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Shifting Paradigm of Perioperative Therapy

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Disclosures

- I am a medical oncologist!
- Advisory role: Deka biosciences, Pfizer, Systimmune

Background

- Cisplatin-based combination therapy is the first peri-operative treatment to demonstrate an overall survival benefit in muscle-invasive bladder cancer (MIBC), with a 5-10% improvement at 5 years.
- However, its use in clinical practice remains limited due to several factors:
  - Patient ineligibility for cisplatin
  - Perceptions of limited effectiveness
  - Patient treatment preferences
  - Barriers to access multidisciplinary care

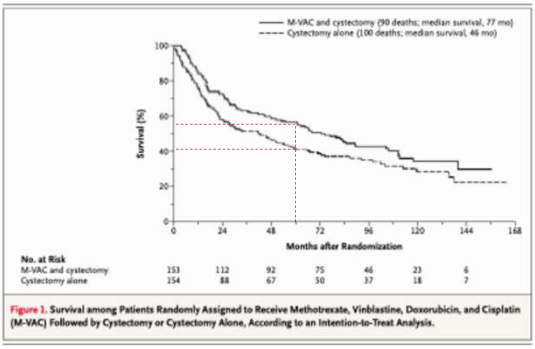

Figure 1. Survival among Patients Randomly Assigned to Receive Methotrexate, Vinblastine, Doxorubicin, and Cisplatin (M-VAC) Followed by Cystectomy or Cystectomy Alone, According to an Intention-to-Treat Analysis.

Grossman et al. NEJM 2003

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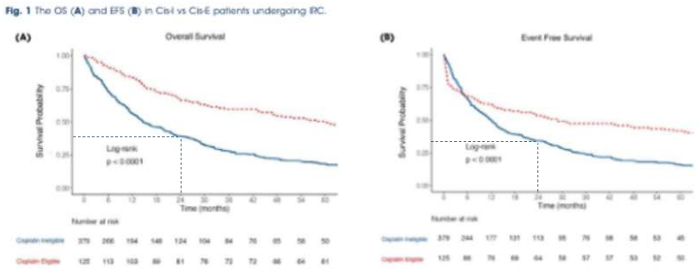
Cisplatin-ineligible patients with MIBC



Majority of cisplatin in-eligible patients experience disease recurrence/death within 2 years

Fazili et al. BJUI 2026

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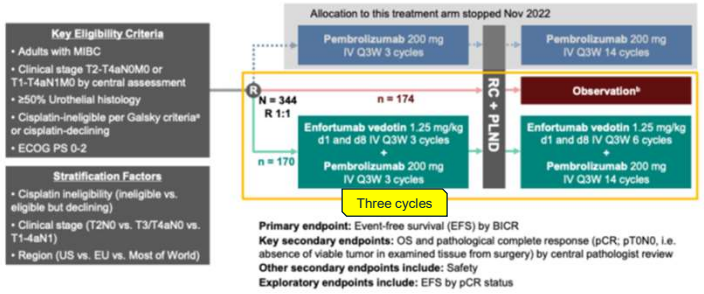
EV/Pembro in cis-ineligible MIBC

KEYNOTE-905/EV-303 Study (NCT03924895)



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

Vulsteke et al. ESMO 2025; NEJM 2026

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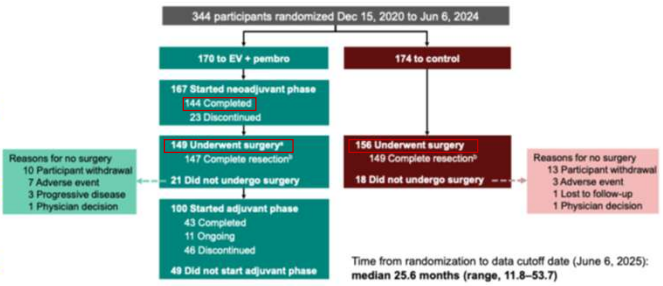
EV/Pembro in cis-ineligible MIBC

Characteristic, n (%)	EV + pembro (N = 170)	Control (N = 174)
Median age (range), years	74.0 (47–87)	72.5 (46–87)
≥65 to <75 years	63 (37.1)	77 (44.3)
≥75 years	78 (45.9)	68 (39.1)
Male	137 (80.6)	131 (75.3)
ECOG PS		
0	102 (60.0)	95 (54.6)
1	47 (27.6)	53 (30.5)
2	21 (12.4)	26 (14.9)
Region		
United States	21 (12.4)	23 (13.2)
European Union	78 (45.9)	77 (44.3)
Most of World	71 (41.8)	74 (42.5)
Cisplatin eligibility status (per Galsky criteria)		
Ineligible	142 (83.5)	139 (79.9)
Eligible but declining	28 (16.5)	35 (20.1)
PD-L1 combined positive score (CPS) ≥10[a]	80 (47.1)	83 (47.7)
Tumor stage at baseline (*centrally assessed using both pathology of TURBT specimen and imaging*)[b]		
T2N0	30 (17.6)	32 (18.4)
T3/T4aN0	133 (78.2)	132 (75.9)
T1-4aN1	7 (4.1)	10 (5.7)
Creatinine clearance		
≥60 mL/min	68 (40.0)	72 (41.4)
≥30 and <60 mL/min	102 (60.0)	101 (58.0)
<30 mL/min	0	1 (0.6)
Pure urothelial carcinoma histology	152 (89.4)	161 (92.5)



Vulsteke et al. ESMO 2025; NEJM 2026

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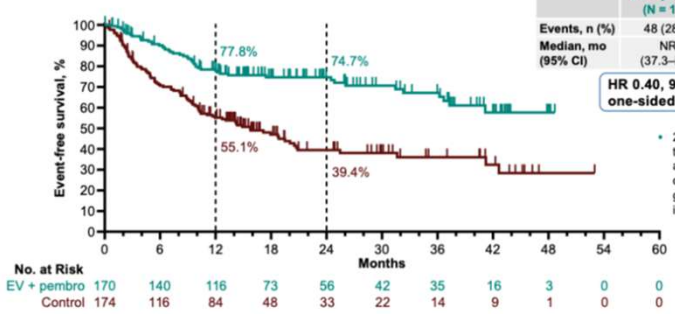
EV/Pembro in cis-ineligible MIBC



	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

Trial	Drug Regimen	2-Year DFS/EFS Rate
CheckMate 274	Nivolumab	~48.5%
AMBASSADOR	Pembrolizumab	~52%

Vulsteke et al. ESMO 2025; NEJM 2026; Bajorin et al. NEJM 2021; Apolo et al. NEJM 2024

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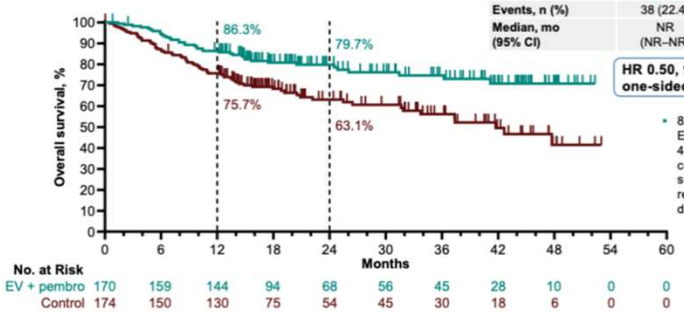
EV/Pembro in cis-ineligible MIBC



	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

Trial	2-Year OS Rate (Active)
CheckMate 274	~76.1% *(ITT)*
AMBASSADOR	~71%

	EV + pembro (N = 170)	Control (N = 174)
pCR, n	97	15
pCR rate, % (95% CI)	57.1 (49.3–64.6)	8.6 (4.9–13.8)

Path CR in cystectomy set: 64%

Vulsteke et al. ESMO 2025; NEJM 2026; Bajorin et al. NEJM 2021; Apolo et al. NEJM 2024

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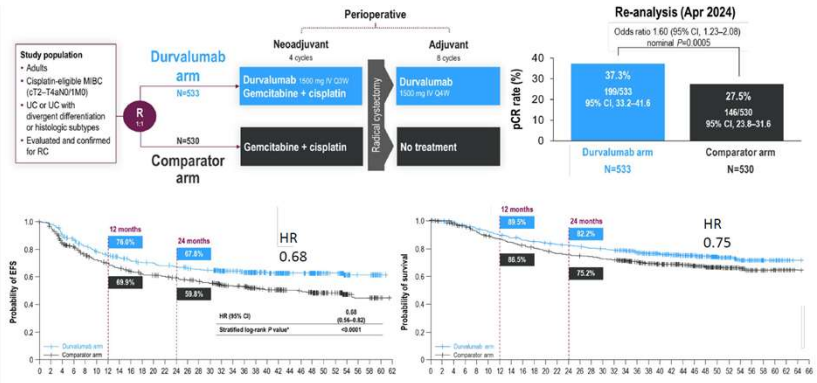
Cisplatin/gem+ durvalumab in MIBC



Powles et al., ESMO 2024; NEJM 2024

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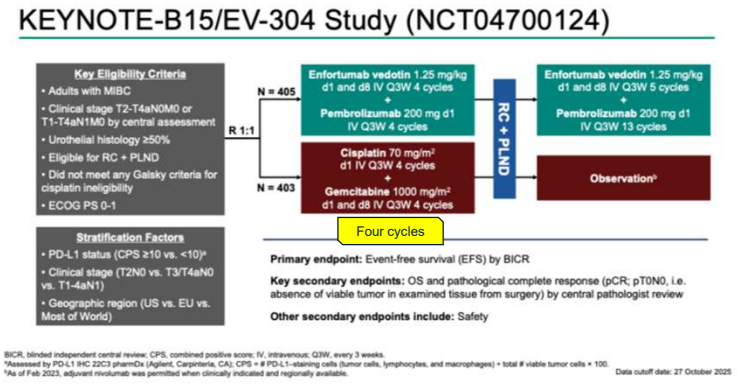
EV/Pembro in cisplatin eligible MIBC



Galsky et al. ASCO GU 2026

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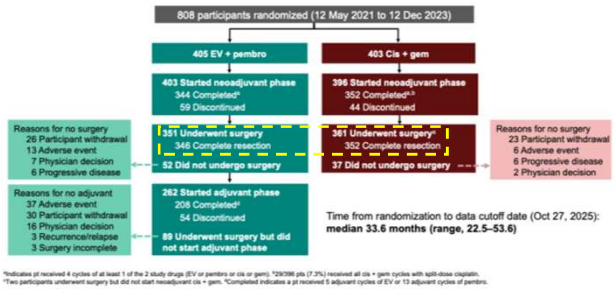
EV/Pembro in cisplatin eligible MIBC



Characteristic, n (%)	EV + pembro N = 405	Cis + gem N = 403
Median age (range), years	66.0 (35–83)	66.0 (37–85)
≥65 years	247 (61.0)	247 (61.3)
Male	327 (80.7)	327 (81.1)
ECOG PS		
0	317 (78.3)	310 (76.9)
1	88 (21.7)	93 (23.1)
Region		
United States	59 (14.6)	59 (14.6)
European Union	206 (50.9)	205 (50.9)
Most of world	140 (34.6)	139 (34.5)
PD-L1 CPS		
≥10	233 (57.5)	230 (57.1)
<10	171 (42.2)	173 (42.9)
Missing	1 (0.2)	0
Tumor stage at baseline (central assessment)[a]		
T2N0	79 (19.5)	77 (19.1)
T3/T4aN0	293 (72.3)	293 (72.7)
T1-4aN1	33 (8.1)	33 (8.2)
Pure urothelial carcinoma histology	370 (91.4)	353 (87.6)
Creatinine clearance		
≥90 mL/min	149 (36.8)	156 (38.7)
≥60 and <90 mL/min	252 (62.2)	245 (60.8)
≥30 and <60 mL/min[b]	4 (1.0)	2 (0.5)

Galsky et al. ASCO GU 2026

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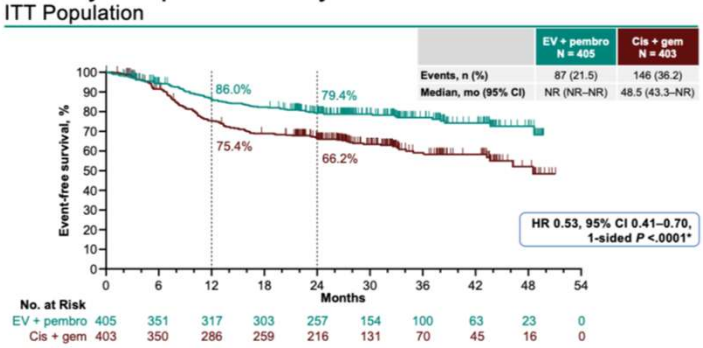
EV/Pembro in cisplatin eligible MIBC

Primary Endpoint: EFS by BICR
ITT Population



Trial	Investigational Arm	Investigational Arm Result
NIAGARA	Durvalumab + GC	67.8%
VESPER	dd-MVAC	66.0%

Galsky et al., ASCO GU 2026; Powles et al., NEJM 2024; Pfister et al. JCO 2022

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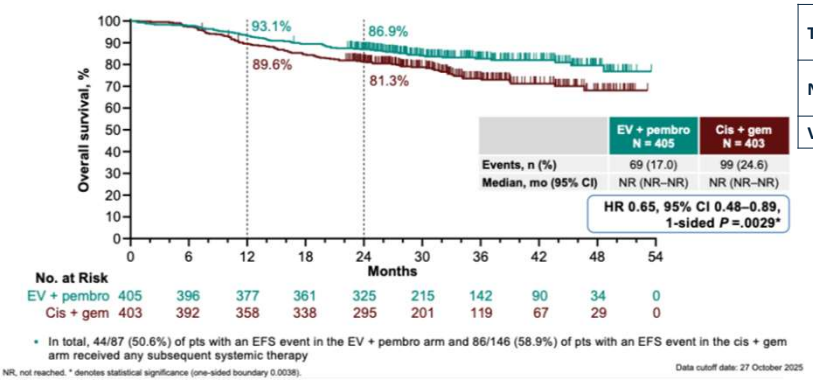
EV/Pembro in cisplatin eligible MIBC



Trial	Investigational Arm	2-Year OS (Investigational)
NIAGARA	Durvalumab + GC	82.2%
VESPER	dd-MVAC	~80%*

	EV + pembro N = 405	Cis + gem N = 403
pCR, n	226	131
pCR rate, % (95% CI)	55.8 (50.8–60.7)	32.5 (28.0–37.3)

Galsky et al., ASCO GU 2026; Powles et al., NEJM 2024; Pfister et al. JCO 2022

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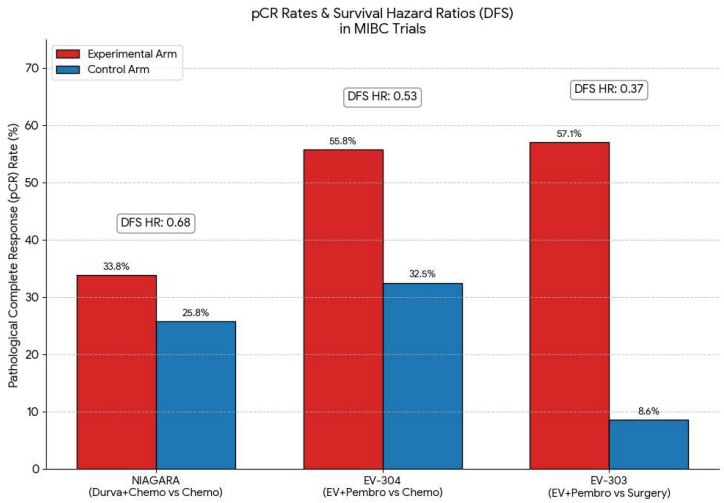

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Individualizing therapy based on co-morbid conditions

Comorbidity / Condition	Enfortumab Vedotin (EV) + Pembrolizumab	Cisplatin + Gemcitabine + Durvalumab
Chronic Kidney Disease	Eligible	**Ineligible** if GFR < 40 mL/min
Peripheral Neuropathy	**Relative contraindication**	**Ineligible**
Diabetes / Hyperglycemia	**High risk**; requires close monitoring.	Requires close monitoring
Hearing Loss	Eligible	**Ineligible**
Heart Failure	Eligible, depending on overall performance status.	**Ineligible**
Performance Status	Eligible if ECOG PS 0–2	**Ineligible** if ECOG PS is ≥ 2.
Autoimmune Disease/Immune suppression	**Contraindication** for IO	**Contraindication** for IO

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Unanswered questions from EV/P trials

- How many cycles of neoadjuvant EV/P enough/ideal?
  - Similar pCR with 3 or 4 cycles
  - Could patients achieving MRD negativity go to surgery earlier?
- Do all patients need surgery? How do we apply these to TMT patients?
- Can we individualize adjuvant component based on response/lack thereof?

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Conclusions

- Enfortumab vedotin and pembrolizumab has changed treatment paradigm for BOTH cis-eligible AND ineligible patients
- Multimodal therapy and multidisciplinary care is crucial (now more that ever) to achieving best oncologic outcomes
- Ongoing studies will help address the lack of data in TMT/bladder sparing space

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Thank you


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Bladder Preservation and Consolidative Therapy in Era of EV/P: Identifying the Right Patient and Timing

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Disclosures

- PADCEV Steering Committee

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EVP Era of Bladder Cancer

Bladder Preservation: Wild West

Operating Less on Localized Dx?

Next Frontier

Consolidative Treatment: Unchartered Territory

Operating More on Advanced Disease?

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EVP ERA: Preservation and Consolidation

Rapidly changing practice

clinical trials or prospective data

Driven by **patients** and **providers**

Goals and **prospective** different in each setting

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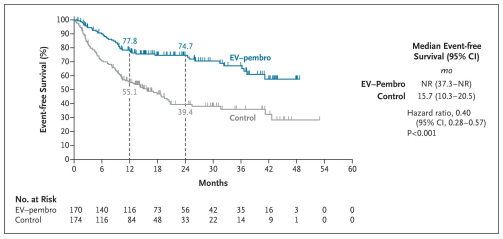
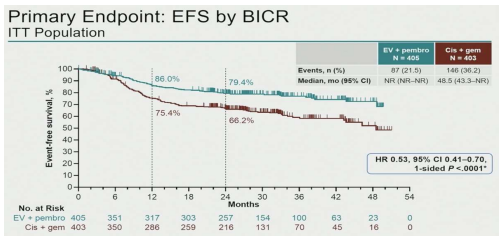
Primary Outcomes - EFS

EV 303/K 905

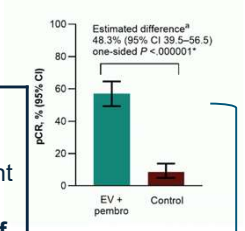


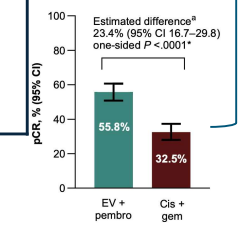
EV 304/K B-15



EFS benefit dependent upon **receipt of surgery** AND **adjuvant therapy**

Secondary Outcomes - pCR





Does high pCR rates mean many do not need **surgery** AND/OR **adjuvant therapy**?

Vulsteke NEJM 2026; Galsky GU ASCO 2026

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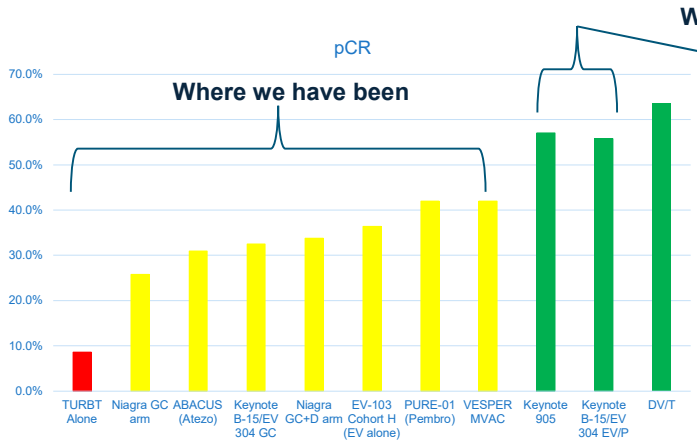

500 patients
149 EV 303/K 905
351 EV 304/K B-15

Improved and
Consistent pCR

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Hypothesis Generation

Cystectomy is **morbid operation** and **not desired** in many

Previous **pCR** rates were **low (~30%)**

pCR correlates with **excellent RFS** and **OS,** historically

If **pCR exceeds 50%,** then cystectomy may be **avoided in many/majority**

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cCR = pCR??

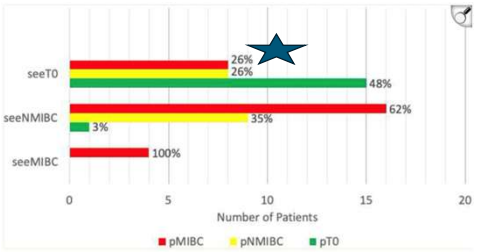
Systematic Endoscopic Evaluation SEE T0 Study

Pts at Fox Chase scheduled for **RC**

Cystoscopy and bx performed endoscopically first

RC completed immediately thereafter

Primary Outcome: **NPV of SEET0**



SeeT0 NPV: 48.4%!!!

Zibelman J Urol 2023

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Sensitivity of Clinical Staging (RULE OUT)

- Cystoscopy – 60-65% (Asad Scand J Urol 2022)
- TURBT – 30-80% (Zibelman J Urol 2023; Kukreja Eur Urol Focus 2018)
- CT – 30-60% (Alam Bladder Cancers 2023) MRI - **60-85%** (Dehghanopour Eur Radiol 2025)
- Cytology - 30-60%
- ctDNA and utDNA (33% sensitivity in ctDNA in RETAIN population presented at Ghatalia GU ASCO 2026)

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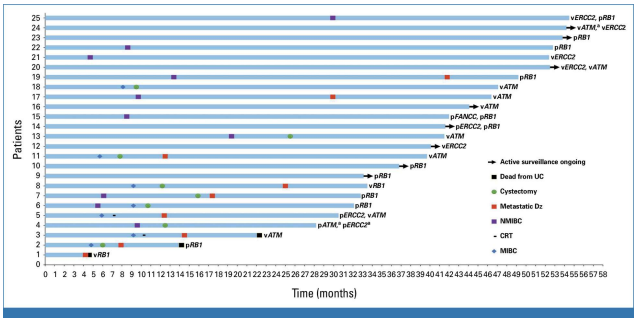
Fate of the RETAINed Bladder?

RETAIN 1

25/70 on AS with cT0 after ddMVAC and mutation

- **8 on AS NED**
- **17 recurrences**
- **8 cystectomies**
- 9 metastasis
- **2-year MFS 72.9%**
- **MFS** and **OS rates** similar to other trials



Geynisman J Clin Oncol 2025

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Preservation at what cost?

Uncertain strategies which will need to be **refined**

- Timing of **cystoscopy**
- Timing of **biopsies** without cause?
- Imaging **modality** and **timing**?
- Consideration of **PROs?**
- Utility of new **biomarkers**?

Systemic versus **Surgical** side effects

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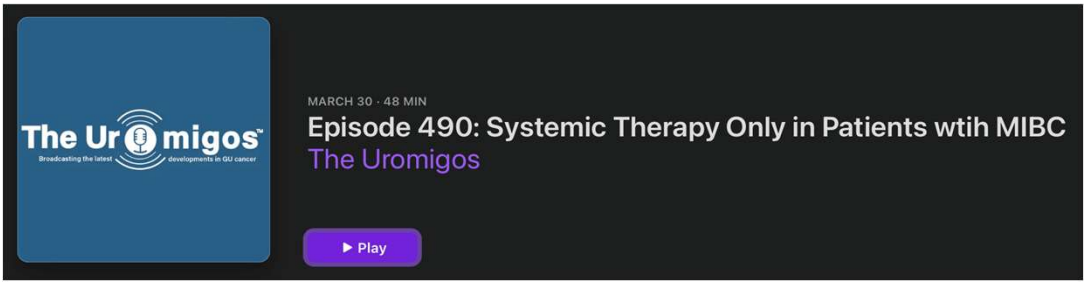
Proposed Trials in Bladder Preservation



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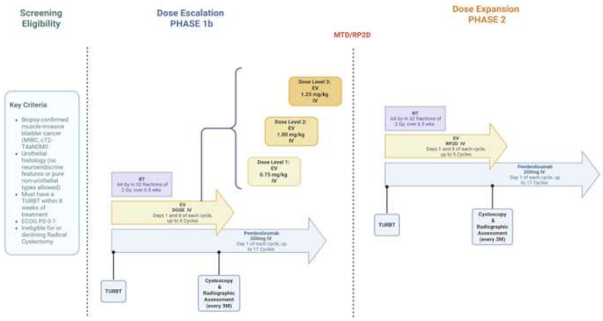
Proposed Trials in Bladder Preservation

EV-PRIME

- Design: **Phase Ib/II** Multicenter IIT study in ~40 pts with cT2-T4a UC
- Treatment: **EV/P and Concurrent Radiation**
- Primary Outcome: **6-month cCR** on cystoscopy/TURBT, cytology, imaging



Bladder Preservation with EVP

- Right **patient** and right **timing**
  - **TBD!**
- Likely already **into practice without data**
- **Single arm prospective studies** planned
- Multi-arm **randomized trials** may be **impossible**
- Many questions need to be **answered**

Consolidative Cystectomy

Locally advanced or oligometastatic disease

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Historical Context of Consolidation

Herr et al, 2001

- **80** patients with advanced or unresectable dx
- ypT0N0 in **30%**
- cCR ≠ pCR
- 33% of patients survived 5 years

Meijer et al, 2013

- **125** pts with advanced or unresectable dx
- ypT0N0 in **26.3%**
- cCR ≠ pCR; cCR PPV of 62.5%
- 54% estimated 5-year OS

Small, single centers
Retrospective
Heavily selected patients
Different systemic therapy regimens

Herr J Urol 2001; Meijer Eur J Surg Oncol 2013

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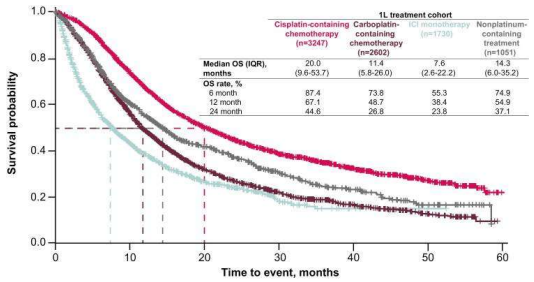
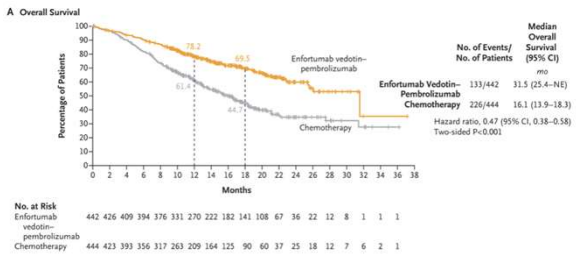
Changing Paradigms

Chemotherapy



Prior to EVP, median OS was 20 months
~5-10% 5-year OS

EVP



EV 302, median OS was 31.5 months
~40-50% 3-year OS

Bilen Oncologist 2023; Powles NEJM 2024

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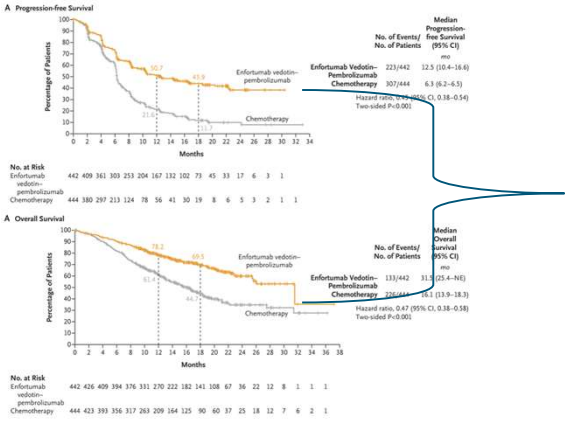
Treatment Dilemmas



Powles NEJM 2024

Due to improved PFS/OS which appear **DURABLE** in **MANY…**

Role of EVP until progression/toxicity?

OR

Expanding role of local consolidation?

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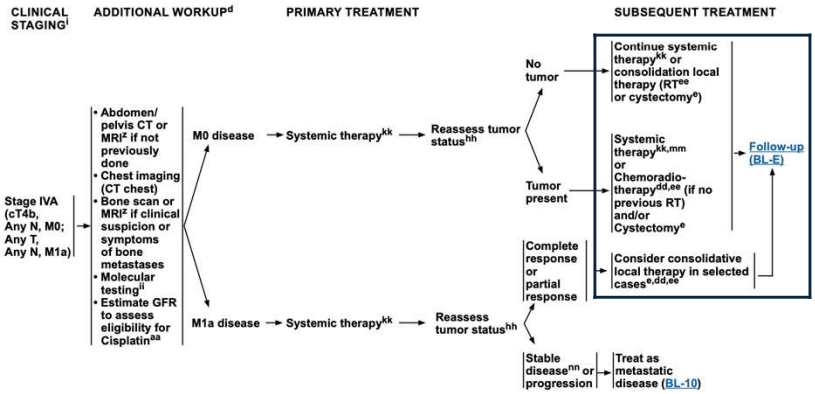
Treatment Considerations - Guidelines



But **which** patients to choose? And **when** to offer consolidation?

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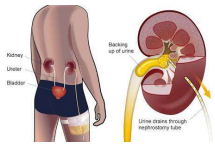
Treatment Considerations - Patient

Local Symptoms

Obstruction
Hematuria
Pain
Lower Urinary Tract Symptoms

Disease Characteristics

Nodal vs Visceral
Number of sites



Costs of Care

Financial Costs
- **EVP ~40-50K per cycle**
- 600K for median 12 cycles EV 302

Systemic Toxicity
- Grade ≥3: 55.9%; Discontinuation 35%
  - **Rash**, Hyperglycemia, **Neuropathy**

Consolidation Risk
- QoL
- Oncologic benefit?
- Complications

Powles NEJM 2024

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Which patients to consider?

STOP!
ALL PATIENTS SHOULD BE DISCUSSED IN MDS/TB!

Obvious Factors

- **Healthy**, Good Performance Status
- **Surgical candidate**
- At **least partial response** on systemic therapy
- Patients with **residual cancer**

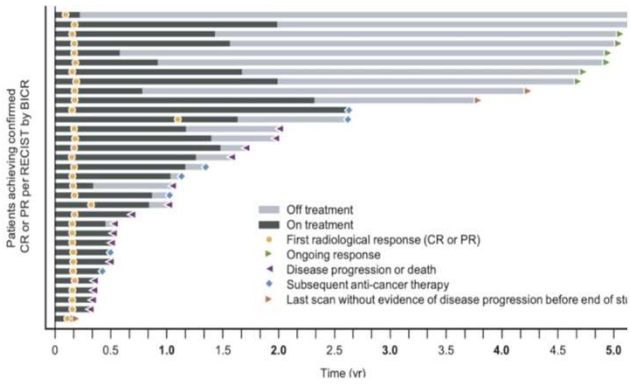
Disease Specific Factors

- **Limited sites** of metastasis
  - **Limited** if any **visceral disease**
- **cN+ disease patients**
- **Obstructed**
- Locally **symptomatic**
- **AE** to systemic therapy

Timing of consolidation?

- **EV-103** (dose escalation and cohort A): Timing of first response **EARLY** at first scans **~2-3 months**
- **Time to cCR ~ 2-4 months**
- **4 cycles** currently being tested in trials

Figure 2. Time to response and DOR in patients achieving confirmed CR or PR by BICR



Rosenberg ESMO 2024

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STUDY	Jang Oncologist 2025	Ghoreifi Urol Oncol 2026	Roberson Eur Urol 2025	McSweeney (Submitted)
Patient #	6	23	28	28
Cycles EVP (IQR)	6 (4-7)	4 (3-8)	6 (4-7)	5
Location UC (%) UTUC (%)	 6 (100) -	 14 (61) 9 (39)	 22 (79) 6 (21)	 24 (86) 4 (14)
cCR prior to surgery (%)	6 (100)	NR	15 (54)	4 (15)
pCR # (%) Downstaged # (%)	6 NA	10 (45) 13 (59)	12 (43) 23 (82)	13 (46) 19 (70)
Surgical Complications	NR	64%; 6 (27%) ≥ 3	57%; 5 (18%) ≥ 3	NR; (11%) ≥ 3
Adjuvant Therapy (%)	0	5 (22)	6 (21)	5 (18)
Cessation of Systemic Therapy (%)	6 (100)	18 (78)	22 (79)	23 (82)
Recurrences/Deaths	0	5/2	3/2	5/1

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Enrolling Clinical Trials

- CAST-AI (NCT06764095)
- CONSOLIdaTE-01 (NCT07048457)

Primary Outcome: **PFS at 12 months**

- CONSOLIDATE (NCT06434350)

Primary Outcome: **Safety and Adverse Events**

- BLAD-RAD01 (NCT 04428554)

Primary Outcome: **Overall Survival**

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Consolidative Treatment

- Changing patient population undergoing cystectomy
- Already **into practice with little data**
- **Single arm prospective studies** planned
- Multi-arm **randomized trials** may be **impossible**
- Many questions need to be **answered!**

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Community Urology: Adapting to Bladder Preservation

Samuel Haywood, MD
Urology of St. Louis

5.18.26

Focus On: Muscle Invasive Bladder Cancer

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Conflicts of Interest: None

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Learning Objectives

- Identify appropriate patients for bladder preservation
- Understand trimodal therapy
- Recognize barriers/solution in the community setting
  - Referring provider
  - Treating provider

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Why Bladder Preservation?

- Not all patients want to lose their bladder
- Limited access to qualified surgeons
- Many patients are suboptimal surgical candidates

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Why Bladder Preservation?

- Not all patients want to lose their bladder
- Limited access to qualified surgeons
- Many patients are suboptimal surgical candidates
- Comparable survival*
- QoL gains
- * = “in well selected patients”

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Why worry about TMT in the community?

- Many patients not ideal cystectomy candidates
- Refuse/unable to obtain care at tertiary center
- Maximize initial TURBT
- Set patient expectations

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Components of Bladder Preservation

What it is	What it is NOT
• Trimodality Therapy	• Radiation alone
• Treatment w/ curative intent	• Palliative care
• Start of the therapeutic relationship	• “One and done”

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Components of Bladder Preservation

- Maximal TURBT
- Concurrent chemoradiation
- Close surveillance

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Complete TURBT

- Pak et al 2014 – higher CR rate
- Efstathiou et al 2012 - ~20% increase in CR rate
- Rodel et al 2002 – complete TUR predicts CR and survival

- TURBT alone in MIBC
  - Herr HW 2001 – 76% OS
  - Solsona et al 2010 – 80% 10 yr CSS

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Who should consider TMT?

Ideal

- cT2
- Unifocal
- Good bladder capacity
- No hydronephrosis
- Complete resection

Relative Contraindications

- Extensive CIS
- Poor bladder function
- Multifocal disease
- Difficulty with surveillance
- Variant histology?

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TMT in the Community Setting

- Non-ideal candidates
- Shared decision making
- Less access to multidisciplinary teams
- Coordination with radiation colleagues
- Patient adherence – commitment to surveillance

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Practical Solutions in the Community

- Build pathways with radiation teams
- Tumor boards (virtual?)
- Standardize protocols to streamline care
  - Operative templates
  - Checklists
  - Followup/surveillance protocols

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Role of the Community Urologist

- TURBT quality
  - Random biopsies?
  - Complete resection?
- Documentation: document location and size
- Set expectations: surveillance, salvage treatments, etc
- Establish relationships

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On the horizon

- Biomarker-driven selection (Genomic assays, MRD markers)
- New combos with radiation
- Improvements in surveillance

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Thank you!

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- Email: shaywood@helios-stl.com

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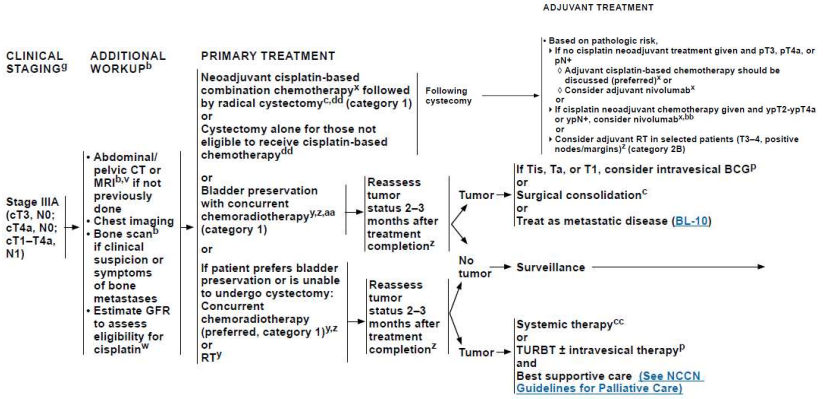
Radiation Treatment in MIBC

Shalini Moningi, MD

No Disclosures

Muscle Invasive Bladder Cancer

Neoadj Chemo + RCx OR TURBT + ChemoRT



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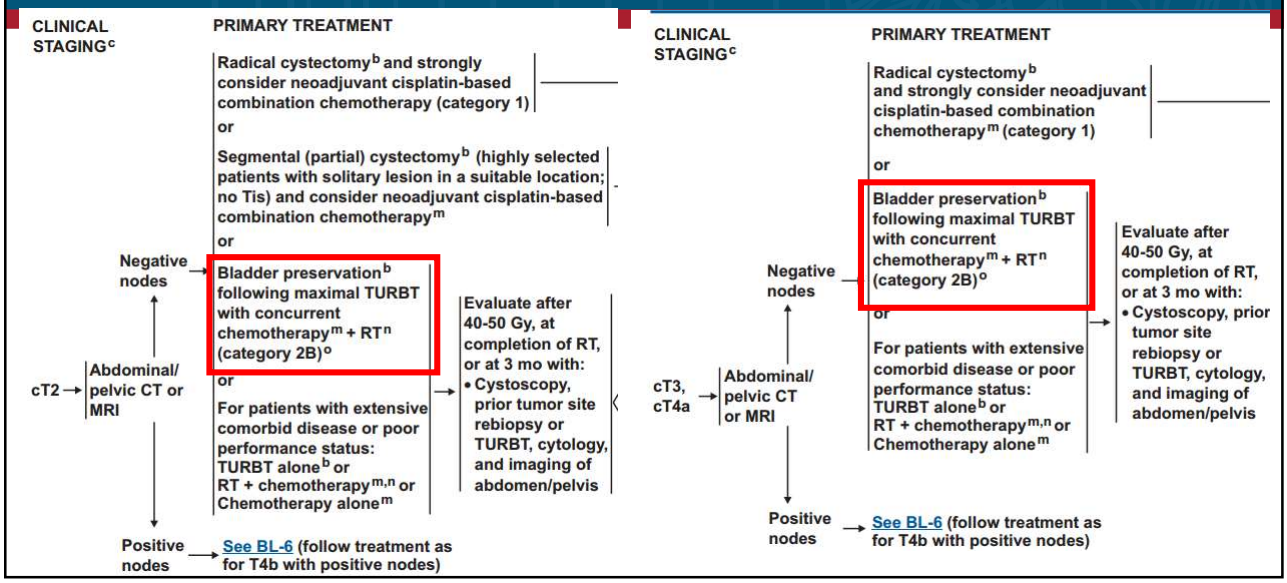
2013 NCCN guidelines



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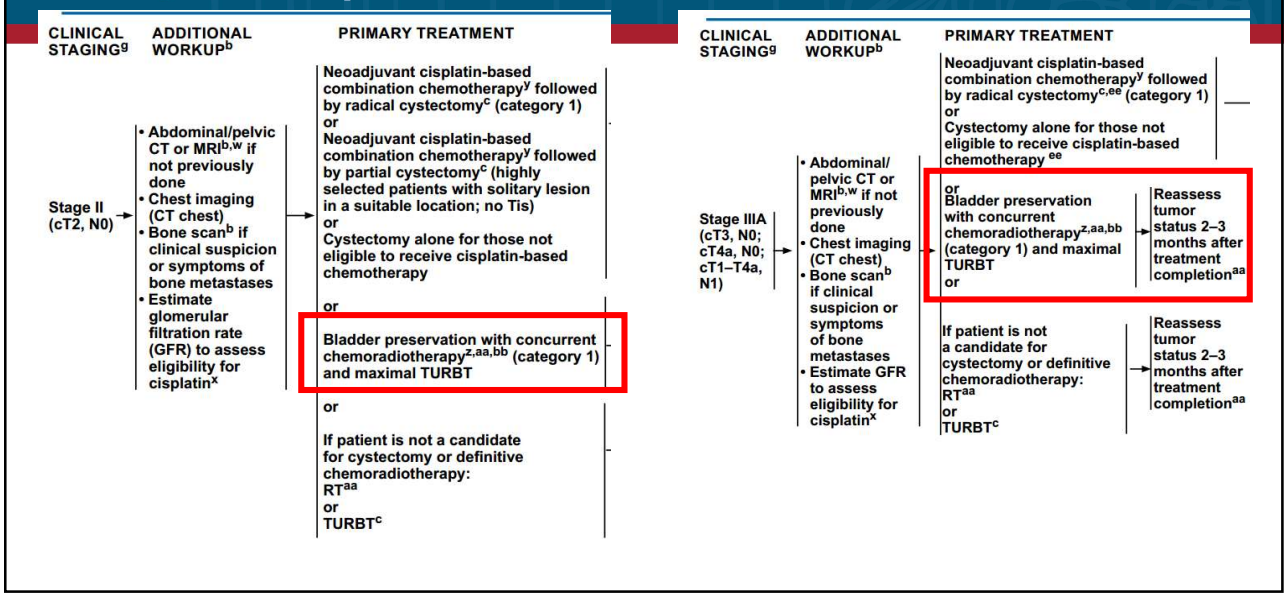
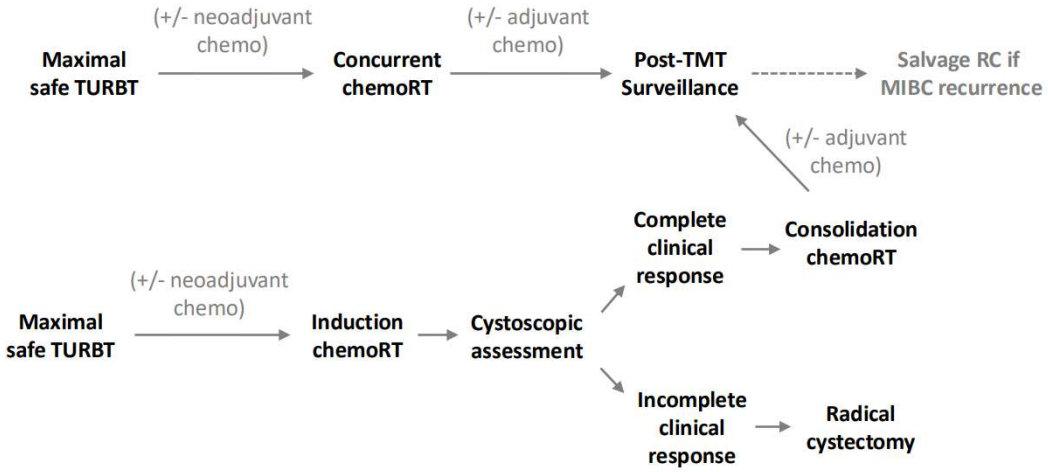
2025 NCCN guidelines



Treatment options

- Non-muscle invasive
  - TURBT + Observation
    - (Ta, T1 Grade 1 w/ Full resection)
  - TURBT + intravesical therapy (BCG, MMC)
    - (G2-3, T1/Tis, residual/multifocal disease)
- Muscle invasive, node negative
  - Radical cystectomy +/- neoadjuvant chemo
  - Partial cystectomy (dome)
  - Bladder preservation / trimodality therapy
- cT4b (pelvic/abd wall invasion)
  - Chemotherapy
  - Chemotherapy -> restage-> consider CRT or Cystectomy
  - CRT

What is Tri-modality Therapy (TMT)?



Chemoradiation for MIBC

Executive Summary of the American Radium Society Appropriate Use Criteria for Radiation Treatment of Node-Negative Muscle Invasive Bladder Cancer

- General paradigm

- Eligibility: cT2-T4 N0 M0, good bladder function
  - Hydronephrosis → high risk for failure (but not absolute contraindication)
- Multidisciplinary evaluation is critical

Dinh IJROBP 2021

Chemoradiation for MIBC

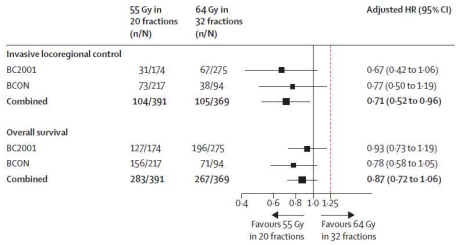
Executive Summary of the American Radium Society Appropriate Use Criteria for Radiation Treatment of Node-Negative Muscle Invasive Bladder Cancer

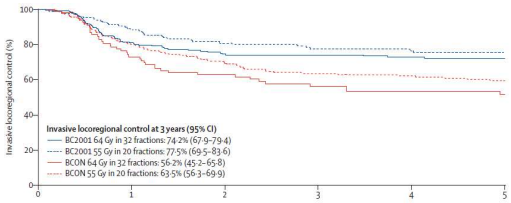
- Concurrent cisplatin-based chemo (or 5-FU/MMC or gem)
  - Consider carbogen or nicotinamide if not chemo candidate (rather than RT alone)
- RT dose 60-66 Gy at 2 Gy/fraction
  - Either continuous course or split course with cystoscopic evaluation
  - Either IMRT or 3D appropriate
- Nodal radiation is optional
  - <10% nodal failure in BC2001 & TROG trials

Dinh IJROBP 2021

55 Gy in 20 preferred in U.K.

- Meta-analysis of 782 patients (BC2001 and BCON trials)
- Either 64 Gy/32 or 55 Gy/20 allowed on trial (not randomized)
- **55 Gy/20 non-inferior** (lower iLRR and similar toxicity)





Choudhury Lancet Oncol 2021

How do RC and TMT Compare?

Radical cystectomy versus trimodality therapy for muscle-invasive bladder cancer: a multi-institutional propensity score matched and weighted analysis

Alexandre R Zlotta, Leslie K Ballas, Andrzej Niemiec†, Katherine Lajkosz†, Cynthia Kuk, Gus Miranda, Michael Drumm, Andrea Mari, Ethan Thio, Neil E Fleshner, Girish S Kulkarni, Michael A S Jewett, Robert G Bristow, Charles Catton, Alejandro Berlin, Srikala S Sridhar, Anne Schuckman, Adam S Feldman, Matthew Wszolek, Douglas M Dahl, Richard J Lee, Philip J Saylor, M Dror Michaelson, David T Miyamoto, Anthony Zietman, William Shipley, Peter Chung, Siamak Daneshmand, Jason A Efstathiou**

Lancet 2023

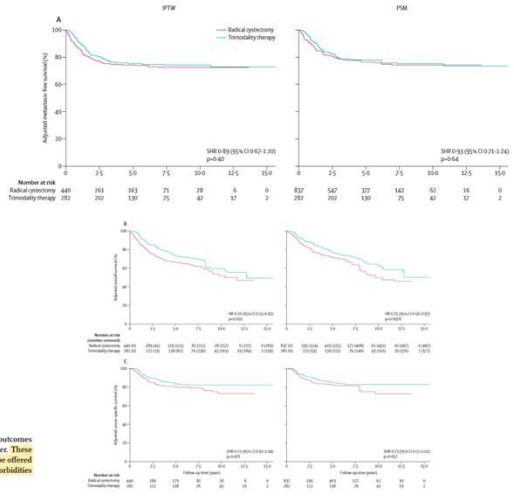
Retrospective analysis of T2-4N0M0 MIBC patients who underwent curative treatment at 3 centers (USC, MGH, Toronto) between 2005-2017

770 patients: 440 RC, 282 TMT

Primary endpoint: MFS
Secondary endpoints: OS, CSS, DFS

Propensity score matching using two techniques

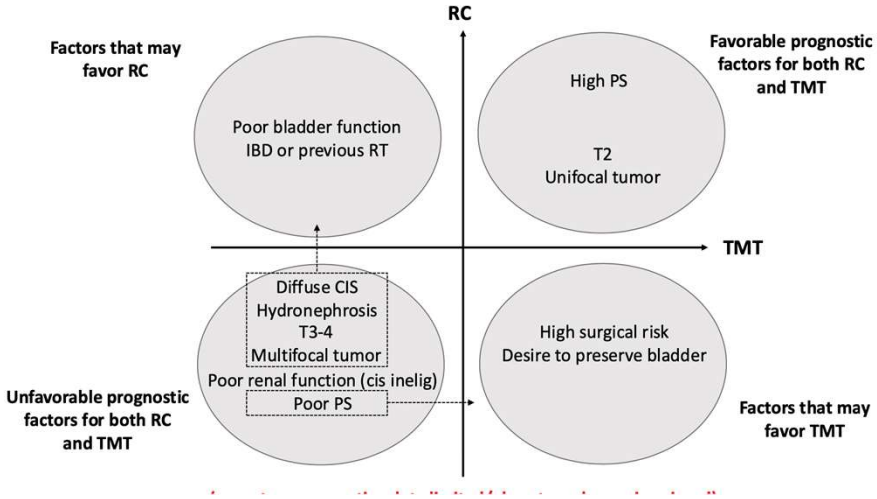
Interpretation This multi-institutional study provides the best evidence to date showing similar oncological outcomes between radical cystectomy and trimodality therapy for select patients with muscle-invasive bladder cancer. These results support that trimodality therapy, in the setting of multidisciplinary shared decision making, should be offered to all suitable candidates with muscle-invasive bladder cancer and not only to patients with significant comorbidities for whom surgery is not an option.



Patients selected for bladder preservation with chemoradiotherapy should *ideally* have the following features

- Unifocal cT2-4, N0, M0
  - N1 in select cases
- Maximal TURBT
  - This can exclude patients with large tumors
- No extensive carcinoma in situ (CIS)
- No hydronephrosis
  - Can try to correct with a stent or percutaneous nephrostomy.
- Good bladder function
- Transitional cell carcinoma (TCC) histology
  - Many trials also allow adeno, squamous cell

Factors that may impact treatment choice



Slide adapted from Dr Kent Mouw

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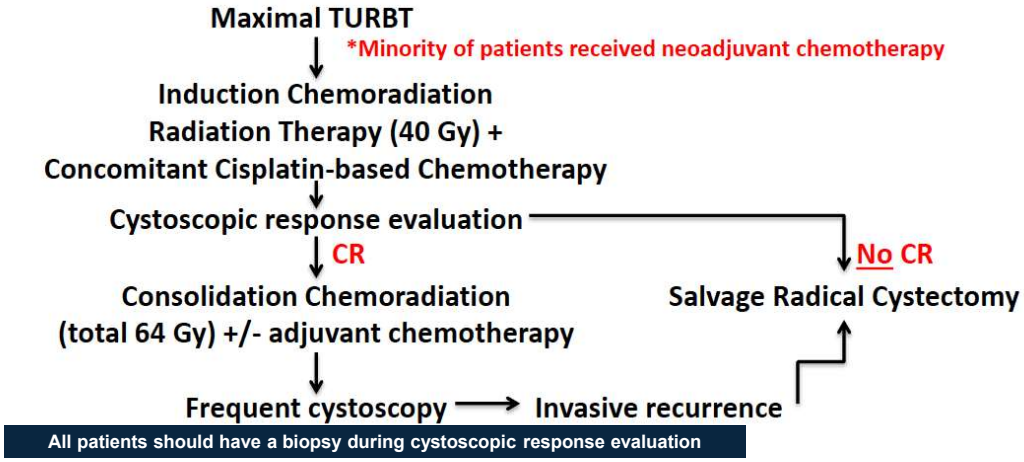
Bladder preservation: treatment paradigms for chemo-RT

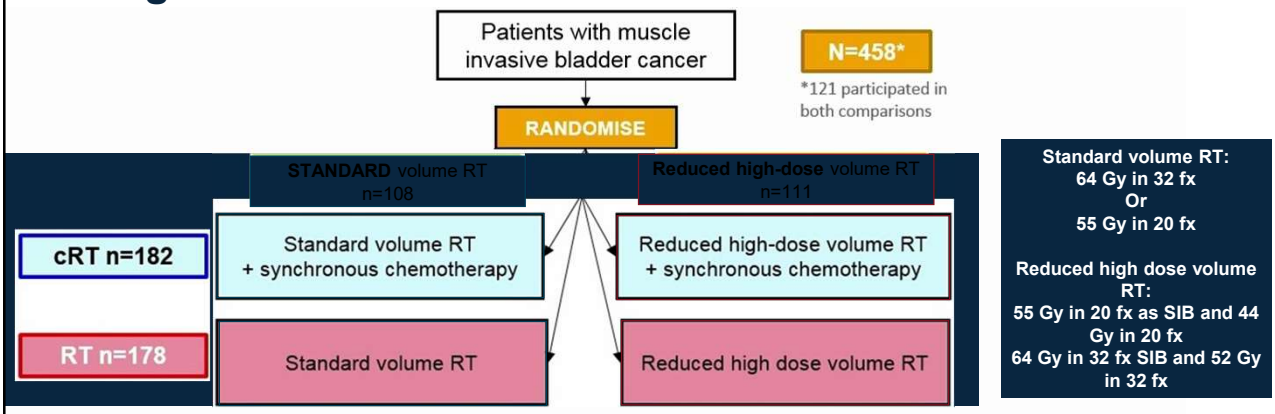
- **Continuous course**
  - Complete entire course of CRT and assess response with TURBT after 3 months
  - Per BC2001: treatment is to bladder only, not elective pelvic LNs
  - As of ~2021, this is the superior regimen (vs split course) because of improved local control with hypofractionated RT
- **Split course / MGH / Shipley protocol**
  - Induction chemoradiation phase
  - Planned break with response assessment with cystoscopy ~ 3 weeks after
  - Per MGH trial: treatment is to bladder and pelvic LNs
  - Consolidation chemoradiation phase or cystectomy

Split course bladder preservation protocol



Note: Although it's an option, I would not recommend this regimen (vs continuous course), given the BC2001 data with hypofractionation

Continuous course chemo radiotherapy: BC2001 trial design



Eligible patients had histologically confirmed T2-T4a N0 M0 MIBC, WHO performance status 0 to 2; GFR> 25ml/min. For radiotherapy (RT) comparison: single tumour at time of invasive disease diagnosis.

Slide courtesy of Dr Nick James and BC2001 team

PRESENTED AT: **2017 Genitourinary Cancers Symposium | #GU17**

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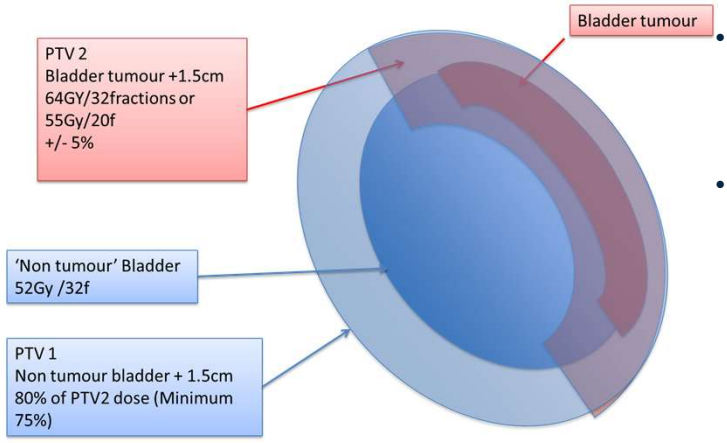
Patients on BC2001 received 1 of 4 possible RT regimens

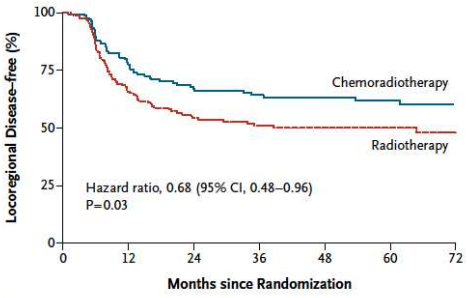


- Standard volume RT:
  - 64 Gy in 32 fx

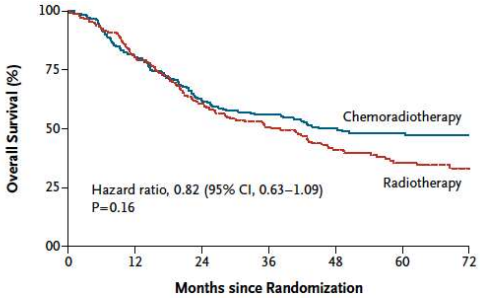
  vs
  - 55 Gy in 20 fx
- Reduced high dose volume RT:
  - 55 Gy in 20 fx as simultaneous integrated boost (SIB) and 44 Gy in 20 fx to whole bladder

  vs
  - 64 Gy in 32 fx SIB and 52 Gy in 32 fx
  - Delivered 80% of maximum dose to the uninvolved bladder and full dose to the tumor

In BC2001, chemoradiotherapy improved locoregional control (vs radiotherapy alone); no change in survival or late toxicity



No. at Risk (no. of events)							
Chemoradiotherapy	182 (35)	108 (14)	76 (3)	66 (1)	56 (1)	46 (1)	25
Radiotherapy alone	178 (54)	96 (16)	69 (4)	58 (1)	44 (0)	35 (1)	18



No. at Risk (no. of events)							
Chemoradiotherapy	182 (35)	144 (33)	111 (11)	94 (9)	75 (3)	62 (1)	39
Radiotherapy alone	178 (35)	141 (34)	104 (17)	85 (15)	60 (7)	41 (2)	20

James, *NEJM*, 2012

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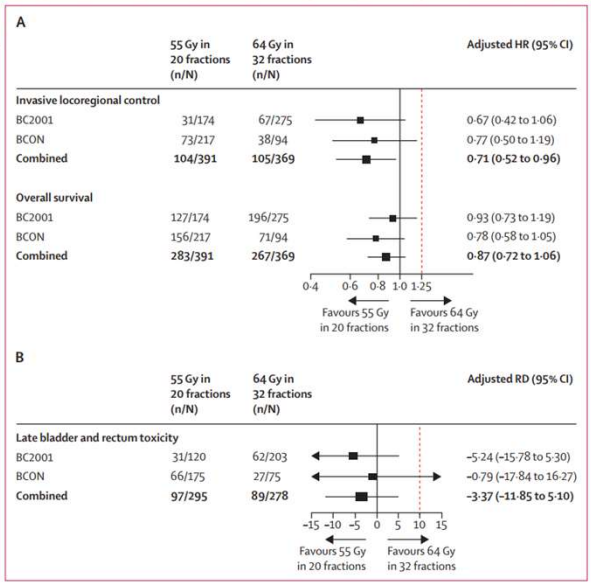
In BC2001 and BCON, hypofractionation (55 Gy / 20 fx) had improved local control vs conventional fractionation (64 Gy / 32 fx)



Choudhury, *Lancet Onc*, 2021

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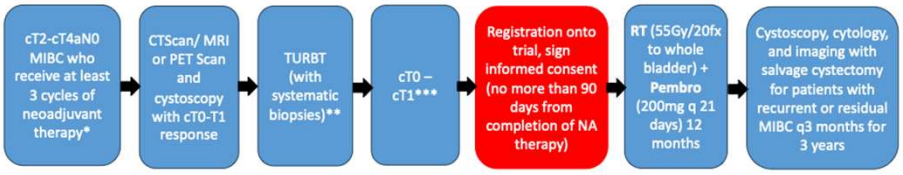
Current Trials

Schema S2427



*Patients who receive NAC as the NAT must have at least 3 cycles of cis-based regimen
**Patients found to have >T1 disease on TURBT will proceed to SOC cystectomy
***Diffuse CIS patients will be excluded (>3 cm area of contiguous CIS or >3 separate locations of CIS on TURBT (dome/posterior/left/right/trigone)

SWOG CANCER RESEARCH NETWORK

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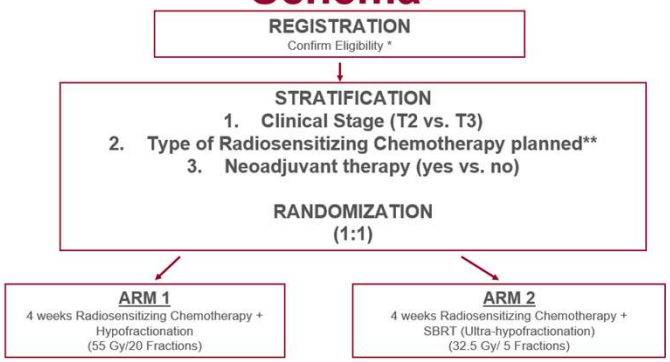
Current Trials

Schema



* See Protocol Section 3.1 for details
** Types of chemotherapy regimens are:
- Cisplatin
- Gemcitabine
- Mitomycin-C/5-Fluorouracil

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Post-op bladder cancer: who needs adjuvant radiation therapy?

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Penn/SWOG post cystectomy risk groups for LRFS		
Stage	**Nodal Risk**	**5-yr LRFS**
Low	pT0 -2	8%
Intermed	pT3-4, R+ in soft tissue and 10+ LN dissected	20%
High	pT3-4, R+ in soft tissue and <10 LN dissected	>40%

Post-cystectomy RT atlas

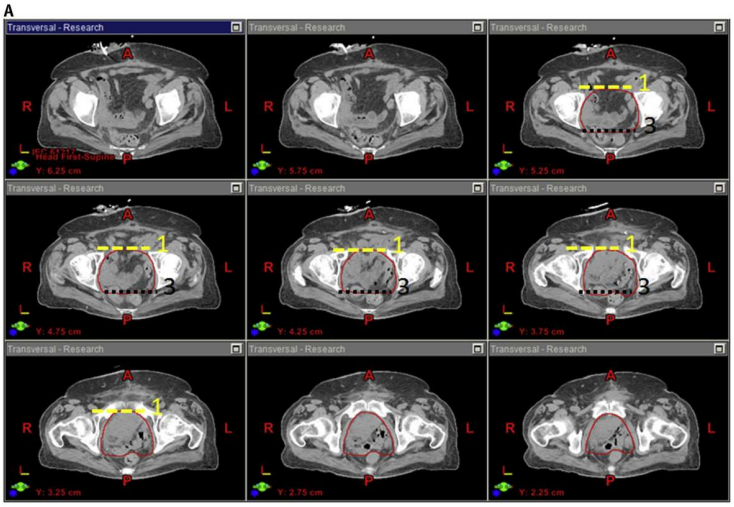

Fig. 3. Representative axial slices showing the cystectomy bed in the (A) upper pelvis and (B, following page) lower pelvis of a female patient.

Baumann, 2016, *IJROBP*

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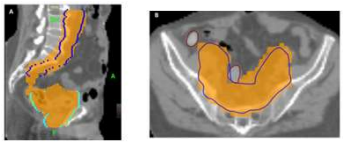
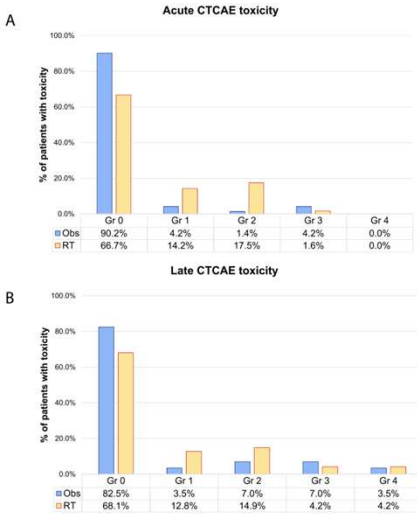
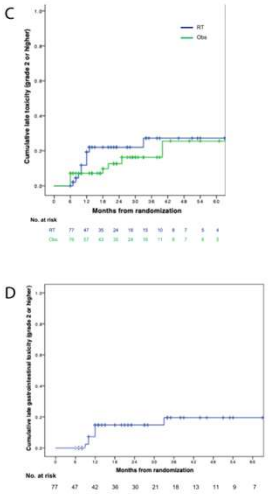
BART trial: evaluates adjuvant RT for high-risk MIBC

- 153 patients w MIBC a 1+ high risk feature: pT3-4, pN1-3, < 10 node yield, R1, or cT3+
- Randomize: observation vs adjuvant IMRT 50.4 Gy to bed and pelvic LNs
- Findings:
  - limited G3+ toxicity with RT
  - cumulative 20% late G2 toxicity







Murthy, *IJROBP*, 2024

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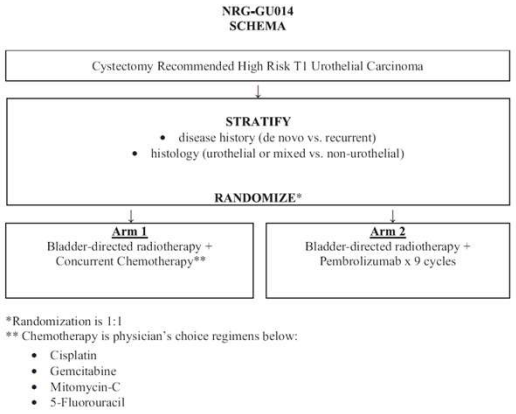
Role of RT in NMIBC

- Can consider RT in High Risk T1; non-cystectomy candidates



Conclusion

- Evolution of Hypo-Fractionated RT and potential role of SBRT for MIBC
- Increased use of Adjuvant RT for high-risk MIBC
- Evolving role of biomarkers in the treatment of bladder cancer

Adjuvant volumes	Components	Description from NRG-GU001
CTV cystectomy bed Include if R+. Dose 54–60 Gy	**Sup**	2 cm above pubic symphysis
	Ant	Post of pubic rami/symphysis. Above and below, contour will stop at the planes defined by extending linesup and inf from the post aspect of symphysis
	Post	Abut the ant 1/3 of the external ano-rectal circumference w/o extending into anorectum. Above the level of rectum, stop posteriorly at plane defined by line going superior from ant border of rectum
	Lat	Medial border obturator internus muscles. Inferiorly, it is at the vaginal wall or prostate bed
	Inf	2-3 mm (1 axial CT slice) above the penile bulb for males, 1 cm below lower pole of obturator foramen for females.
CTV LNs		Trim LNs at pelvis, muscle, bone Do not trim at bowel bc risk of marginal miss LN CTV mirror high-risk prostate LN CTV
	Pelvic LNs: Always include (R0 or R+) R0: 45–50.4 R+: 54–60	**distal common iliac, internal iliac, external iliac, obturator** Sup at L5-S1 Externals iliacs extend inf to top of femoral heads Int iliacs extentinf until no longer visible, or exit through greater sciatic notch Expand by 7 mm in ant, post, lat dimensions
	Presacral LNs: Include if R+ 54–60 Gy	From L5-S1 to S2-3. Include 1-1.5 cm of tissue ant to sacrum and between vessels Sup at inf border of iliac contours Inf at top of pubic symphysis 1 cm width of tissue medial to obturator internus muscles, from ant border or ilium to post border or ilium
OARs	**ostomy bag**	for patients with non-continent diversions sim and treat with empty bag
	Bowel	entire bowel space, inc bowel, cecum, colon. sup at 3 cm above sup extent of LN CTV
	Rectum	from RS junction sup to level of iscial tuberosities inf
	Pelvic bones	Start 1 cm sup above nodal CTV and go 1 cm inf of CTV