Retrospective non-interventional, multicenter study on the effectiveness and safety of intravesical bacillus Calmette-Guerin in patients with non-muscle-invasive bladder: Real-world experience from six hospital centers in Greece.

Angelopoulos Panagiotis[1], Markopoulos Titos[1], Lazarou Lazaros[1], Skolarikos Andreas[1], Stamatakos Panagiotis[2] Papadopoulos I Georgios[2], Fragkoulis Charalampos[2], Ntoumas Konstantinos[2], Moulavasilis Napoleon[3], Levis Panagiotis[3], Papanikolaou Dimitrios[4], Sokolakis Ioannis[4], Hatzimouratidis Konstantinos[4], Tzanetakos Charalampos[5], Psarra Marina[5], Mavridoglou George[6], Skriapas Konstantinos[7] Akrivou Dimitra[7], Karagiannis Dimitrios[7], Noutsos Christos[8], Georgiou Andreas[8], Hastazeris Konstantinos[8], Gourzoulidis George[5], Mitropoulos Dionysios[3]

[1]2nd Department of Urology, Sismanogleio Hospital, Athens Medical School, Athens, Greece
[2]Department of Urology, General Hospital of Athens G. Gennimatas, Athens, Greece
[3]1st Department of Urology, "Laiko" Gen. Hospital, University of Athens Medical School, Greece
[4]2nd Urology Department of Medical School, Aristotle University of Thessaloniki, Greece
[5]Health Through Evidence GP, Athens, Greece
[6]University of the Peloponnese, Kalamata, Greece
[7]Department of Urology General Hospital of Larissa, Greece
[8]Department of Urology General Hospital G.Hatzikosta Ioannina, Greece

INTRODUCTION

- Urinary bladder cancer is the most common malignancy of the urinary tract malignancy and ranks as the ninth most common cancer globally [1].
- More than 70% of new bladder cancer diagnoses are various forms of non−muscle-invasive bladder cancer (NMIBC) which include noninvasive papillary carcinoma (Stage Ta), carcinoma in situ (CIS), and tumors invading the submucosa (stage T1) [2].
- Approximately 50% of the new bladder cancer cases are low grade, noninvasive papillary tumors having low risk (<5%) of progression, whereas high grade T1 tumors have much risk of progression [3].
- Bacillus Calmette-Guerin (BCG) has been an established adjuvant treatment (to transurethral resection (TUR) which significantly reducing the recurrence and progression of NMIBC.
- Many prospective, randomized trials have confirmed that BCG's efficacy in reducing tumor recurrence, progression, and mortality [4-6].
- SII-ONCO-BCG is a live freeze-dried preparation derived from attenuated strain of Mycobacterium bovis (BCG Moscow I, Russian strain). The reconstituted product contains 1−19.2 x 108 colony-forming units.
- Although its clinical benefits have been demonstrated previously, up-to-date efficacy and safety data are available, as real-world studies complement clinical trial data, providing a more comprehensive understanding of how treatments perform in diverse patient populations and real-world clinical settings.

OBJECTIVE

- The present retrospective, observational, multicenter, chart-review study was designed to generate real-life effectiveness and safety data of SII-ONCO-BCG in patients with intermediate- and high-risk NMIBC in Greece

METHODS

- In this retrospective, observational, multicenter, chart-review study, medical records from six hospital centers: Laiko General Hospital, Sismanoglio General Hospital, Papageorgiou General Hospital, Hatzikosta General Hospital, G.Gennimatas General Hospital and General Hospital of Larissa were analyzed.
- Eligible patients were adults with histologically confirmed stage Ta, T1 NMIBC, or CIS after diagnostic transurethral resection of bladder tumor (TURBT) who received at least nine intravesical SII-ONCO-BCG (80 mg) treatment instillations (at least one maintenance course after the induction course) between January 2016 and December 2023.
- Baseline demographic and disease characteristics of patients were extracted from six hospital centers.
- The primary outcomes evaluated were the recurrence-free survival (RFS) and progression-free survival (PFS).
  - Recurrence was defined as any urothelial carcinoma (UC) reappearance within the urinary bladder after the initial TURBT. With an interval of less than 3 months being considered as a residual tumor
  - Progression was defined as stage or grade advance (such as pathology report of Ta to T1-4 or T1 to T2-4).
- The primary outcomes of RFS and PFS were estimated as the time from the date of surgery (TURBT) to the recurrence and progression event after a 3, 2-, and 1-year follow-up, respectively.
- The secondary outcome was the incidence of adverse events (AE) over 3 years with the severity of AEs documented and categorized from grade 1 to 3 according to the Cleveland Clinic Approach of BCG Toxicity
- RFS and PFS were analyzed by the Kaplan-Meier (KM) method. All statistical analyses were conducted using the latest version of statistical software package IBM SPSS.

RESULTS

Patient characteristics

- A total of 162 patients receiving SII-ONCO-BCG 80 mg were enrolled in the study (Table 1).
- Among all patients, 145 (89.5%) patients were men with a mean age of 70 years (range, 44-92 years; 54.3% ≥70 years), of whom 59 (36.4%) were current smokers.
- The most frequent comorbidities were cardiovascular diseases (72 [44.4%] patients) and diabetes mellitus (15 [9.3%]).
- Pertaining to tumor characteristics, 103 (63.6%) patients had T1, 43 (26.5%) had Ta, 21 (12.9%) had concurrent CIS, and 124 (76.5%) had high grade tumor (Table 1).
- Among other available data, 72.7% of patients had a single tumor, 62.2% had tumors smaller than 3 cm, and 81.7% had primary tumors (Table 1).

Table 1: Baseline patient characteristics

Group parameters	Total (n=162)
Age, mean ± SD (range), year	70.0 ± 9.4 (44-92)
≥65 years, No. (%)	118 (72.8)
≥70 years, No. (%)	88 (54.3)
Sex, n (%)	
Male	145 (89.5)
Female	17 (10.5)
Smoking n (%)	
Smoking	59 (36.4)
Ex-Smoker	20 (12.3)
Comorbidities n (%)	
Cardiovascular diseases	72 (44.4)
Respiratory diseases	10 (6.2)
Diabetes mellitus	15 (9.3)
Primary tumor	
Primary	81.7%
Recurrent	18.3%
Number of tumors	
Single	68.7%
Multifocal	31.3%
T category n (%)	
T1	103 (63.6)
Ta	43 (24.1)
T1HG	89 (54.9)
CIS n (%)	
Pure	20 (12.3)
Concurrent	17 (10.5)
Any CIS,	37 (22.8)
Tumor diameter	
<3 cm	62.2%
≥3 cm	37.8%
Tumor grade	
Low grade	23.5%
High grade	76.5%

Primary outcomes: disease recurrence and progression

- Disease recurrence occurred in 21 (13.0%), 23 (14.2%), and 24 (14.8%) of the 162 patients during the 1st, 2nd, and 3rd year of follow-up (Table 2).
- The corresponding 1-, 2-, and 3-year RFS rates were 87.0% (95% CI, 81.8%-92.3%), 85.8% (80.4%-91.2%), and 85.2%, (79,7%-90.7%), respectively (Table 2).
- A KM curve shows probability of RFS over 3 years (Figure 1).
- Pertaining to disease progression, four (2.5%), five (3.1%), and five (3.1%) patients experienced progression during the 1st, 2nd, and 3rd year of follow-up (Table 2).

Table 2: Survival analyses results

Outcomes	Total (n=162)
Median follow up, months (range)	28.9 (5-36)
Recurrence-free survival analysis	
1-year recurrence, No (%)	21 (13%)
1-year recurrence-free survival 95% CI	87%, (81.8% - 92.3%)
2-years recurrence, No (%)	23 (14.2%)
2-years recurrence-free survival 95% CI	85.8%, (80.4% - 91.2%)
3-years recurrence, No (%)	24 (14.8%)
3-years recurrence-free survival 95% CI	85.2%, (79.7% - 90.7%)
Progression-free survival analysis	
1-year progression, No (%)	4 (2.5%)
1-year Progression-free survival, 95% CI	97.5% (95.1%-99.9%)
2-year progression, No (%)	5 (3.1%)
2-year Progression-free survival, 95% CI	96.9% (94.2%-99.6%)
3-year progression, No (%)	5 (3.1%)
3-year Progression-free survival, 95% CI	96.9% (94.2%-99.6%)

CI: confidence interval.

RESULTS (continued)

- The corresponding 1-, 2-, and 3-year PFS rates were 97.5% (95.1%-99.9%), 96.9% (94.2%-99.6%), and 96.9% (94.2%-99.6%), respectively (Table 2).
- A KM curve shows the probability of PFS at the end of 36 months (Figure 2).

Figure 1 Figure 1: Kaplan–Meier survival curve of 3-year recurrence-free survival

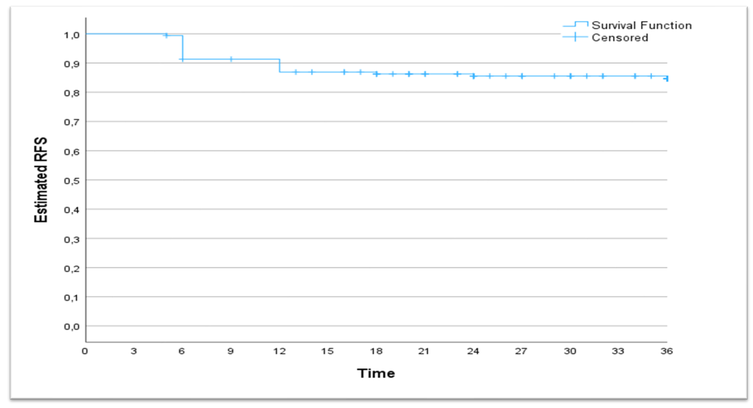
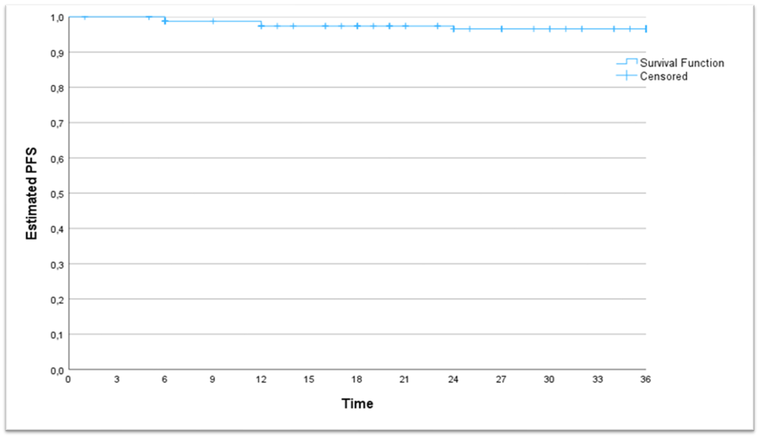


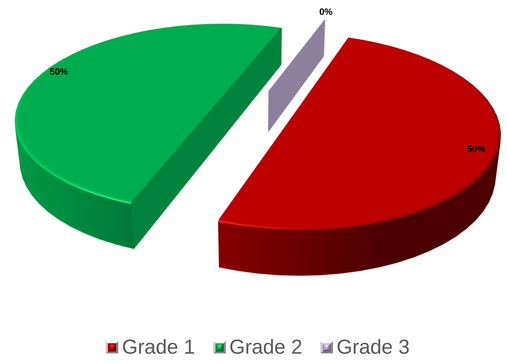
Figure 2: Kaplan–Meier survival curve of 3-year progression-free survival.



Secondary outcome: adverse events

- The analysis indicated that 14.8% patients experienced at least one AE during the 3 years follow-up period.
- All the AEs were grade 1 (50%) and grade 2 (50%).

Figure 3: Adverse Events grade



CONCLUSIONS

- **Based on this real-world evidence study, SII-ONCO-BCG was found to be an effective and safe therapy for patients with intermediate- and high-risk NMIBC in routine clinical practice.**
- **The present study provides valuable clinical insights for the management of patients with NMIBC.**

References

1.Antoni S, et al. European urology. 2017;71(1):96-108.
2. Braasch MR, et al. European Urology Supplements. 2009;8(7):549-555.
3. Braasch MR, et al. BJU international. 2008;102(9 Pt B):1254-1264.
4.Sylvester RJ, et al. The Journal of urology. 2005;174(1):86-91; discussion 91-82.
5.Lamm DL, et al. The New England journal of medicine. 1991;325(17):1205-1209.
6.Böhle A, et al. The Journal of urology. 2003;169(1):90-95.

For more information please contact:
George Gourzoulidis,
Health Through Evidence GP, Athens, Greece
Email: g.gourzoulidis@hte.gr
www.hte.gr

Poster presented at: ISPOR—The Professional Society for Health Economics and Outcomes Research; Barcelona, Spain, November 17–20, 2024