 (22.4)	68 (39.1)
Median, mo (95% CI)	NR (NR–NR)	41.7 (31.8–NR)

HR 0.50, 95% CI 0.33–0.74, one-sided *P* =.0002*

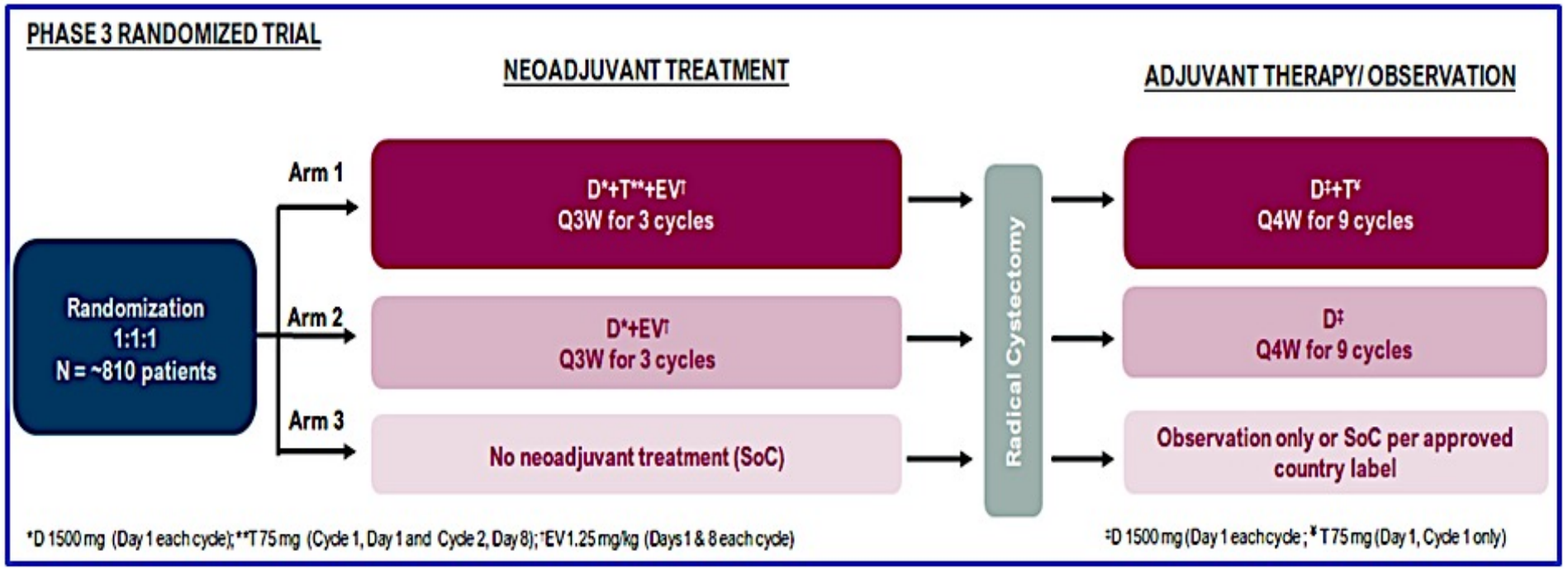
- 8/170 pts (4.7%) in the EV + pembro arm and 46/174 (26.4%) in the control arm received subsequent therapy for recurrent/metastatic disease

Christof Vulsteke, ESMO 2025; *N Engl J Med* 2026;394(13):1257-69.

Neoadjuvant

Phase 3 Study of Durvalumab (D) + Tremelimumab (T) + Enfortumab Vedotin (EV) or D + EV In Neoadjuvant Cisplatin-Ineligible Muscle-Invasive Bladder Cancer (VOLGA)

Adjuvant



Primary Endpoints

* Pathologic complete response
* Event-free survival (EFS)

Secondary Endpoints

* OS, DSS, QOL
* Pathologic downstaging to <pT2N0M0
* Safety / Tolerability

Interim Analysis of the Phase III VOLGA Trial Demonstrated Significant Improvement in Event-Free and Overall Survival With Perioperative Durvalumab Plus Neoadjuvant EV in Muscle-Invasive Bladder Cancer

Press Release: May 14, 2026

“High-level results from a planned interim analysis of the VOLGA Phase III trial showed perioperative treatment with durvalumab in combination with neoadjuvant enfortumab vedotin (EV) demonstrated statistically significant and clinically meaningful improvements in event-free survival (EFS) and overall survival (OS) in patients with muscle-invasive bladder cancer (MIBC) versus standard of care. Patients were ineligible for or had declined cisplatin-based chemotherapy. Patients in the comparator arm had a radical cystectomy (surgery to remove the bladder) with or without approved adjuvant treatment.

Perioperative durvalumab plus tremelimumab in combination with neoadjuvant EV demonstrated a statistically significant and clinically meaningful improvement in EFS and a favourable trend for OS; however, the OS data were not statistically significant at this planned interim analysis and will be formally reassessed at a subsequent analysis.”

https://www.astrazeneca.com/media-centre/press-releases/2026/imfinzi-ev-improves-efs-os-in-bladder-cancer.html

RTP RESEARCH TO PRACTICE

Conclusions

New Era in management of Cis-Ineligible MIBC

Case Presentation

65-year-old male with new diagnosis of Muscle Invasive Bladder Cancer

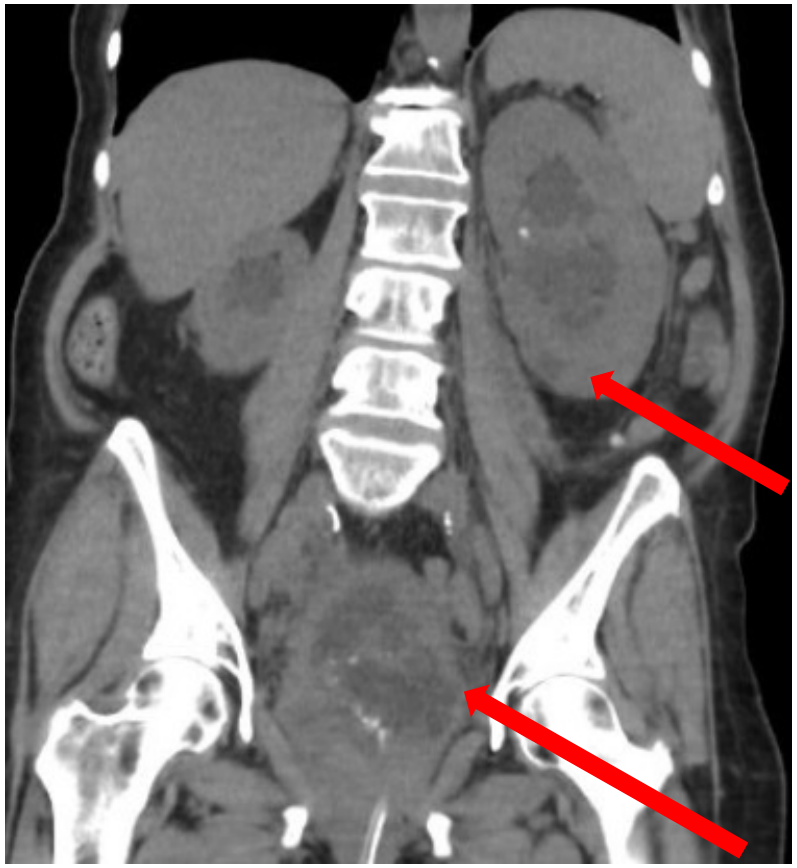
History of Present Illness:

65-year-old male presented with a year-long history of left flank pain and hematuria after intense workout.

CT chest did not reveal any evidence of metastatic disease, but the CT urogram was consistent with left sided mild hydronephrosis. Upon evaluation by Urology, he underwent TURBT that showed high grade urothelial cancer with muscularis propria invasion.

Therefore, patient was referred to medical oncology with the new diagnosis of

T3N0M0 muscle invasive bladder cancer with Left sided hydronephrosis



PreTURBT Image

Past Medical History:

Childhood asthma, mild hypertension, eczema

Past Surgical History:

Knee surgery

Family History:

Mother with uterine cancer, brother with prostate cancer

Social History:

Works as a hairdresser, does not drink alcohol, does not smoke cigarettes but using marijuana occasionally, No IVDU.

Married with a 30-year-old healthy son

Current Medications:

Multivitamin, Albuterol as needed, Cortisone cream as needed

Muscle Invasive Bladder Cancer Treatment Approach:

Patient is Cisplatin Ineligible with ***creatinine clearance of 45*** and therefore started on the Neoadjuvant regimen with

Enfortumab Vedotin/Pembrolizumab, followed by cystoprostatectomy and LN dissection that revealed pathologic complete response and completed the adjuvant therapy with 6 more cycles of enfortumab and 14 cycles of pembrolizumab.

Patient remains cancer free 3 years later

Discussion Questions

Now that perioperative pembrolizumab/enfortumab vedotin is available for cisplatin-ineligible patients with MIBC, are you recommending it in most cases? In which ones, if any, are you not?

Tolerability and Toxicity Profile of Enfortumab Vedotin

Margarita Huober, AGNP, AOCNP

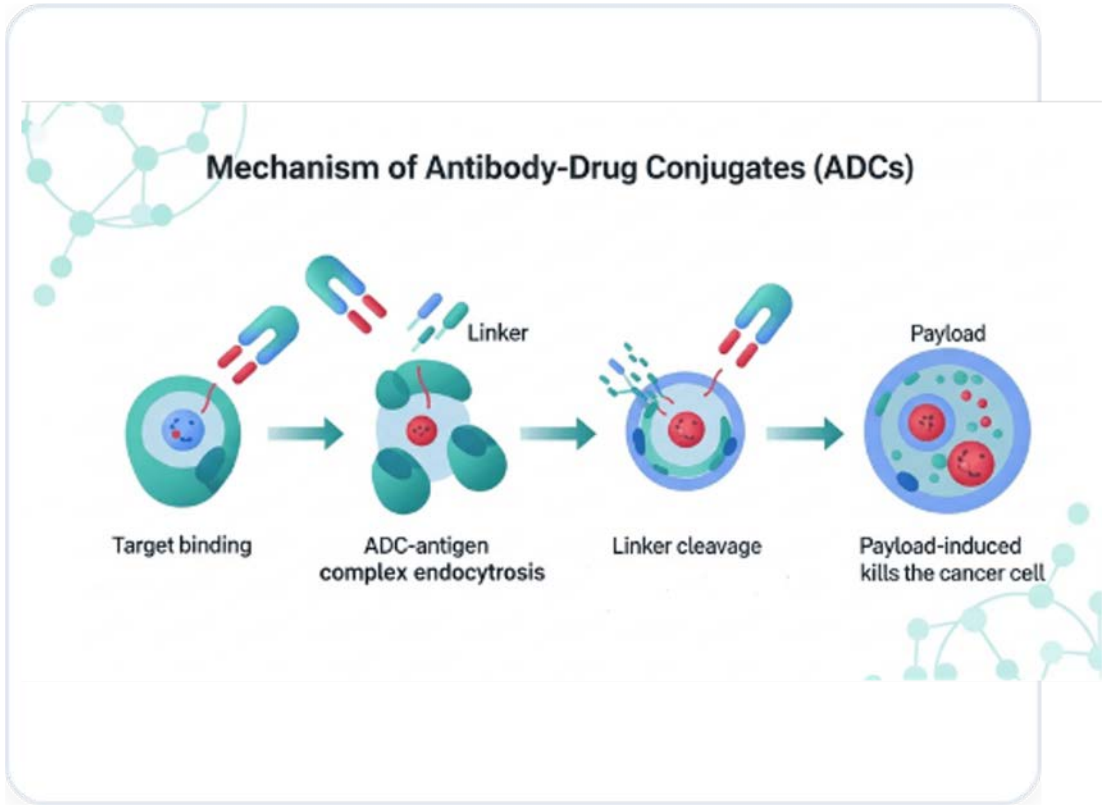
Stanford Health Care

SELECTIVE CYTOTOXIC DELIVERY

How It Works

Enfortumab Vedotin (EV) is a precision-targeted **Antibody-Drug Conjugate (ADC)**

- **The Target:** High affinity for **Nectin-4**, a protein found in ~97% of bladder cancers
- **The Payload:** MMAE, a potent chemotherapy-like medicine, is attached to the antibody
- **The Action:** The antibody binds to the cancer cell and releases the payload directly inside
- **Result:** Disrupts cell cycle, leading to the death of the cancer cell



MMAE: monomethyl auristatin E; Nectin-4: cell surface adhesion molecule.

SPECTRUM & INCIDENCE OF EV-RELATED ADVERSE EVENTS

Skin Reactions

Any Grade: ~67% | Grade 3+: ~14%

Median Onset: 0.6 months (Early)

Peripheral Neuropathy

Any Grade: ~50% | Grade 3+: ~7%

Median Onset: 6 months (Cumulative)

Hyperglycemia

Any Grade: ~12% | Grade 3+: ~6%

Median Onset: 0.5 months (Rapid)

Ocular Disorders

Any Grade: ~21% | Grade 3+: <1%

Secondary: Fatigue, Dry eye, Blurred vision

All-Cause Grade ≥3 TRAE INCIDENCE: ~56%

EV: enfortumab vedotin; G: grade; TRAE: treatment-related adverse event.

EV TOXICITY VS. PEMBRO IRAE

Toxicity	EV	Pembro	Quick Clinical Tip
Skin Rash	Flexural (groin, axillae); Onset: Days 1–14	Trunk-first, diffuse; Onset: Weeks–Months	**Steroids fix pembro, not EV**
Neuropathy	~50%; Symmetric, sensory, Gradual/Cumulative	~1%; Asymmetric, motor, Acute onset	**Slow over cycles → EV** **Sudden + weakness → Pembro**
Hyperglycemia	Common (6% G≥3); Gradual; No autoantibodies	Rare (1%); New-onset T1DM with DKA; **+ Antibodies**	**Check T1DM Antibodies** **Positive result → Pembro**
Ocular	~21% (Dry eye, blur); Nectin-4 in epithelium	Rare (Uveitis)	**Almost always EV** **Uveitis with pain/photophobia → Pembro**

IRAE: immune-related adverse event; DKA: diabetic ketoacidosis | EV: enfortumab vedotin | G: grade | T1DM: type 1 diabetes mellitus

Postow MA, et al. **N Engl J Med.** 2018;378(2):158-168. Powles T, et al. **N Engl J Med.** 2024;390(10):875-888. Vulsteke C, et al. **N Engl J Med.** 2026. Yajima S, et al. **JAMA Netw Open.** 2025;8(3):e250250.

EV SKIN TOXICITY: CLINICAL MANAGEMENT

DOSE MANAGEMENT

G1: Continue | G2–3: Hold → Resume same dose or reduce| Recurrent G3 or G4: discontinue

Grade 1

<10% BSA

- Moderate topical steroids (Triamcinolone)
- Emollients
- Antihistamines

Grade 2

10–30% BSA

- High-potency topical steroids
- Antihistamines
- Consider Dermatology referral

Grade 3

>30% BSA / ADL

- High-potency topicals (Clobetasol 0.05%)
- Prednisone 0.5–1 mg/kg
- Urgent Derm consult / consider inpatient care

Grade 4

EMERGENCY

- Immediate specialized inpatient (Burn Unit/ICU)
- Intensive management (SJS/TEN protocols)

BSA: Body Surface Area; **G1-4:** Toxicity Grade; **SJS: Stevens-Johnson syndrome; TEN:** Toxic Epidermal Necrolysis

Postow MA, et al. **N Engl J Med.** 2018;378(2):158-168. Powles T, et al. **N Engl J Med.** 2024;390(10):875-888. Vulsteke C, et al. **N Engl J Med.** 2026. Yajima S, et al. **JAMA Netw Open.** 2025;8(3):e250250.

EV PERIPHERAL NEUROPATHY: MANAGEMENT

Dose Reductions: 1.25 mg/kg → 1.0 mg/kg → 0.75 mg/kg → 0.5 mg/kg

G1: MILD

CLINICAL DEFINITION

Asymptomatic paresthesia or loss of DTRs; no functional impact

"I have a slight tingle in my toes, but I can walk normally."

CONTINUE EV
MAINTAIN 1.25 MG/KG

G2: MODERATE

CLINICAL DEFINITION

Sensory loss interfering with function (e.g., buttoning clothes)

"Picking up coins is hard and I'm clumsy with buttons."

WITHHOLD EV
RESUME 1.25 MG/KG IF ≤G1

G2: RECURRENT

CLINICAL DEFINITION

Functional interference repeating after prior G2 event

"The numbness is back. It's getting harder to do daily tasks."

WITHHOLD EV
RESUME 1.0 MG/KG IF ≤G1

G3+: SEVERE

CLINICAL DEFINITION

Severe symptoms; limiting self-care ADLs (bathing, feeding)

"I cannot dress myself and I feel very unsteady."

DISCONTINUE
PERMANENT CESSATION

ADL: activities of daily living | **DTR:** deep tendon reflex | **EV:** enfortumab vedotin | **G:** grade

Postow MA, et al. **N Engl J Med.** 2018;378(2):158-168. Powles T, et al. **N Engl J Med.** 2024;390(10):875-888. Vulsteke C, et al. **N Engl J Med.** 2026. Yajima S, et al. **JAMA Netw Open.** 2025;8(3):e250250.

EV HYPERGLYCEMIA MANAGEMENT

SCREENING	SCREENING & MONITORING Check Baseline HbA1c before C1D1. Monitor blood glucose before each cycle	**PRIOR TO CYCLE 1** **Early identification of risk factors is critical**
FDA DOSING	WITHHOLD THRESHOLD Glucose >250 mg/dL → Withhold EV until glucose improves to ≤250 mg/dL	**HOLD → RESUME** **Resume at** Same Dose **(No reduction required)**
TREATMENT	ADA STANDARDS Metformin is first-line for drug-induced insulin resistance; some patients may require **insulin**	**FIRST-LINE** **Most cases controlled without stopping EV**
FATAL WARNING	DKA SAFETY EDUCATION Educate on thirst, polyuria, nausea, and confusion	**URGENT EDUCATION** **Report symptoms immediately**

DKA: diabetic ketoacidosis | EV: enfortumab vedotin | HbA1c: hemoglobin A1c

Postow MA, et al. **N Engl J Med.** 2018;378(2):158-168. Powles T, et al. **N Engl J Med.** 2024;390(10):875-888. Vulsteke C, et al. **N Engl J Med.** 2026. Yajima S, et al. **JAMA Netw Open.** 2025;8(3):e250250.

EV OCULAR TOXICITY

RECOGNITION

- Dry eye, blurred vision, irritation
- Pain or foreign body sensation

PREVENTION

- Artificial Tears (4x daily)
- Avoid contact lenses
- Warm compresses + lid hygiene

MONITORING

- Baseline vision exam pre-Cycle 1
- Evaluate for vision changes at every visit

DOSE MODIFICATION

- Refer to Ophthalmology
- Withhold/Reduce if symptomatic

Starting	1.25 mg/kg
1st Redux	**1.0 mg/kg**
2nd Redux	**0.75 mg/kg**
3rd Redux	**0.5 mg/kg**

EV: enfortumab vedotin

Chen H, et al. **Front Immunol.** 2024;15:1495137.

EV TOXICITY: TAKEAWAYS

RECOGNIZE EARLY

- Skin: Typically early onset
- Neuropathy: Cumulative burden
- Hyperglycemia: risk for DKA
- Ocular: Corneal surface / dry eye

ACT EARLY

- Hold or adjust based on severity
- Check **glucose** each cycle
- Start artificial tears Day 1

TOXICITY DRIVERS

- EV: Skin, neuropathy, hyperglycemia
- IO: Systemic (GI, lung, endocrine)
- Overlap exists → evaluate carefully

WHY THIS MATTERS

- Prevent irreversible toxicity (Neuro)
- Maintain treatment intensity
- Avoid delays in curative care

EV: enfortumab vedotin; IO: immunotherapy; DKA: Diabetic Ketoacidosis

Postow MA, et al. **N Engl J Med.** 2018;378(2):158-168. Powles T, et al. **N Engl J Med.** 2024;390(10):875-888. Vulsteke C, et al. **N Engl J Med.** 2026. Yajima S, et al. **JAMA Netw Open.** 2025;8(3):e250250.

CASE PRESENTATION: BALANCING EFFICACY AND TOXICITY WITH ENFORTUMAB VEDOTIN

INITIAL PRESENTATION

MK is 65 yo Male

Self-employed Electrician

"I can't afford to lose use of my hands."

CANCER DIAGNOSIS

cT3aN0M0 Muscle-Invasive Bladder Cancer (High-Grade)

BASELINE RISK

Type 2 Diabetes (HbA1c 7.4%) + Grade 1 Neuropathy

CONTRAINDICATION

Cisplatin-ineligible (CrCl 45 mL/min)

MANAGEMENT GOAL

Deliver Neoadjuvant EV + Pembro → Radical Cystectomy

| Pre-Treatment ctDNA: 1.8 MTM/mL (Positive)

EMERGING TOXICITY WITH FUNCTIONAL IMPACT

Cycle 1: Day 10

- Flexural Rash (G1): Resolved with emollients + Triamcinolone 0.1% BID.
- Result: Fully resolved; no dose change.

Cycle 2: Day 15–21

- Neuropathy (G2): Progressive fingertip numbness.
- Functional Impact: Dropping tools; slower motor tasks.
- Dilemma: Risk of irreversible injury vs. finishing Cycle 3.

PRE-TX ctDNA:
1.8 MTM/mL

→

POST-C2 ctDNA:
0.0 MTM/mL

Molecular Response Confirmed

BID: twice daily | **G1/G2:** Grade 1/2 | **EV:** enfortumab vedotin | **ctDNA:** circulating tumor DNA

MANAGEMENT DECISION & PRE-OP REASSESSMENT

DECISION

Stopped Neoadjuvant Therapy early (after 2 cycles) to avoid irreversible neuro-toxicity

PREOPERATIVE RE-ASSESSMENT

- Cystoscopy: No visible tumor; clear bladder wall
- Imaging: No measurable mass; no lymphadenopathy

NEUROPATHY MANAGEMENT

- Gabapentin: Titrated to 300 mg TID
- Referrals: OT + Diabetes optimization
- Stability: No rapid reversal; G1–2 stable

OT: occupational therapy; **TID:** three times daily; **G1–2:** toxicity grade 1–2

SURGICAL OUTCOME & TEACHING POINTS

FINAL PATHOLOGY

ypT0N0 (pCR)

NODAL STATUS

0/16 Nodes

RECOVERY

Return to Work

CLINICAL TAKEAWAYS

- Act Early: **Intervene at G1–2 neuro in high-risk (T2DM) patients to preserve livelihood**
- ctDNA Kinetics: **Molecular clearance (1.8 → 0.0) can support an early transition to surgery**
- Stability is the Goal: **Holding treatment is damage control; do not wait for full neuro-recovery**
- Perioperative Priority: **Deliver enough therapy to clear disease, but stop before permanent toxicity**

ctDNA: circulating tumor DNA; **EV:** enfortumab vedotin; **G1-2:** Grade 1-2; **pCR:** pathological complete response; **T2DM:** type 2 diabetes

Discussion Questions

If a patient with MIBC experiences tolerability issues during neoadjuvant pembrolizumab/enfortumab vedotin therapy, do you always attempt to continue both agents in the adjuvant setting? What is your threshold for discontinuing one or both?

Agenda

Introduction: Basic Biology of Nonmetastatic Urothelial Bladder Cancer (UBC)

Module 1: Systemic Therapy for Cisplatin-Eligible Patients with Muscle-Invasive Bladder Cancer (MIBC)

Module 2: Evolving Approach to Systemic Therapy for Cisplatin-Ineligible Patients with MIBC

Module 3: Immune Checkpoint Inhibitors in Non-Muscle-Invasive Bladder Cancer

Module 4: Novel Intravesical Therapies for Nonmetastatic UBC

Immune Checkpoint Inhibitors in NMIBC

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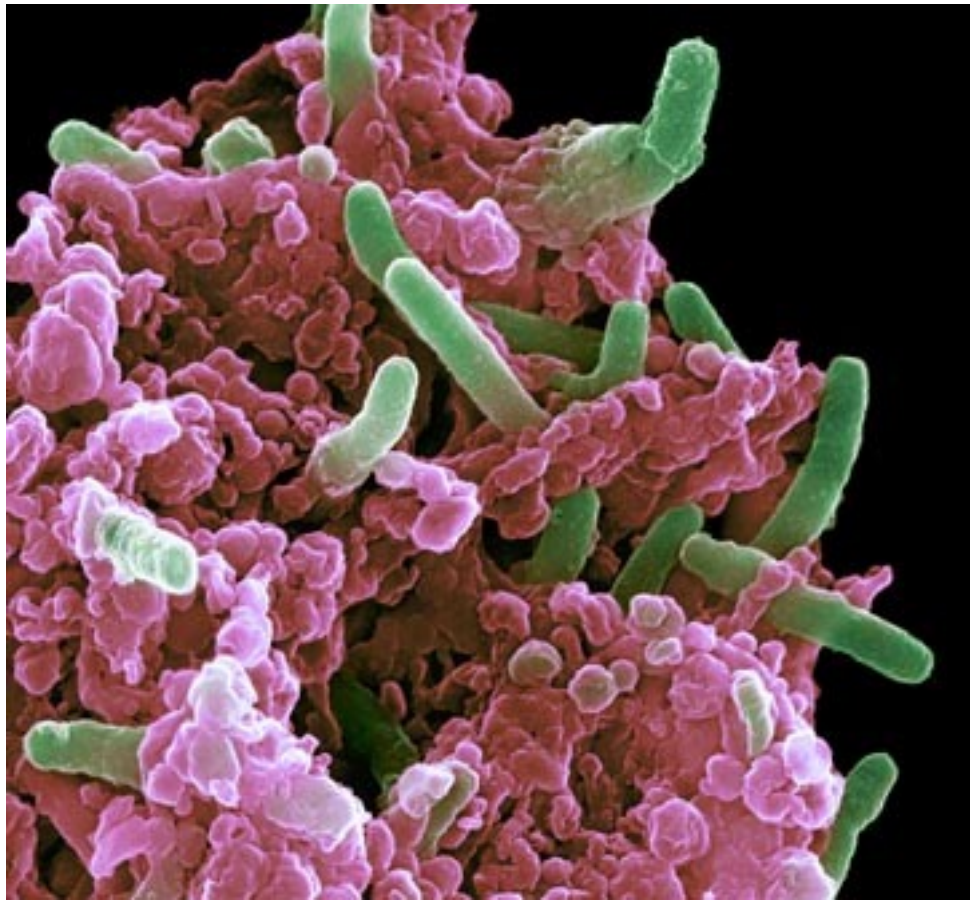
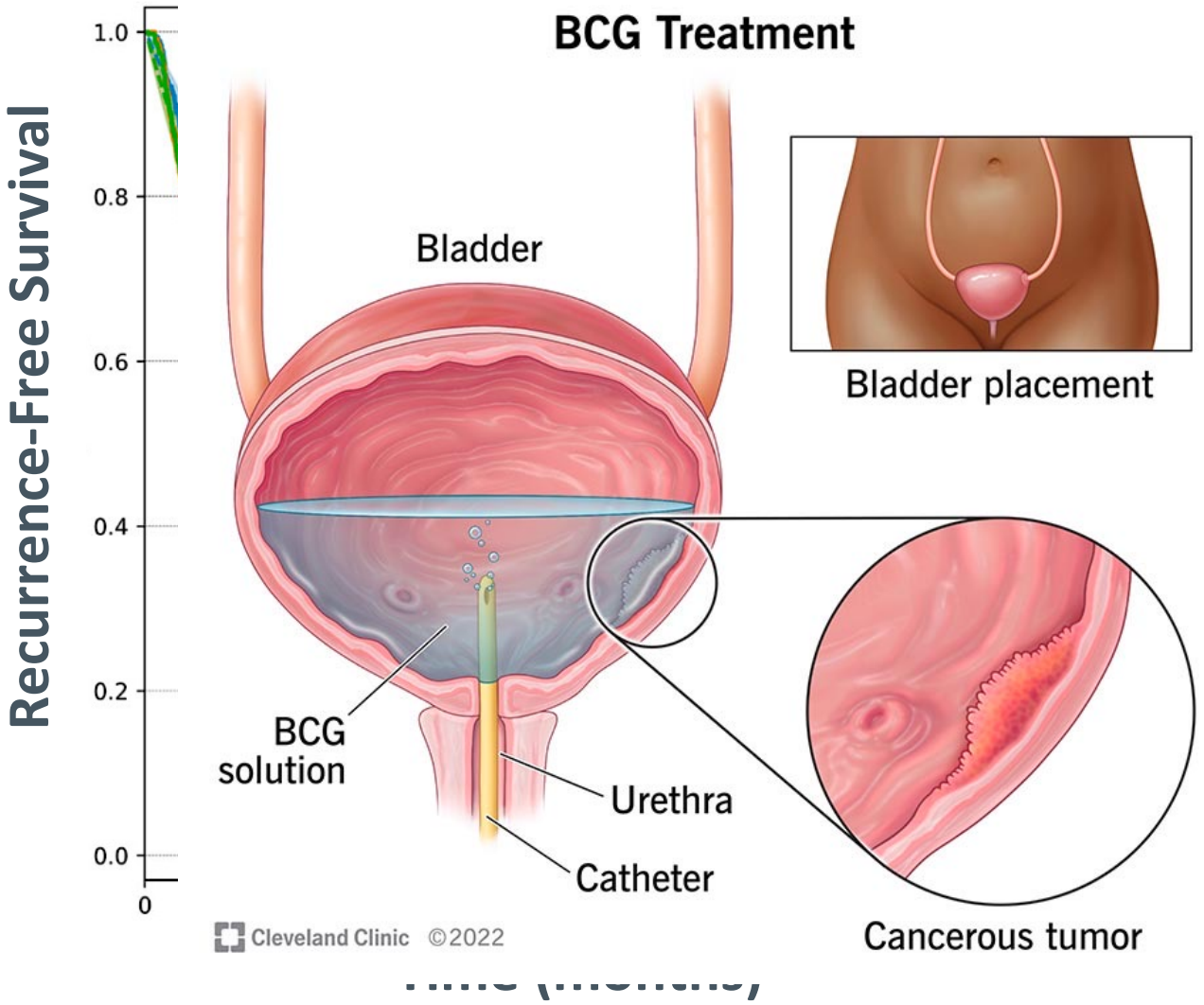
BCG is the Standard of Care for treatment-naïve NMIBC

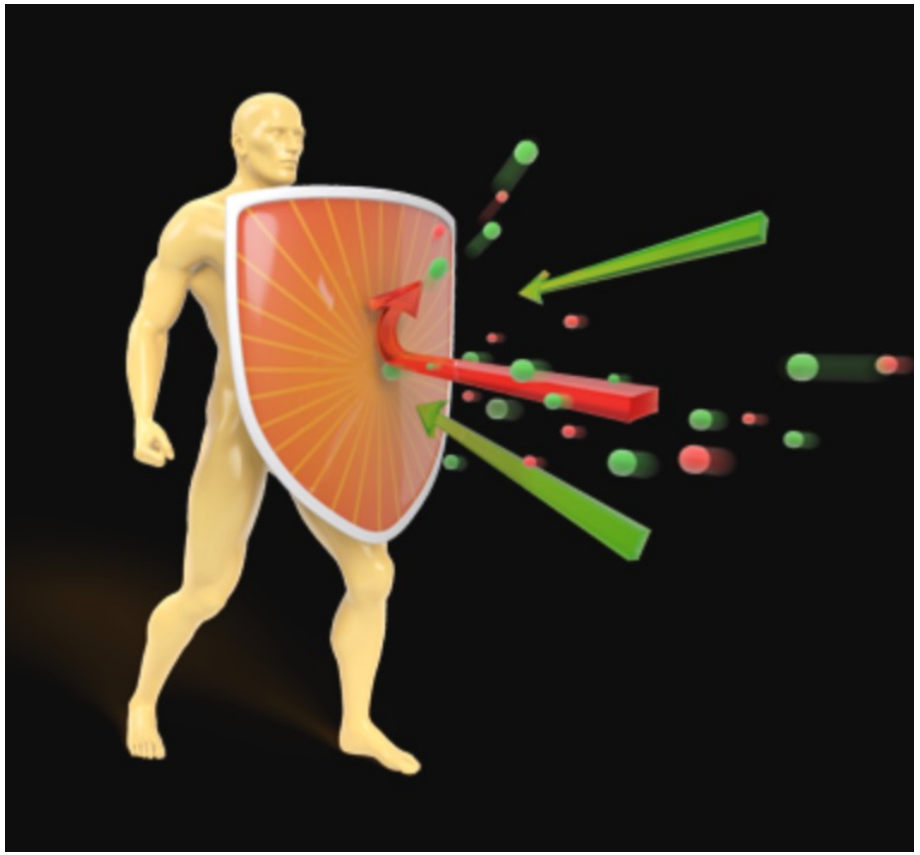




Nature Medicine 2011, Subiela et al BJUI 2026

Why add PD-1 immunotherapy to BCG?

- Immunologically
  - BCG makes cancer cells increase PD-1
    - "Shield" against immune cells
    - PD-1 therapies "remove the shield"

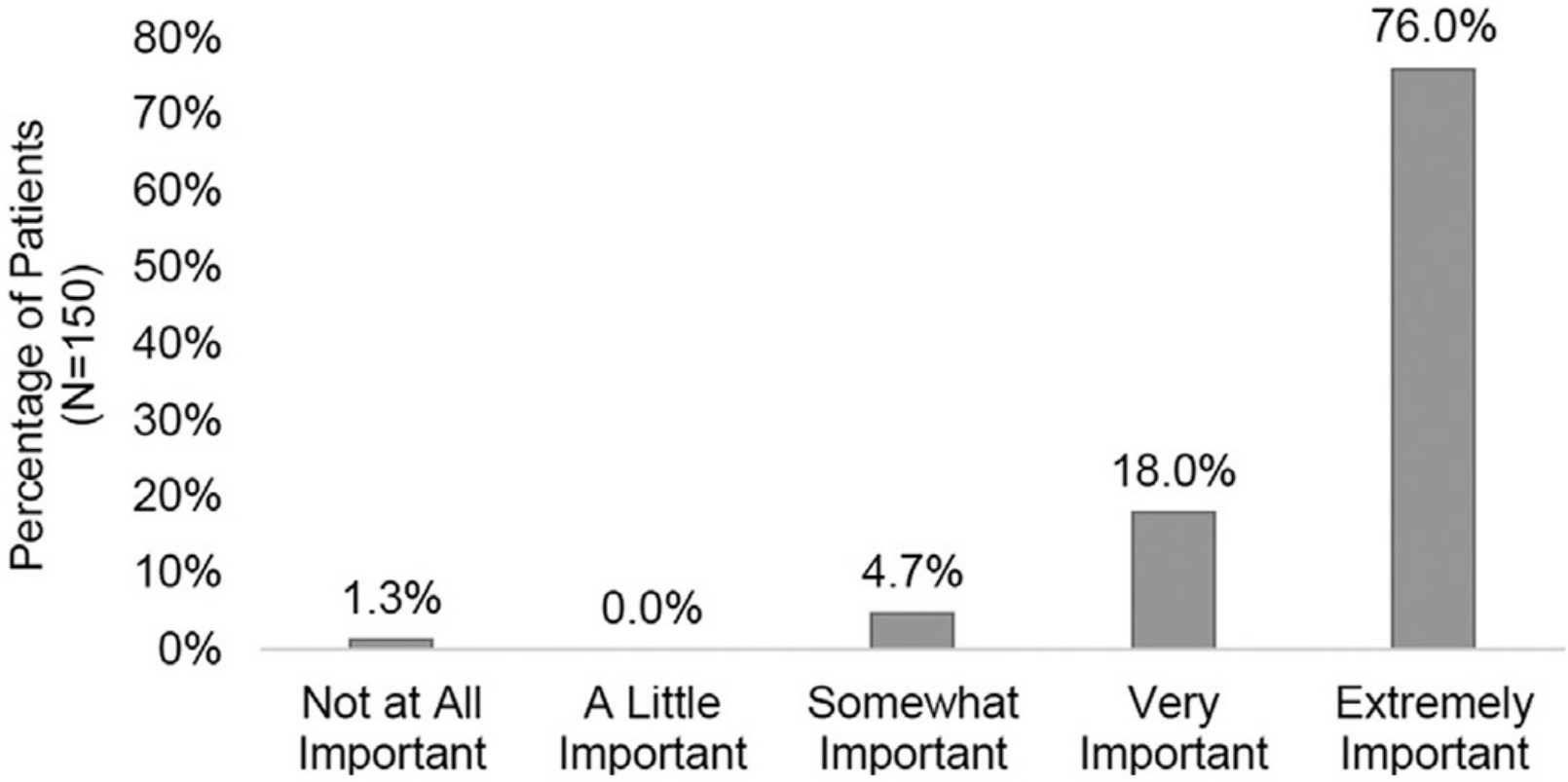


- Clinically
  - Avoids cystectomy (potentially!)
  - Synergy of 2 immunotherapies
    - BCG addresses localized disease
    - PD-1 addresses any disease beyond the urothelium

Wang et al OncoTarg and Therapy 2018, Fukumoto Ann Surg Onc 2018, Hashizume et al Oncotarget 2018, Lim et al Front Immunol 2021

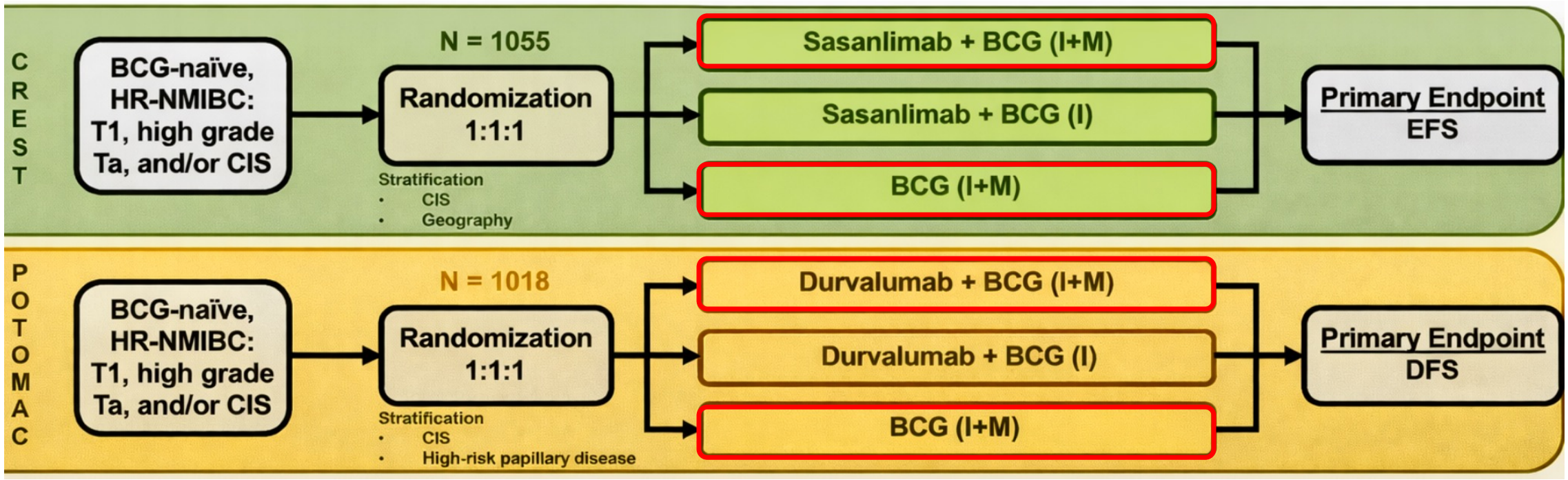
The Patient Perspective?

How important is it to keep the bladder and avoid cystectomy?



Kopenhafer L et al, Urol Oncol 2024

Studies to discuss today



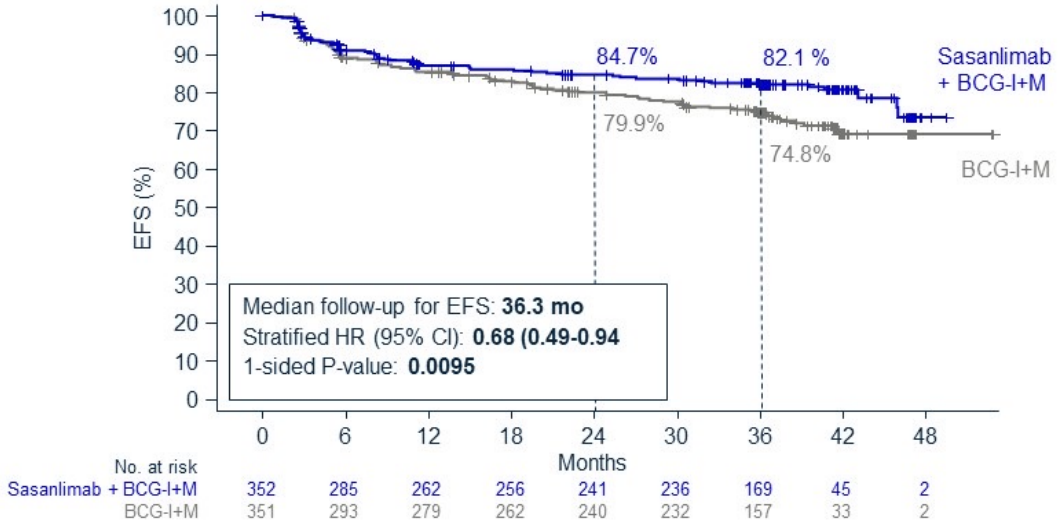
HR-NMIBC = High-risk Non-muscle invasive bladder cancer; I = Induction; M = Maintenance; EFS = Event-free survival; DFS = Disease-free survival

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

CREST

2 years BCG

2 years Sasanlimab



EFS HR 0.68

primary endpoint

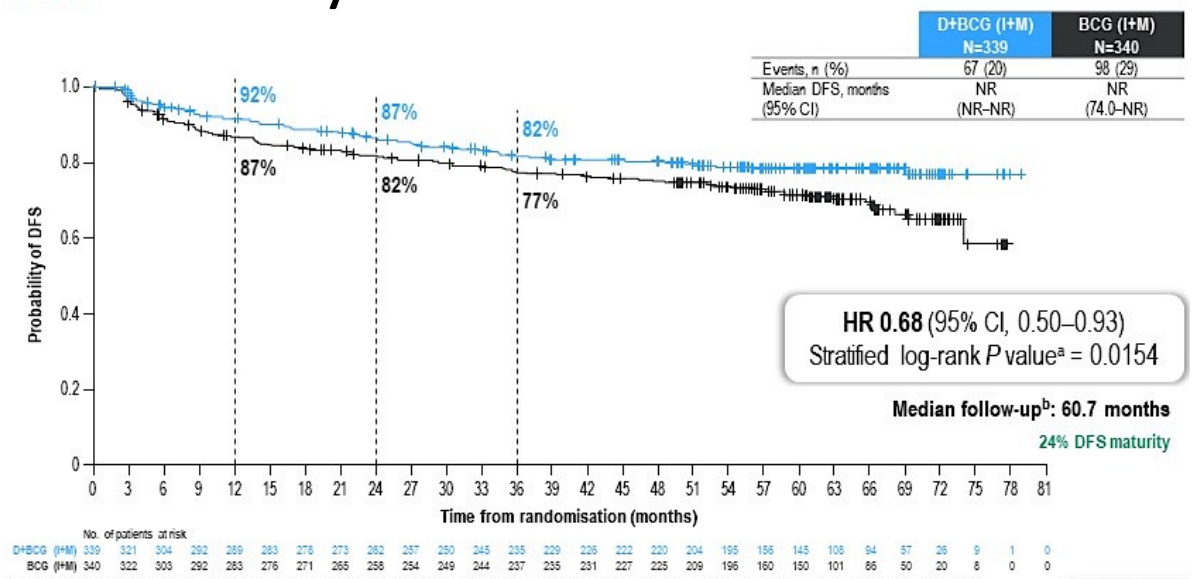
OS HR 1.13 (0.68-1.87)

Gr 3 TRAE 29% vs 5.4%

POTOMAC

2 years BCG

1-year Durvalumab



EFS HR 0.68

primary endpoint

OS HR 0.8 (0.53-1.20)

Gr 3 TRAE 21% vs 4%

Shore NS et al, AUA 2025 / Nat Med 2025, De Santis M et al, ESMO 2025 / Lancet 2025, Hahn GU ASCO 2026

Impact on Practice

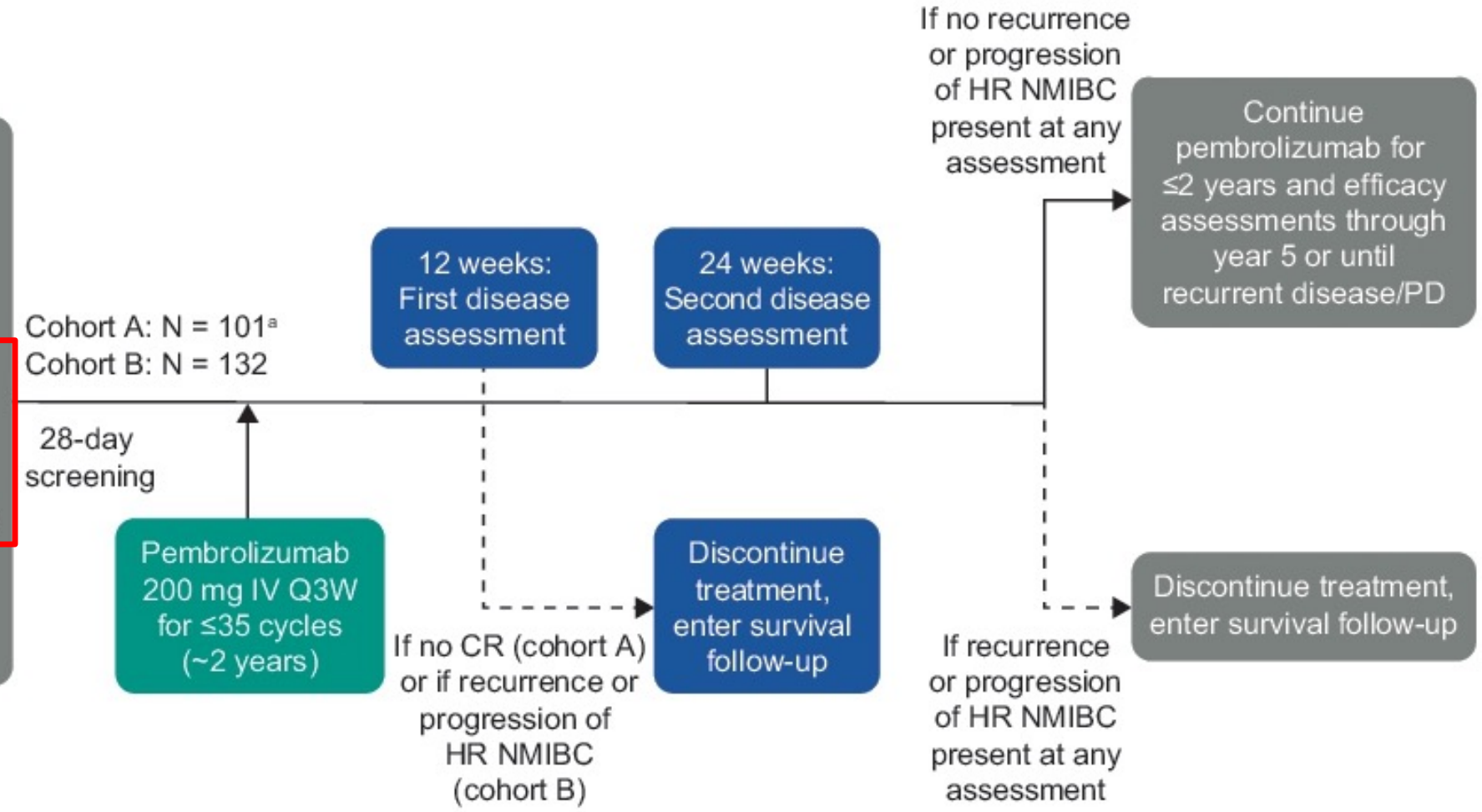
- Either Sasanlimab or Durvalumab combined with BCG induction and maintenance **may** become an option for high-risk BCG-naïve NIMBC
  - Benefit mostly in T1 (highest risk) population
  - Awaiting KEYNOTE-676 trial in similar population
- Are autoimmune side effects worth it?
  - How to balance EFS (positive), OS (immature) and Toxicity (real)?
  - Likely will allow some patients to avoid cystectomy
  - But… multiple later-line therapies available for NMIBC
- Who will be giving this therapy? Urologists? Medical Oncologists?

Can we “save” PD-1 for BCG-unresponsive patients?

KEYNOTE 057

Key Eligibility Criteria

- Patients with HR NMIBC (per US FDA criteria) unresponsive to BCG who declined to undergo or were ineligible for RC
- Cohort A: CIS with or without papillary disease (high-grade Ta or any T1)
- Cohort B: papillary tumors only (high-grade Ta or any T1) without CIS
- TURBT ≤12 weeks prior to first dose of trial treatment
- ECOG PS 0-2



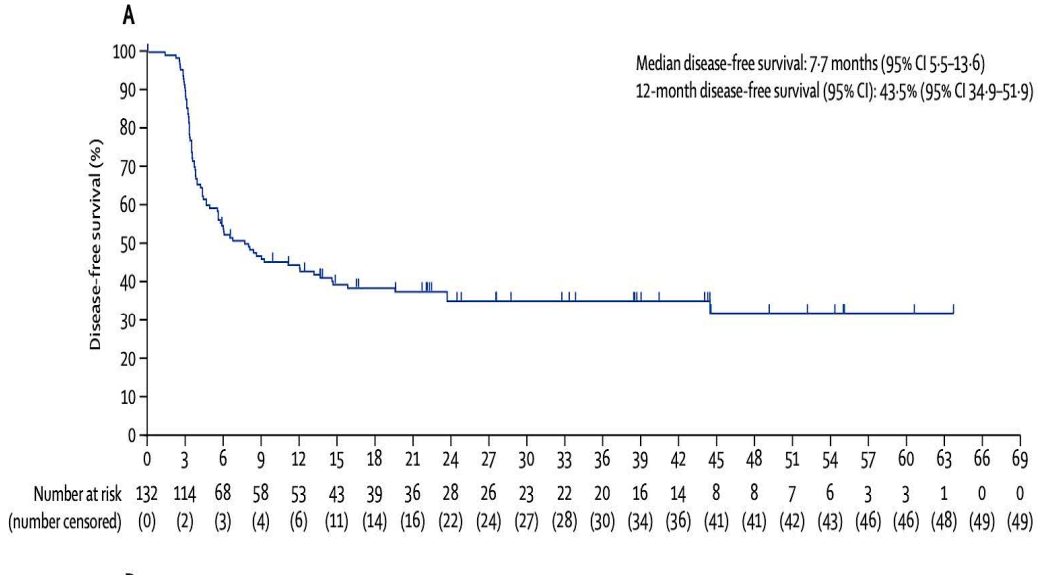
Li et al ASCO 2024

KEYNOTE 057: Pembrolizumab for High-risk (HR) BCG-unresponsive NMIBC

HR NMIBC **with** CIS

- 41% CR rate at 3 months
  - Median duration of CR 16.2 month
  - 9.3% (n=9) remain in CR at 45 months

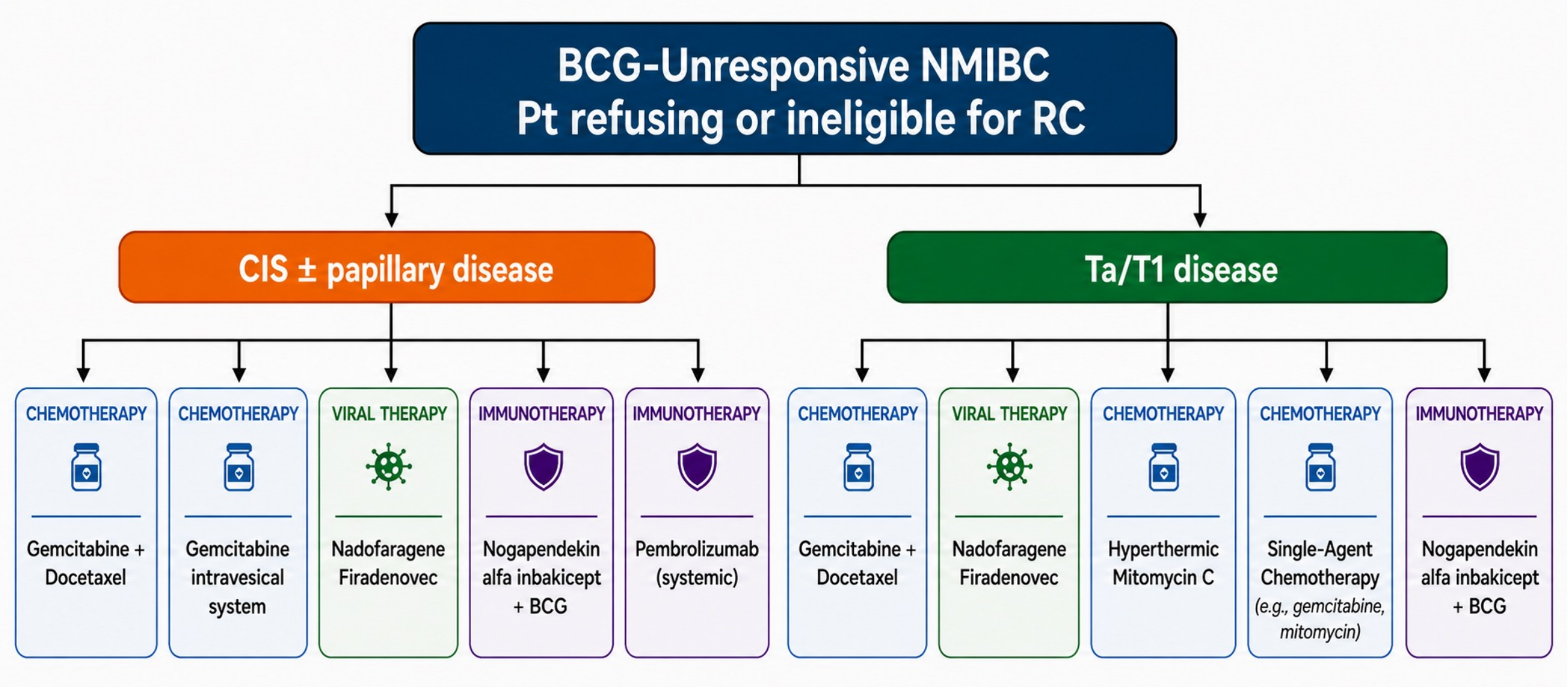
HR NMIBC **without** CIS



- 12 month DFS: 43%
- 36 month DFS: 33%

Balar et al Lancet Onc 2021, Necchi et al Lancet Onc 2024

Many intravesical options for BCG-unresponsive NMIBC!

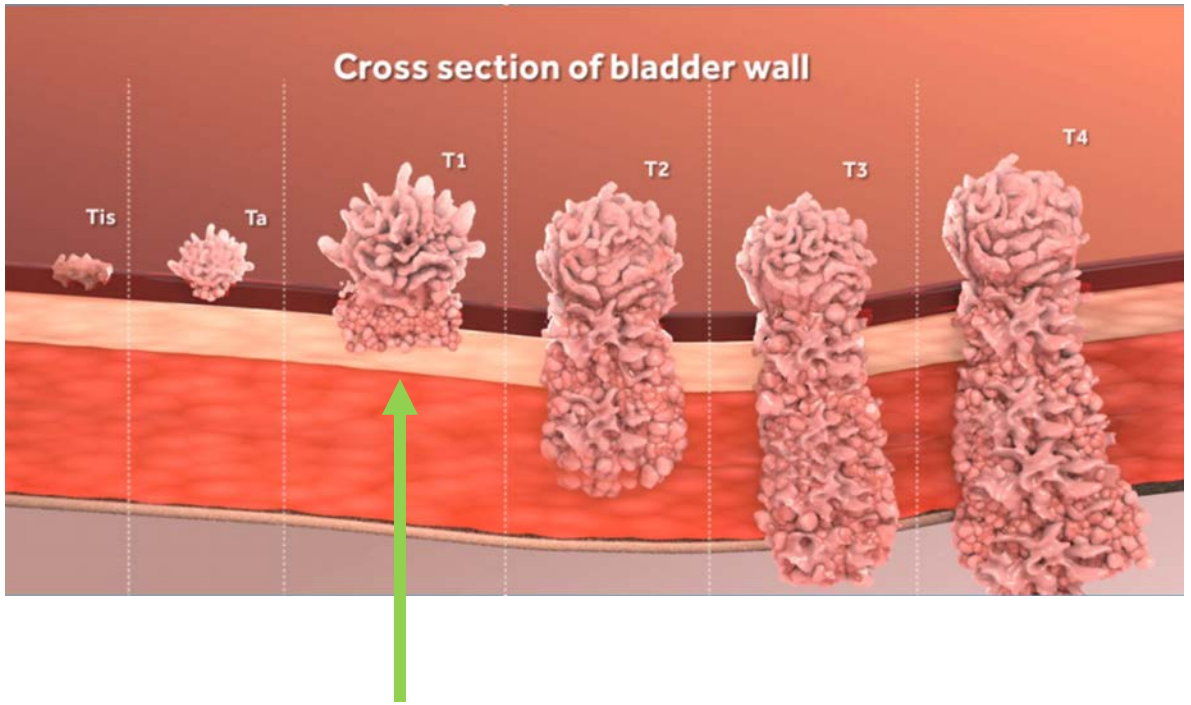


Adapted from: Li and International Bladder Cancer Group, Eur Urol, 2024

Case Presentation

Clinical Case

- 62 yo M with second-hand tobacco exposure as a child, and new hematuria
  - Urine cytology suspicious (Paris IV)
- Cysto/TURBT: HG T1 NMIBC
- SH: Avid outdoorsman, enjoys rock-climbing
  - “I do not want to have a cystectomy… ever”

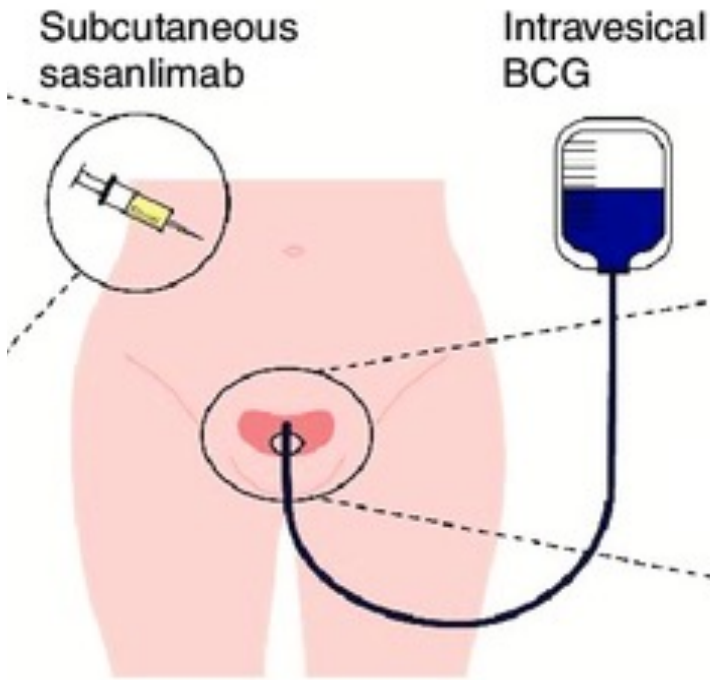


Follow up with Urology

- Discusses role of BCG, about a 30-50% chance of relapse
- “Isn’t there anything we can do to improve chances of cure?”
- Enrolls in the Phase 3 trial of Sasanlimab + BCG

Clinical Case

- Tolerates therapy well overall
- Course c/b hypothyroidism requiring levothyroxine
  - Grade 1 pruritis responsive to antihistamines/topical steroid
- Cystoscopy/TURBT negative after induction, and maintains in a CR at present
- Still mountaineering!



Steinberg et al Fut Med 2024

Discussion Questions

Which patients with NMIBC represent ideal candidates for anti-PD-1/PD-L1 antibodies in combination with BCG? If this strategy were to reach the clinic, would you prefer it for all patients with high-risk disease, or are there some for whom you would still opt for BCG alone or some other strategy?

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Module 4: Novel Intravesical Therapies for Nonmetastatic UBC

Novel Intravesical Therapies for Nonmetastatic UBC

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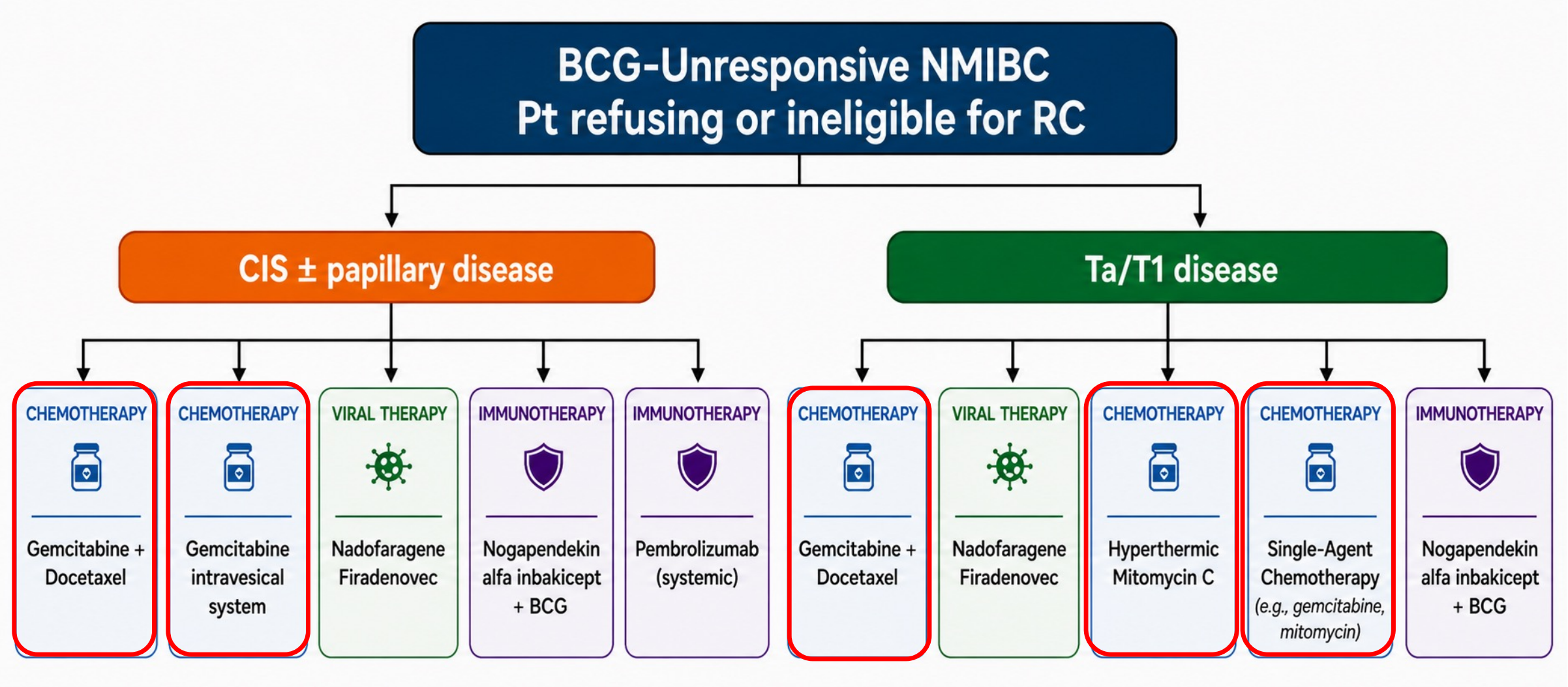
San Francisco, California

@DrTFriedlander UCSF

Many intravesical options for BCG-unresponsive NMIBC!



Adapted from: Li and International Bladder Cancer Group, Eur Urol, 2024

Intravesical Chemotherapy for NMIBC

Pros

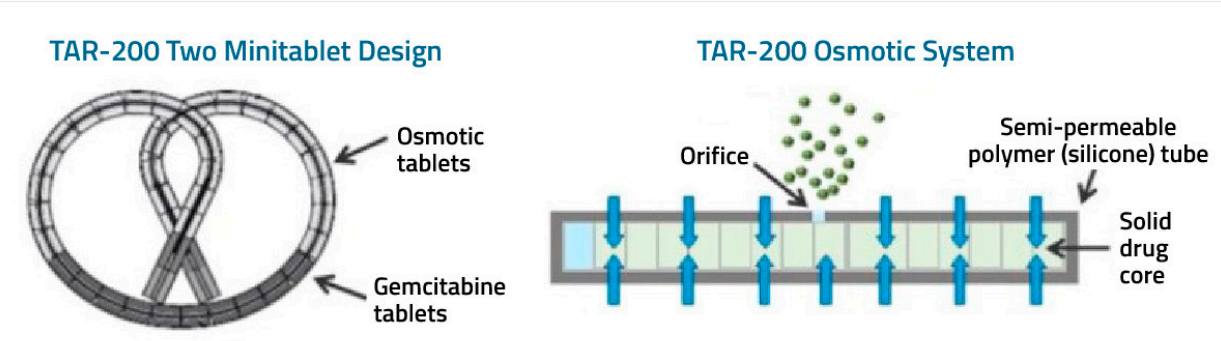
- Delivered directly to cancer cells
- High concentration in urine
- Generally well-tolerated
- Years of safety and efficacy data
- Cost is low

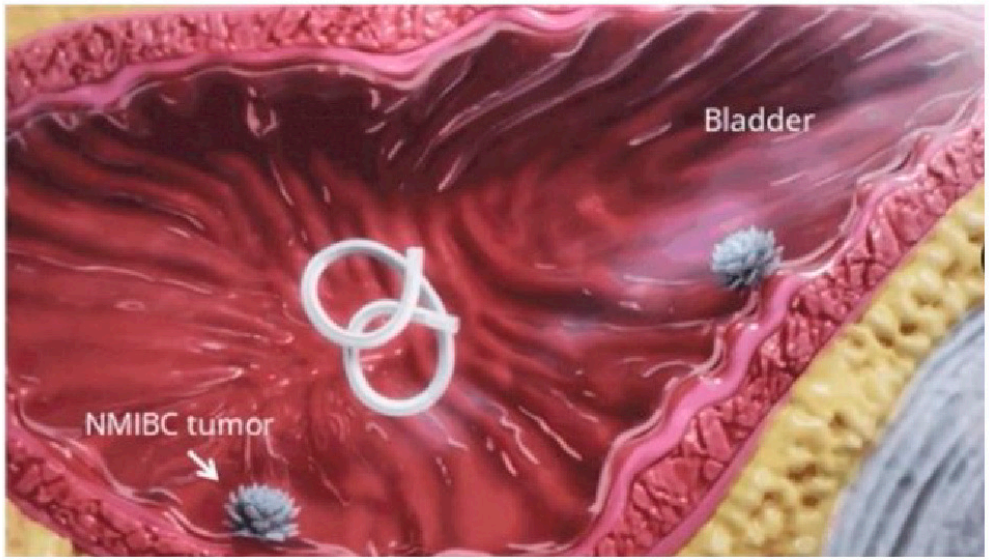
Cons

- Short drug exposure (1h)
- Diluted by urine over time
- Repeated catheterizations (weekly x 6 induction)
- Less effective in later lines

Intravesical Gemcitabine Delivery Device (TAR-200)

- Silicone tube containing solid gemcitabine
  - Continuous release over 3 weeks
  - No systemic exposure
  - Fewer office visits
  - Well tolerated
  - But does it work…?





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

NCT04640623

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

R

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

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

- TAR-200 Monotherapy *Cohort 4* (N=52) — *Enrollment completed*

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

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

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

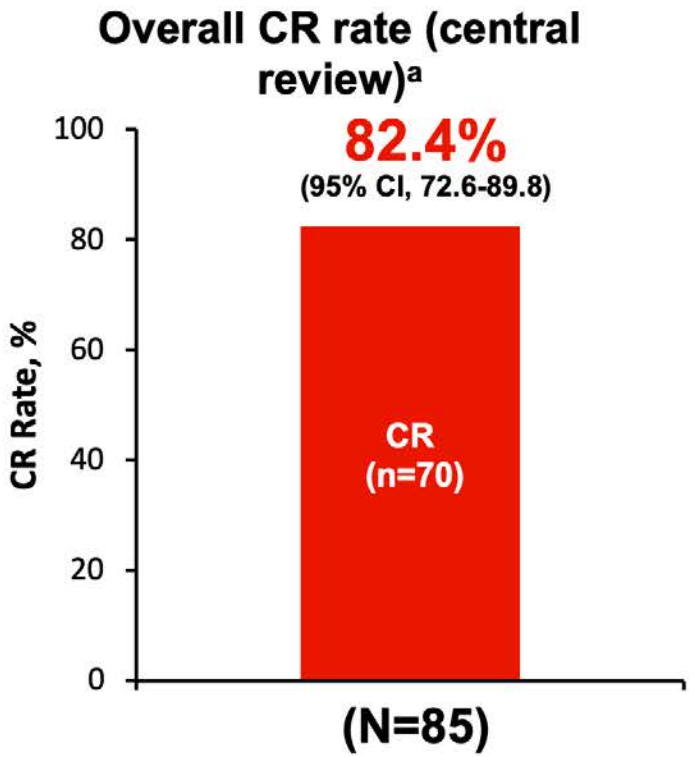
Cohort 4:
Primary end point
- DFS

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

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

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

Most patients respond…



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

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

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

FDA Breakthrough Therapy Designation

Daneshmand S, et al. *J Clin Oncol*. 2025 Nov 20;43(33):3578-3588.

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

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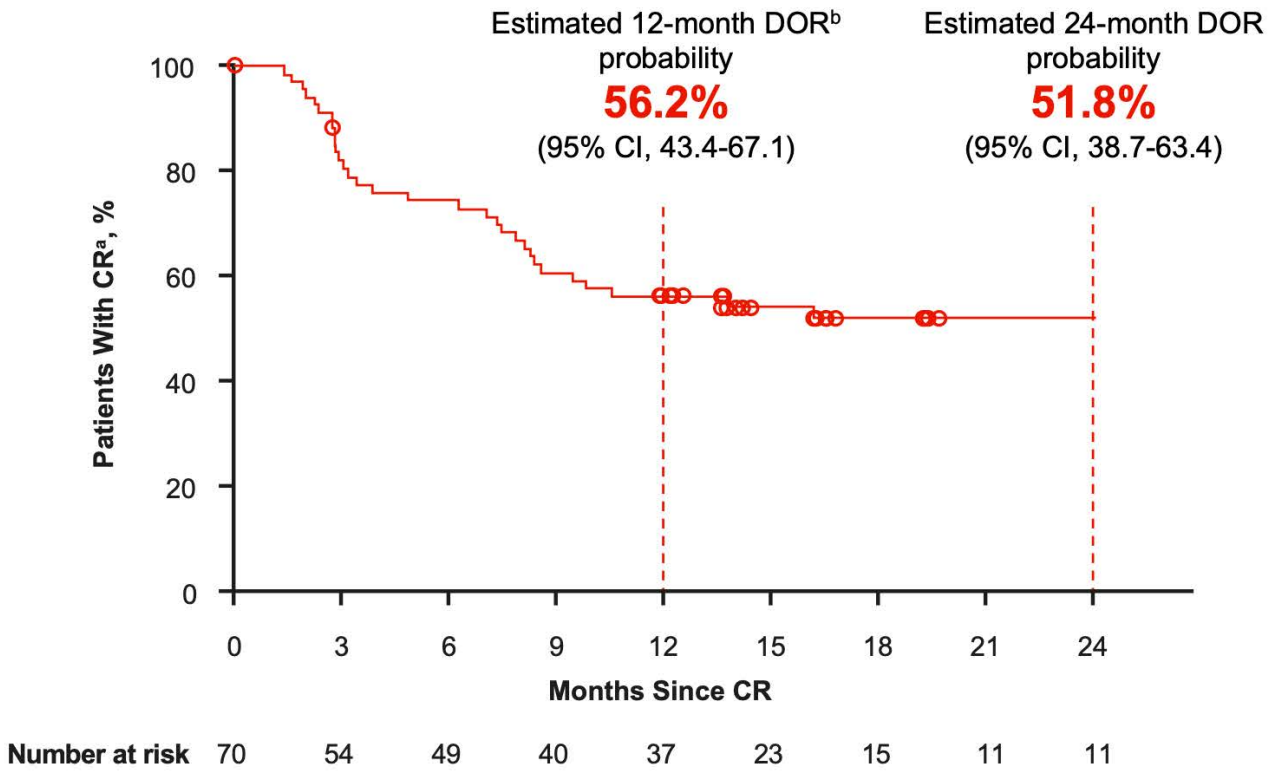
…and some responses are durable!



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

Daneshmand S, et al. *J Clin Oncol*. 2025 Nov 20;43(33):3578-3588.

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

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Treatment is generally well-tolerated

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

Patients With E...nts, n (%)	TAR-200 Monotherapy *Cohort 2* (N=85)[c]	
	Any Grade	Grade ≥3
	71 (83.5)	11 (12.9)
e,f		
	37 (43.5)	0
	34 (40.0)	0
	21 (24.7)	0
	19 (22.4)	1 (1.2)
	14 (16.5)	0
	9 (10.6)	4 (4.7)
	7 (8.2)	2 (2.4)
	7 (8.2)	0
Noninfective cystitis	6 (7.1)	0
Urinary incontinence	5 (5.9)	0

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

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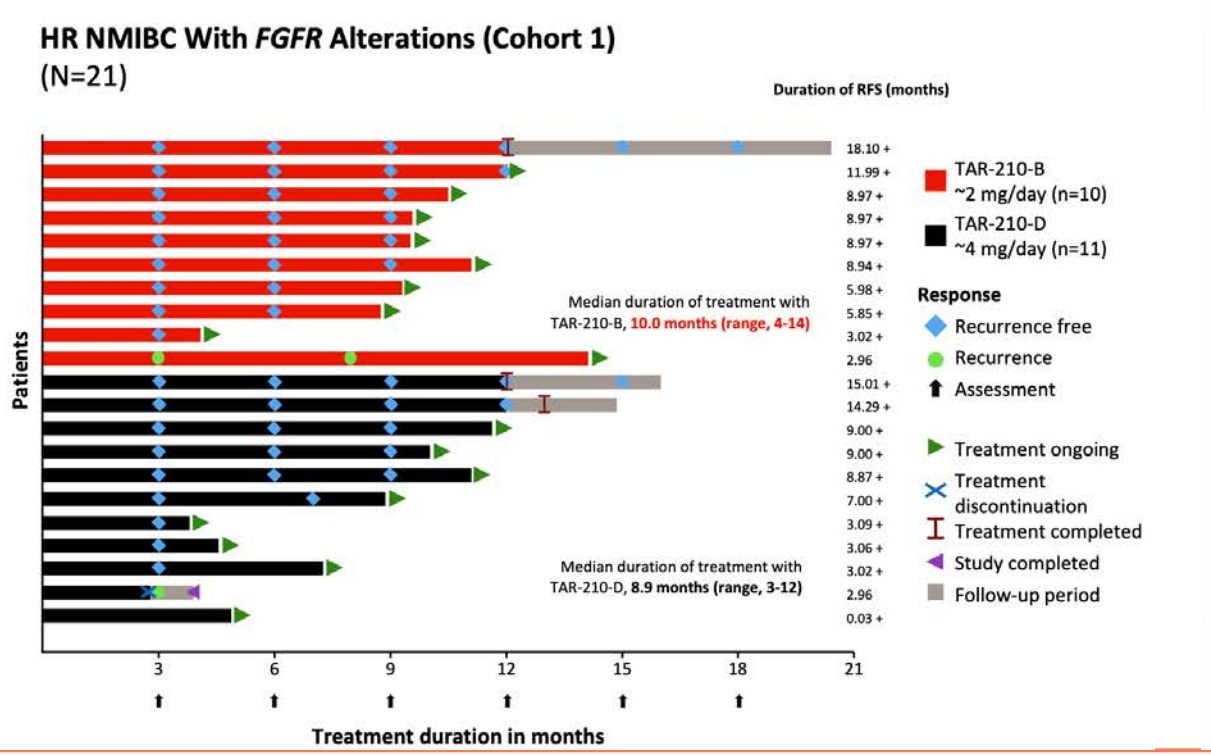
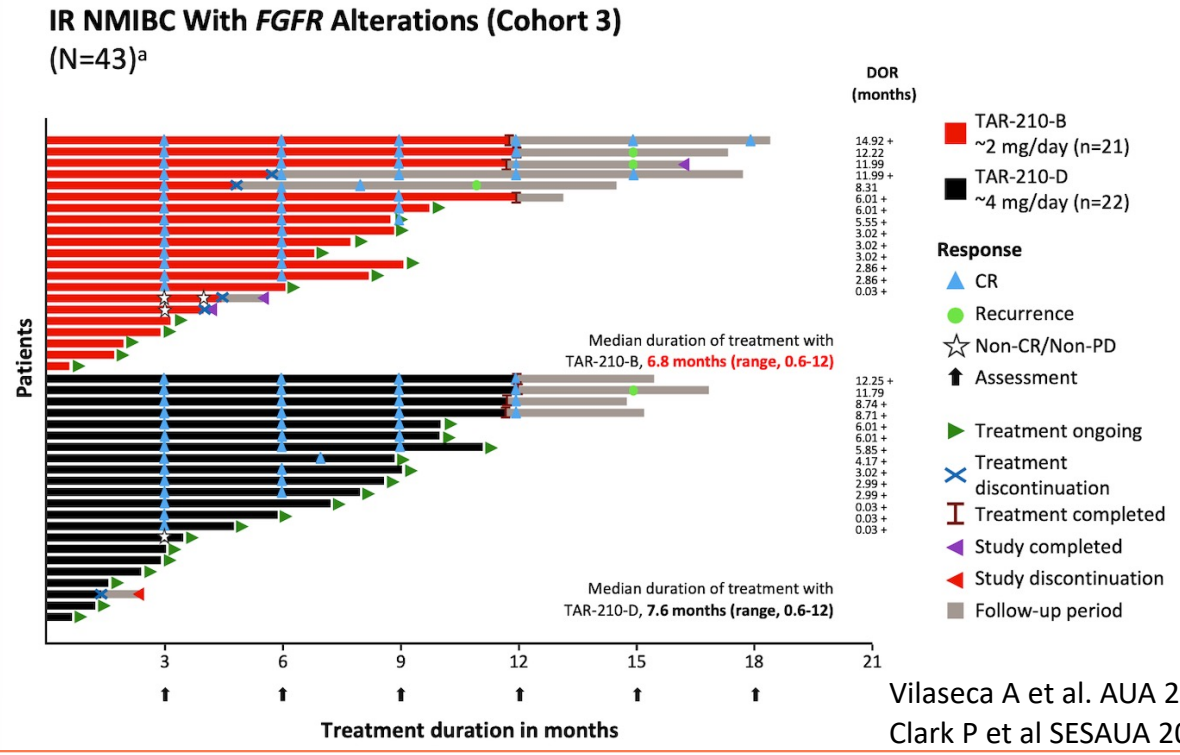
Why gemcitabine? Why not other agents?

- FGFR mutations present in 30-60% of NMIBC tumors
- TAR-210 – delivers erdafitinib (FGFR–inhibitor) in place of gemcitabine
- Phase 1 trial in FGFR-mutated, recurrent NMIBC





Vilaseca A et al. AUA 2024;
Clark P et al SESAUA 2025

What's next?

MoonRISe-1: An Open-Label, Multicenter, Randomized Phase 3 Study to Evaluate Efficacy and Safety of TAR-210 vs Intravesical Chemotherapy in Patients With *FGFR*-Altered, Low-Grade IR NMIBC

Key eligibility criteria

- Adults (aged ≥18 years)
- Histologically confirmed **IR NMIBC** (diagnosed ≤90 days prior to randomization):
  - Ta LG/grade 1
    - Primary
    - Recurrent
  - —*or*—
  - Ta LG/grade 2
    - Primary
    - Recurrent
- With **≥1 risk factor**[a]
- Susceptible *FGFR2/3* alterations by central or local tissue or urine testing

Stratification factors

- Anticipated choice of intravesical chemotherapy
- Newly diagnosed vs recurrent disease
- Cystoscopic assessment method (white light vs enhanced assessment method)

1:1 (N≈540) → **R**

TAR-210
(n≈270)
Q12W for 1 year

Investigator's choice of intravesical chemotherapy
(n≈270)
MMC or gemcitabine
QW for 4 to 6 doses (induction) and maintenance for 6 months to 1 year

Primary end point

- Disease-free survival[b]

Secondary end points

- Time to next-line treatment
- High-grade recurrence-free survival
- Progression-free survival
- Rate of diagnostic and therapeutic urological interventions
- Safety and tolerability

NCT06319820

- All visible papillary disease must be fully resected prior to randomization
- Assessments of recurrence or progression include urine cytology, cystoscopy, for-cause TURBT or biopsy of bladder lesions, ultrasound, and urography
- The follow-up phase for patients meeting the primary end point is up to ≈5 years

[a]Risk factors include multiple Ta LG tumors, tumors ≥3 cm, early (<1 year) recurrence, frequent (>1 per year) recurrences, or recurrence after prior adjuvant intravesical chemotherapy. [b]Disease-free survival defined as time from randomization to first documented recurrence of any-grade NMIBC, disease progression, or death from any cause, whichever occurs first.
LG, low grade; MMC, mitomycin C; NMIBC, non–muscle-invasive bladder cancer; Q12W, every 12 weeks; QW, every week; R, randomized; TURBT, transurethral resection of bladder tumor.

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

Case Presentation

Clinical Case

- 4/2022: New hematuria and dysuria, frequency.
  - CT Urogram: 2.9 cm x 4.3cm x 4.1 cm exophytic bladder trigone mass
  - TURBT: HG Ta NMIBC
- 5/2022 – 8/2022: **BCG induction and maintenance**
- 8/2022: Bladder bx: HG Ta NMIBC
  - **Intravesical gemcitabine** x 6 doses
- 11/2022: Persistent HG Ta NMIBC

Clinical Case

- 3/2023 – 1/2024: **Intravesical Gemcitabine + Docetaxel** x 15 doses
- 4/2024 – recurrence in bladder: HG papillary T1
- 5/2024 – 9/2024: **Repeat BCG** x 9 doses
- 11/2024 – Recurrence with 2 papillary HG tumors
- 1/2025 - Starts monthly **TAR-200** (intravesical gemcitabine delivery device)
  - Well tolerated, mild dysuria, mild urgency
- 6/2025 – Cystoscopy/cytology: No recurrence, Paris II
- Remains without recurrence now 1.5 years later!

Discussion Questions

Now that the gemcitabine intravesical system has received FDA approval, how are you integrating it into patient care? How do you choose among the gemcitabine intravesical system, pembrolizumab or intravesical vaccine therapy for individual patients with NMIBC after BCG failure?

Are you currently ordering biomarker testing for your patients with nonmetastatic UBC? Do you think TAR-210 is likely to reach the clinic in the near future, and if so, how do you envision using it?

Tolerability/Toxicity Profile and Other Practical Considerations with Novel Intravesical Therapies

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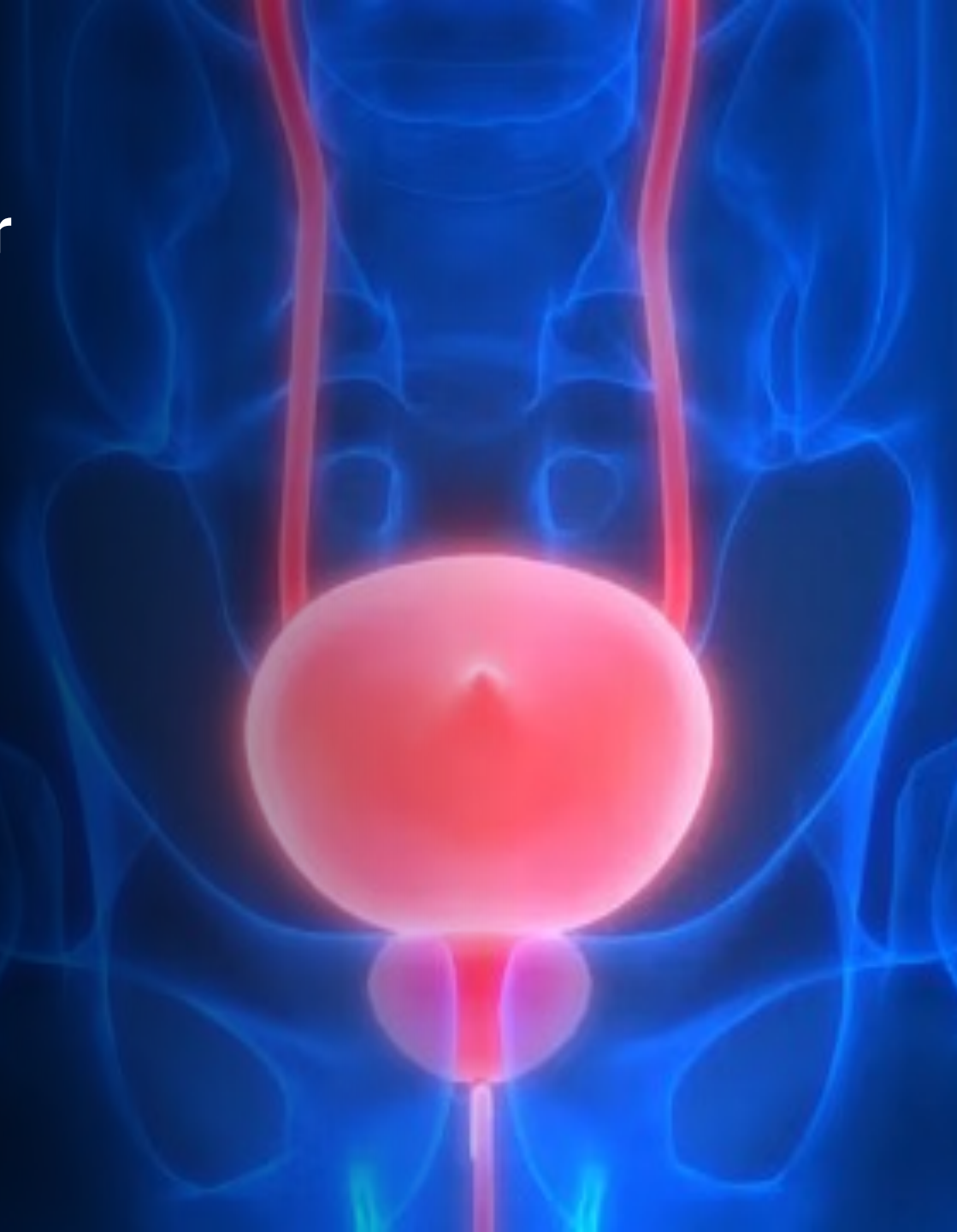
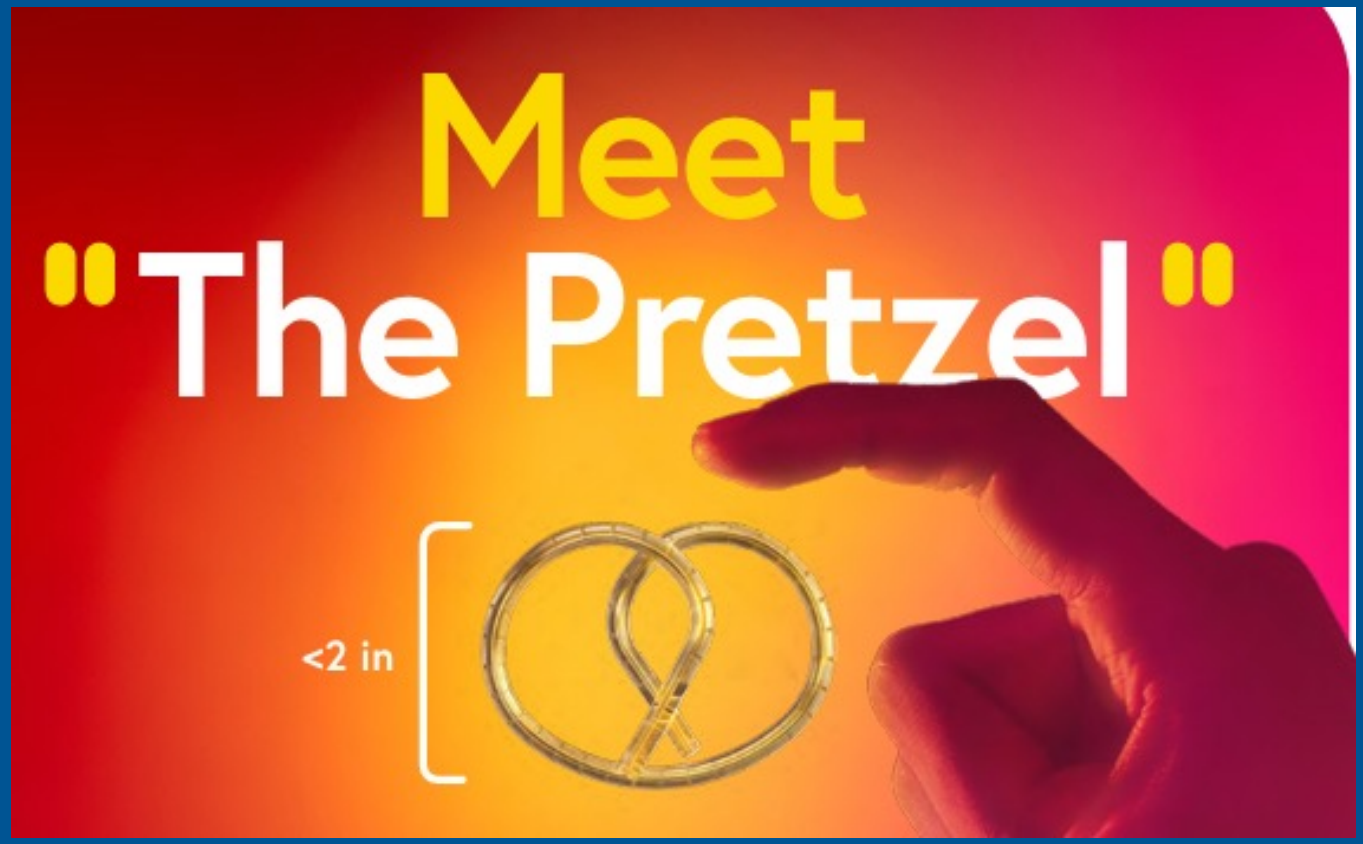


Agenda

- Logistics of insertion and removal of the gemcitabine intravesical system and TAR-200
- Incidence of urinary issues (eg, urinary frequency, urinary tract infection/pain, dysuria, micturition urgency, hematuria) related to the gemcitabine intravesical system; optimal strategies to mitigate these effects
- Spectrum, frequency and severity of systemic toxicities with the gemcitabine intravesical system; appropriate monitoring and management protocols
- Incidence, severity and management of local and systemic side effects noted with TAR-200

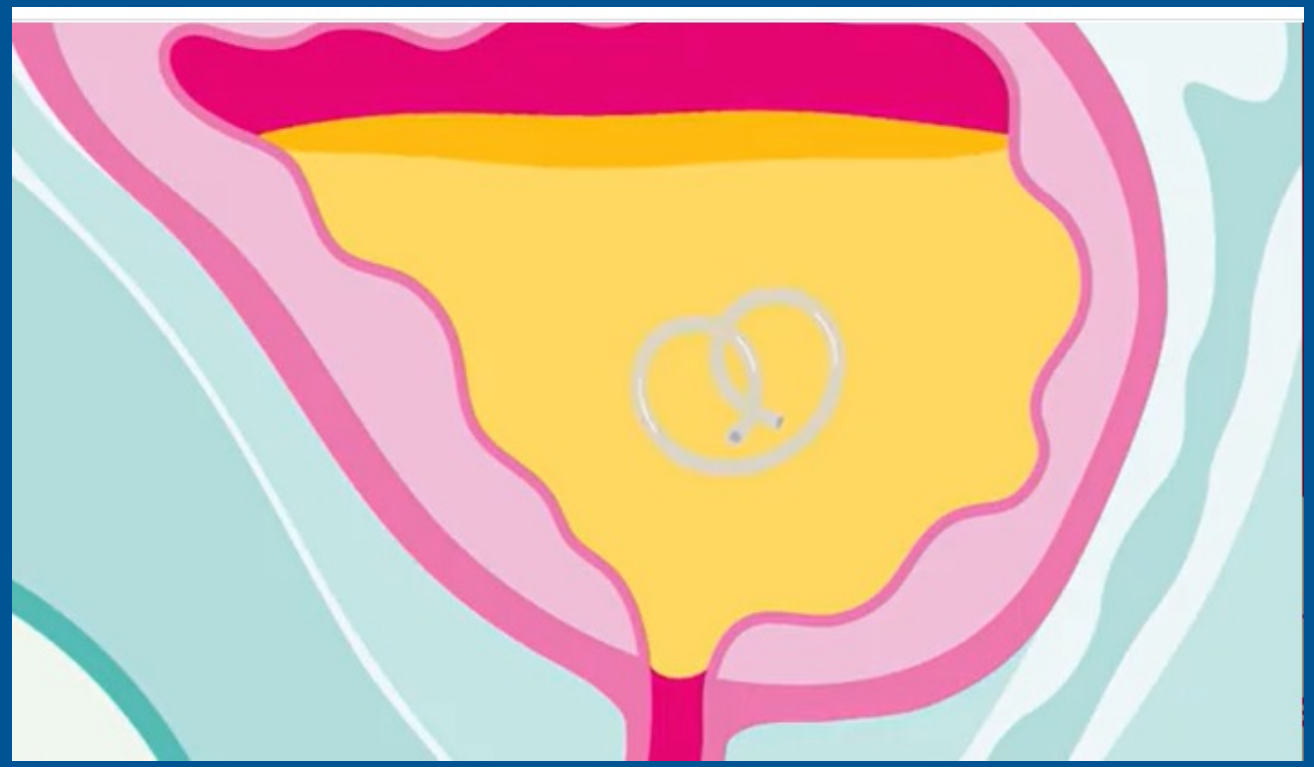
What is TAR 200 (iDRS)?
SunRISe-1 Trial

- Gemcitabine intravesical system is indicated for the treatment of adult patients with Bacillus Calmette-Guérin (BCG)-unresponsive, non-muscle invasive bladder cancer (NMIBC) with carcinoma *in situ* (CIS), with or without papillary tumors (HG T1/Ta)
- **Given in 14 doses over 2 years**
- Inserted q3 weeks x 6 months (8 doses) then once q12 weeks for up to 18 months (6 doses)



Gemcitabine Intravesical System Insertion: APP/MD

- Pass a urinary catheter via urethra into bladder
- Then, pass the gemcitabine intravesical system into the urinary catheter.
- The gemcitabine intravesical system will uncurl and straighten as it is passed into the urinary catheter, afterward resuming its curled shape.
- The urinary catheter will be removed, and the gemcitabine intravesical system will remain in the bladder.



Treatment-Related Adverse Events (AEs) – TAR-200 Monotherapy (Cohort 2) N=85

Safety Outcome	Any Grade n (%)	Grade ≥3 n (%)
Patients with treatment-related AEs	71 (83.5)	11 (12.9)
Pollakiuria	37 (43.5)	0
Dysuria	34 (40.0)	0
Micturition urgency	21 (24.7)	0
UTI	18 (21.2)	1 (1.2)
Hematuria	14 (16.5)	0
Urinary tract pain	9 (10.6)	4 (4.7)

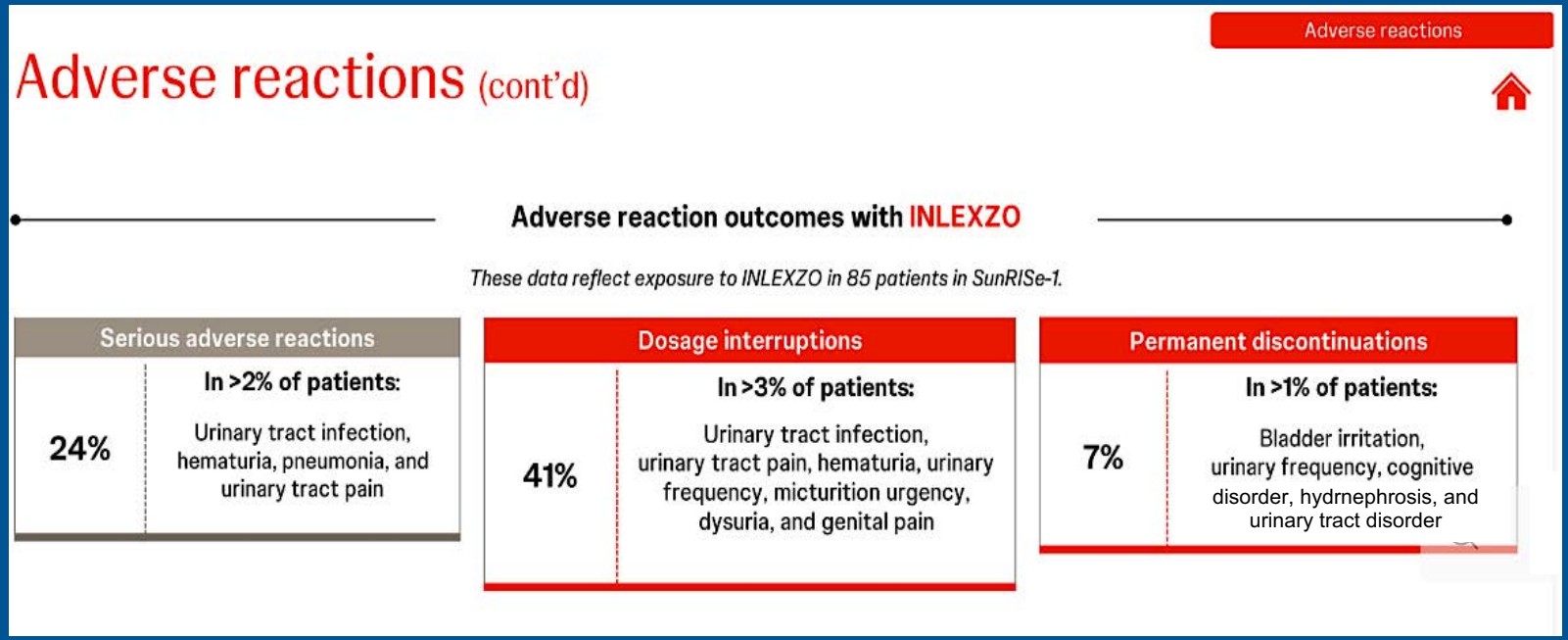
Treatment-related AEs leading to TAR-200 interruption occurred in 27 patients (31.8%), with urinary tract pain (5.9%), hematuria (4.7%), and pollakiuria (4.7%) being the most frequent TAR-200–related AEs.

Most interruptions were limited to one to two doses, and most patients resumed treatment.

Three patients (3.5%) discontinued TAR-200 because of treatment-related AEs, including noninfective cystitis (two patients) and pollakiuria and urinary tract disorder

Daneshmand, S et al
J Clin Oncol. 2025;43(33):3578-3588. doi:10.1200/JCO-25-01651

Incidence of ADVERSE SIDE EFFECTS



There are detectable levels of gemcitabine in urine 7 days after placement w/o detection in plasma

The toxicity profile of iDRS as reported in published clinical trials is characterized by dysuria, UTI, overactive bladder (OAB) symptoms, and hematuria (generally low grade)

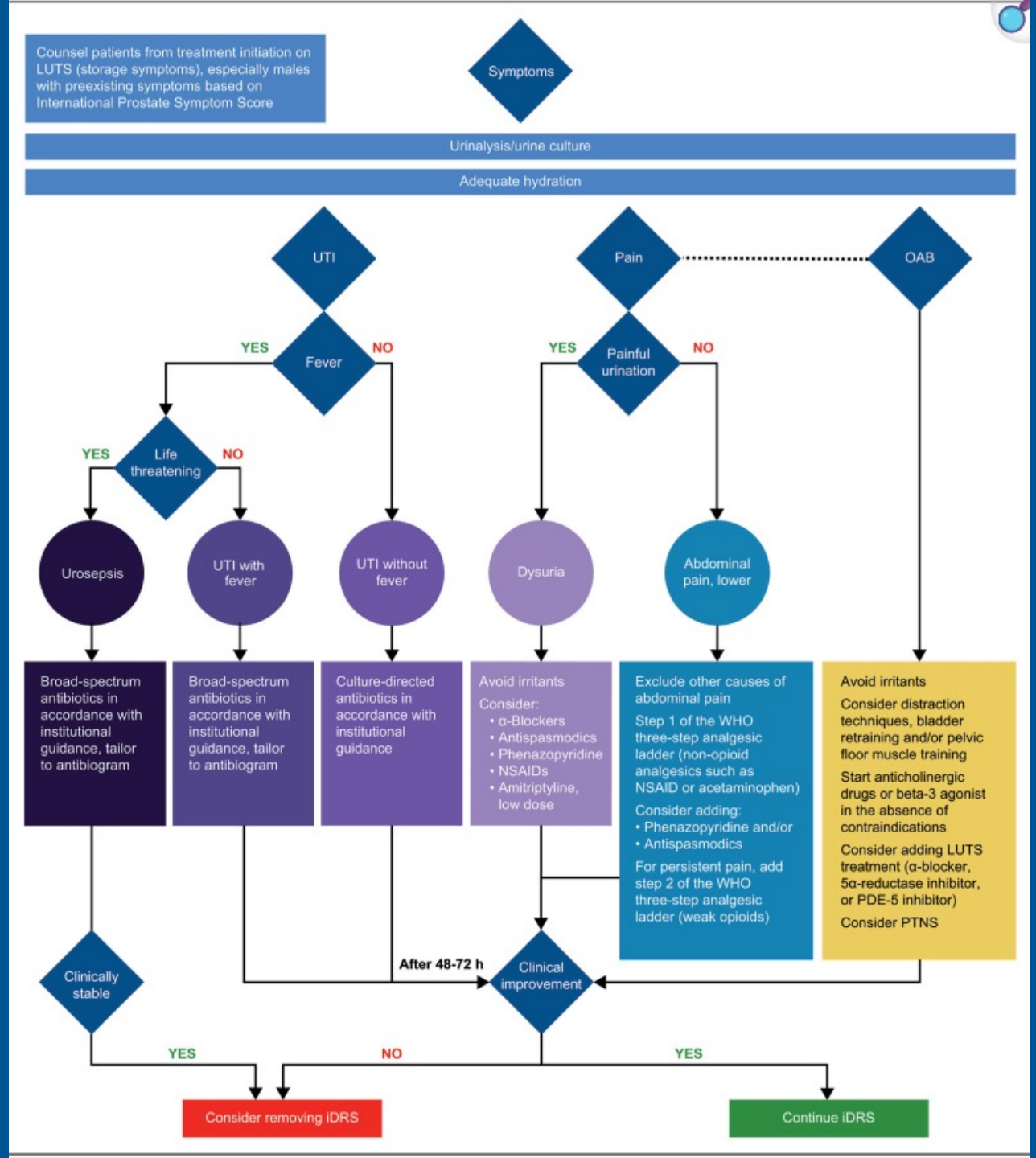
Monitor Hgb, increase Cr/lipase, AST/ALT, Na, K +UA/MICRO REFLEX CX

Clinical Management of iDRS in the Treatment of Bladder Cancer

Asymptomatic bacteriuria	Continue iDRS			
UTI without fever	Continue iDRS if clinical improvement is seen on antibiotic treatment	Consider removal/delaying insertion of new iDRS if no clinical improvement 48-72h after antibiotics	Resume iDRS after complete resolution of infection and negative urine culture	
UTI without fever	Continue iDRS if clinical improvement is seen on antibiotic treatment	To avoid risk of infection, current iDRS can remain in bladder for at least 48h of antibiotics	Remove/delay insertion of new iDRS if no clinical improvement after 48-72h of antibiotics	Resume iDRS after complete resolution of infection and negative urine culture
Urosepsis	Remove iDRS as soon as patient is clinically stable on broad spectrum antibiotics	Consider resumption of iDRS after complete resolution of infection and negative urine culture	Consider proactive UTI prevention strategy	

Pradere B et al. *Curr Opin Urol*. 2025;36(1):123-133

Expert Panel Recommendations for Managing Toxicity from iDRS



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Case Presentation

Case of Roy, 83 yo male for TAR 200

Roy has BCG-unresponsive high-risk non–muscle invasive bladder cancer (NMIBC), specifically recurrent high-grade papillary urothelial carcinoma with prior CIS despite multiple adequate courses of BCG.

- PMH: BPH, LUTS, hematuria, bladder cancer, diabetes, arthritis, hypertension, peptic ulcer disease, decreased vision, hearing, low back pain. Former smoker.

Key points from the timeline:

- 8/1/25 TURBT showed:
  - HG Ta disease + CIS
  - No muscle invasion identified
- Rapid recurrence shortly after BCG is particularly concerning because recurrence within months of BCG strongly suggests treatment resistance rather than undertreatment.
- 11/5/25 TURBT then showed:
  - invasive high-grade papillary urothelial carcinoma with lamina propria invasion (T1)
  - No muscle present in specimen, so complete staging was limited
- 12/17/25 repeat re-resection was reassuring:
  - only focal atypia/scar, muscle negative/clear
  - no residual T1 identified

Clinical Course

Discussed RC, gem/doce, TAR200/gemcitabine intravesical system (CIS), nogapendekin alfa inbakicept-pmln (given w/ BCG as it induces the proliferation of NK cells and CD8+ T cells to destroy tumor cells), Nadofaragene (vector-based gene therapy to encode for interferon-alpha2b into the bladder wall cells, turning them into factories that produce this protein to fight cancer cells).

Roy chose TAR200/gemcitabine intravesical system and s/p 4 instillation

2/3/26: Cystoscopy: TAR200 #1 inserted without difficulty after prep and drape through UPC device. No evidence of recurrent tumor, TAR200 in correct place confirmed on cystoscopy

02/23/26: TAR200 #2

02/24/26: Cytology Atypical Urothelial Cells (Paris System III)

3/12/2026 TAR200 #3

4/7/2026: TAR200 #4

- Induction is 8 doses given every 3 weeks. Full surveillance cystoscopy with cytology will be done at removal of #4, no recurrence seen

- Break x 2 weeks d/t TAR200 unavailability
- Hydration as best prevention of urinary symptoms.

- His schedule:
- May 12th cysto: TAR200 #5 insertion
- June 2nd cysto: TAR200 removal and insertion of #6
- June 23rd cysto: TAR200 removal and insertion of #7
- July 14th cysto: TAR200 removal and insertion of #8
- August 4th cysto: TAR200 removal only

Approaches to dysuria: Urge, burn, repeat….

Hydration, Hydration!
Skip an insertion or remove sooner

Most pain resolves after a week
ATC Ibuprofen 600 mg x 1 week +/- Tylenol
Mirabegron 50 mg daily for OAB
Oxybutynin for bladder spasms (less incontinence and leakage during sex)
Alpha blocker
Hydroxyzine for bladder pain (blocks mast cells & inflammation)
Timed voiding and eliminating bladder irritants

NMIBC, Hematuria, BPH/LUTS, Diabetes, Hypertension, Arthritis, poor vision

Social: Married/support system,Former smoker, Older adult needs, Healthcare access/follow-up, Possible caregiver dependence

Psychological: Anxiety about recurrence, coping with chronic illness, stress from ongoing treatment, fear of progression, Impact on independence

Discussion Questions

How is the gemcitabine intravesical system tolerated relative to traditional intravesical delivery of gemcitabine? How do the two delivery methods stack up in terms of practical requirements?

What are the most frequently observed adverse events with TAR-210? How is intravesical delivery of erdafitinib tolerated relative to conventional systemic delivery?

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