# Poster Session 3: Oncology–Bladder
# Saturday, June 28, 2025 • 16:00–17:30

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## MP 3.1

### The gut microbiome as a potential mediator of BCG response in non-muscle-invasive bladder cancer patients

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**Introduction:** Gut microbiome has emerged as a potential driver of systemic immune checkpoint blockade (ICB) immunotherapy efficacy in various malignancies. Antibiotic (ATB) intake is known to modulate gut microbiota in a deleterious manner, potentially reducing the efficacy of ICB. We hypothesized that ATB intake prior to the initiation of intravesical bacillus Calmette-Guérin (BCG) immunotherapy, the gold-standard treatment for high-risk non-muscle-invasive bladder cancer (NMIBC), may influence treatment response.

**Methods:** We conducted a single-site, retrospective study of 622 NMIBC patients who received BCG immunotherapy at CHU de Québec from 2009–2019. ATB intake was collected from prescriptions and medical records up to 12 months prior to BCG initiation. Recurrence-free survival was evaluated using Kaplan-Meier analysis, and both uni- and multivariate Cox proportional hazards models were applied. We performed an in vivo experiment with C3H mice, which received a broad-spectrum ATB regimen either for one week or continuously. Mice were injected subcutaneously with MBT-2 bladder cancer cells and treated weekly with intratumoral BCG. To investigate the potential cause-effect relationship between the gut microbiome and BCG response, we performed fecal microbiome transfer (FMT) in the same bladder cancer mouse model pre-treated with ATB, using fecal samples collected at baseline from NMIBC patients who responded favorably or unfavorably to BCG.

**Results:** Of the 622 NMIBC patients, 77 (12%) were exposed to ATB within three months before BCG initiation, while 545 (88%) were not. ATB-exposed patients showed a significantly reduced recurrence-free survival compared to unexposed patients (HR 1.96, 95% CI 1.36–2.83, p=0.0002). Fluoroquinolones were prescribed in over 70% of cases, and their combination with other antibiotics was associated with a shorter recurrence-free survival compared to fluoroquinolone alone or other ATB classes. In the mouse model, extended ATB treatment reduced the antitumor activity of BCG compared to control (p<0.01). FMT from non-responder patients significantly reduced the antitumor efficacy of BCG compared to responder patients, suggesting that gut microbiota may influence BCG response.

**Conclusions:** This large study demonstrates a detrimental effect of ATB intake within three months prior to BCG therapy in NMIBC patients. Preclinical data suggest that FMT and alterations in gut microbiota composition due to extended ATB intake may impair the antitumor efficacy of BCG, reinforcing the potential role of the microbiome in modulating the response to BCG immunotherapy. These findings underscore the importance of judicious ATB prescribing practices prior to BCG initiation to potentially optimize NMIBC treatment outcomes and enhance BCG efficacy.

*Acknowledgements: The authors would like to acknowledge the Weston Family Foundation for their generous financial support of this study.*

## MP 3.2

### The role of methylnaltrexone in the length of hospital stay and bowel recovery after radical cystectomy: A retrospective review

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**Introduction:** Postoperative ileus (POI) is a frequent complication after radical cystectomy (RC) and contributes to extended length of hospital stay (LOS). Alvimopan, a peripherally acting μ-opioid receptor antagonist (PAMORA), reduces LOS and improves bowel recovery after RC but is unavailable in Canada. This study investigated the impact of adding methylnaltrexone (MNTX), a PAMORA available in Canada, to the enhanced recovery after surgery (ERAS) protocol on LOS and POI.

**Methods:** This single-center, retrospective review included patients undergoing RC for bladder cancer (October 2021 to August 2024). MNTX (12 mg SC pre-incision, then daily for up to six days post-surgery) was added to the ERAS protocol in May 2023. Patients undergoing additional surgeries (e.g., bowel resection) or taking preoperative narcotics were excluded. The primary outcome was LOS, with secondary outcomes including time to flatus, time to bowel movement, inability to tolerate oral diet by day 7, nasogastric tube placement, POI, and 30-day emergency visits. Logistic regression and Mann-Whitney U tests were applied.

**Results:** Among 294 cases, 191 patients were included (82 MNTX, 109 controls). Median age was 71 (IQR 66–77), 79% were male, and 89% had an epidural. LOS was significantly shorter in the MNTX group (median 6 days [5, 7]) compared to controls (median 7 days [6, 7], p<0.001). There was no difference in POI (16.0% vs. 18.3%, p=0.826) or other secondary outcomes (all p>0.05), and complication rates were comparable. Univariate analysis showed no significant association between MNTX and POI (OR 0.85, 95% CI 0.39–1.85, p=0.679), but MNTX was significantly associated with reduced LOS (W=5836, p=0.0002).

**Conclusions:** MNTX as part of the ERAS protocol for RC was associated with a shorter LOS, but no significant difference in bowel recovery. Given the potential healthcare cost savings, MNTX appears beneficial, although further prospective studies are needed to confirm these findings.

## MP 3.3

### A cost-utility analysis of enfortumab vedotin and pembrolizumab vs. nivolumab plus gemcitabine-cisplatin in advanced urothelial carcinoma

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**Introduction:** Combinations of enfortumab vedotin plus pembrolizumab (EV-302; EV+P) and nivolumab plus gemcitabine-cisplatin (CHECKMATE 901; N+GC) have demonstrated progression-free and overall survival benefits in patients with locally advanced and metastatic urothelial carcinoma; however, these agents are expensive and their cost-effectiveness has not been well described. Our objective was to assess the clinical and cost-effectiveness of these strategies vs. conventional platinum-based therapy.

**Methods:** We developed a pan-Canadian policy model as an individual-level state transition model in R to assess new treatments in bladder cancer with submodules for non-muscle-invasive, muscle-invasive, and metastatic disease. For this study, we

**MP 3.3. Table 1. Cost-utility analysis**

| Treatment | Total cost ($) (95% CI) | Total QALYs (95% CI) | Incremental cost ($) (95% CI) | Incremental QALY (95% CI) | ICER ($/QALY)* |
|---|---|---|---|---|---|
| Gemcitabine-cisplatin | 261 296 (248 021–276 027) | 1.57 (1.43–1.80) | Reference | Reference | Reference |
| Nivolumab + gemcitabine-cisplatin | 455 513 (437 943–470 699) | 1.96 (1.76–2.14) | 194 217 (183 212–203 212) | 0.39 (0.15–0.62) | 499 448 |
| Enfortumab vedotin + pembrolizumab | 769 262 (747 206–787 317) | 2.92 (2.52–3.36) | 507 966 (490 593–524 587) | 1.35 (0.95–1.87) | 375 170** |

*Vs. gemcitabine-cisplatin. **Strategy demonstrates extended domination over nivolumab + gemcitabine-cisplatin.

considered these agents within the first-line metastatic setting. Downstream elements of this metastatic module have previously been validated vs. published decision models. Key transition probabilities were obtained from clinical trial data and used a network meta-analysis to establish comparative effectiveness. Patient utilities were gathered using validated questionnaires at three Canadian tertiary care centers. Costs were sourced from literature review. A total of 10 000 patient-level simulations and 50 probabilistic sensitivity analyses were run to assess model and parameter uncertainty. A time horizon of 10 years with a 1.5% discount rate and provincial ministry of health perspective were used for the model.

**Results:** In the reference base case, gemcitabine-cisplatin (GC) treatment was associated with a total cost of $261 296 CAD ($248 021–276 027) and 1.57 (1.43–1.80) QALYs (Table 1). N+GC was more effective with a total QALY gain of 1.96 (1.76–2.14) but more expensive at $455 513 CAD ($437 943–470 699). EV+P was the most effective and most costly treatment option, with a total QALY improvement of 2.92 (2.52–3.36) and a cost of $769 262 CAD ($747 206–787 317). The incremental cost-effectiveness ratio (ICER) was $375 170 CAD/QALY for EV+P compared to GC alone. Given a higher effectiveness at a lower ICER, this demonstrated extended domination over N+GC; however, neither treatment strategy was considered cost-effective using conventional willingness-to-pay thresholds of $100 000/QALY.

**Conclusions:** Both EV+P and N+GC were more effective and more costly than conventional GC. Despite being the most effective option with the lowest (relative) ICER, EV+P was not cost-effective vs. GC.

*Acknowledgements: Funded by the Canadian Institutes of Health Research Project Grant awards, 390221 (Bridge funding) and PJT 173386.*

## MP 3.4

### Incorporating longitudinal followup information for dynamic prognostication in patients with non-muscle-invasive bladder cancer

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**Introduction:** Non-muscle-invasive bladder cancer (NMIBC) has high progression rates, leading to substantial healthcare costs. Patients who progress to muscle-invasive disease face worse outcomes, emphasizing the need for better risk stratification. Current risk calculators use predictors from a single time point, such as initial TURBT. This study aimed to determine whether longitudinal features, such as cumulative cystoscopy and cytology results, can improve predictive performance.

**Methods:** This retrospective study included NMIBC patients treated from 2005–2022 at two academic centers in Ontario, Canada. Two datasets were created: a static dataset with baseline data from initial TURBT (age, stage, grade, concomitant carcinoma in situ) and a longitudinal dataset with the baseline data and time-series features. Both datasets were split into training (80%) and testing (20%) sets, with the same random survival forest model applied to each. Performance was assessed using the concordance index (C-index).

**Results:** A total of 818 patients were included, of which 164 were used for testing. The longitudinal model demonstrated improved predictive performance, achieving a C-index of 0.988 (95% CI 0.987–0.990) in the training set and 0.752 (95% CI 0.640–0.854) in the testing set compared to the static model's C-index of 0.932 (95% CI 0.913–0.949) in training and 0.692 (95% CI 0.537–0.811) in testing. While initial stage and age were key predictors in the static model (Figure 1), the longitudinal model identified significant time-series features, such as the total number of suspicious or abnormal cytologies and the time elapsed since the last suspicious or abnormal result (Figure 2).

**Conclusions:** This study demonstrates that incorporating longitudinal features may improve predictive accuracy for NMIBC progression. Dynamic followup data may enable precise risk stratification and optimized treatment decisions. External validation is needed to confirm generalizability.

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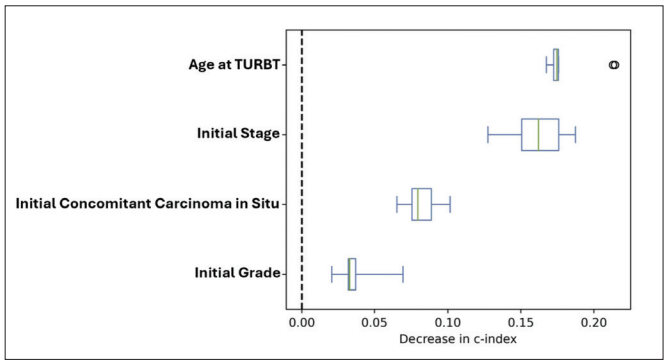
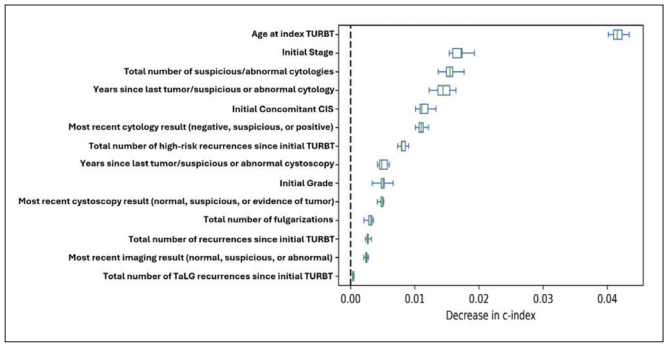
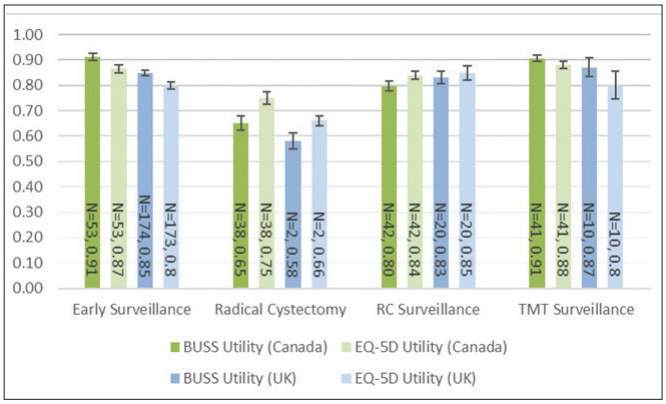



**MP 3.4. Figure 1.** Permutation importance test for variables included in the static model. Each box represents the 25th and 75th percentiles, with the center line indicating the median decrease in C-index and the whiskers extending to 1.5 times the IQR.




**MP 3.4. Figure 2.** Permutation importance test for variables recorded over time included in the longitudinal model. Each box represents the 25th and 75th percentiles, with the center line indicating the median decrease in C-index and the whiskers extending to 1.5 times the IQR.




**MP 3.5. Figure 1.** Bladder cancer utilities in NMIBC and MIBC patients in Canada and the U.K.

## MP 3.5

### A comparison of bladder cancer health utilities in Canada and the U.K.

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**Introduction:** The Bladder Utility Symptom Scale (BUSS) is a preference-based psychometric and utility instrument to measure health-related quality of life (HRQoL) in bladder cancer (BCa). It has undergone rigorous internal and external validation in Canadian patients, and can be used in all phases of BCa (non-muscle-invasive [NMIBC], MIBC, and metastatic). In this study, we assessed BUSS performance in novel patient cohorts in Canada and the U.K.

**Methods:** In Canada, patients at three tertiary care centers were prospectively recruited into representative BCa health states. Patients completed EQ-5D-5L and BUSS at recruitment and whenever their health state changed. Life and Bladder Cancer (LABC) was a cross-sectional and longitudinal study at National Health Service hospitals in the U.K. For this analysis, patients completed EQ-5D-5L and BUSS as part of routine followup at nine months after TURBT. Given the timing of LABC, patients were correspondingly sampled in NMIBC surveillance, radical cystectomy (RC), post-RC surveillance, and post-trimodal therapy (TMT) surveillance. Surveillance states ended upon recurrence/progression. Descriptive statistics and pairwise comparisons within each cohort were used to assess utility scores.

**Results:** In the U.K., 206 patients were recruited. Most (n=174) were in NMIBC surveillance (EQ-5D-5L/BUSS respective utility 0.80/0.85). Twenty patients were post-RC (0.85/0.83), 10 were post-TMT (0.80/0.87), and two were RC (0.66/0.58). In Canada, 174 patients were in analogous health states. Mean utilities (EQ-5D-5L/BUSS, respectively) were 0.87/0.91 for NMIBC surveillance (n=53), 0.75/0.65 for RC (n=38), 0.84/0.80 for post-RC (n=42), and 0.88/0.91 for post-TMT (n=41). Overall health utilities were similar between Canada and the U.K. (Figure 1). In particular, surveillance health state utilities were significantly higher than those for RC ($p<0.05$). Measured utilities also mirrored identical relationships between BUSS and EQ-5D-5L in both countries. Finally, BUSS utilities better identified significant differences between health states, indicating improved discrimination vs. EQ-5D-5L.

**Conclusions:** Health state utilities were comparable across Canada and the U.K., lending face validity and external validation to the BUSS outside of a Canadian context. Similar trends in the relationship of BUSS to EQ-5D-5L utilities and of the BUSS to detect clinically important health state differences were seen in both jurisdictions.

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## MP 3.6

### A comparison of disease-specific and generic health utility instruments in bladder cancer patients

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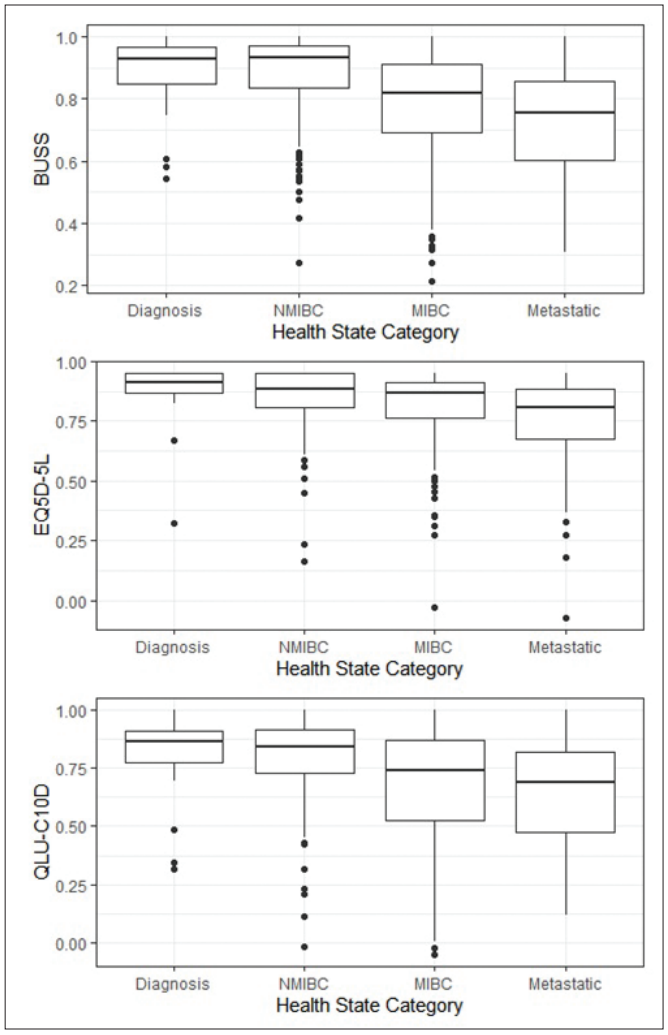
**Introduction:** Health utilities are important preference-based measures of health-related quality of life (HRQoL). We previously obtained utilities for 17 health states in bladder cancer (BCa); however, predicted utilities differ based on the measurement tool. Our aim was to compare utilities from generic (EQ-5D-5L), cancer-specific (EORTC QLU C10D), and BCa-specific (Bladder Utility Symptom Scale [BUSS]) instruments.

**Methods:** In this prospective, multicenter study, BCa patients recruited from three tertiary care centers across Canada completed each validated utility instrument. Health states were clustered into representative categories of diagnosis, non-muscle-invasive (NMIBC), muscle-invasive (MIBC), and metastatic BCa. Descriptive statistics summarized utility scores. Linear mixed models with a random intercept were fit to compare utility scores within each instrument. Pairwise comparisons across health states and instruments were performed, with adjustment for multiple comparisons.

**Results:** A total of 406 BCa patients completed at least one utility instrument with 464 total observations across up to three visits. Overall, BUSS utilities were slightly higher than EQ-5D-5L for early stage (0.927–0.931 vs. 0.885–0.910) and slightly lower for advanced disease (0.756–0.818 vs. 0.808-0.865), while QLU-C10D utilities were universally lower for each category (0.841–0.864 and 0.688–0.742, respectively) (Figure 1). There was a moderate to strong correlation between instruments (r=0.52–0.86). Pairwise comparisons yielded significant differences in BUSS vs. EQ-5D-5L for NMIBC (higher utilities +0.024, $p<0.01$) and MIBC (lower utilities -0.036, $p<0.01$). QLU-C10D utilities were significantly lower than either instrument (-0.057 to -0.136, $p<0.05$), reflecting an emphasis on non-BCa health domains. Differences in utility between clinically important health state transitions were more often significant when assessed with BUSS and QLU-C10D, indicating improved discrimination for cancer-specific instruments.

**Conclusions:** Differing instruments provided varied HRQoL utility estimates for BCa patient health. BUSS and QLU-C10D appeared to capture more significant differences between health state categories, but scores were lowest for QLU-C10D. Given the higher discrimination for health transitions and the inclusion of BCa-specific health domains, we suggest using the BUSS to measure HRQoL and utilities in BCs patients for future research.

*Acknowledgements: Funded by the Canadian Institutes of Health Research Project Grant awards, 390221 (Bridge funding) and PJT 173386.*




**MP 3.6. Figure 1.** Health utilities by health state category and utility instrument.

## MP 3.7

### A systematic review/meta-analysis on perioperative stenting/dwell time and postoperative outcomes in patients undergoing radical cystectomy and urinary diversion for bladder cancer

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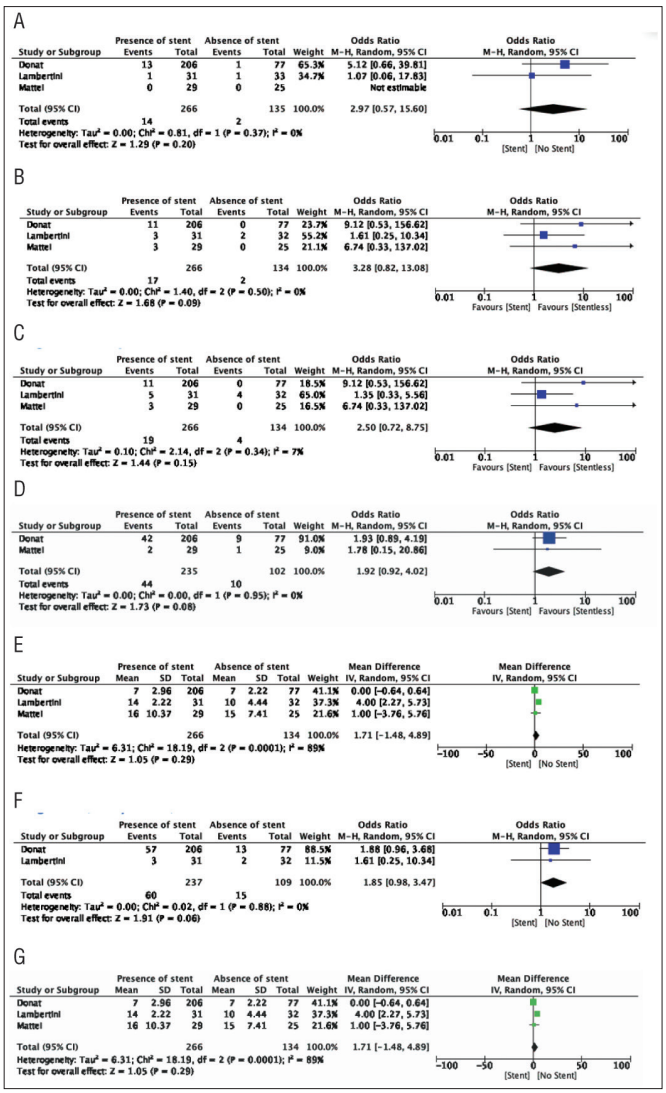


**MP 3.7. Figure 1.** Postoperative complications following stent vs. stentless RCUD. (A) Urinary leak; (B) uretero-ileal stricture; (C) postoperative obstruction; (D) Postoperative UTI; (E) ureteral reimplantation; (F) readmission within 30 days; (G) length of stay.

**Introduction:** Ureteral stents are used to protect the uretero-enteric anastomosis during radical cystectomy and urinary diversion (RCUD); however, complications can occur from their use. The objective of this study was to perform a systematic review of perioperative stenting strategies and postoperative outcomes in patients undergoing RCUD for bladder cancer.

**Methods:** This review was published via PROSPERO (CRD42024558468) and conducted following the Preferred Reporting Items for Systematic Reviews and Meta-analyses. Medline, Medline In-Process, Embase, and the Cochrane Central Register of Controlled Trials were searched. The study population included adult patients with localized or locally advanced bladder cancer (T1-T4, N1-3, M0) who underwent RCUD (including ileal conduit, continent pouch, and neobladder). The index intervention was the presence of a (external) stent. The comparator intervention included the absence of a stent or internal stent. Prospective comparative (randomized and non-randomized) studies published until June 2024 were included. All outcomes were included in the analysis. Risk of bias assessments were undertaken.

**Results:** The search yielded 1516 abstracts. After removing duplicates, 1432 studies were screened based on titles and abstracts, which identified nine articles for full-text review. Three studies were excluded due to incorrect study design (n=2) and inappropriate setting (n=1). Six prospective, comparative studies (740 patients) were included. There were no significant differences between the use or omission of ureteral stents (three studies) during RCUD with any of the UEA complications (urinary leak: OR 2.97, 95% CI 0.57–15.60; ureteroenteric stricture: OR 3.28, 95% CI 0.82–13.08; UTI: OR 1.92, 95% CI 0.92–4.02; ureteral obstruction: OR 3.88, 95% CI 0.73–20.53); however, the outcomes did trend towards stent-less RCUD (Figure 1). Two studies compared the use of an internal stent to an external (extracorporeal) stent. No differences were identified in postoperative outcomes; however, internal stents were associated with a longer stent retention time (30 days) but shorter length of stay (4–7 days) (Figure 1). Early stent removal (five days) was associated with reduced urinary tract infections and hospital readmission (n=1) (Figure 1). There was a high/serious risk of bias with all studies.
**Conclusions:** The role of perioperative stenting during RCUD in preventing uretero-enteric complications remains equivocal and does not favor one approach over another. Shorter stent duration/omission of stents may be associated with better postoperative outcomes. This review highlights the need for further high-quality, randomized studies examining perioperative stenting during RCUD.

## MP 3.8

### Impact of stent duration, antibiotic use, and stent type on urinary complications in post-radical cystectomy patients

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**Introduction:** The management of stents following radical cystectomy is critical for optimizing patient outcomes; however, the usual postoperative pathway for stent removal can greatly vary between institutions and surgeons. This retrospective cohort study aimed to inform clinical procedures for stent removal by evaluating the effects of stent duration and type and antibiotic use on post-stent removal urinary infections and readmission rates.
**Methods:** This was a retrospective study including 259 patients who underwent a radical cystectomy with urinary diversion (Ileal conduit, Indiana, or neobladder) from 2020–2024. The primary outcomes were post-stent removal urinary infection rates and readmission rates. Secondary outcomes evaluated post-stent removal urine leak rates and stricture rates. Chi-squared test and logistic regression were used for statistical analysis.
**Results:** Antibiotic use at the time of stent removal was not associated with a difference in infection rates ($X2=(1, N=259)=3.58$, $p=0.058$) or in readmission rates ($X2=(1, N=259)=0.344$, $p=0.558$). Stent duration (> or <10 days) was not associated with a difference in post-removal infection rates. Stent type (feeding tube or single J stent) was not associated with a difference in infection rates, although these were slightly more frequent with single J stents (21%) compared to feeding tubes (16%). There were insufficient occurrences of urine leak and anastomotic stricture to draw any conclusions on the effect of stent type and duration on these.
**Conclusions:** This study indicates that stent duration and antibiotic administration at removal do not significantly influence urinary infection or readmission rates post-radical cystectomy. The findings suggest a need for standardized stent management protocols to enhance patient outcomes and warrant further investigation into effective strategies to reduce urinary complications in this patient population.

## MP 3.9

### Survival outcomes stratified by AJCC clinical stage in urachal carcinoma of the bladder using the National Cancer Database

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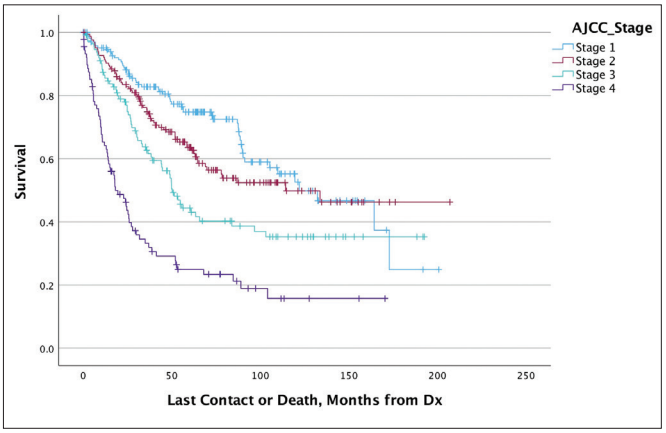
**Introduction:** Urachal carcinoma is a rare condition with limited survival data available in the literature. This study aimed to analyze overall survival outcomes and clinical management patterns in patients diagnosed with urachal carcinoma of the bladder.
**Methods:** The National Cancer Database (NCDB) was queried for cases of urachal carcinoma (ICD C67.7) of the bladder from 2004–2021. Descriptive analyses were conducted to compare AJCC clinical stage with sociodemographic and clinical treatment variables. Kaplan-Meier analysis was used to determine overall median survival.
**Results:** A total of 560 patients with urachal carcinoma were identified according to our selection criteria. Age distribution among the groups was as follows: 26.1% were under 50 years, 20.2% were 50–59 years, 27.7% were 60–69 years, 14.6% were 70–79 years, and 11.4% were 80 years or older ($p<0.001$). In terms of sex distribution, 56.8% of patients were male and 43.2% were female. A higher proportion of males had stage 1 cancer (62.9%), while females had a higher proportion in stage 4 (55.8%) ($p<0.001$). Median overall survival decreased with advancing stage: 18 months for stage 4, 50 months for stage 3, 114 months for stage 2, and 122 months for stage 1 ($p<0.001$) (Figure 1).
**Conclusions:** This large patient cohort provides insights into the sociodemographic and clinical treatment patterns among patients with urachal carcinoma of the bladder. Given the low incidence of urachal carcinoma, these results may serve as a guide for physicians and support informed, multimodal treatment decisions.




**MP 3.9. Figure 1.** KM curves for median overall survival by cancer stage.

## MP 3.10

### Inflammatory complete blood count prognostic biomarkers in patients with non-muscle-invasive bladder cancer

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**Introduction:** Non-muscle-invasive bladder cancer (NMIBC) is a heterogeneous disease with a high risk of recurrence and in some cases, progression to muscle-invasive disease. Clinical factors are used to risk-stratify patients, but there remains a need for useful and accessible biomarkers. Prior work has suggested that accessible biomarkers derived from the complete blood count may be useful to categorize the risk of clinical events in patients with NMIBC.
**Methods:** Using a previously published cohort of consecutive patients with NMIBC who received BCG at our institution, we extracted complete blood count values taken within 90 days prior to initial diagnostic surgery. The value closest to surgery was used. Clinical outcomes were obtained through chart review.

The absolute values of neutrophils, monocytes, lymphocytes, and granulocytes, along with derived ratios, were calculated to assess their relationship with clinical outcomes, including recurrence or progression to invasive disease.
**Results:** A total of 257 patients with available complete blood counts were included in this study. Median followup of these patients was 33 months, with 85 (33%) patients experiencing at least one recurrence, and 24(9%) experiencing progression to invasive disease. Moreover, 81 (32%) patients had a re-TURBT following diagnosis. Of the markers evaluated, the ratio of monocytes to lymphocytes (MLR) demonstrated the greatest prognostic value. On Cox multivariable regression analysis adjusted for age (>70 vs. ≤70), smoking status, grade, and stage, this ratio resulted in a partial hazard ratio for recurrence of 2.1 (95% CI 0.96–4.47). Similarly, the partial hazard ratio for progression was 3.80 (95% CI 1.00–14.44). Further, among the patients who had a second-look surgery, those in the highest MLR tertile had a higher proportion of residual cancer and upgrading present (p=0.04).
**Conclusions:** This exploratory analysis suggests that the MLR may be a useful prognostic marker to identify patients at higher risk of recurrence and progression. Further research is needed to validate and implement use of complete blood count derived biomarkers into clinical practice.
*Acknowledgements: Funded by the Clinician-Scientist Award from the Fonds de recherche de Québec-Santé.*

## MP 3.11
### Correspondence of cystoscopy with pathology findings in the evaluation of bladder cancer: A systematic review and meta-analysis

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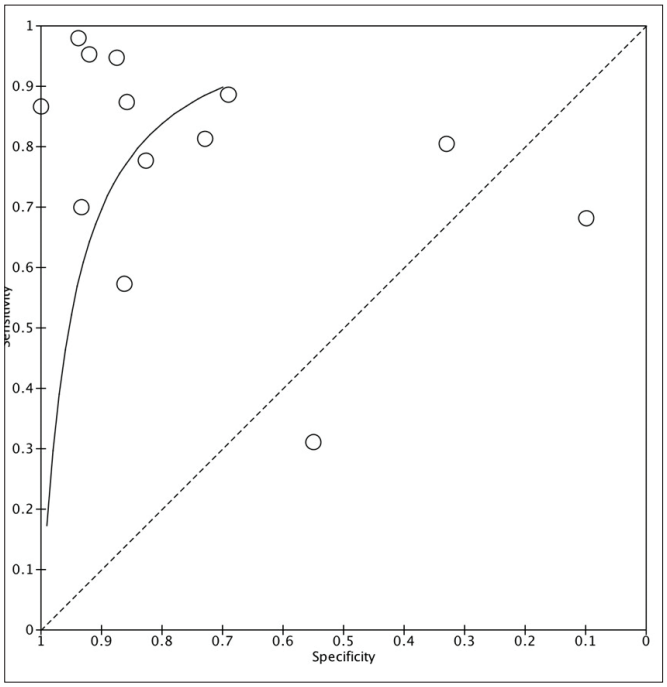
**Introduction:** The diagnosis and treatment non-muscle-invasive bladder cancer relies on the capacity of cystoscopy surveillance to detect bladder tumors. In this systematic review, we evaluated the literature to support cystoscopy as a diagnostic test for pathology-confirmed bladder cancer. We further aim to ascertain what features at cystoscopy may be prospectively used to develop a scale for image-based adjudication of recurrences for a prospective clinical trial.
**Methods:** The systematic review was registered in PROSPERO. We reviewed MEDLINE/Pubmed, Cochrane, and EMBASE databases from 1995–2024 for English- or French-language studies to address the research question: What is the utility of recorded images and video at cystoscopy to correctly predict the pathologic diagnosis among patients investigated for bladder cancer? Study selection was independently performed in duplicate, with consensus discussion with a third reviewer to resolve differences, with data collated with the aid of Rayyan. The QUADAS-2 scale was used to assess the risk of study bias.
**Results:** Of 1165 extracted studies, we included 31 studies that reported on the correspondence of cystoscopy findings with pathology findings. Among studies with consecutive cystoscopy cohorts, seven evaluated patients under investigation for bladder cancer, and 16 evaluated both patients with prior bladder cancer and those under investigation for bladder cancer. The sensitivity and specificity of white light cystoscopy from studies with per-lesion comparison to pathology are shown in Figure 1. Qualitatively, diagnostic results were lower for flat lesions than for papillary lesions, with the accuracy of grade prediction low among studies assessing this. Five studies reported data evaluating conserved photos or videos, with no significant differences in reported diagnostic test performance. Overall, most studies were at low risk of bias in the areas assessed. Nonetheless, limitations include the heterogeneity of clinical contexts and the detail of available information, with many studies indirectly related to our study question. Further, results on alternative cystoscopy methods (e.g., narrow-band imaging) were not included in our analysis.
**Conclusions:** While relatively few studies directly address this topic, the current literature indicates that cystoscopy has high diagnostic value to detect pathology-confirmed bladder cancer. Lesion features may help indicate the level of diagnostic accuracy, while current data does not support the reliable diagnosis of grade at cystoscopy.




**MP 3.11. Figure 1.**

## MP 3.12
### Secondary tumors in orthotopic neobladder using isolated gut segment post-radical cystectomy for urothelial carcinoma: A systematic review

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**Introduction:** Urothelial carcinoma recurrence of an orthotopic neobladder created from bowel segment is a rare occurrence. The usage of bowel segments to create neobladder following cystectomy for urinary diversion is growing, yet there remains a large gap in the literature about recurrence in neobladder. We carried out the first systematic review to outline current details of urothelial cancer recurrences in a neobladder, including diagnostic approach, management, and long-term prognosis.
**Methods:** We carried out a systematic review searching databases PubMed (MEDLINE), Scopus, and Web of Science. Only studies reporting on urothelial carcinoma recurrence of the neobladder with or without multifocal disease were reported. A quality assessment tool was used to ensure all studies met quality standards.
**Results:** Fifteen studies were included in the systematic review meeting inclusion criteria. Fourteen of these studies were cases in men where pT3 disease was the most prevalent (29%). The most common symptomology was macroscopic hematuria seen in eight patients (53.33%). Management varied among cases and included adjuvant chemotherapy regimens and surgical interventions consisting of endoscopic resection to robotic neocystectomy and nephroureterectomy. The followup period for these patients was up to 38 months, and 55% of patients did not see a recurrence.
**Conclusions:** The nature of recurrence is hypothesized to be due to seeding of urothelial cells into the non-urothelial surfaces compatible for both implantation and growth. We present the first systematic review to report on recurrence rates and details of diagnosis and outcomes of various management regimens for urothelial carcinoma of the neobladder.

## MP 3.13

### The Cretostimogene Grenadenorepvec Expanded-Access Program in patients with non-muscle-invasive bladder cancer unresponsive to bacillus Calmette-Guérin

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**Introduction:** Current guidelines, including those from the Canadian Urological Association (CUA), recommend that patients diagnosed with high-risk, BCG-unresponsive non-muscle-invasive bladder cancer (HR BCG-UR NMIBC) undergo radical cystectomy; however, many patients are unwilling to undergo such a morbid intervention or are unfit due to competing medical risks. Therefore, a considerable unmet medical need exists for clinically effective, well-tolerated, and readily available bladder-sparing treatment options for patients with HR BCG-UR NMIBC. Cretostimogene grenadenorepvec is an oncolytic immunotherapy with a dual mechanism of action. It selectively replicates in and lyses bladder cancer cells with retinoblastoma (Rb)-E2F pathway alterations. The subsequent release of virus- and tumor-specific antigens initiates antitumor immune activation amplified by the GM-CSF transgene, a potent cytokine. Based on preliminary efficacy and safety results from the ongoing phase 3 BOND-003 study, cretostimogene received both fast-track and breakthrough therapy designations from the U.S. FDA for BCG-UR NMIBC with CIS indication. The Cretostimogene Expanded-Access Program (EAP) (NCT06443944) is an open-label, expanded-access clinical trial designed to provide cretostimogene to a diverse population of real-world patients with BCG-UR NMIBC with CIS who may not otherwise be eligible for enrollment in clinical trials.

**Methods:** Pragmatic, real-world eligibility criteria include: age ≥18 years, ECOG performance status of 0–3, pathologically confirmed BCG-UR CIS ± HG Ta/T1 disease after completion of adequate BCG treatment. Patients who received prior intravesical treatment may be considered. Intravesical cretostimogene will be administered in combination with n-dodecyl-β-D-maltoside (DDM), an excipient that enhances adenoviral delivery for six weekly doses during the induction phase, followed by three weekly maintenance cycles quarterly through month 12, then every six months through month 24. Re-induction is permitted. Additionally, patients with partial response, defined as persistent but improved disease at week 25 or subsequent time points, may receive continued doses of cretostimogene at the discretion of the investigator. Primary disease assessments include serial cystoscopy, urine cytology, axial imaging, and directed bladder biopsies, as clinically indicated, with local review of pathologic samples. Co-primary endpoints include safety and complete response at any time. The incidence of adverse events will be reported using the Medical Dictionary for Regulatory Activities (MedDRA) and CTCAE v5.0. Secondary outcomes include duration of response, progression-free survival, radical cystectomy-free survival, patient-reported outcomes, and health-related quality of life measures.

**Results:** This is an ongoing trial.

**Conclusions:** A broad cross-section of geographically diverse clinical sites with socioeconomically diverse patient populations has been identified. The study is open and actively recruiting.

*Acknowledgements: Funded by CG Oncology.*

## MP 3.14

### Health utilities and health-related quality of life for patients on BCG

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**Introduction:** For patients with non-muscle-invasive bladder cancer (NMIBC), intravesical BCG therapy remains a mainstay of treatment to decrease the recurrence and progression of disease; however, treatment administration, local, and systemic adverse effects may impact the health-related quality of life (HRQoL) for patients undergoing BCG treatment. Using health utilities as preference-based measures of HRQoL, we evaluated the utility of NMIBC patients on BCG therapy compared to patients off of therapy.

**Methods:** In this prospective, multicenter study, we previously recruited bladder cancer patients from outpatient clinics at three Canadian tertiary care centers in 17 representative bladder cancer health states. Patients completed three validated utility instruments: EQ-5D-5L, EORTC Quality of Life Utility – Core 10 Dimensions, and Bladder Utility Symptom Scale (BUSS). For this study, patients with NMIBC in surveillance states following TURBT were assessed. We evaluated multiple timeframe definitions for patients on BCG in order to capture the HRQoL impact of BCG therapy. The primary definition included health utility measurement within the first week of treatment. Secondary definitions included within the first 24 hours (strict), the first two weeks (lenient), and the first month of treatment (lenient). Descriptive statistics were used to summarize utility scores for patients on and off BCG treatment. Two-tailed comparisons with Student's t-test were performed, with $p<0.05$ to indicate statistical significance.

**Results:** A total of 98 patients with NMIBC on surveillance were recruited and completed HRQoL questionnaires, with three patients completing multiple visits (n=101 total observations). Of these, 91 patients (n=94 observations) were off therapy and seven patients (n=7 observations) were on BCG therapy. Mean BUSS utilities were 0.907 (SD 0.115) for patients off therapy vs. 0.894 (SD 0.175) for patients within the first week of BCG treatment in the primary definition (p=0.78). Strict definitions reflecting the first 24 hours of treatment yielded slightly lower utilities (0.883, SD 0.189), and lenient definitions of two weeks and one month yielded slightly higher utilities (0.901, SD 0.152), although these were not statistically significant and remained below those of patients off therapy.

**Conclusions:** BCG treatment is well tolerated overall, with minimal impact on measured health utilities for patients undergoing therapy compared to those off therapy. These results were similar across strict and lenient timeframe definitions for measuring HRQoL. Future studies are needed with targeted recruitment of patients with significant adverse events to assess the potential dis(utility) attributable to BCG treatment in those who are intolerant to treatment.

*Acknowledgements: Funded by the Canadian Institutes of Health Research Project Grant awards, 390221 (Bridge funding) and PJT 173386.*

## MP 3.15

### Ex-vivo culture to evaluate dynamic changes in the tumor microenvironment following durvalumab treatment

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**Introduction:** While the tumor microenvironment is critical to the mechanism of action of anti-PD-1/PD-L1 checkpoint inhibitions, limitations exist to understand this using in-vitro and in-vivo models. With bladder and prostate cancer representing cancer sites wit,h respectively, strong and poor responses to PD-1/PD-L1 inhibition, we sought to use ex-vivo culture of fresh cancer patient tissue samples to better understand changes that occur in the tumor microenvironment following durvalumab therapy, specifically the macrophage phenotype.

**Methods:** Following optimization of techniques, fresh prostate or bladder biopsies from patients undergoing radical prostatectomy (RP) or radical cystectomy (RC) were cultured in paired samples treatment with durvalumab or isotype control. After 72 hours, flow cytometry assessed a panel of myeloid cell markers.

**Results:** For both bladder and prostate tissues, cell viability after 72 hours was not significantly different between paired treatment groups (RC, n=35: isotope 93% [95% CI 91–96%] vs. durvalumab 94% [92–96%]; RP, n=35: isotype 92% [91–94%] vs. durvalumab 92% [90–93%]). Further, an anticipated treatment effect was seen in both tissues, with a significant decrease in PD-L1 positive macrophages (CD45+CD11b+HLA-DR+) in RC patients and PD-L1 positive immune (CD45+) cells in RP patients. In prostate tissues, there was a significant increase in the intensity of ROS expression in inflammatory macrophages (CD11b+HLA-DR+CCR7+) in durvalumab-treated tissue vs. control. For bladder tissues, there was a non-significant decrease (p=0.05) in the proportion of mixed inflammatory macrophages (CD45+CD11b+HLA-DR+CCR7+B7-H3+), with active phagocytosis with durvalumab vs. control. The heterogeneity of patient and tumor characteristics is a limitation.

**Conclusions:** Our detailed cytometric analysis of ex-vivo cultured biopsies from bladder and prostate cancer patients demonstrated relatively few detectable changes in macrophage phenotype following durvalumab treatment, despite the anticipated decrease in the expression of PD-L1. Further research is needed to validate our findings, with our results demonstrating the limitations that exist to detect immunotherapy-induced immune cell changes ex-vivo.

*Acknowledgements: Supported by a externally funded research grant from AstraZeneca.*

## MP 3.16

### The impact of radiotherapy on the bladder tumor micro–environment and associated B-cell response using an orthotopic murine model

*Iman Sadri[1,2], Eva Michaud[2], Jose Joao Mansure[2], Leonardo Jurado[2], Fatima Inigo[2], Wassim Kassouf[1,2]*

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**Introduction:** Radical cystectomy, the standard treatment for invasive bladder cancer (MIBC), significantly impacts quality of life, highlighting the need for bladder-sparing therapies like radiotherapy. Radiotherapy induces DNA damage and modulates immune responses, with immune cell infiltration linked to tumor response. While T-cell responses to radiation are well studied, the effects on B cells in the tumor micro-environment remain unclear. This study examined the impact of radiation on B cells in an orthotopic murine bladder cancer model.

**Methods:** 6x109 MB49 bladder cancer cells were injected transurethrally into 40 10-week-old female C57BL/6 mice. Bladder cancer development was monitored by hematuria and/or ultrasound. Mice with hematuria were randomized into radiation and control groups. The radiation group received six sessions of 6 gray (Gy) over 10 days using CT-guided bladder radiation. Mice were euthanized upon reaching humane endpoints (20% weight loss or abnormal behavior). Post-euthanasia, radical cystectomy was performed, and tumors underwent H&E staining. Tumor presence was confirmed by a pathologist, followed by immunohistochemistry (IHC) staining for plasma cells (CD138) and germinal center B cells (CD19). HALO AI (v4.0) software quantified cell counts from the IHC slides.

**Results:** Thirty-five mice were successfully catheterized and instilled with the MB49 cells. All mice developed hematuria. The radiation group survived longer than controls (21.19 vs. 9.58 days, p<0.001). Necropsy identified 13 tumors in controls and eight in the radiation group. Immune cell quantification found 1961 (±1143) plasma cells/mm² and 33 (±82.36) germinal center B cells in controls, yielding a plasma-to-germinal-B-cell ratio of 424 (±458). The plasma cell ratio was significantly greater in the radiation group (p=0.007); however, there was no significant association between radiation and plasma cell (p=0.17) or germinal center B cell density.

**Conclusions:** This is the first study examining B cells in the context of radiation therapy for MIBC. The findings may provide insights into biomarkers and predictors of treatment success, enabling future patient stratification and personalized therapies.