IP02-31

Treatment Patterns and Clinical Outcomes in Patients with Bacillus Calmette-Guérin (BCG)-unresponsive High-risk Non-muscle Invasive Bladder Cancer with Carcinoma in Situ

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Key Takeaways

Most HR-NMIBC patients with CIS initiate intravesical chemotherapy after BCG failure without achieving durable responses, highlighting a high unmet need for efficacious bladder-sparing treatments for this population.

Conclusions

In patients with BCG-unresponsive HR-NMIBC with CIS:

- Despite the recommended standard-of-care being RC, analyses using real-world data demonstrated that most patients initiated bladder-sparing treatment, primarily intravesical chemotherapy, within 1 year of adequate BCG therapy
- Intravesical therapies did not provide durable responses, as evidenced by the short median time-to-recurrence with or without progression of 6.94 months

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Acknowledgments

The authors thank the participants and investigators for their participation in the study. Yi Zhe (Izzy) Wang, PhD (contracted researcher of Johnson & Johnson Innovative Medicine) contributed significantly in data analysis. Jyotsana Dixit, PhD (SIRO Medical Writing Pvt. Ltd., India) provided editorial assistance. Sandeep Chavan (SIRO Medical Writing Pvt. Ltd., India) provided graphic designing support.

Disclosures

Stephen B. Williams: Consultant and advisory board- Janssen, Merck, Photocure, Valar labs.

The study was funded by Johnson & Johnson Innovative Medicines.

Introduction

- Non-muscle invasive bladder cancer (NMIBC) accounts for more than 75% of newly diagnosed bladder cancers[1]. Approximately 25% of NMIBC cases are classified as high-risk (HR)[1,2]
  - Among these, carcinoma in-situ (CIS) represents an aggressive subtype, with an increased likelihood of recurrence and progression[2,3]
- Up to 40% of HR-NMIBC patients become unresponsive to the standard-of-care in frontline therapy, Bacillus Calmette-Guérin (BCG) treatment[4,5], which poses a significant clinical challenge[6,7,8]
  - Clinical guidelines recommend radical cystectomy (RC) as the standard treatment for these patients, despite its associated risks of morbidity, mortality, and reduction in quality-of-life[7]
- Real-world data on treatment regimens and downstream outcomes are sparse for patients with BCG-unresponsive HR-NMIBC with CIS[3]

Objective

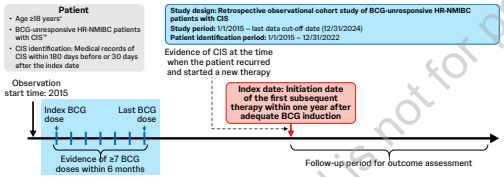
- **This study aims to report treatment patterns and clinical outcomes in patients with BCG-unresponsive HR-NMIBC with CIS in a real-world setting**

Methods

Data sources

- Patients with NMIBC, both newly diagnosed and recurrent or prevalent cases, were identified from the American Urology Association Quality (AQUA) Registry, which collects real-world data from more than 2,200 active providers in the US
- De-identified patient records from AQUA were integrated and linked with corresponding de-identified patient records in Komodo's Healthcare Map, a healthcare claims database, that enhances the electronic health record data by capturing healthcare resource utilization and treatments that may have taken place outside the AUA network
- Further inclusion and exclusion criteria for the analysis are described in (**Figure 1**)

Figure 1: Study design and patient's eligibility criteria



*FDA guidance-based definition of BCG-unresponsive patients: Those patients who have received at least 7 BCG treatments ≤6 months and initiated a non-BCG treatment within the next 12 months. Baseline period: 6-month period prior to index date. †All patients were required to have a minimum 1 year of follow-up post adequate BCG treatment.

BCG, Bacillus Calmette-Guérin; CIS, carcinoma in-situ; FDA, Food and Drug Administration; HR-NMIBC, high-risk non-muscle invasive bladder cancer.

Study Outcomes

- Baseline demographic and clinical characteristics
- Subsequent treatments received within 12 months of adequate BCG treatment
- Clinical outcome: Time-to-recurrence with or without progression
  - Defined as time from index date to the earliest occurrence of any of the following:
    - Evidence of small, medium, or large TURBT
    - Evidence of biopsy
    - Evidence of a change in treatment
    - Evidence of disease progression (MIBC or T-stage ≥T2)
    - Evidence of metastasis

Statistical Analysis

- Baseline demographics, clinical characteristics, and treatment patterns were summarized using descriptive statistics
- Kaplan Meier analysis was used to assess time-to-recurrence with or without progression
  - Outcomes among patients initiating different types of intravesical chemotherapy were compared using log-rank test

BCG, Bacillus Calmette-Guérin; MIBC, muscle-invasive bladder cancer; TURBT, transurethral resection of bladder tumor; T-stage, tumor-stage.

Results

Baseline demographics and clinical characteristics

- Patient demographics: Mean age 72 years, predominantly male (84.4%), White (93.2%), non-Hispanic or Latino (97.2%) (**Table 1**)
- After completing adequate BCG treatment, 282 HR-NMIBC patients with CIS initiated a subsequent non-BCG treatment within 12 months
- Most patients (67.4%) had CIS alone without concomitant papillary disease
- The median duration from adequate BCG treatment completion to non-BCG treatment initiation was 142 days or 4.7 months

Table 1: Patient demographics and clinical characteristics

Characteristic	N=282
Age, mean (SD)	72 (8.27)
Age, median (IQR)	74 (67–80)
Age category, n (%)	
<65	51 (18.1)
65–69	42 (14.9)
70–74	52 (18.4)
≥75	137 (48.6)
Sex, n (%)	
Male	238 (84.4)
Female	44 (15.6)
Race, n (%)*	
White	207 (93.2)
Black or African American	11 (5.0)
Native American and Alaska Native	1 (0.5)
Asian or Pacific Islander	2 (0.9)
Other	1 (0.5)
Ethnicity, n (%)**	
Not Hispanic or Latino	206 (97.2)
Hispanic or Latino	6 (2.8)
Median follow-up (IQR) (months)	33.7 (21.1–54.5)
Year of index date, n (%)	
2015–2019	166 (58.9)
2020–2023	116 (41.1)
Tumor stage, n (%)	
Tis	190 (67.4)
Tis + T1	75 (26.6)
Tis + Ta	17 (6.0)
Number of BCG doses received at index, median (IQR)	9 (8–12)
Time between index BCG and first non-BCG subsequent treatment, days, median (IQR)	324 (246–413)
Time from completion of adequate BCG treatment period to initiation of first non-BCG subsequent treatment, days, median (IQR)	142 (64–231)
Time between index and last BCG dose, days, median (IQR)	153 (131–174)

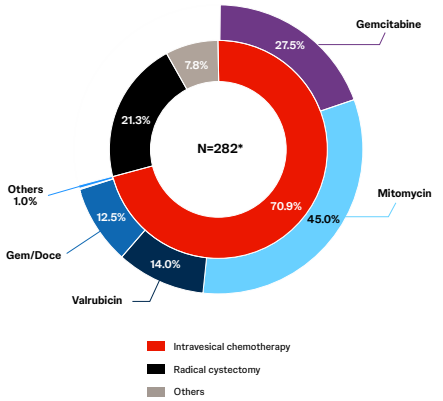
*Calculated out of 222 patients with known race information. **Calculated out of 212 patients with known ethnicity information.

BCG, Bacillus Calmette-Guérin; CIS, carcinoma in-situ; IQR, interquartile range; SD, standard deviation; Tis, carcinoma in situ; T1 and Ta, tumor stages.

Treatment patterns

- While RC is the standard-of-care in this population, only ~20% of patients received RC after becoming BCG unresponsive, indicating a desire for bladder sparing therapy (**Figure 2**)
- The majority (70.9%) of these patients received intravesical chemotherapy (**Figure 2**)
  - 45.0% mitomycin
  - 27.5% gemcitabine
  - 14.0% valrubicin
  - 12.5% gemcitabine-docetaxel
  - 1.0% others

Figure 2: Type of subsequent non-BCG treatment

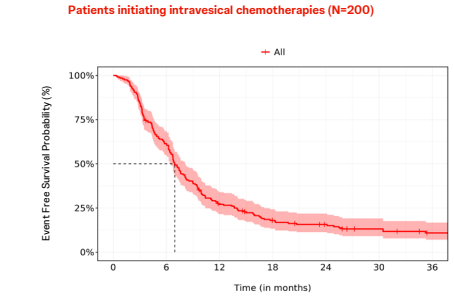


*Total number of patients initiating subsequent non-BCG treatment within 1 year of adequate BCG (7 BCG doses within 6 months).
Note:The inner circle denotes the treatments received by the BCG-unresponsive HR-NMIBC patients with CIS. Outer circle denotes different categories of intravesical chemotherapies received by the BCG-unresponsive HR-NMIBC patients with CIS.
BCG, Bacillus Calmette-Guérin; CIS, carcinoma in-situ; Doce, docetaxel; Gem, gemcitabine; HR-NMIBC, high risk-non-muscle invasive bladder cancer.

Time-to-recurrence with or without progression

- Among patients who started intravesical chemotherapy as subsequent treatment (n=200), the median time-to-recurrence with or without progression was 6.94 (95% confidence interval [CI]: 6.41, 8.12) months, with 84% experiencing recurrence with or without disease progression within 24 months after starting the treatment (**Figure 3**)
- No significant difference was found in time-to-recurrence with or without progression across types of intravesical chemotherapy (log-rank test p>0.05)

Figure 3: Time-to-recurrence with or without progression after initiating subsequent intravesical chemotherapy



Time (in months)	0 m	6 m	12 m	18 m	24 m	30 m	36 m
N at Risk	200	122	52	32	25	18	12
Survival Probability	100%	61%	27%	18%	16%	13%	11%

N	Events	Median (months)	95% CI
200	178	6.94	6.41–8.12

BCG, Bacillus Calmette-Guérin; CI, confidence interval; CIS, carcinoma in-situ; EFS, event-free survival; LCL, lower confidence limit; m, months; NMIBC, non-muscle invasive bladder cancer; UCL, upper confidence limit.

Limitations

- The electronic medical record database, linked with healthcare claims, does not capture detailed clinical information, including test results and reasoning for procedures such as TURBT and biopsy, which may limit our ability to accurately interpret and confirm potential recurrence events
- The AQUA Registry primarily collects data from community urologists and other urologic care providers. Therefore, information on patient's non-urological medical care (e.g., non-cancer-related comorbidities managed outside of specific institutions) may be incomplete or unavailable
- Participation in the AQUA Registry is voluntary and may not fully reflect the diversity of urologic practice across the US, potentially limiting the generalizability of results to populations beyond those represented in the registry
- Mortality data was not available at the time of initial data analysis and therefore not considered as part of the outcomes assessment

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Presented by Stephen B. Williams at American Urological Association (AUA) Annual Meeting 2025; April 26–29, 2025; Las Vegas, Nevada, USA