Outcomes and Healthcare Resource Utilization of Patients Receiving Definitive Versus Non-Definitive Treatment for Muscle-Invasive Bladder Cancer: a Real-World Analysis within the Veterans Affairs System

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INTRODUCTION

- Approximately 50% of patients with muscleinvasive bladder cancer (MIBC) do not receive definitive treatments (DT), including radical cystectomy (RC) or chemoradiation (CRT), despite established survival benefits¹⁻⁴.
- Retrospective real-world data were used to better understand and compare demographic, clinical characteristics, survival outcomes, and healthcare resource utilization (HCRU) and associated costs among patients with MIBC receiving DT vs. no definitive treatment (NDT).

METHODS

- Patients from the United States Veterans Affairs System diagnosed with MIBC between 2010-2019 were identified via a validated natural language processing (NLP) model analyzing pathology reports of transurethral resection of bladder tumor (TURBT) and supplementary chart review⁵.
- Index date was defined as the first date of MIBC diagnosis. All eligible patients had baseline periods of ≥ 12 months pre-index and follow-up periods of >3 months post-index.
- Baseline characteristics were summarized and compared by omnibus (i.e., global) tests.
- The impact of treatment groups on overall survival (OS) was visualized by unadjusted Kaplan-Meier plot and tested by a multivariable Cox model with time-dependent covariates.
- All-cause and bladder-cancer specific (BCspecific) HCRU and associated costs were summarized on a per-patient per-year (PPPY) basis, and differences across treatment groups were assessed by omnibus (i.e., global) tests.

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RESULTS

- We identified **1,524 patients with MIBC**, of whom 650 received NDT, 740 were treated with RC, and 134 were treated with CRT.
- Patients who received NDT were older at MIBC **diagnosis** (median age in years: 78 [NDT], 68 [RC], 72 [CRT]; p<0.001).
- An OS advantage was observed for patients receiving DT vs. NDT in both unadjusted Kaplan-Meier plot (Figure 1) and the multivariable Cox model (adjusted hazard ratios (HR): 0.49 [RC], 0.65 [CRT]; both, p<0.001).
- Patients receiving NDT had lower, but nevertheless substantial unadjusted all-cause and **BC-specific total costs** compared to those receiving DT (**Table 1**).
- Inpatient HCRU and costs were highest for patients receiving RC. Outpatient HCRU and costs were highest for patients receiving CRT (**Table 1**).



FIGURE 1: Unadjusted Kaplan-Meier plot of treatment groups

TABLE 1: Unadjusted all-cause and BC-specific HCRU and costs

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Variable	Туре	No Definitive Treatment (n=650)	Radical Cystectomy (n=740)	Chemoradiation (n=134)	p-value
Total Costs (USD) , PPPY, Median (IQR)	All-cause	46,418 (18,885–106,638)	74,535 (37,415–158,778)	68,465 (37,255–146,860)	<0.001ª
	BC-specific	9,299 (2,213–28,263)	24,513 (11,271–68,002)	14,085 (4,179–26,029)	<0.001 ^a
Inpatient Visits					
Patients with ≥ 1 visit, n (%)	All-cause	411 (62.2)	721 (97.4)	104 (77.6)	<0.001 ^b
	BC-specific	195 (30.0)	651 (88.0)	40 (29.9)	<0.001 ^b
Number of visits, PPPY, Mean (SD)	All-cause	1.8 (2.6)	1.9 (2.4)	1.7 (2.3)	<0.001ª
	BC-specific	0.5 (1.1)	0.7 (1.0)	0.3 (0.6)	<0.001ª
Costs (USD), PPPY, Median (IQR)	All-cause	7,475 (0–46,380)	37,017 (15,199–98,875)	19,727 (1,353–62,217)	<0.001ª
	BC-specific	0 (0–4,898)	18,518 (7,502–53,634)	0 (0–1,768)	<0.001ª
Outpatient Visits					
Patients with \geq 1 visit, n (%)	All-cause	645 (99.2)	739 (99.9)	134 (100.0)	0.13 ^b
	BC-specific	614 (94.5)	730 (98.7)	132 (98.5)	<0.001 ^b
Number of visits, PPPY, Mean (SD)	All-cause	59.8 (44.1)	63.3 (39.0)	90.3 (55.4)	<0.001ª
	BC-specific	9.1 (10.1)	10.7 (11.8)	20.3 (19.4)	<0.001ª
Costs (USD), PPPY,	All-cause	25,776 (12,250-48,406)	24,362 (13,714–43,075)	39,918 (19,987–64,110)	<0.001ª
Median (IQR)	BC-specific	5,431 (1,655–15,601)	3,777 (1,274–10,433)	11,723 (3,361–22,073)	<0.001ª

aKruskal-Wallis p-value; bChi-Square p-value. Costs were adjusted to the 2022 medical care component of the consumer price index. BC, bladder cancer. HCRU, healthcare resource utilization. USD, US dollar. PPPY, per-patient per-year. IQR, interquartile range. SD, standard deviation

REFERENCES:

1. Patel M, Gadzinski AJ, Bell AM, et al. Interprofessional Consultations (eConsults) in Urology. Urol Pract. May 2021;8(3):321-327

2. Westergren DO, Gårdmark T, Lindhagen L, Chau A, Malmström PU. A Nationwide, Population Based Analysis of Patients with Organ Confined, Muscle Invasive Bladder Cancer Not Receiving Curative Intent Therapy in Sweden from 1997 to 2014. J Urol. Nov 2019;202(5):905-912 3. Gray PJ, Fedewa SA, Shipley WU, et al. Use of potentially curative therapies for muscle-invasive bladder cancer in the United States: results from the National Cancer Data Base. Eur Urol. May 2013;63(5):823-829.

4. ohn JB, Varughese MA, Cooper N, et al. Treatment Allocation and Survival in Patients Diagnosed with Nonmetastatic Muscle-invasive Bladder Cancer: An Analysis of a National Patient Cohort in England. *Eur Urol Focus*. Mar 2021;7(2):359-365. 5. Yang R, Zhu D, Howard LE, et al. Context-Based Identification of Muscle Invasion Status in Patients With Bladder Cancer Using Natural Language Processing. *JCO Clin Cancer Inform*. Jan 2022;6:e2100097.

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KEY TAKEAWAY



Patients receiving NDT were older and had worse overall survival compared to those receiving DT.

Patients receiving NDT were older, had

costs compared to those receiving DT.

significantly worse survival, and

incurred lower but still substantial



Although NDT was associated with lower total costs than DT, the overall costs remain substantial. However, these costs within the VA may not reflect those in other systems or populations (e.g., Medicare, Commercial) or costs within specific timeframes.



Further studies are needed to evaluate other impacts of DT and NDT on patients including productive life-years lost and the physical and emotional burden.

These findings highlight unmet needs among MIBC patients receiving NDT and underscore the requirement for more tolerable novel therapies to improve the prognosis of these patients.

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DISCLOSURES

RZ and SD have no disclosures to report. BL, RH, EOC, JG report employment with J&J. KK is a shareholder in J&J and CG Oncology. HS employment with J&J and ownership of J&J stocks. SB owns J&J stocks and was a J&J employee at the time of study. SJF consultant to Janssen, Astellas, Bayer, Pfizer, Sanofi, Sumitomo, Novartis, Astra Zeneca, Merck, and Eli Lilly SBW reports advisory board and consultant fees from Janssen, Merck, Photocure, Valar Labs and serves as BJUI section editor. APM reports honoraria from UpToDate and is a co-creator of intellectual property owned by the University of Southern California related to a prognostic panel for urinary bladder cancer. JI, SM, JP, CE, AD report research funding paid to the lab by: Merck, Janssen, Exact Sciences, Astellas, Delfi Diagnostics, Guardant Health, Photocure, AstraZeneca Pharmaceuticals, Reinvestment Partners, Prostatype Genomics, Novartis, Vir Biotechnology, Coloplast corporation, **Roche Pharmaceuticals**



