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Real-World Evidence on Patients with Non-Muscle Invasive Bladder Cancer Treated with BCG Therapy

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Summary

- Less than 49% of high-risk non-muscle invasive bladder cancer (NMIBC) patients receive Bacillus Calmette Guerin (BCG) adequate therapy
- Only 11% of patients in this cohort underwent radical cystectomy after BCG treatment
- Significant unmet need exists in this cohort of BCG treated patients

Introduction and Objective

- NMIBC accounts for ~70% of bladder cancer cases1, of which ~40% are high grade (HG).
- HG NMIBC patients are at significant risk of recurrence and progression if untreated. BCG is the standard treatment for HG NMIBC. However, many patients fail to respond to BCG.[2,3,4]
- Significant unmet need exists for patients who are unresponsive to BCG and are ineligible for or unwilling to have radical cystectomy, an invasive surgical procedure. Real-world data such as that extracted from patient medical charts can evaluate contemporary patient experience and outcomes and provide insights into the unmet need in this patient population.
- This retrospective patient medical chart study aimed to assess the treatment patterns and real-world practice outcomes of NMIBC patients who were treated with BCG.

Methods

- A web-based retrospective chart review, approved by an independent Institutional Review Board, was conducted with qualifying physicians.
- Each eligible physician could either be an actively practicing urologist or oncologist meeting the predetermined conditions and was willing to provide at least 3 patient charts **(Table 1)**.
- Data on diagnosis of NMIBC, treatment choices, and patient outcomes post-BCG therapy were extracted from the patient charts.
- Descriptive statistics were conducted and comparisons between groups were tested for statistical significance at 95% confidence levels.

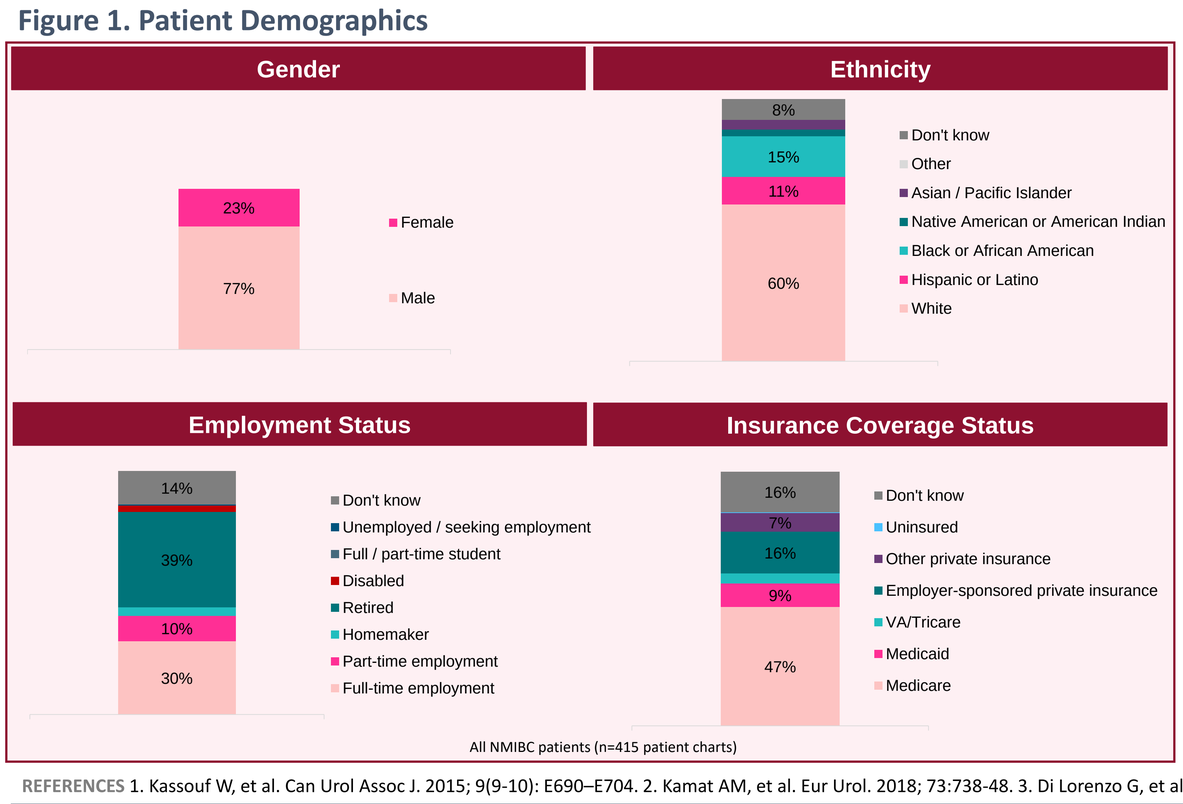
Table 1. Screening Criteria for Eligible Physicians and Patient Medical Charts

Physicians (must have met all criteria)
1. Board certified or board eligible urologist or oncologist
2. Active clinical practice (post-residency) for 2-30 years
3. Spent at least 70% (if oncologist) and 50% (if urologist) of their professional time in providing direct patient care
4. Treated at least 50 patients with solid tumors (if oncologist) in a typical month
5. Treated the following solid tumor patients in a typical month: - Bladder Cancer or - Urothelial Carcinoma or - Transitional Cell Carcinoma
6. In a typical month, seen at least: - 10 patients with NMIBC (CIS, Ta, T1) - 5 patients with muscle invasive bladder cancer (MIBC) (T2, T3) (if oncologist) - 5 patients with metastatic bladder cancer (T4) (if oncologist) - 5 NMIBC patients with high-risk bladder cancer (Ta, T1 Cis); any T1 and/or G3 and/or Cis - At least 3 BCG-unresponsive patients
7. Familiar with treatment options for NMIBC like: - BCG, radical cystectomy, mitomycin C (if oncologist), valstar, gemcitabine (if oncologist), PD-(L)1 inhibitors (if oncologist)
Patient Charts (must have met at least one criterion)
1. Treated at least once with BCG
2. Refractory to BCG therapy - defined as persistent high-grade disease at 6 months despite adequate BCG treatment - also includes any stage/grade progression by 3 months after the 1st BCG cycle
3. Experienced relapse after BCG therapy - defined as recurrence of high-grade disease after achieving a disease-free state at 6 months after adequate BCG therapy
4. Intolerant to BCG therapy - defined as disease persistence as a result of inability to receive adequate BCG therapy

Results

- Charts for 415 patients were collected from 94 physicians (73 urologists and 21 oncologists).
- Mean age of the selected cohort was 67 years (range 44-90 years).
- Other demographics in **Figure 1**.
- At diagnosis, ~69% patients reported hematuria and ~38% with frequent urination.
- High-risk NMIBC patients accounted for 41%, while intermediate-risk patients were ~43%.
- 60% of all included patient charts showed failure to BCG.

Figure 1. Patient Demographics

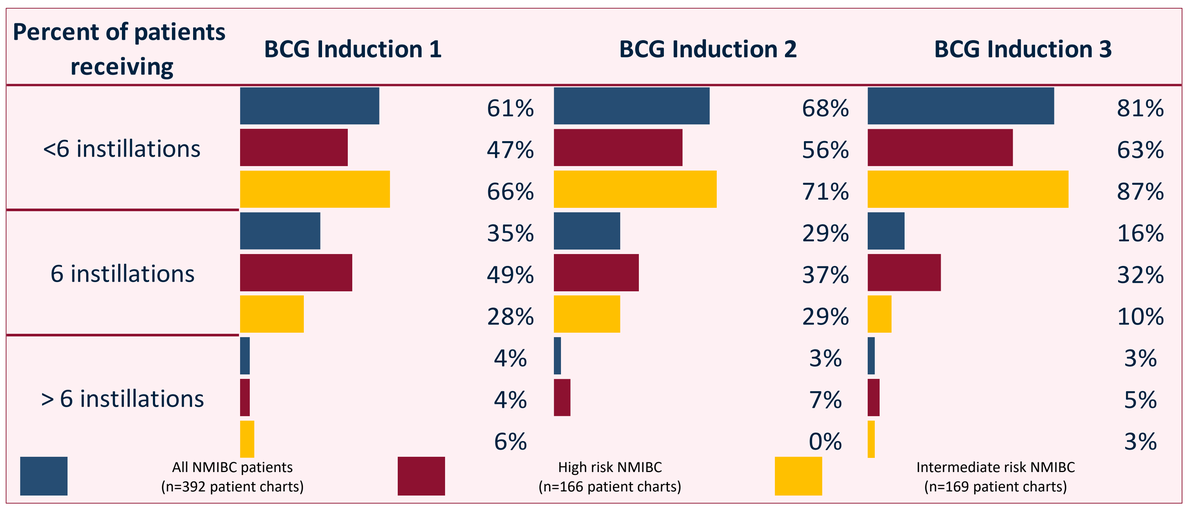


Results

Treatment Patterns

- In this study cohort, almost all patients (94%) received BCG therapy; other 6% were ineligible to receive BCG.
  - Other than BCG, 20% of patients received intravesical or systemic chemotherapy, excluding those who received a single instillation of intravesical chemotherapy following a transurethral resection of bladder tumor (TURBT).
- Receiving full course of 6 instillations of BCG during the 1st induction course was defined as adequate dosing of BCG **(Figure 2)**
  - Only 29% repeated BCG induction after the 1st full course.
  - Less than half (49%) of the high-risk patients received adequate BCG at 1st induction.
  - Less than 10% received >6 instillations during any induction course in any cohort.
- Overall, ~15% of patients received at least one maintenance course after BCG induction.
- Rate of radical cystectomy was quite low in the overall cohort (11%); average of 5 months between failure of BCG 1st induction to radical cystectomy for all patients
  - Significantly more high-risk patients underwent radical cystectomy than intermediate-risk patients (18% vs. 4%; $p<0.05$).

Figure 2. BCG Instillations per Induction Course by Risk Stratification



Reasons for Treatment Choices

- Tolerability/side effects (64%) and limited or lack of efficacy (30%) were cited as the top reasons for not completing the 1st induction course of BCG **(Figure 3)**.
- Physicians reported that patients received additional therapies after 1st BCG induction primarily due to poor outcomes defined by disease recurrence (38%). Other common reasons for use of additional therapies were being in a high-risk category (28%), use of adjuvant therapy (28%), and lack of efficacy (26%) **(Figure 6)**.
- Physicians cited using a "wait and watch" approach in 30% of their patient charts to avoid additional treatments **(Figure 7)**.
  - Low risk patients (23%) are significantly more likely to being monitored rather than treated further compared to high-risk patients (4%) ($p<0.05$).
  - BCG shortage was also cited to be a reason for discontinuation post the induction course.

Figure 3. Reasons for Incomplete BCG First Induction Course by Risk Stratification

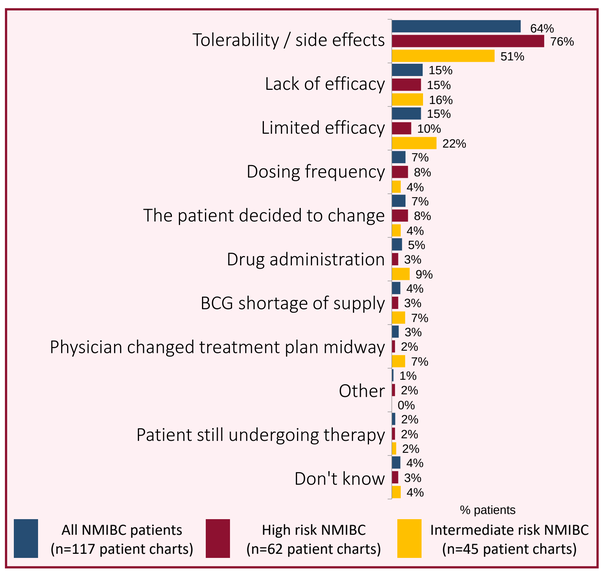


Figure 4. Reasons for Therapies after BCG First Induction Course by Risk Stratification

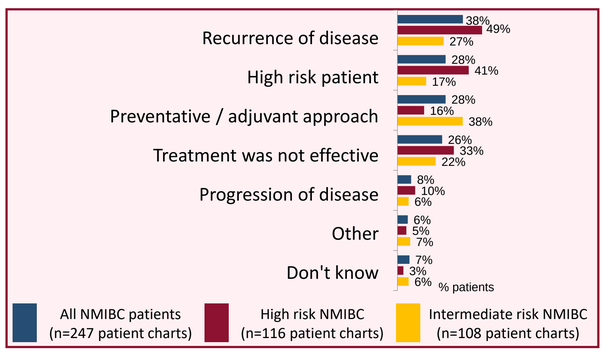
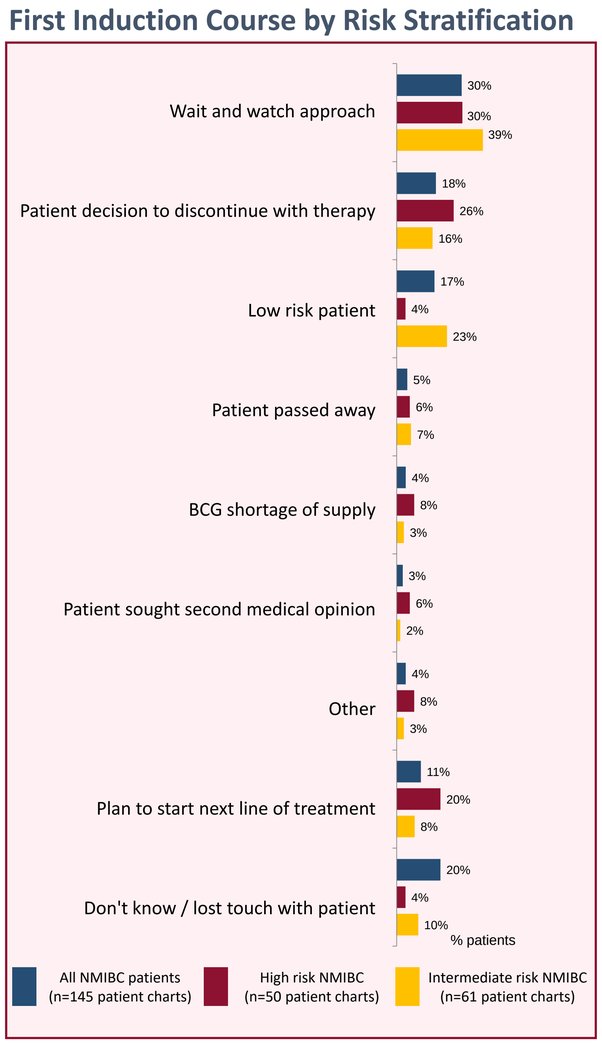


Figure 5. Reasons for No Therapies after BCG First Induction Course by Risk Stratification



Conclusions and Implications

- This chart analysis of NMIBC patients provides robust estimates of real-world treatment patterns and reasons for treatment choices by patients and physicians.
- Most NMIBC patients fail to receive adequate BCG inductions, significantly deviating from guideline recommendations.
- Tolerability issues, lack of adherence to treatment protocols, limited treatment efficacy, disease recurrence, and BCG shortage are contributing to inadequate BCG treatment.
- There is a significant unmet need for new and innovative therapies in patients who are ineligible or unwilling to undergo invasive surgical procedures such as radical cystectomy.

REFERENCES 1. Kassouf W, et al. Can Urol Assoc J. 2015; 9(9-10): E690–E704. 2. Kamat AM, et al. Eur Urol. 2018; 73:738-48. 3. Di Lorenzo G, et al. Cancer. 2010; 116:1893-900 4. Babjuk M, et al. Eur Urol. 2017; 71:447-61 DISCLOSURES This study was funded by FerGene.