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Front-line treatment and recurrence patterns among patients with high-risk non–muscle-invasive bladder cancer with papillary carcinoma or carcinoma in situ following Bacillus Calmette-Guérin or other intravesical therapies

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Key Takeaway

Current intravesical options, including BCG, show limited durability, underscoring the need for more effective, bladder-sparing treatments in 1L patients with HR-NMIBC

Conclusions

In this real-world study of Medicare-insured patients with HR-NMIBC with CIS or papillary carcinoma, over 60% of patients experienced recurrence within 12 months of initiating 1L treatment with BCG or other IVTs

While a large majority of patients with HR-NMIBC completed the induction phase, approximately half had adequate maintenance

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Disclosures

M. D. Fabrizio is an employee of MedStar Georgetown University Hospital and has served in a consulting role for Johnson & Johnson, Dendreon, Teleflex Medical, and Specialty Networks, and has served on speaker's bureau for Astellas Pharma, Bayer, Pfizer, and Sumitomo Pharma Oncology. M. Singhal is an employee and stockholder of Johnson & Johnson. B. Emond, C. Rossi, R. Bungay, S. Liu, and D. Pilon are employees of Analysis Group, ULC/Inc., a consulting company that has provided paid consulting services to Johnson & Johnson. A. R. Khaki is an employee of Stanford University School of Medicine and has received grants from Johnson & Johnson, Pfizer, 23andMe, and Acrivon Therapeutics outside of this work.

Background

- High-risk non-muscle invasive bladder cancer (HR-NMIBC) is associated with a high disease burden and substantial likelihood of recurrence and progression, requiring close surveillance and management through multiple interventions[1,2]
- Intravesical Bacillus Calmette-Guérin (BCG) is recommended by the National Comprehensive Cancer Network (NCCN®) as front-line (1L) therapy for HR-NMIBC, with additional intravesical therapies (IVTs) recommended for patients who become unresponsive to BCG[3]
- Patients who experience disease recurrence after treatment with BCG or other IVTs have few effective bladder-sparing treatment options and experience poor long-term clinical outcomes[4-6]
- There is limited real-world data describing treatment patterns and recurrence among treatment-naïve patients with HR-NMIBC with carcinoma in situ (CIS) or papillary carcinoma in the US

Objective

- To describe real-world treatment patterns and disease recurrence among patients in the US with HR-NMIBC receiving BCG or other IVTs in 1L HR-NMIBC

Methods

Data source

- SEER-Medicare Data (01/01/2007–12/31/2022) were used, which linked the US National Cancer Institute's (NCI) Surveillance, Epidemiology, and End Results (SEER) cancer registry (containing cases diagnosed since 1973) with the Centers for Medicare & Medicaid Services (CMS) Medicare claims database
- Data were de-identified and complied with the Health Insurance Portability and Accountability Act (HIPAA) regulations

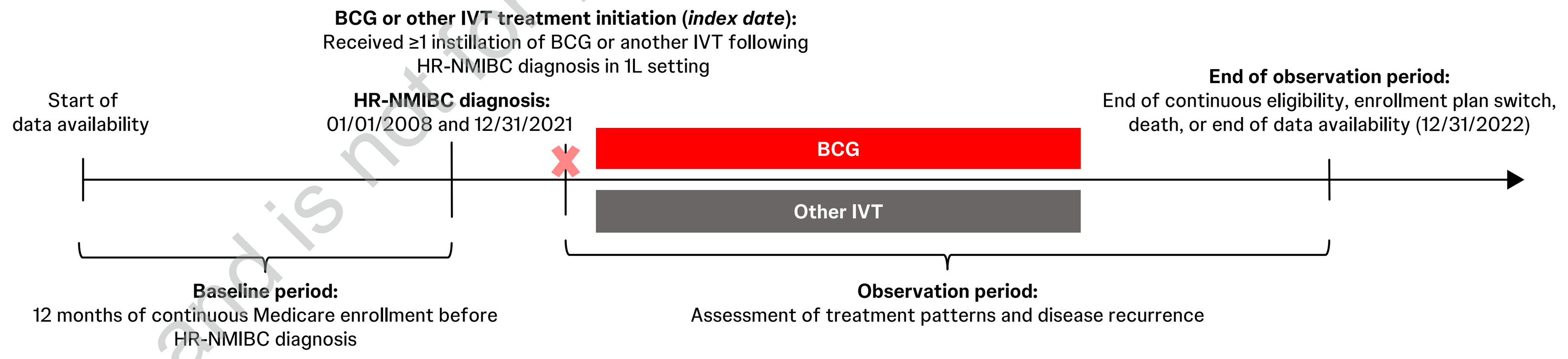
Study design and study population

- A retrospective longitudinal study was conducted (**Figure 1**)
- Patients aged ≥65 years with HR-NMIBC with CIS or with papillary carcinoma who initiated treatment with BCG or other IVTs (i.e., mitomycin, gemcitabine, valrubicin, docetaxel, epirubicin), with no prior treatments for HR-NMIBC were included (**Figure 2**)
- The index date was defined as the date of the first instillation for BCG or other IVTs (i.e., start of 1L therapy)
- The baseline period was defined as the 12-month period of continuous enrollment prior to HR-NMIBC diagnosis, while the observation period spanned from the index date until the earliest of end of continuous enrollment, plan switch, death, or end of data availability (12/31/2022)

Study measures and statistical analysis

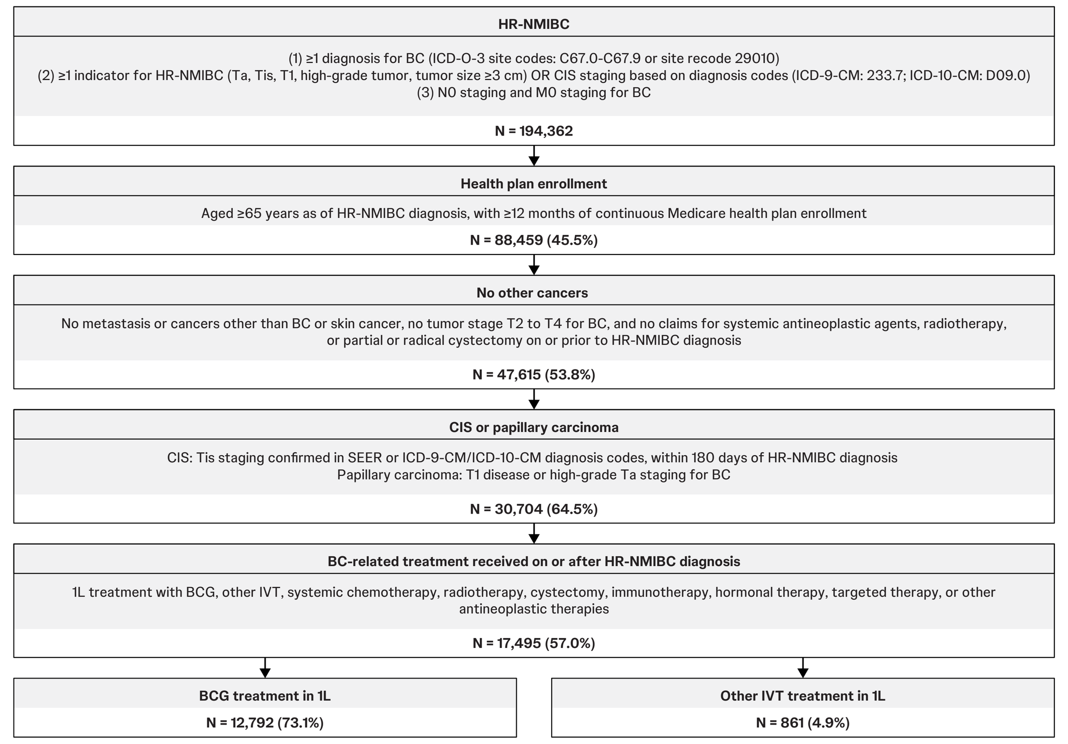
- Patient characteristics and treatment patterns following HR-NMIBC diagnosis were summarized using means, standard deviations, and medians for continuous variables, and frequencies and proportions for categorical variables
- Disease recurrence during the observation period was evaluated using Kaplan-Meier (KM) time-to-event analysis
  - Disease recurrence was defined as reinitiation of the same therapy after a gap (BCG: ≥180-day gap; other IVT: ≥90-day gap), transurethral resection of bladder tumor (TURBT), biopsy, or initiation of a new treatment (i.e., alternative IVT, systemic chemotherapy, radiotherapy, cystectomy, immunotherapy [including pembrolizumab], hormonal therapy, or other antineoplastic therapy)

Figure 1: Study design scheme



1L: front-line; BCG: Bacillus Calmette-Guérin; HR-NMIBC: high-risk non-muscle invasive bladder cancer; IVT: intravesical therapy.

Figure 2: Sample selection



1L: front-line; BC: bladder cancer; BCG: Bacillus Calmette-Guérin; CIS: carcinoma in situ; HR-NMIBC: high-risk non-muscle invasive bladder cancer; ICD-9-CM/ICD-10-CM: International Classification of Disease, Ninth/Tenth Revision, Clinical Modification; ICD-O-3: International Classification of Diseases for Oncology, Third Edition; IVT: intravesical therapy.

Results

Patient characteristics

- Among 17,495 patients initiating 1L treatment for HR-NMIBC, 12,792 (73%) received BCG (mean age: 76 years; 79% male; 91% White) and 861 (5%) received other IVTs (mean age: 77 years; 76% male; 93% White) (**Table 1**)

Table 1: Baseline patient characteristics

	BCG treatment in 1L N = 12,792	Other IVTs in 1L N = 861
Age at diagnosis, mean ± SD [median]	76.3 ± 6.6 [75.6]	76.9 ± 7.0 [75.9]
Male sex, n (%)	10,061 (78.7)	652 (75.7)
White race, n (%)	11,619 (90.8)	797 (92.6)
Year of diagnosis, n (%)		
2008-2011	2,055 (16.1)	58 (6.7)
2012-2015	3,282 (25.7)	240 (27.9)
2016-2019	5,058 (39.5)	319 (37.0)
2020-2021	2,397 (18.7)	244 (28.3)
US region, n (%)		
West	5,594 (43.7)	305 (35.4)
Northeast	3,032 (23.7)	197 (22.9)
South	2,735 (21.4)	157 (18.2)
Midwest	1,431 (11.2)	202 (23.5)
Residential setting, n (%)		
Urban	11,260 (88.0)	734 (85.2)
Rural	1,532 (12.0)	127 (14.8)
Medicare plan enrollment, n (%)		
Fee-for-Service	8,607 (67.3)	653 (75.8)
Medicare Advantage	4,185 (32.7)	208 (24.2)
Quan-CCI, mean ± SD [median]	1.7 ± 1.8 [1.0]	2.0 ± 1.9 [2.0]
Urinary tract infection, n (%)	4,193 (32.8)	295 (34.3)
Smoking, n (%)	3,442 (26.9)	295 (34.3)
Kidney stone, n (%)	1,527 (11.9)	111 (12.9)

1L: front-line; BCG: Bacillus Calmette-Guérin; CCI: Charlson Comorbidity Index; IVT: intravesical therapy; SD: standard deviation; US: United States.

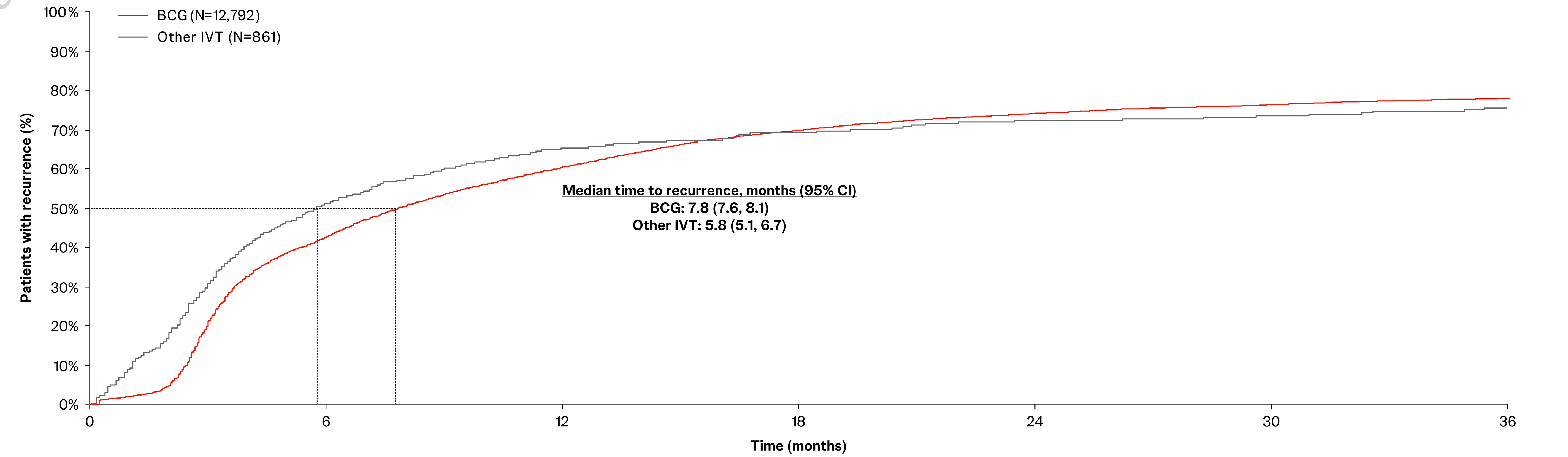
Treatment patterns

- Among BCG-treated patients, 56% initiated BCG within 3 months of HR-NMIBC diagnosis, 84% received adequate induction (≥5 instillations within 70 days), and 54% received adequate induction plus maintenance (≥7 instillations within 274 days)
- Among other IVT-treated patients, most were treated with mitomycin (64%), gemcitabine (25%), or gemcitabine + docetaxel (5%)

Disease recurrence

- For BCG-treated patients, median time to recurrence was 7.8 months (95% confidence interval [CI]: 7.6, 8.1), with KM recurrence rates of 21% at 3 months, 43% at 6 months, 61% at 12 months, and 74% at 24 months
- For patients treated with other IVTs, median time to recurrence was 5.8 months (95% CI: 5.1, 6.7), and KM recurrence rates were 30% at 3 months, 51% at 6 months, 65% at 12 months, and 72% at 24 months

Figure 3. Time to disease recurrence among patients with HR-NMIBC who initiated BCG or other IVTs in 1L



	6	12	18	24	30	36
BCG						
Number at risk	7,085	4,631	3,056	2,326	1,903	1,578
Recurrence rate	43%	61%	70%	74%	76%	78%
Other IVT						
Number at risk	402	257	189	139	109	78
Recurrence rate	51%	65%	69%	72%	74%	76%

1L: front-line; BCG: Bacillus Calmette-Guérin; CI: confidence interval; HR-NMIBC: high-risk non-muscle invasive bladder cancer; IVT: intravesical therapy.

Limitations

- This study is subject to limitations common to retrospective claims analyses, including potential coding inaccuracies, missing data, and incomplete documentation, which may result in misidentification of study variables
- The HR-NMIBC diagnosis date was defined as the earliest available indicator (i.e., staging or diagnosis codes) in the data, which may not reflect the true disease onset, particularly for cases diagnosed before data availability (i.e., prior to 2008)
- As the dataset did not include clinical measures of disease recurrence, an algorithm to identify recurrence events was applied; however, some events may have been misclassified or not captured
- Findings may not be generalizable to patients without Medicare insurance coverage

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