

Podium Session 4: Oncology - Bladder/Kidney/Other

Monday, June 29, 2026 • 9:10–10:10

Cite as: *Can Urol Assoc J* 2026;20(6Suppl1):S15-7. <http://dx.doi.org/10.5489/cuaj.9811>

POD 4.1

Cystectomy-free survival following cretostimogene grenadenorepvec in high-risk BCG-unresponsive non-muscle-invasive bladder cancer with carcinoma in situ: Results from BOND-003 cohort C

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Introduction: Cretostimogene is an oncolytic immunotherapy with dual mechanisms of action. It replicates in and lyses cancer cells with Rb-E2F pathway alterations, while simultaneously amplifying an anti-tumor immune response, further mediated by the GM-CSF transgene. BOND-003 (NCT04452591) is a phase 3 study evaluating the efficacy and safety of cretostimogene in patients with HR BCG-unresponsive (UR) NMIBC. We report data on radical cystectomy performed post-recurrence or progression.

Methods: A total of 112 patients with HR BCG-UR NMIBC with CIS were enrolled. Treatment included six weekly inductions, followed by three weekly maintenance cycles every three months at year 1 and every six months during years 2–3. Repeat induction was permitted at month 3. Response assessments included serial cystoscopy, urine cytology, and mandatory mapping biopsy at 12 months, with centralized pathology review. The primary endpoint is CR at any time. Cystectomy-free survival (CFS) and progression-free survival (PFS) are key secondary endpoints.

Results: As of the June 23, 2025 data cutoff (median followup of 25.8 months), the CR rate at any time is 75.5% (83/110) (95% CI 66.3–83.2%). Kaplan-Meier estimates of 12- and 24-month DoR are 64.2% (95% CI 52.5–73.8%) and 60.1% (95% CI 48.2–70.0%), respectively, with a median DoR of 27.9 months (95% CI 14.3–NE%) and ongoing. The 12- and 24-month CR rate is 46.4% (51/110) (95% CI 36.8–56.2%) and 41.8% (46/110) (95% CI 32.5–51.6%), respectively. The 12- and 24-month CFS rates are 89.2% (95% CI 81.3–93.9%) and 81.3% (71.8–87.8%), respectively, with median CFS not reached. Among 18 patients who underwent radical cystectomy post-disease recurrence or progression, 15 (83.3%) had NMIBC or pT0 on final pathology. At 12 and 24 months, 96.4% (106/110) are free from $\geq$ T2 progression. No grade 3+ TRAEs were reported.

Conclusions: Cretostimogene may offer distinct advantages with its MOA, efficacy, durability, and safety profile for the treatment of HR BCG-UR NMIBC.

Funding: Funded by CG Oncology.

POD 4.2

Suicide risk among patients with urologic malignancies in Canada

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Introduction: Patients with urologic malignancies face distinctive psychological challenges related to cancer diagnosis, treatment, and survivorship. Prior studies suggest that cancer survivors, particularly those with hormonally driven or quality-of-life-altering malignancies, may be at increased risk of suicide, although population-level evidence across urologic cancer sites remains limited.¹⁻³ We evaluated suicide risk among patients with urologic malignancies and identified associated sociodemographic factors using national census-linked data.

Methods: We used data from five Canadian Census Health and Environment Cohorts linking the 1996, 2001, 2006, 2011, and 2016 census cycles to the

Canadian Cancer Registry and the Canadian Vital Statistics Database. Adults aged 25 years and older residing outside Quebec were followed for seven years after each census cycle. Weighted logistic regression models were used to estimate the odds of suicide by cancer site, adjusting for demographic and socioeconomic characteristics. Colorectal cancer served as the reference group.

Results: Compared with colorectal cancer, individuals diagnosed with urologic malignancies demonstrated higher adjusted odds of suicide. Prostate cancer was associated with the highest risk (odds ratio 5.84, 95% CI 3.20–10.66), followed by bladder cancer (odds ratio 4.85; 95% CI 1.98–11.88). Kidney cancer demonstrated a non-significant elevation in suicide risk. Higher suicide odds were also observed among younger adults, individuals who were separated or divorced, those with higher educational attainment, rural residents, and residents of Alberta or the Territories.

Conclusions: Patients with prostate and bladder cancer remain at substantially increased risk of suicide despite improving oncologic outcomes. Consistent with prior population-based studies, these findings support the integration of systematic psychosocial screening and targeted mental health interventions into urologic oncology survivorship care. I-3

Acknowledgements: This study was conducted using de-identified data accessed through Statistics Canada under the authority of the Statistics Act. This abstract was presented at the European Association of Urology Annual Congress 2026.

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POD 4.3

Incidental testicular masses in infertile men: Are we over-treating?

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Introduction: Incidental small testicular masses are increasingly detected during scrotal ultrasonography for male infertility evaluation. This study aimed to assess the prevalence, characteristics, management strategies, and outcomes of such masses in a contemporary cohort of patients presenting with infertility.

Methods: We conducted a retrospective review of more than 600 men attending the fertility clinic from a prospectively collected database, including 75 men with incidental small testicular masses discovered on scrotal US between 2018 and 2025. Masses were defined as hypoechoic or mixed-echogenic lesions < 1 cm. Data collected included patient demographics, lesion characteristics (number, size, laterality, location, vascularity, calcifications, and associated findings), baseline tumor markers, initial managements (surveillance vs. intervention), indications for intervention, pathology results, followup duration, and outcomes. Patients under surveillance underwent serial imaging and clinical followup. Statistical analyses included descriptive summaries (means, medians, and frequencies) using standard methods.

Results: The cohort had a mean age of 37 years (range 24–60). Lesions were single in 73.3% and hypoechoic in 80.0%, with a mean maximum diameter of 5.0 mm (range 1–9). Associated findings included epididymal cysts (13.3%) and varicocele (12.0%). The baseline tumor markers were normal in most cases. Initial management was active surveillance in 88.0% (n=66), with a mean followup of 23.2 months (range 6–84). Intervention was performed in 10.7% (n=8): partial orchiectomy (n=4), radical orchiectomy (n=3), and biopsy (n=1), primarily for suspicious fea-

tures (37.5%) or during sperm retrieval procedures (37.5%). Pathology revealed benign findings in 75% (Leydig cell, n=3; benign lesion, n=3) and malignancy in 25% (teratoma, n=1; seminoma, n=1). Two men required delayed interventions for interval growth, both of which revealed seminoma. No cases of advanced disease or recurrence were observed.

Conclusions: Incidental small testicular masses in infertile men are frequently benign and remain stable over time, supporting active surveillance as a safe initial management strategy. Intervention is warranted for interval growth or suspicious imaging features, with low malignancy rates and excellent oncologic outcomes. These findings reinforce the role of conservative management to preserve fertility.

POD 4.4

Genomic alterations in geriatric renal cell carcinoma

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Introduction: Renal cell carcinoma (RCC) has a median diagnosis age of around 65 years. The somatic alterations landscape in elderly patients remains poorly understood. We aimed to better characterize the genomic alterations in geriatric RCC patients.

Methods: This retrospective cohort focused on 943 cases of clear-cell RCC (ccRCC) from the Cancer Genomics of the Kidney (CAGEKID) dataset in the exploratory phase and 118 cases from the McGill University Biobank in the validation phase. Patients were divided into two groups: elderly (≥ 65 years old) and younger (< 65 years old). A previously validated 12-gene panel was used to compare age-specific mutation frequencies and associations with cancer-specific survival (CSS), disease-free survival (DFS), and overall survival (OS).

Results: In age-stratified analyses of the CAGEKID cohort, PBRM1 and KDM5C mutations were enriched in elderly tumors (PBRM1 OR 1.61, $p=0.0005$; KDM5C OR 1.9, $p=0.01$). Canonical PBRM1-SETD2 co-mutation and BAP1-PBRM1 mutual exclusivity in both age groups were preserved, but with a novel elderly-specific signal of ATM-BAP1 co-mutation (OR 5.65, $p=0.001$). BAP1 mutation was independently associated with significantly worse CSS, DFS, and OS in elderly patients. VHL mutation showed stage-specific effects, with worse OS and DFS in low-stage elderly tumors only. SETD2 mutation showed a distinct age-dependent prognostic direction. In low-stage tumors, elderly SETD2-mutated cases had worse survival, whereas in high-stage tumors, the trend was reversed, with better outcomes among elderly patients compared to younger ones.

Conclusions: While core drivers (VHL, PBRM1, and BAP1) are shared across ages, elderly ccRCC shows distinct co-mutation networks and chromatin-modifying alterations, including SETD2. The prognostic impact of these alterations varies by age and stage, indicating distinct biologic and clinical behavior in geriatric ccRCC.

POD 4.5

Effectiveness of BCG for patients with non-muscle-invasive bladder cancer and concomitant autoimmune disorders may be altered by changes in the local immune microenvironment

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Introduction: Identification of patients less likely to respond bacillus Calmette Guérin (BCG) for high-grade non-muscle-invasive bladder cancer (NMIBC) is an unmet need, particularly given the other novel therapeutics soon to be available. Chronic inflammation of the bladder and biological aging, especially if associated with mucosal immune exhaustion with the presence of chronic tertiary lymphoid structures (TLSs), can lead to ineffective local anti-tumor immune responses. We hypothesize that comorbidities, such as autoimmune disorders (AID), would be associated with chronic mucosal inflammation/TLS formation within the bladder tumor microenvironment and suboptimal response to repeated BCG.

Methods: We first assessed a cohort of patients with high-grade NMIBC and any diagnosis of an AID, including age- and sex-matched controls. Evaluation of immune cell infiltration patterns and TLS presence in tumors was performed using multiplex immunofluorescence assays. Secondly, a murine model of spontaneous autoimmunity was subjected to chronic N-butyl-N-(4-hydroxybutyl) nitrosamine (BBN) carcinogen exposure and treated using repeated intravesical BCG followed by local and systemic immune profiling.

Results: The clinical cohort consisted of 11 patients with concomitant AID that received BCG and 20 patients with no AID. Histopathologic evaluation and multiplex immunofluorescence-based tumor spatial profiling of those tumors from patients with an AID exhibited increased peri-tumoral TLS formation and higher immune infiltration prior to initiating BCG. In the in vivo studies, autoimmunity-prone mice exhibited a shorter time to tumor induction after exposure to BBN and greater TLS formation within the bladder mucosa as compared to control mice. Systemic immune profiling showed an increase in splenic exhausted B cells and M2-like macrophages following repeated BCG treatment.

Conclusions: Herein, we provide the first evidence demonstrating autoimmunity-induced accelerated immune aging and mucosal immune exhaustion as potential factors underlying differential response to BCG. Future work will identify larger cohorts of patients to replicate these observations and assess any association with response rates. The ultimate goal would be to use these clinical characteristics, alongside pathologic assessments of pre-treatment tumor immune microenvironment, to determine the optimal first-line adjuvant therapy.

POD 4.6

Component and total healthcare-related costs of bladder cancer in a universal healthcare system

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Introduction: Bladder cancer (BCa) is the most expensive per-patient cancer to treat in Canada and the U.S., and represents a substantial economic burden; however, there is limited information on the component costs that contribute to this overall burden. This is the first study to segment the mean unadjusted per-patient cost into individual BCa health states in a universal healthcare system.

Methods: We used population and registry data housed at the Institute for Clinical Evaluative Sciences (ICES; Ontario, Canada) that captures 96% of cancer diagnoses in the province. We divided the BCa journey into health states to capture clinically relevant disease states, spanning non-muscle-invasive (NMIBC), muscle-invasive (MIBC), and metastatic BCa patients. The accuracy of these codes was then separately validated against a subset of local patients in manual chart review. Costs of BCa were calculated by capturing inpatient, ambulatory, outpatient, and emergency care, physician and non-physician billings, laboratory, cancer and dialysis clinics, chemotherapy and drug benefit costs, mental health, long-term, complex and continuing care, and home care services. These costs were derived using validated costing macros at ICES and were reported descriptively for 30-day and total cost periods. Costs include both the direct costs associated with BCa care and those of comorbid conditions.

Results: A total of 29 230 BCa patients were diagnosed and followed longitudinally in ICES data from 2003 to present. Mean unadjusted per-patient costs for the total time period of each health state and on a 30-day basis are reported in Table 1. The most expensive costs per 30 days were recorded in radical cystectomy, trimodal therapy, and end-of-life health states. High total costs for surveillance health states, despite low per 30 days costs, reflected long durations of time with comorbid care. Inpatient care was the largest driver of healthcare costs apart from chemotherapy, and had the highest relative cost contribution for radical cystectomy, urothelial tract recurrence, and end-of-life care.

Conclusions: The lifetime economic burden of BCa care is expensive. We report clinically relevant health state-based costs of BCa and important component drivers of cost. These serve as a contemporary baseline reference for costing, planning policy, and decision-modeling studies.

Funding: Canadian Institutes of Health Research Project Grant awards, 390221 (Bridge funding) and PJT 173386.

POD 4.6. Table 1. Mean total per-patient costs for bladder cancer patients by health state

Health state	Cost per 30 days	SD	Total cost	SD	% inpatient cost burden
TURBT	\$4798.43	\$8393.78	\$8,270.12	\$7642.72	37.7%
Early surveillance* (≤ 2 years)	\$2095.86	\$4336.25	\$20,659.95	\$33 247.36	18.6%
Late surveillance* (> 2 years)	\$1476.59	\$3436.49	\$67 863.36	\$113 787.73	20.2%
Radical cystectomy	\$20 000.36	\$21 545.90	\$46 097.64	\$29 742.88	68.8%
Post-radical cystectomy surveillance*	\$2500.49	\$4613.73	\$82 589.96	\$119 871.57	24.9%
Trimodal therapy	\$10 957.17	\$8857.67	\$32 085.04	\$19 606.76	10.3%
Post-TMT surveillance*	\$2451.65	\$4132.52	\$55 722.90	\$84 196.52	24.7%
Neoadjuvant chemotherapy	\$9387.76	\$5384.49	\$30 711.70	\$15 135.61	6.8%
Adjuvant chemotherapy	\$8765.10	\$6408.35	\$44 600.23	\$49 218.45	9.4%
Urothelial tract recurrence	\$7073.65	\$7460.61	\$19 917.37	\$15 369.89	52.1%
End of life	\$11 288.11	\$11 816.74	\$31 275.99	\$32 386.03	54.1%

*Surveillance health states include treatment of comorbid conditions over this time.