2025 DEBATES AND DIDACTICS in Hematology and Oncology

EMORY WINSHIP CANCER INSTITUTE
National Cancer Institute-Designated Comprehensive Cancer Center
Where Science Becomes Hope

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This activity is jointly provided by Partners for Advancing Clinical Education and Bio Ascend

VS

DEBATE: Ileal conduit versus neobladder post-cystectomy

THE ARGUMENT FOR AN ILEAL CONDUIT

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July 26th, 2025

VS

DEBATE: Optimal Approach to Muscle Invasive Bladder Cancer

PERIOPERATIVE CHEMOIMMUNOTHERAPY (the NIAGARA regimen)

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Disclosures

Research support: Medicenna, Pliant Therapeutics, Astellas, Duality Biologics, Macrogenics, Merck, Xencor, Acrivon Therapeutics, Adcentrx, Surface Oncology

Consulting: Gilead, Exelixis, EMD Serono, Pfizer, Astra Zeneca, Xencor

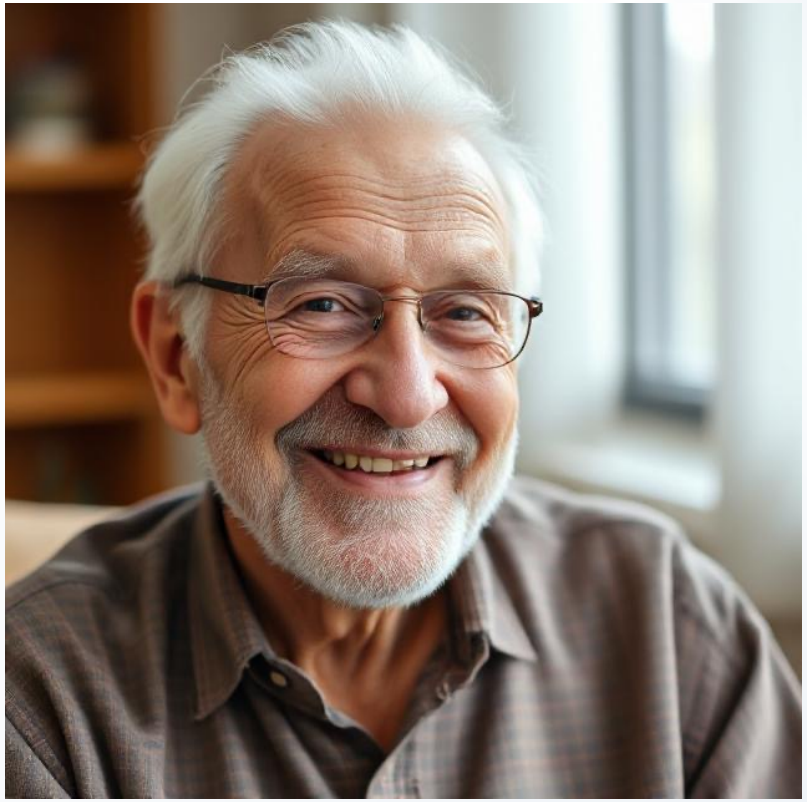
Ben

Ben is Dr. Narayan's and my **74-year-old patient with muscle-invasive bladder cancer**

TURBT shows **high-grade UC with 20% squamous differentiation with invasion into the muscularis propria**

CT chest and urogram show **hazy perivesical stranding with mild L hydronephrosis. Prominent L ext iliac LN, mild FDG avidity on FDG PET.** No metastatic lesions

His CrCl is **52 mL/min.**



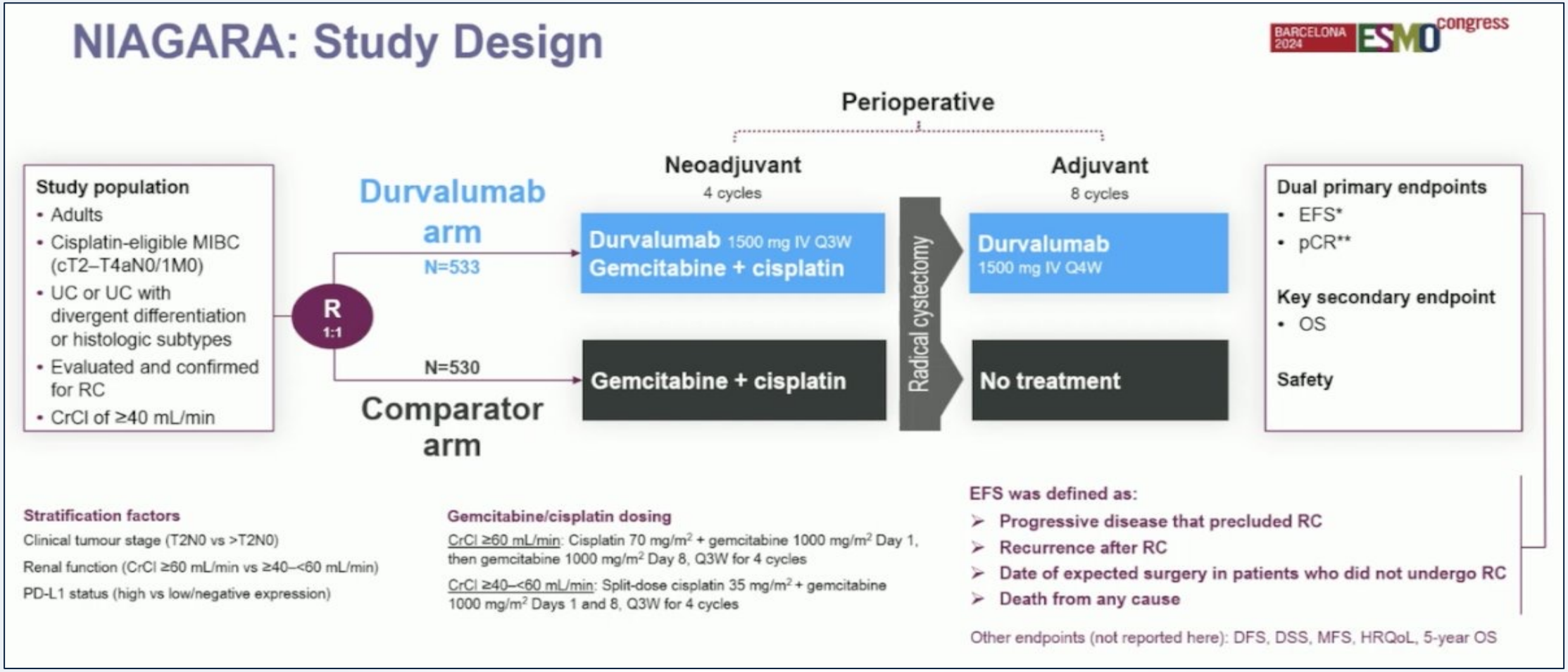
If only we had…

A phase 3, randomized trial showing overall survival benefit (category 1 data)

That reflected our real-world population in terms of:

- Divergent differentiation allowed
- Imperfect renal function allowed
- Split-dose cisplatin allowed
- N1 disease allowed

NIAGARA: Perioperative chemoimmunotherapy in MIBC

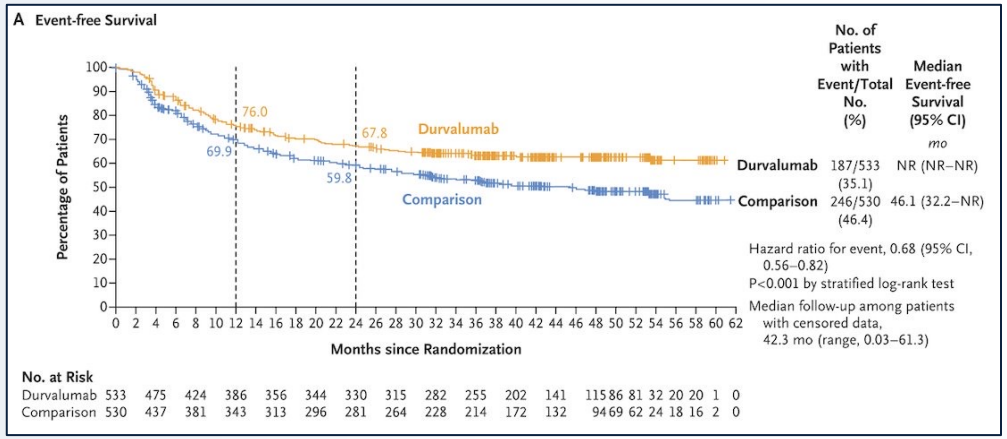


Powles, T. ESMO 2024.

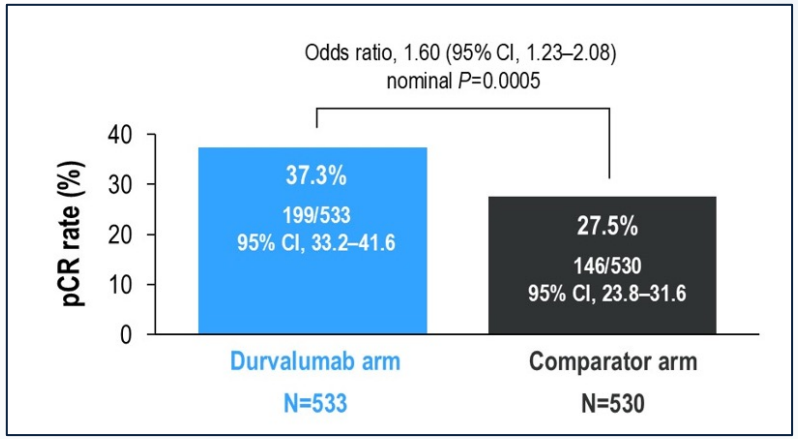
Perioperative chemotherapy improves survival in MIBC

Co-primary endpoints

Event-free survival ✓

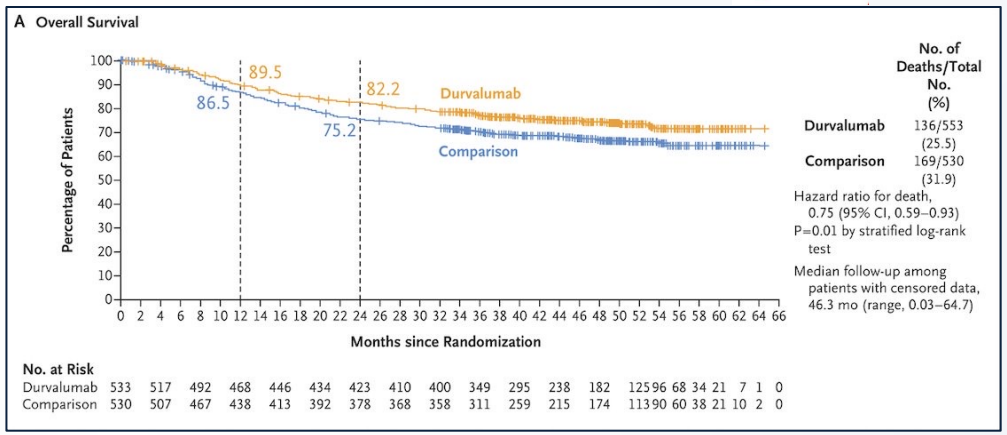


Pathologic CR rate ✗



Key secondary endpoint

Overall survival ✓



Powles, T. (2024). NEJM 391: 1773-1786.

NIAGARA doesn't require extrapolation to your patients

(because patients like yours were included)

15% divergent differentiation

60% > T2N0

5% N1

~20% with CrCl 40-60

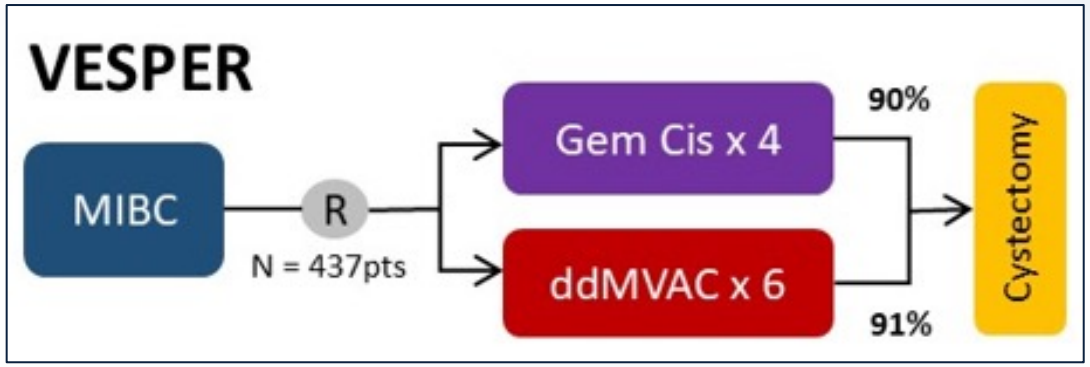
Characteristic	Durvalumab (N=533)	Comparison (N=530)
Invasive urothelial carcinoma, not otherwise specified	457 (85.7)	441 (83.2)
Urothelial carcinoma with squamous differentiation	38 (7.1)	49 (9.2)
Urothelial carcinoma with glandular differentiation	10 (1.9)	15 (2.8)
Urothelial carcinoma with other histologic subtype	28 (5.3)	25 (4.7)
Tumor stage — no. (%)§¶		
T2N0	215 (40.3)	213 (40.2)
Higher than T2N0	318 (59.7)	317 (59.8)
Regional lymph-node stage — no. (%)§		
N0	505 (94.7)	500 (94.3)
N1	28 (5.3)	30 (5.7)
Creatinine clearance — no. (%)		
≥60 ml/min/1.73 m^2	432 (81.1)	430 (81.1)
40 to <60 ml/min/1.73 m^2	101 (18.9)	100 (18.9)

Powles, T. (2024). NEJM 391: 1773-1786.

How does perioperative GC-durvalumab compare to ddMVAC?

VESPER: ddMVAC x6 vs GC x4

- pCR 42% vs 36%
- 3-year PFS 66% *v* 56%, HR 0.70 (0.51-0.960)
- 5-year OS 66% vs 57%, HR 0.71 (0.52-0.97)
- Cost: increased toxicity

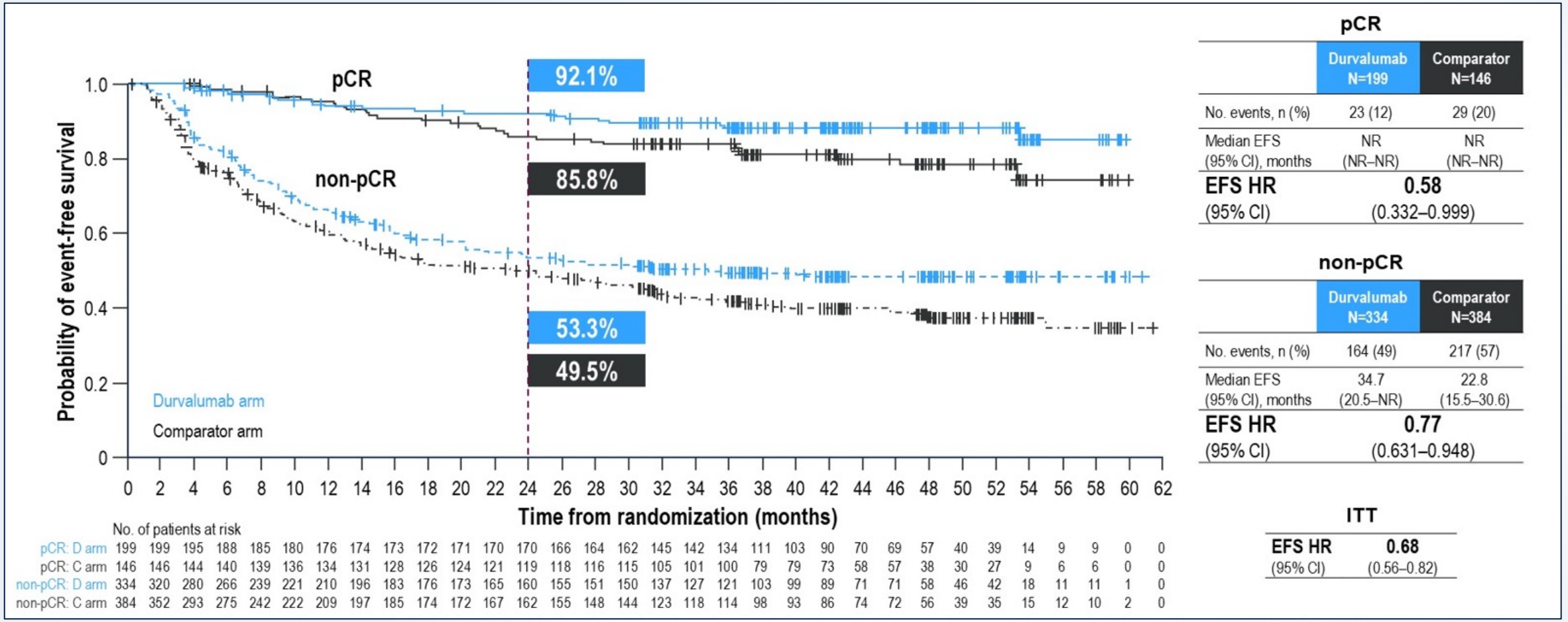


- VESPER included 95% cT2N0 (~5% cT3-4) – NOT representative
- 20-30% of MY patients can get ddMVAC (renal/cardiac function)
- 6 cycles of ddMVAC?! Aspirational…and toxic
- In 2014, 32% received **any** neoadjuvant cisplatin

ddMVAC vs GC is an intellectual exercise that doesn't apply to most patients with MIBC

Pfister, C. (2024). Lancet Oncology 25(2): 255-264.
Duplisea, J. (2019). Can Urol Assoc J 13(2): 24-28.
Plimack, E. ASCO GU 2025.

Perioperative durvalumab improved survival in the pCR and non-pCR groups



pCR

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

non-pCR

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

ITT

EFS HR	**0.68**
(95% CI)	(0.56–0.82)

Galsky, ASCO GU 2025.

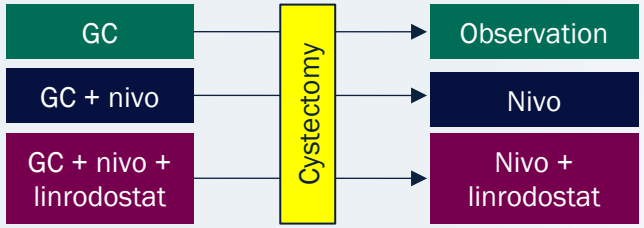
Dr. Narayan may tell you that we need a 4 arm, 4000-patient trial to determine the contribution from the components of the sandwich…

I have bad news for him.

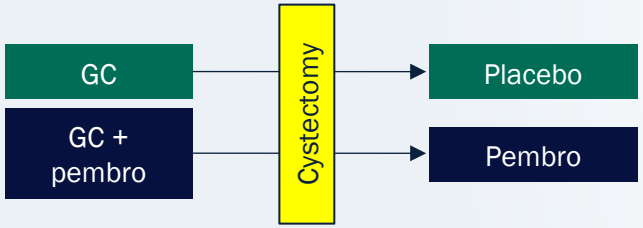
ALL ongoing phase 3 MIBC trials are perioperative trials

Cisplatin +/- IO paradigm

ENERGIZE

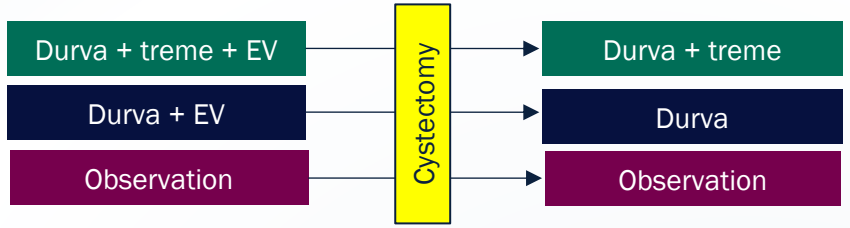


KEYNOTE-866

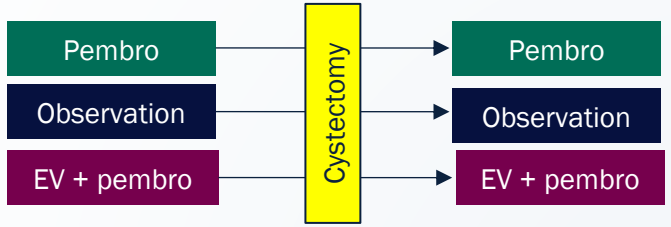


EV-containing paradigm

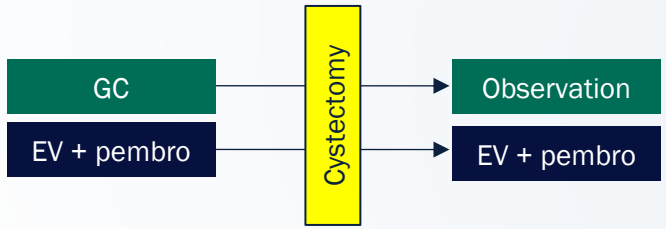
VOLGA (cis-ineligible)



EV-303 (cis-ineligible)



EV-304 (cis-eligible)



Take home messages

- The addition of perioperative durvalumab to neoadjuvant GC improves EFS and OS
- Inclusion criteria that reflect a real-world population
- pCR rate with GC+durvalumab rivals those seen with ddMVAC
- EFS and OS were improved with the additional of durvalumab even with patients who had a pCR
- Most patients can't get ddMVAC – so shouldn't we give them the best possible neoadjuvant treatment available to them?
- Nervous about overtreatment/toxicity with adjuvant durvalumab? Just WAIT for adjuvant enfortumab vedotin

As I place Ben's split-dose gem-cis orders for next week, I'm adding durvalumab. Are you?