Abstract #453

Disease Progression among Patients who Receive Available Bladder Preservation Therapies after Failure of BCG Therapy in the SEER-Medicare Data

Min Yang, MD, PhD[1]; Mihaela V. Georgieva, PhD[1]; Jinlin Song, PhD[2]; Iryna Bocharova, BA[1]; Kun Qian, MSc[2]; Amy Guo, PhD[3]; Ashish M. Kamat, MD[4]

[1] Analysis Group, Inc., Boston, MA, USA [2] Analysis Group, Inc., Los Angeles, CA, USA [3] FerGene, Cambridge, MA, USA [4] Department of Urology, Division of Surgery, University of Texas MD Anderson Cancer Center, Houston, TX, USA

Background

- Bacillus Calmette-Guérin (BCG) therapy after transurethral resection of the bladder tumor (TURBT) is the standard treatment for high grade (HG) non-muscle-invasive bladder cancer (NMIBC) patients, but up to 50% fail to maintain a response within 5 years[1–3]
- For patients with HG NMIBC after BCG failure, treatment options remain limited, with cystectomy being guideline recommended treatment but many patients will attempt bladder preservation therapies (BPTs)[4–6]

Objective

- Examine real-world utilization and outcomes (progression-free survival and time-to-progression) associated with available BPTs after BCG treatment among patients with HG NMIBC

Methods

Data source and study population

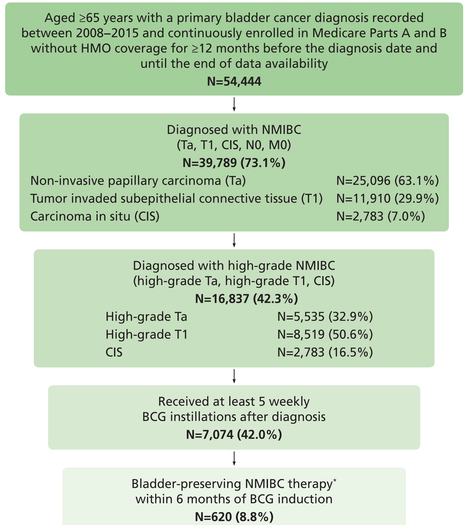
- This study used the linked Surveillance, Epidemiology and End Results (SEER)-Medicare data (2007–2016)
- Eligible patients received at least one BCG induction course (≥5 consecutive weekly instillations) after diagnosis, and initiated BPT within six months of the last consecutive BCG instillation (**Figure 1**)
  - Index date: the date of BPT initiation following BCG induction
  - Baseline period: 12 months prior to the index date
- Patients who progressed before the index date were excluded, where progression was identified as initiation of treatment for muscle-invasive bladder cancer (MIBC), radical cystectomy, and/or presence of metastases

Study outcomes and statistical analysis

- Demographic and clinical characteristics prior to BPT initiation were described using the mean (standard deviation [SD]) and median values for continuous variables and frequency distributions for categorical variables
- BPT agents after BCG treatment were summarized using counts and proportions
- Progression-free survival (PFS), time-to-progression (TTP), and time-to-metastasis (TTM) were assessed using Kaplan-Meier analysis
  - PFS: time from index date to progression or death due to bladder cancer. Patients were censored for non-bladder cancer causes of death or at the end of data availability
  - TTP and TTM: similar to PFS, except that patients who died due to any cause were censored

Methods (continued)

Figure 1. Sample selection flowchart



BCG, Bacillus Calmette-Guérin; HMO, health maintenance organization; NMIBC, non-muscle invasive bladder cancer.
* BPT for NMIBC included BCG + interferon alpha, docetaxel, doxorubicin, epirubicin, gemcitabine, mitomycin C, nab-paclitaxel, thiotepa, valrubicin, gemcitabine + docetaxel, and gemcitabine + mitomycin C.[1,4]

Results

Sample characteristics (Table 1)

- 620 patients met the inclusion/exclusion criteria and initiated BPT (**Figure 1**)
- Majority (50.5%) were diagnosed with HG T1 tumor, 31.1% with HG Ta, and 18.4% with CIS
- Mean CCI score: 1.4 (SD=1.7)
- Most common comorbidities: hypertension (86.0%), dyslipidemia (78.9%), and urinary tract infection (78.2%)
- Most commonly used BPT agents: mitomycin C (66.0%), followed by BCG + interferon alpha (22.9%), valrubicin (4.0%), doxorubicin (2.9%), and gemcitabine (2.1%)

Results (continued)

Table 1. Patient characteristics

	N=620
Demographic characteristics	
Age at index date (years), mean (SD) [median]	77.5 (6.8) [77.0]
Male, n (%)	483 (77.9%)
Race, n (%)	
White, non-Hispanic	589 (95.0%)
Black, non-Hispanic	13 (2.1%)
Other*	18 (2.9%)
Clinical characteristics	
Tumor stage at diagnosis, n (%)	
High-grade Ta	193 (31.1%)
High-grade T1	313 (50.5%)
CIS	114 (18.4%)
Year of diagnosis, n (%)	
2008–2010	212 (34.2%)
2011–2013	228 (36.8%)
2014–2015	180 (29.0%)
Bladder-preserving therapy, n (%)	
Mitomycin C	409 (66.0%)
BCG and interferon	142 (22.9%)
Valrubicin	25 (4.0%)
Doxorubicin	18 (2.9%)
Gemcitabine	13 (2.1%)
Other‡	13 (2.1%)
Number of TURBTs prior to index date, mean (SD)	2.5 (1.3)
BCG induction	
Number of instillations received, mean (SD) [median]	5.9 (0.4) [6.0]
≥5 instillations received, n (%)	528 (85.2%)
BCG maintenance (≥1 instillation received), n (%)	77 (12.4%)
CCI score,§ mean (SD)	1.4 (1.7)
Common CCI comorbidities,§ n (%)	
Diabetes	235 (37.9%)
Chronic pulmonary disease	192 (31.0%)
Peripheral vascular disease	160 (25.8%)
Congestive heart failure	120 (19.4%)
Renal disease	110 (17.7%)
Other common comorbidities, n (%)	
Hypertension	533 (86.0%)
Dyslipidemia	489 (78.9%)
Urinary tract infection	485 (78.2%)
Other malignancies	208 (33.5%)
Anxiety/depression	203 (32.7%)
Alzheimer's disease	18 (2.9%)

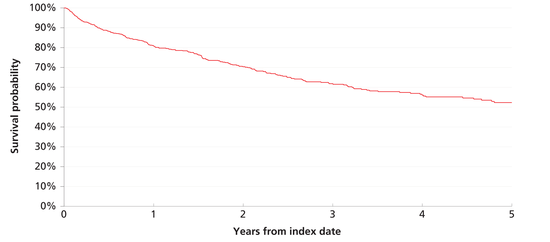
BCG, Bacillus Calmette-Guérin; BPT, bladder-preserving therapy; CCI, Charlson Comorbidity Index; HG, high grade; NMIBC, non-muscle invasive bladder cancer; SD, standard deviation; TURBT, transurethral resection of bladder tumor.
* Other races included Asian, Hispanic, North American Native, other, and unknown; ‡ Other BPTs included thiotepa, epirubicin, docetaxel, nab-paclitaxel, and the combination therapies of gemcitabine and docetaxel, and gemcitabine and mitomycin C; § Comorbidities were assessed in the 12 months prior to the index date. The CCI has been modified to exclude malignancies and metastatic solid tumors. Only the 5 most common CCI comorbidities were reported.

Results (continued)

Survival outcomes

- The rate of PFS was 80.9%, 61.8%, and 52.3% at 1, 3, and 5 years (**Figure 2**)
- In the TTP analysis, disease progression occurred in 18.7%, 36.4%, and 45.4% of patients at 1, 3, and 5 years (**Figure 3**)
  - Disease progression was predominantly identified by presence of metastases, which accounted for 40.5%, 50.0%, and 50.2% of all identified progression events within 1, 3, and 5 years of BPT initiation (**Table 2**)
- Metastases were present in 9.5%, 24.8%, and 32.6% of patients at 1, 3, and 5 years

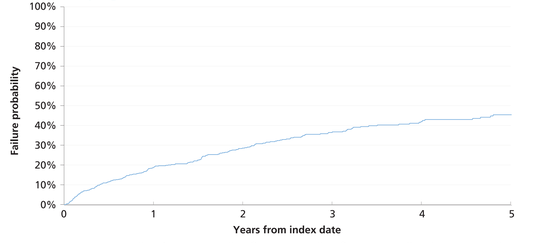
Figure 2. Progression-free survival



	Year 1	Year 2	Year 3	Year 4	Year 5
Number at risk	434	298	200	123	84
PFS rate	80.9%	70.4%	61.8%	56.0%	52.3%

PFS, progression-free survival.

Figure 3. Time-to-progression



	Year 1	Year 2	Year 3	Year 4	Year 5
Number at risk	434	298	200	123	84
Progression rate	18.7%	28.5%	36.4%	42.0%	45.4%

Results (continued)

Table 2. Progression events over five years among patients who progressed

	Metastases	Radical cystectomy	MIBC treatments*	Total cumulative events
Over 1 year	45 (40.5%)	39 (35.1%)	27 (24.3%)	111 (100.0%)
Over 3 years	93 (50.0%)	56 (30.1%)	37 (19.9%)	186 (100.0%)
Over 5 years	104 (50.2%)	62 (30.0%)	41 (19.8%)	207 (100.0%)

MIBC, muscle invasive bladder cancer.
* Guideline-recommended MIBC treatments included chemoradiation (cisplatin/carboplatin + radiotherapy), cisplatin/carboplatin + gemcitabine, DDMVAC (dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin), atezolizumab, pembrolizumab, nivolumab, gemcitabine + paclitaxel, and combination therapy of ifosfamide, doxorubicin and gemcitabine.[4,5]

Limitations

- General limitations of using claims data also applied to this study, including potential incorrect records and inability to capture services or treatments received outside of the Medicare plan
- Progression to MIBC was assessed using a composite proxy measure based on relevant treatment and diagnosis codes, which may underestimate the progression rate

Conclusions

- **Disease progression occurs in 18.7%, 36.4%, and 45.4% of patients at 1, 3, and 5 years following available BPT after BCG therapy**
- **Development of metastatic disease accounts for 40.5%, 50.0%, and 50.2% of all identified progression events within 1, 3, and 5 years of BPT initiation**
- **A high unmet need remains for novel bladder-sparing therapies to improve outcomes in this difficult-to-treat population**

References

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Corresponding author: Amy Guo, PhD; email: Amy.Guo@fergene.com

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