Cite as: *Can Urol Assoc J* 2019;13(2Suppl2):S9-30. http://dx.doi.org/10.5489/cuaj.5793

Published online January 3, 2019.

POD-1.1

Surgical castration in the management of metastatic prostate cancer: Current trends in androgen-deprivation therapy

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Introduction: The majority of cases of metastatic prostate cancer in North America are treated with pharmaceutical androgen-deprivation therapy, rather than the gold standard treatment of surgical castration (SC). A previous cost analysis by the same authors has identified the potential for significant cost-savings through increased use of SC in the treatment of metastatic prostate cancer. Here, we aim to identify current practice patterns and attitudes of urologists regarding the treatment of metastatic prostate cancer.

Methods: An electronic survey was developed with the aim of assessing current practice patterns and attitudes in the treatment of metastatic prostate cancer. Information collected included practice demographics and current practices in the treatment of metastatic prostate cancer. This survey was distributed via email to approximately 700 urologists across Canada. Responses were tabulated and quantitative and qualitative analyses were performed.

Results: Survey responses were obtained from urologists in all 10 Canadian provinces and included urologists practicing in both academic and community settings. Fifty percent of respondents indicated they only sometimes offer SC, while 37% of respondents stated that they do not routinely offer SC as a treatment for metastatic prostate cancer. Eighty-one percent of respondents estimated that currently <5% of their patients have been treated with SC. Factors preventing wider adoption of SC included perceived negative attitudes of patients towards SC, invasiveness of surgery, and lack of operating room availability. Seventy-two percent of respondents felt that SC is an underused treatment and 66% agreed that urologists should more actively offer SC. Seventy-five percent of respondents stated they would like to see more data on the cost-effectiveness of SC.

Conclusions: SC is likely an underused treatment modality with potential for significant cost-savings in the treatment of metastatic prostate cancer in Canada and abroad. Further study of patient attitudes toward SC is warranted.

POD-1.2

A high percent-free PSA in the setting of biochemical recurrence after radical prostatectomy is associated with poorer outcomes: A validation study using prospectively collected biobank specimens

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Introduction: The role of percent-free prostate-specific antigen (%fPSA) in the management of patients who have undergone radical prostatectomy (RP) and subsequently relapsed is unclear. Our team previously conducted a retrospective study of 308 patients and found that %fPSA of ³15 in the setting of biochemical recurrence (BCR) confers a more aggressive disease, manifesting in faster development of CRPC, metastasis, and death. However, this retrospective study has its intrinsic limitations, in particular, the %fPSA tests were performed at random and at various time points after BCR. To validate our previous findings, we propose to use biobank specimens collected prospectively when patients were first diagnosed with BCR.

Methods: Biobank specimens of all patients with undetectable PSA after RP and then develop BCR (PSA ≥0.2) were included. Biobank samples were analyzed for %fPSA. Patients were stratified according to the %fPSA cutoff of 15% (Group 1 <15% and Group 2 ≥15%). Multivariable logistic regression analysis was performed to predict covariates associated with a higher %fPSA. Cox proportional hazard models were performed to evaluate androgen-deprivation therapy (ADT)-free, metastasis-free, CRPC-free, cancer-specific (CSS), and overall survival (OS).

POD-1.2. Table 1. Clinical information of patients

	% fPSA <15 (Group 1)	% fPSA ≥15 (Group 2)	p
Number of patients	126 (81.8)	28 (18.2)	
Mean age (SD)	61.5 (7.2)	63.2 (6.8)	0.266
Race, n (%)			0.747
White	110 (87.3)	25 (89.3)	
Black	6 (4.8)	0 (0.0)	
Asian	5 (4.0)	1 (3.6)	
South Asian/Indian	3 (2.4)	1 (3.6)	
Other	2 (1.6)	1 (3.63)	
Mean total PSA at diagnosis (SD)	11.5 (16.2)	8.6 (6.4)	0.025
Mean prostate weight at surgery, g (SD)	43.8 (18.0)	48.0 (18.1)	0.269
Surgery (histopathology at RP)			
Primary Gleason score, n (%)			0.105
3	80 (63.5)	12 (42.9)	
4	45 (35.7)	16 (57.1)	
5	1 (0.8)	0 (0.0)	
Secondary Gleason score, n (%)			0.214
3	38 (30.2)	13 (46.4)	
4	76 (60.3)	12 (42.9)	
5	12 (9.5)	3 (10.7)	
pT stage, n (%)			0.973
T2a	18 (14.3)	3 (10.7)	
T2b	1 (0.8)	0 (0.0)	
T2c	46 (36.5)	11 (39.3)	
T3a	43 (34.1)	10 (35.7)	
T3b	18 (14.3)	4 (14.3)	
pN stage, n (%)			0.958
N0	68 (54.0)	15 (53.6)	
N1	6 (4.8)	1 (3.6)	
NX	52 (41.3)	12 (42.9)	
Intraductal, n (%)	17 (13.5)	6 (21.4)	0.287
Cribriform, n (%)	2 (1.6)	3 (10.7)	0.014

PSA: prostate-specific antigen; RP: radical prostatectomy; SD standard deviation.

Results: A total of 154 men were included (Table 1). Patients in Group 2 were more likely to receive ADT (42.9% vs. 24.8%; hazard ratio [HR] 2.3; 95% confidence interval [CI] 1.09–4.9; p=0.03), develop metastatic disease (21.4% vs. 7.9%. HR 8.16; 95% CI 1.59–41.77; p=0.04), and become castrate-resistant (CRPC) (14.3% vs. 4%; HR 495; 95% CI 1.18–206521; p=0.04). Time from surgery to the start of ADT was shorter in Group 2 (38.2 months) vs. Group 1 (45.1 months) (p=0.03). Time from surgery to metastasis was shorter in Group 2 (28.4 months) vs. Group 1 (63.4 months) (p=0.018). There was no difference in CSS.

Conclusions: Patients with %fPSA of ³15 were started on ADT earlier, and they progressed to CRPC and metastatic stage earlier. %fPSA of ≥15 in

the setting of BCR after RP is an indicator of a more aggressive disease, and it can potentially be used as a simple and cheap biomarker. Unlike in the diagnostic setting, a higher %fPSA ratio portends a worse clinical outcome. This validates our previous findings.

POD-1.3

Factors associated with treatment completion and survival in patients with metastatic, castration-resistant prostate cancer undergoing radium-223 therapy in Ontario

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Introduction: Radium-223 (Ra-223) prolongs the survival and improves the quality of life of patients with metastatic castration-resistant prostate cancer (mCRPC) to bones. However, using Ra-223 comes with unique challenges compared to other mCRPC therapies. Hence, we aimed to study real-world Ra-223 utilization patterns, and to identify factors predicting treatment completion and patient survival.

Methods: In this retrospective chart analysis, we extracted data on 198 mCRPC patients treated with Ra-223 from January 2015 to October 2016 at four cancer centres in Ontario, to analyse the rate of Ra-223 completion, reasons for early Ra-223 discontinuation, patient survival, and survival differences in patients completing Ra-223 vs. patients receiving <6 cycles. In addition, we used logistic regression analyses and Cox proportional hazards models to define predictive factors of treatment completion and survival.

Results: In this cohort of patients mostly pretreated with abiraterone and/or enzalutamide (92.4%), half of who were also post-docetaxel (51.5%), the Ra-223 completion rate was 46.5%, and the actuarial median survival 13.3 months. The main reason for early Ra-223 discontinuation was disease progression, and Ra-223 non-completion was associated with a shortened median survival of 8.1 months (range 6.0–12.2) vs. 18.7 months (15.3–22.3) in men completing Ra-223 ($p<0.0001$). Lymph node metastases and high baseline prostate-specific antigen (PSA) were independent predictors of early treatment discontinuation. Early Ra-223 discontinuation, anemia, high PSA, prior skeletal related events, visceral metastases, and being referred for Ra-223 therapy were independent predictors of worse survival.

Conclusions: Despite a lower completion rate than observed under clinical trial conditions, the real-world results achieved with Ra-223 are encouraging. If prospectively validated, predictive factors identified in our cohort might become instrumental to select mCRPC patients most likely to complete and to benefit from Ra-223.

The study was made possible by a grant-in-aid to U. Emmenegger by Bayer Inc., Canada. U. Emmenegger is supported by the Joseph and Silvana Melara Cancer Fund.

POD-1.4

Partial orchiectomy: A review of the Princess Margaret Cancer Centre experience

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Introduction: Radical orchiectomy (RO) is the gold standard treatment for a suspicious testicular lesion. Organ-sparing surgery can be considered in the setting of a solitary functioning unit or bilateral tumours. It has also been suggested as an alternative to RO for small lesions. The aim of this study was to report the experience of partial orchiectomy (PO) at our centre.

Methods: We performed a retrospective review of our prospectively maintained testicular cancer database at the Princess Margaret Cancer Centre, analyzing PO.

Results: A total of 77 patients underwent a PO between 1983 and 2018. The mean age was 31.3 years (range 17–56). A lesion was palpable in 70 (90.9%) patients. The mean size of lesion was 14.1 mm (range 3–35). Thirty-nine (50.6%) patients underwent a PO due a small lesion, 30 (39%) to a solitary functioning testis, six (7.8%) due to bilateral lesions, one (1.3%) for an assumed benign lesion, and one (1.3%) was not documented. The mean followup was 55 months (range 1–258). Histological analysis revealed a benign lesion in 25 (32.5%) patients. A positive surgical margin was noted in six patients (7.8%). None of these patents developed a local or distant recurrence. Sixteen (20.8%) patients subsequently had a RO following an initial PO at a mean interval of 9.8 months (range 0–46). The reasons for subsequent RO included a radiologically detected lesion in seven patients, a palpable lesion in four patients, a positive surgical margin in three patients, and a pathological finding in two patients. Malignant histology was present in 12 (75%) of the RO specimens. Of the patients who initially presented with no metastatic disease (n=57), seven (12.3%) patients subsequently developed a nodal recurrence. None of these had a positive margin at PO. All were salvaged with adjuvant treatment and are currently disease-free. There have been two disease-specific deaths in the series, both however, initially presented with widespread metastatic disease. There were no reported Clavien-Dindo grade 3–5 complications.

Conclusions: Organ-sparing surgery is a safe and feasible approach to small testicular lesions. A proportion of small testicular lesions are benign and it can potentially avoid the necessity for a RO.

POD-1.5

Second cancer incidence and competing causes of death in patients with early stage seminoma: A population-based study comparing radiation therapy vs. chemotherapy

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Introduction: The purpose of this study is to examine the incidence of second cancers (SC) and evaluate the causes of death in patients with stage I or II seminoma treated in British Columbia (BC), and compare outcomes between patients managed with radiation therapy (RT), chemotherapy (CT), or active surveillance (AS).

Methods: Consecutive patients with stage I or II seminoma (n=1549) diagnosed in BC between 1984 and 2013 were identified from the BC

Cancer Registry and included in this study. Patients were managed with RT (n=663), CT (n=259), or AS (n=624). Data was extracted from the registry and verified by individual patient chart review. Cumulative incidence rates and mortality rates were computed using competing risk analysis, and compared using the Fine and Gray model. The 10-year testicular-cancer mortality (TCM), second cancer-related mortality (SCM), cardiovascular mortality (CVM), treatment-related mortality (TRM), and all-cause mortality (ACM) were calculated, from diagnosis date.
Results: After a median followup of 14 years (RT group: 21.5 years, CT group: 10 years, AS group: 8 years), the 15-year overall survival was 91.4%. Only nine patients died due to seminoma, while six died from treatment-related toxicity, 46 from SC, 52 from cardio-pulmonary causes, and 30 from other reasons. The 10-year rate for ACM was 5.67% (4.72% RT group vs. 8.06% CT group vs. 5.75% AS group; p=ns), for TCM was 0.62% (0.60% RT vs. 1.83% CT vs. 0.22% AS; p=ns), for SCM was 1.66% (1.53% RT vs. 2.52% CT vs. 1.29% AS; p=ns), for CVM was 1.43% (1.37% RT vs. 0.84% CT vs. 1.87% AS; p=ns), and for TRM was 0.45%, with the difference between treatment groups being statistically significant (0.15% RT vs. 1.55% CT vs. 0.32% AS; p=0.014). All six of the treatment-related deaths were due to chemotherapy-associated toxicity (some events occurred during salvage therapy, groups for analysis were based on initial treatment). A total of 115 patients developed SCs, and the cumulative incidence (CI) of SC at 15 years was 5.9% for patients who received RT, 8.6% for those who had CT, and 4.9% for patients managed with AS. The higher CI for patients treated with CT vs. RT, was not statistically significant (p=0.08).
Conclusions: Patients with early-stage seminoma have excellent outcomes and very low cancer-related mortality rates (0.62% at 10 years). We report significantly higher treatment-related mortality rates with the use of chemotherapy (1.55%) as compared to RT or AS. We found no statistically significant difference in the CI of SCs for patients treated with RT vs. CT in our patient population. Longer followup for the CT group is required to confirm trends evident in our analysis.

POD-1.6

Activity of cabozantinib after PD-1/PD-L1 immune checkpoint blockade in metastatic clear-cell renal cell carcinoma

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POD-1.6. Table 1. Best response to cabozantinib therapy for mccRCC

		Best response to cabozantinib n (%)			
	n	PR	SD	PD	Unevaluable
All patients	69	23 (33)	32 (46)	12 (17)	2 (3)
By prior ICB type					
ICB alone	37	16 (43)	15 (41)	5 (14)	1 (3)
ICB + VEGF	24	6 (25)	12 (50)	5 (21)	1 (4)
ICB + other	8	(1 (13)	5 (63)	2 (25)	
By prior ICB duration					
<6 months	42	12 (29)	22 (52)	8 (19)	
>6 months	27	11 (41)	10 (37)	4 (15)	2 (7)

ICB: immune checkpoint blockade; mccRCC: metastatic clear-cell renal cell carcinoma; VEGF: vascular endothelial growth factor.

Introduction: Cabozantinib is approved for metastatic clear-cell renal cell carcinoma (mccRCC) based on trials in which the vast majority of patients were immune checkpoint blockade (ICB)-naive. We analyzed the activity of cabozantinibin mccRCC patients who had progressed on ICB.
Methods: We included 69 patients with mccRCC who received cabozantinib after progression on ICB alone or in combination with vascular endothelial growth factor (VEGF) or other therapies. Baseline characteristics, best response (investigator-assessed), time to treatment failure (TTF), and overall survival (OS) were analyzed, adjusted for known prognostic factors, including the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) criteria.
Results: Median age was 62 years (range 37–78). Median number of prior therapies was 2 (range 1–10). Median time on prior ICB was 3.9 months (range <1–38). Type of prior therapy was ICB single agent (54%) or in combination with a VEGF inhibitor (35%) or other therapies (12%). At time of cabozantinib initiation, IMDC risk groups were 6% good, 67% intermediate, and 27% poor. Best response was 33% PR, 46% SD, 17% PD, 3% unevaluable (Table 1). Median followup after cabozantinib initiation was 12 months. At time of analysis, 35% (n=24) remained on cabozantinib and median TTF was 6.6 months (95% confidence interval [CI] 5.3–8.5). Of those discontinuing cabozantinib, 58% (n=26) received additional therapy. At time of analysis, 62% (n=43) were alive, with one-year OS rate of 53% (95% CI 37–66%).
Conclusions: Cabozantinib is active in patients treated after PD-1/PD-L1-based ICB, independent of prior combination therapy with VEGF inhibitors, with 79% achieving disease control at minimum. These results support the continued use of cabozantinib, irrespective of ICB timing.
Equal contribution: AAL, BAM.

POS-1.1

A high baseline neutrophil-to-lymphocyte ratio in men with metastatic castrate-sensitive prostate cancer treated with chemohormonal therapy predicts a longer interval to castration resistance

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Introduction: There is extensive literature on neutrophil-to-lymphocyte ratio (NLR) in castrate-resistant prostate cancer (CRPC). However, little is known about the role of NLR in metastatic castrate-sensitive prostate cancer (mCSPC). Furthermore, there is a lack of predictive baseline biomarkers of benefit from androgen-deprivation therapy (ADT) plus docetaxel chemotherapy (D) in mCSPC. Hence, the primary objective of this study was to analyze the correlation of NLR with time from mCSPC diagnosis to CRPC.
Methods: We studied hematological parameters of 70 men with mCSPC undergoing ADT plus D from June 2014 to August 2018 at Odette Cancer Centre, Toronto. NLR was calculated a three time points: before start of ADT, before D, and following D. The cutoff for high vs. low NLR was determined using the median of the group at each time point (i.e., 3.425 for before ADT, 3.000 for before D, and 2.925 for after D). Kaplan-Meier progression-free survival (PFS) curves, PFS hazard ratios (HR), and median PFS were calculated. All statistical analyses were performed in R (version 3.5.0).
Results: With a median followup of 645 days, 30 (42.9%) men progressed to CRPC after a median time of 271 days (range 6–750). A high NLR before ADT was associated with prolonged time to CRPC, with a HR of 0.47 (95% confidence interval [CI] 0.23–0.94; p=0.03). High NLRs before D and following D also correlated with a longer time to CRPC, but these findings were not statistically significant (HR 0.88; 95% CI 0.46&ndn-dash;1.69; p=0.7 and HR 0.76; 95% CI 0.39–1.48; p=0.4, respectively).
Conclusions: If validated, a high baseline NLR might emerge as an easy available biomarker identifying men with mCSPC benefiting most from ADT plus D vs. patients that may be candidates for treatment intensification beyond chemohormonal therapy. Longer followup of our cohort will enable us to also study the association between NLR and overall survival.
This study was supported by the Joseph and Silvana Melara Cancer Fund.

POS-1.2

Poor bone health is common in men diagnosed with metastatic castrate-sensitive prostate cancer

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Introduction: Prostate cancer patients in general are at increased risk of poor bone health relative to average, healthy ageing males. As opposed to men with metastatic, castrate-resistant prostate cancer, patients with metastatic castrate-sensitive prostate cancer (mCSPC) are not routinely administered antiresorptive agents, such as denosumab or zoledronic acid. There is a paucity of data on the prevalence of poor baseline bone health in men with mCSPC.

Methods: We conducted a retrospective review of mCSPC patients treated at Sunnybrook Odette Cancer Centre in Toronto from 2014–2017 to extract key clinical characteristics and osteoporosis risk factors, and to determine the rate of bone mineral density (BMD) assessments. For patients that underwent a BMD assessment, T-scores and the Canadian Association of Radiologists and Osteoporosis Canada (CAROC) 10-year fracture risk were extracted.

Results: A total of 118 patients (78 with de novo mCSPC, 40 with recurrent mCSPC) were identified, of which 60 (51%) had a baseline BMD assessment (35 de novo, 25 recurrent). Of the patients with a baseline BMD, 34 (57%) had either osteopenia or osteoporosis T-scores. Specifically, of the de novo mCSPC patients, 13 (37%) had a normal BMD, 17 (49%) had osteopenia, and four (11%) osteoporosis; of the recurrent mCSPC patients, 12 (48%) had a normal BMD, 11 (44%) had osteopenia, and two (8%) osteoporosis. While there was no significant difference in the distribution of normal BMD/osteopenia/osteoporosis in de novo vs. recurrent mCSPC, patients with de novo disease more commonly presented with osteoporosis risk factors, such as lower body mass index (p=0.045) and absent vitamin D/calcium supplementation (p=0.038). Twelve patients with recurrent mCPSC (48%) had been exposed previously to androgen-deprivation therapy as part of their treatment for localized prostate cancer.

Conclusions: Almost two-thirds of men with de novo or recurrent mCSPC present with either osteopenia or osteoporosis at diagnosis, and might be candidates for antiresorptive therapy aside from vitamin D and calcium supplementation.

This study was supported by the Joseph and Silvana Melara Cancer Fund.

POS-1.3

Real-world use of radium-223 in patients with castration-resistant prostate cancer and bone metastases

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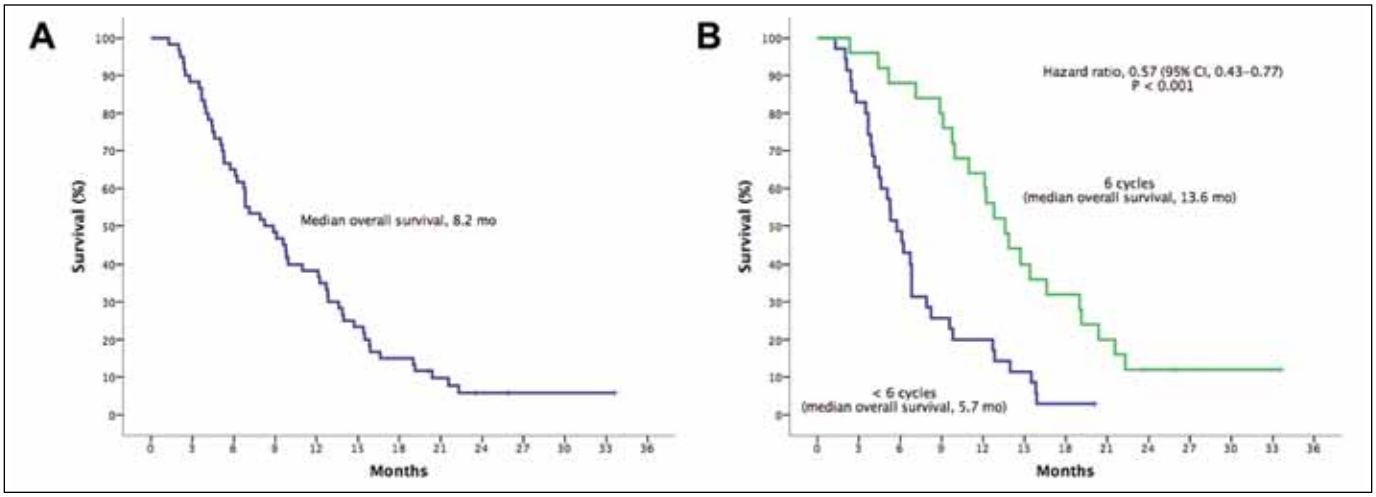
Introduction: Radium-223 dichloride (radium-223), an alpha-emitting agent that mimics calcium and targets bone metastases, is FDA-approved for the treatment of metastatic castration-resistant prostate cancer (CRPC). We report our experience and outcomes of men with metastatic CRPC treated with radium-223.

Methods: We performed a retrospective analysis of men with CRPC and bone metastases treated with radium-223. We examined demographic data, radium-223 therapy details, overall survival, biochemical responses, and adverse events.

Results: Sixty patients were treated with radium-223. Median age was 73 years; median prostate-specific antigen (PSA) and alkaline phosphatase (ALP) prior to radium-223 therapy were 99 ug/L and 154 U/L, respectively. The majority of patients had received previous therapies, including docetaxel (62% of patients), abiraterone (72%), and enzalutamide (68%). Only 42% of patients received all six cycles of radium-223. Median overall survival was 8.2 months. Patients who had all six cycles of radium-223 compared to those who had <6 cycles had longer overall survival (13.6 vs. 5.7 months; p<0.001) (Fig. 1). Previous treatment with docetaxel, abiraterone, and/or enzalutamide did not alter survival. Thirteen patients (22%) had a >25% reduction in PSA and 33 patients (55%) had a >25% reduction in ALP. Seventy-two percent of patients experienced an adverse event (AE): 42% were grade 3–4 and none were grade 5 events.

Conclusions: Radium-223 appeared effective and relatively well-tolerated in heavily pretreated patients. Patients who received all six cycles of radium-223 had improved overall survival. The use of previous therapies did not change overall survival, suggesting that radium-223 is suitable in pretreated patients.



POS-1.3. Fig.1. Kaplan-Meier estimates of ***(A)*** overall survival and ***(B)*** overall survival stratified by number of radium-223 cycles (6 cycles vs. <6 cycles).

POS-1.4

IKKε inhibition by BX795 promotes a senescence phenotype in advanced prostate cancer

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Introduction: Prostate cancer (PCa) is the third most common cause of cancer-related death in Canadian men. Advanced PCa often evolves from a hormonosensitive (HS) to a lethal castration-resistant (CR) state. Our lab has previously demonstrated that CR cells exhibited a constitutive overexpression of IKKε. The tumour growth was significantly decreased when cells were depleted in IKKε. We also showed that IKKε expression regulated the C/EBP-β transcription factor to activate the IL-6 promotor. We believe that IKKε is likely implicated in the development of CR. Since senescence induced by androgen-deprivation therapy (ADT) promotes the maintenance of HS state in PCa cells, we hypothesize that IKKε expression prevents ADT-induced senescence.
Methods: In our laboratory, we have two CR cell lines and two HS cell lines. DU145 cell lines are subcutaneously injected in our mouse model, and when the tumour reaches 400 mm^3, BX795 is administered intraperitoneal.
Results: Proliferation of CR cells dramatically decreased by BX795 administration compared to HS cells. This was confirmed by EdU incorporation assay. After four days of treatment, CR cells have an increased SA-b-Galactosidase staining, whereas the HS cells do not stain. After six days of treatment, the size of CR cells increased compared to HS cells. The inhibition of IKKε activity by BX795 also increased p21 and p15 in CR cells. Moreover, the treatment induced a polynuclear morphology in CR cell lines. Overall, BX795 injection in a mouse model results in a decrease in tumour volume while having no effect on mouse behavior and body weight.
Conclusions: Our study suggests that IKKε is likely involved in PCa progression and that inhibiting its activity in CR cells, they express a senescent phenotype. These results suggest a possible involvement of IKKε in the development of a CR state and justifies further studies addressing the potential of IKKε as a therapeutic target.

POS-1.5

Loss of PTEN decreases prostate cancer cell intrinsic type I interferon response

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Introduction: Prostate cancer (PCa) is the most commonly diagnosed cancer in Canadian men and is characterized by a dysregulated immune response, which is influenced by cancer cell-intrinsic genetic aberrations. Loss of the tumour suppressor gene phosphatase and tensin homolog (PTEN) occurs in 20–30% of PCa tumours. Our findings from PCa patient tumours demonstrate that loss of PTEN expression correlates with decreased Type I Interferon (IFN1) pathway marker pSTAT3, suggesting that PTEN has a role in regulating the immune response by impacting IFN1 signaling. This findings also indicate a potential role of PTEN in evolution of immunologically cold tumour microenvironment, in additional to imparting an aggressive disease phenotype.
Methods: To further characterize these associations, we assessed cell-intrinsic IFN1 responses using NanoString gene expression analysis and secreted cytokine profiling of PCa cells with variable PTEN expression and androgen receptor status. We observed distinct response patterns at baseline and following treatment with IFN1 agonists. We generated PTEN knockout derivatives of PCa cells and observed statistically significant differences in expression patterns of IFN1 pathway genes in PTEN-deficient cells during normal growth and following treatment with IFN1 agonists.
Results: Genes involved in innate immune signaling, antiviral responses, and most importantly immune evasion, were significantly decreased in PTEN-knockout cells. Additionally, PTEN-knockout cells had significantly decreased secreted levels of major inflammatory and chemotactic cytokines, including CXCL1 and CXCL10 compared to PTEN-intact PCa cells.
Conclusions: Given the significance of the cross-talk between cancer cells and surrounding immune cells in cancer progression, these findings are important in elucidating the specific contribution of cell-intrinsic pathways to the PCa tumour microenvironment. This investigation may lead to exploitation of PCa cell-intrinsic IFN1 pathways for rational design and use of immune-based therapies to improve management of PCa.

POS-1.6

Impact of autophagy in PARP inhibitor resistance in prostate cancer

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Introduction: Prostate cancer (PCa) is the most frequently diagnosed cancer in North American men. Over time, one in four patients develops a resistance against hormonotherapy and/or chemotherapy, making PCa difficult to treat. Recently, new therapies, such as PARP inhibitors (PARPis), have been tested in clinic for PCa. Several studies show that these compounds improve the life expectancy of patients. It is well-known that resistance to PARPis is partially mediated by autophagy in ovarian and breast cancer. To date, no studies have shown this possible link in PCa.
Methods: We have determined olaparib sensitivity in five different PCa cell lines, three AR-positive (LNCaP, 22Rv1, and LNCaP-C4-2b) and AR-negative (PC3 and DU145) by clonogenic assay. Levels of LC3II and p62, important autophagy factors, were measured in all cell lines after treatment with olaparib by western blot. To confirm our results, we established stable LC3 double tagged (mCherry-GFP) PCa cell lines and observed the dynamics of autophagic flux using confocal microscopy.
Results: Our results show that PC3 and DU145 are less sensitive to olaparib. These cell lines have a higher basal level of autophagy and a non-canonical autophagy, respectively, compared to AR-positive ones. We observed an induction of autophagy after olaparib treatment in PC3 cell lines. 22Rv1, LNCaP, and LNCaP-C4-2b have increasing sensitivity to olaparib. Interestingly, we observed an induction of autophagy in LNCaP-C4-2b after olaparib treatment as compared to the other AR-positive cell lines. We determined that the mTORC pathway is implicated in this induction of autophagy after olaparib treatment.
Conclusions: The autophagic flux seems to have a role in the development of resistance to PARPis. In fact, the autophagy level increases significantly after treatment induction. In the future, we intend to determine how this possible resistance is regulated. To do so, we will measure the role of AR in the sensitivity to PARPis. Understanding the role of autophagy in PCa progression may lead to strategies to inhibit this resistance mechanism. In the future, combinations of inhibitors of autophagy with agents such PARPis may increase the durability of response and further improve outcomes of patients with aggressive PCa.
Cell Imaging Core Facility of CRCHUM. Canadian Urological Oncology Group.

POS-1.7

Real-world Canadian experience with SpaceOAR™ hydrogel rectal spacer for prostate cancer radiotherapy

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Introduction: SpaceOAR™ is a new hydrogel product used in radiation oncology to displace the rectum away from the prostate to decrease radiation dose and toxicity to the rectum.

Methods: The Cross Cancer Institute is one of the first Canadian sites using the SpaceOAR™. From October 2017 to September 2018, 15 patients have had the SpaceOAR™ attempted either prior to commencing external beam radiotherapy or after having a prostate brachytherapy implant. Patients treated with external beam radiotherapy had a planning computed tomography (CT) prior to SpaceOAR™ insertion, with a repeat planning CT and fused magnetic resonance imaging (MRI) performed one week after the procedure. Patients treated with prostate brachytherapy had a postoperative dosimetric CT prior to SpaceOAR™ insertion and a repeat postoperative dosimetric CT with fused MRI performed one month after the procedure.

Results: Twelve patients have had SpaceOAR™ inserted prior to initiating external beam radiotherapy, with a mean thickness of 12.26 mm at midgland (range 0–18.90). In patients planned with standard fractionation radiotherapy (n=8), the V70Gy, V50 Gy, and V40 Gy were reduced from 23.3% to 10.7%, from 43.2% to 30.2%, and from 53.3% to 45.9%, respectively. In two patients treated with prostate brachytherapy, the RV100 was reduced from 2.0 cc to 0.7 cc. Two patients had unsuccessful attempts, one with SpaceOAR™ inserted into the rectal wall (without any subsequent complication) and another case aborted due to inability to place the SpaceOAR™ safely.

Conclusions: SpaceOAR™ is a safe product that requires training and expertise that can effectively reduce rectal dose for external beam radiotherapy or prostate brachytherapy patients.

POS-1.8

Impact of putative chemopreventative agents on prostate cancer diagnosis

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Introduction: Prostate cancer (PCa) is the most common non-cutaneous cancer in Canadian men and the third most common cause of cancer death in males, accounting for 10% of all male cancer deaths in Canada. Several observational and randomized studies have shown that use of commonly prescribed medications, including those used for the treatment of diabetes and hypercholesterolemia, is associated with improved survival in various malignancies, including PCa. There has not been any large population-based study examining the effects of these and other commonly prescribed medications, such as proton pump inhibitors (PPI), on the rate of PCa diagnosis over more than 20 years of followup.

Methods: We conducted a retrospective population-based study using data from the Institute of Clinical Evaluative Sciences (ICES), including all male patients aged 65 and above in Ontario who have had a negative first prostate biopsy between 1994 and 2016. We assessed the impact of commonly prescribed medications on PCa diagnosis. The analyzed medications included statins (hydrophilic and hydrophobic), most commonly used diabetes drugs (metformin, insulins, sulfonylureas, and thiazolidinediones), PPIs, 5-alpha reductase inhibitors, and alpha-blockers. Time-dependent Cox regression proportional hazards models

POS-1.8. Table 1. Multivariable analysis for (A) "Ever" vs. "Never; and (B) cumulative drug use to assess predictors of prostate cancer diagnosis

	A. "Ever" vs. "Never"		B. Cumulative drug use	
Variable	**HR (95% CI)**	**p**	**HR (95% CI)**	**p**
Age category 70–74 (reference 66–69)	1.069 (1.0041–1.1I39)	0.036	1.071 (1.0057–1.14)	0.032
Age category 75–79 (reference 66–69)	1.041 (0.96–1.12)	0.325	1.043 (0.962–1.13)	03
Age category 80–84 (reference 66–69)	1.2 (1.065–1.36)	0.002	1.208 (1.069–1.365)	0.0023
Age category 85-89 (reference 66–69	1.11 (0.89–1.39)	0.342	1.118 (0.892–1.4)	0.33
ADG score	1.0005 (0.997–1.002)	0.687	0.999 (0.997–1.002)	0.69
Rurality index	1.004 (1.0034–1.0064)	<0.001	1.005 (1.003–1.006)	<0.001
Index year	0.979 (0.973–0.985)	<0.001	0.978 (0.972–0.984)	<0.001
Glaucoma eye drops	0.96 (0.809–1.158)	0.72	0.989 (0.93–1.05)	0.723
5-ARI	0.92 (0.817–1.04)	0.2	0.995 (0.974–1.01)	0.65
Alpha-blockers	1.065 (0.979–1.15)	0.14	0.994 (0.98–1.008)	0.45
Hydrophobic statins	0.98 (0.896–1.07)	0.668	0.993 (0.982–1.005)	0.294
Hydrophilic statins	0.83 (0.731–0.94)	0.004	0.972 (0.95–0.99)	0.013
Insulin	0.6 (0.26–1.36)	0.22	1.012 (0.879–1.165)	0.861
Metformin	0.79 (0.644–0.968)	0.02	0.985 (0.958–1.01)	0.314
Sulphonylurea	1.24 (0.99–1.55)	0.06	1.024 (0.993–1.057)	0.12
Thiazolidinedions	0.67 (0.24–1.84)	0.44	0.867 (0.6625–1.13)	0.303
Pantoprazole	1.06 (0.91–1.23)	0.41	1.02 (0.996–1.057)	0.083
All other PPI	0.94 (0.858–1.047)	0.29	0.99 (0.97–1.01)	0.398
Chloroquine	1.19 (0.854–1.68)	0.29	1.05 (0.942–1.175)	0.366
Dipyridamole	1.16 (0.8–1.689)	0.4	1.016 (0.945–1.09)	0.658

ADG: Aggregated Diagnosis Group; ARI: alpha-reductase inhibitor; HR: hazard ratio; CI: confidence interval; PPI: proton pump inhibitor.

were performed to determine predictors of PCa diagnosis. Medication exposure was time-varying and modeled as "ever" vs. "never" use or as cumulative exposure.
Results: A total of 51 415 men were analyzed over a mean followup time of 8.06 years (standard deviation [SD] 5.44). Overall, 10 466 patients (20.4%) were diagnosed with PCa, 16 726 (32.5%) had died, and 1460 (2.8%) patients died of PCa. On multivariable analysis for PCa diagnosis, increasing age and rurality index were associated with a higher PCa diagnosis rate, while a more recent index year and use of hydrophilic statins were associated with a lower diagnosis rate in both "ever" vs. "never" and cumulative models (Table 1).
Conclusions: Hydrophilic statins are associated with a clinically and statistically significant lower PCa diagnosis. To our knowledge, this is the first study demonstrating a clear advantage of hydrophilic over hydrophobic statins in PCa prevention.

POS-1.10

Prostate biopsy trends and results over a 20-year period in a high-volume tertiary centre

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Introduction: Prostate biopsies (PBx) are the gold standard for the diagnosis of prostate cancer (PCa). Nevertheless, the usage and optimal timing of this procedure has evolved over time, especially with the introduction of prostate-specific antigen (PSA), magnetic resonance imaging (MRI), additional biomarkers, and genomic classifiers. We present the diagnosis and rate of positive biopsies over 20 years in a high-volume tertiary centre.
Methods: Our institutional database of PBx was queried and the indications and rate of positive PBx was analyzed over time. Only patients undergoing a first PBx with a PSA <10 ng/dl in our centre were included. Patients were stratified into four groups: Group 1, January 1998 to December 2002; Group 2, January 2003 to December 2007; Group 3, January 2008 to December 2012; Group 4, January 2013 to June 2018). Furthermore, in an attempt to discover the predictors of a positive PBx, a multivariable logistic regression model was performed.
Results: A total of 13 343 patients were analyzed, with a mean age of 62.7 years (standard deviation [SD] 8.34), a PSA of 5.38 ng/dl (SD 2.25), and prostate volume of 48.32 cc (SD 24.65). Table 1 shows changes in age, PSA, indications for PBx, PV, digital rectal examination (DRE), transrectal ultrasound (TRUS), clinically significant PCa (Gleason score >7), and percentage of positive PBx over the different periods of time. Less than 1% of the patients had an MRI (Canadian Health System does not cover MRI for primary PBx). In the multivariable model age (Beta 0.178; 95% confidence interval [CI] 0.10–0.012; p< 0.001), PSA (Beta 0.221; 95% CI 0.045–0.053; p< 0.001), suspicious DRE (Beta 0.036; 95% CI 0.021–0.056; p<0.001), PV (Beta -0.277; 95% CI -0.006–(-)0.005; p<0.001), suspicious TRUS (Beta 0.190; 95% CI 0.175–0.206; p<0.001), and time period (Beta 0.079; 95% CI 0.030–0.045; p<0.001) were all predictors of a positive PBx.
Conclusions: Rate of PCa diagnosis (and clinically significant PCa) in PBx has increased over time, reaching more than 60% in the most recent time period. Currently, more than half of the diagnoses correspond to Gleason >7. This could be driven by an increased usage of PSA, additional biomarkers and new imaging modalities.

POS-1.11

Digital rectal examination variability before prostate biopsy

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Introduction: Digital rectal examination (DRE) is used as part of the evaluation before a prostate biopsy (PBx). The utility of the DRE has been questioned in large series, but certainly experience plays a role in its utility.
Methods: We used our institutional database of PBx and analyzed the performance of the referral DRE (rDRE) compared to the DRE done at the moment of the biopsy (DREPBx) by a high-volume physician. Likewise, we compared the prediction of the transrectal ultrasound (TRUS) for the detection of clinically significant nodules.
Results: We included 19821 patients who had a transrectal PBx from 2005–2018 in our centre, with a mean (standard deviation [SD]) age of 64.02 (8.3) years, prostate-specific antigen (PSA) of 14.92 (287.13) ng/dl, and prostate volume of 49.75 (29.22) cc. Mean (SD) number of cores taken was 13 (3). Only 7.3% of the biopsies were done with magnetic resonance imaging guidance and 42.8% of the patients had at least one previous PBx. The most common PBx indication was elevated PSA (66.4%), followed by palpable nodule in 15.4% and active surveillance followup in 15.1%. From the referral note, 22.3% had a suspicious rDRE vs. 28.2% in the DREPBx. On the other hand, the TRUS reported a nodule in 44.9%. Finally, 53.3% of the PBx were positive for prostate cancer (PCa) (53.8% of these had Gleason >7). Table 1 shows the sensitivity and specificity of the rDRE, DREPBx, and TRUS. The concordance between rDRE and DREPBx was moderate (kappa 0.494).
Conclusions: DREPBx seems to outperform the rDRE. This suggests that experience has a significant impact and rDRE can be avoided if we already have an indication for PBx (i.e., elevated PSA). TRUS has a better sensitivity, but the specificity is lower that DRE.

POS-1.10. Table 1. Changes over time

	1998–2002 (n=4307)	2003–2007 (n=4693)	2008–2012 (n=4376)	2013–2018 (n=3373)	p
Age, mean (SD)	63.48 (8.38)	62.52 (8.34)	62.37 (8.34)	62.87 (8.33)	<0.001
PSA, mean (SD)	5.65 (2.37)	5.16 (2.24)	5.24 (2.17)	5.58 (2.18)	<0.001
Indication for PBx (PSA %)	65.8%	71.7%	74.5%	72.1%	<0.001
Prostate volume, mean (SD)	58.20 (29.30)	47.27 (24.23)	44.12 (20.84)	44.11 (20.69)	<0.001
Suspicious DRE (%)	48.6%	34.8%	26.9%	26.8%	<0.001
Suspicious TRUS (%)	51.0%	45.8%	46.2%	55.3%	<0.001
PCa diagnosis (%)	45.0%	47.5%	52.2%	62.7%	<0.001
Clinically significant PCa diagnosis (Gleason >7) (%)	67.4%	46.3%	61.8%	67.4%	<0.001

DRE: digital rectal exam; PBx: prostate biopsy; PCa: prostate cancer; PSA: prostate-specific antigen; SD: standard deviation; TRUS: transrectal ultrasound.

POS-1.11. Table 1. Sensitivities and specificities of rDRE, DREPBx, and TRUS

	Sensitivity	Specificity
rDRE	25.06%	80.88%
DREPBx	34.98%	79.47%
TRUS	55.6%	67.32%

DREPBx: digital rectal exam prostate biopsy; rDRE: referral digital rectal exam; TRUS: transrectal ultrasound.

POD-2.1

Clinical practice patterns of immediate intravesical chemotherapy following transurethral resection of bladder tumour in Canada

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Introduction: Current evidence supports the use of a single postoperative dose of intravesical chemotherapy following bladder tumour resection for non-muscle-invasive bladder cancer (NMIBC). However, several studies have demonstrated a wide variation in the use of postoperative intravesical chemotherapy in various health jurisdictions around the globe. Our goal was to assess current practice patterns among urologists in the Canadian healthcare system with regard to postoperative chemotherapy instillation.
Methods: Institutional review board approved our study. An electronic questionnaire was distributed to urologists across Canada via email in June 2018. An initial invitation to participate was followed by two reminder emails. Descriptive statistics were performed on the collected data.
Results: A total of 130 Canadian urologists completed our survey. The overall response rate was 17.6% and included urologists from all 10 Canadian provinces; 43.1% of respondents work in academic setting and 22.3% have received urologic oncology fellowship training. A majority (76.9%) of respondents perform from 2–10 transurethral resections of bladder tumour (TURBT)/month. The median years in practice was 10 years (interquartile range [IQR] 7.5–16.25).Eighty-one urologists (62.3%) send urine culture before TURBT. Forty-nine (37.9%) do not use intravesical chemotherapy post-TURBT or have rarely used it, and only four (3.1%) use it in for all resections. Mitomycin C is the primary agent for 60.0% of urologists, followed by epirubicin (19.2%). Common reasons to not administer intravesical chemotherapy included logistical barriers (65.3%), side effects (48.9%), lack of access to agent (22.4%), and a perceived limitation of clinical evidence (22.4%). Sixty-nine (53%) responders believe that less than 10% of their patients receive intravesical chemotherapy post-TURBT. Interestingly, if alternatives to mitomycin C were available with decreased toxicity, comparable efficacy, increased availability, and decreased cost, 102 (78.5%) urologists would consider such agents in their practice.
Conclusions: Immediate intravesical chemotherapy instillation following TURBT has been reasonably well-accepted across Canada. However, if guideline adherence is a measure of healthcare quality, much needs to be done to eliminate logistical barriers to treatment and to address safety concerns regarding intravesical therapy.

POD-2.2

Are most patients >75 years old eligible for neoadjuvant chemotherapy prior to radical cystectomy?

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Introduction: Neoadjuvant chemotherapy (NAC) has shown benefit in conjunction with radical cystectomy (RC) for urothelial carcinoma. Given higher comorbidities, current treatment options offered to older patients are frequently more conservative than for younger patients. In addition, older participants generally accounted for a minority of patients in initial trials that tested the efficacy of NAC, including the Grossman landmark trial.[1] Patients in this trial were considered eligible for NAC based on their hepatic, hematological, renal, and SWOG performance status. The median age of enrolment was 63 years, and 56% of total patients were below the age of 65. We aim to describe the comorbidities of patients >75 years old who underwent a RC and the proportion of those patients considered candidates for NAC in order to identify the strongest factor that negates chemotherapy eligibility.
Methods: In this retrospective cohort study, we used our institutional database to obtain patients >75 years old who underwent a RC and looked into their comorbidities and their eligibility for receiving NAC according to standard criteria. We also did a multivariate logistic regression model including the criteria for chemotherapy ineligibility, including Eastern Cooperative Oncology Group (ECOG) ≥2, chronic kidney disease (CKD; estimated glomerular filtration rate [eGFR] <60 ml/min], hearing loss, peripheral neuropathy, and severe heart failure (NYHA class III or higher), to identify the strongest predictor to be not considered as chemotherapy eligible.
Results: We found 242 patients who fit the above criteria. Median age at diagnosis was 77.9 years (standard deviation [SD] 4.6) and at RC was 79.9 years (SD 15.6); 77.3% of patients were male. The indication for surgery was mainly as a curative treatment of muscle-invasive urothelial carcinoma (58.3%), with 48.2% who had muscle-invasive disease since the first diagnosis and 45.8% who received some intravesical therapy (bacillus Calmette-Guérin or chemotherapy). Body mass index was 27.02 (SD 24.46) kg/m^2, 66.5% were current or former smokers (27.7% >30 pack/year), 21.7% had diabetes mellitus, 12.2% had a prior myocardial infarction (3.5% had NYHA III or higher), 10.4% had chronic obstructive pulmonary disease, and 23% had a history of a prior primary cancer. Of the total, 10.2% had an eGFR <60 ml/min, 7.8% had hearing loss, and 1.4% had peripheral neuropathy. Median Charlson score was 7 (interquartile range 6–8) and 94.4% had an ECOG 0–1. Considering the previous, 75.6% of the patients were considered chemotherapy-eligible. In the univariate analysis, CKD had the strongest correlation against chemo eligibility (-0.592; p<0.001), and in the multivariate logistic regression model, again the strongest predictor to be considered chemotherapy-ineligible was CKD (odds ratio [OR] 0.343; 95% confidence interval [CI] -0.425 to -0.315; p<0.001).
Conclusions: Most of the patients >75 years old who are candidates for a RC could be considered eligible for NAC. The most frequent factor that negatively affects chemotherapy eligibility is CKD. Age should not preclude the consideration for chemotherapy in these patients.

Reference:

1. Grossman HB, Natale RB, Tangen CM, et al. Neoadjuvant chemotherapy plus cystectomy compared with cystectomy alone for locally advanced bladder cancer. *N Engl J Med* 2003;349:859-66. https://doi.org/10.1056/NEJMoa022148

POD-2.4

Neoadjuvant chemotherapy prior to bladder-sparing chemoradiation for patients with muscle-invasive bladder cancer

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Introduction: Cisplatin-based neoadjuvant chemotherapy (NAC) prior to cystectomy improves survival in muscle-invasive bladder cancer (MIBC). NAC is rarely given before chemoradiation (CRT), as these patients are often cisplatin-ineligible. However, as younger, fitter, cisplatin-eligible patients opt for bladder preservation, NAC in this setting warrants re-evaluation.
Methods: From 2008–2017, 58 consecutive MIBC patients received NAC followed by CRT at Princess Margaret and Durham Regional Cancer

Centres. Gemcitabine cisplatin NAC was given for 2–4 cycles, followed by external beam radiation (EBRT, 60–66 Gy) over six weeks, with concurrent weekly cisplatin (CC) at 40 mg/m^2. Kaplan-Meier analysis was used for survival.
Results: Main reasons for CRT were pt preference (60%) and comorbidities (34%). At diagnosis, median age was 72 years (45–87), and most had Eastern Cooperative Oncology Group (ECOG) 0 (60%) or 1 (34%). Median CrCl was 58.7 ml/min and 24% had hydronephrosis. Patients had stage II (64%), III (21%), and IV disease with regional nodal metastases (10%). Histologies included pure transitional cell carcinoma (81%), squamous differentiation (16%), plasmacytoid (2%), and micropapillary (2%) variant. Most patients completed planned NAC (95%) and EBRT (98%); 40% completed CC. Seventy percent of residual tumour received maximal transurethral resection (TURBT). Median followup was 19.3 months. Median overall survival (OS) was not reached. Two-year OS and disease-specific survival (DSS) rates were 74.0% (95% confidence interval [CI] 57.7–84.9) and 88.3% (95% CI 78.5–98.1), respectively. Two-year bladder-intact disease-free survival (BIDFS) was 64.2%; 15.5% received salvage cystectomy, 15.5% of patients recurred distantly, and 6.9% died of metastatic disease. On multivariate analysis, OS was associated with stage and hydronephrosis, and BIDFS with stage and residual disease on cystoscopy.
Conclusions: NAC followed by CRT achieves encouraging OS and DSS compared to reported outcomes of contemporary cystectomy series. These results support this bladder-sparing approach in MIBC patients eligible for NAC.

POD-2.5

Robot-assisted radical cystectomy vs. open radical cystectomy: A meta-analysis of oncological-, perioperative-, and complication-related outcomes

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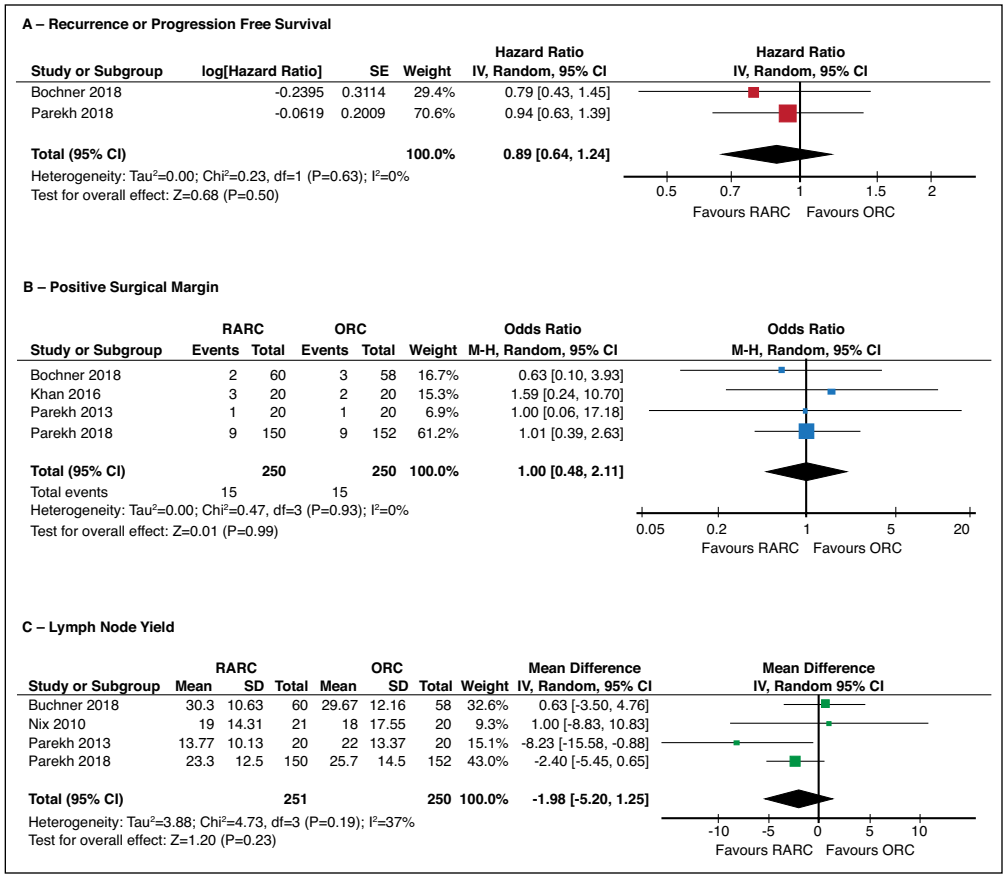
Introduction: Robotic-assisted radical cystectomy (RARC) has been increasingly adopted for the treatment of muscle-invasive bladder cancer. How outcomes from this approach compare to open radical cystectomy (ORC) is uncertain.
Methods: As of August 1, 2018, we performed a systematic review and meta-analysis of randomized controlled trials (RCTs) to compare outcomes of patients treated by RARC vs. ORC. The primary outcome was oncological recurrence/progression-free survival. Secondarily, we examined other surrogate oncological endpoints, perioperative outcomes, and complications. We used random-effects models for all meta-analyses due to clinical heterogeneity.
Results: We identified five unique RCTs involving 560 participants. We found no difference between RARC and ORC in oncological outcomes, including recurrence/progression-free survival (hazard ratio 0.89; 95% confidence interval [CI] 0.64–1.24) (Fig. 1A), surgical margin rates (odds



POD-2.5. Fig.1.

ratio 1.00; 95% CI 0.48–2.11) (Fig. 1B), or lymph node dissection yield (mean difference 1.98; 95% CI -5.2–1.25) (Fig. 1C). Analysis of patterns of recurrence considering local (pelvic) vs. distant/abdominal sites indicated a statistically significant differences in recurrence pattern between RARC and ORC (p=0.04). Lastly, we found advantages in estimated blood loss for RARC (difference 281 cc; 95% CI -435 to -125), but increased operative time (difference 75 minutes; 95% CI 26–123). No difference was identified in hospital length of stay (0.5 days; 95% CI -1.15–0.14) or complication rates (any grade: odds ratio [OR] 0.82; 95% 0.53–1.25; Clavien-Dindo grade ≥3: OR 1.08; 95% CI 0.69–1.67).
Conclusions: These data support the oncological safety of RARC, however, potential differences in recurrence patterns requires further study. Moving forward, further developing enhanced recovery after surgery (ERAS) programs and surgery with high-volume providers will improve outcomes for patients undergoing radical cystectomy. The relative contribution of robotic surgery is less certain.

POD-2.6

Heterogeneity of immune checkpoint inhibitor response in advanced malignancies according to patient sex: A systematic review and meta-analysis of overall survival data

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Introduction: There are known sex-related differences in immune response. A previous analysis suggested men derive greater benefit from immunotherapy than women for treatment of advanced solid organ malignancies. However, methodological concerns and subsequent trials placed these results in doubt. Thus, we performed an updated, comprehensive meta-analysis assessing the benefit of immunotherapy in oncology according to patient sex.
Methods: We performed a systematic review of PubMed, MEDLINE, Embase, and Scopus from inception to June 16, 2018 for randomized clinical trials assessing immune checkpoint inhibitors on overall survival (OS) in advanced cancers, compared to standard systemic therapy, with data stratified by patient sex. Data were abstracted according to PRISMA guidelines by a single reviewer with independent verification by two additional authors. Risk of bias was assessed using the Cochrane tool. Pooled hazard ratios (HR) and 95% confidence intervals (CI) were calculated among men and women using random-effects models, and heterogeneity was assessed between the two estimates using a test for interaction.
Results: Twenty eligible trials reporting on 8140 (66·8%) men and 4053 (33·2%) women were included. There was an OS benefit of immunotherapy for both men (HR 0.73; 95%CI 0.67–0.81) and women (HR 0.79; 95%CI 0.69–0·91), however, we found no significant difference when comparing this benefit between genders (p=0·35). Subgroup analyses according to disease site, line of therapy, class of immunotherapy, and study methodology recapitulated these findings. Subgroup analysis according to the proportion of women included suggested a trend towards a significantly larger benefit for male patients among studies with fewer women (pheterogeneity=0.06).
Conclusions: Stratified analyses demonstrated no significant effect of patient sex on the efficacy of immunotherapy in the treatment of advanced cancers using overall survival. Under-representation of subgroups may lead to erroneous results.

POS-2.1

Disparities associated with disease presentation and poor survival among Asian patients with upper tract urothelial carcinoma

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Introduction: Data on clinical characteristics, pattern of initial surgical treatment, and survival in Asian patients with upper tract urothelial carcinomas (UTUC) is limited. In most cancers, minority populations, such as African Americans and Hispanics, have shown poorer outcomes than Caucasians. To our knowledge, most epidemiological data on UTUC has mainly focused on African Americans and Caucasians, and thus neglected the Asian populations, which represent >5% of the U.S. population and are rapidly increasing. Our study aims to evaluate potential differences in disease stage at diagnosis, surgical management for localized disease, and survival outcomes for Asian patients with UTUC.
Methods: Patients diagnosed with UTUC from 1988–2014 were identified in the Surveillance, Epidemiology, and End Results (SEER) database. Demographic and socioeconomic variables, such as marital and insurance status, were analyzed. Multivariable logistic regression was used to assess predictors of metastatic disease at diagnosis. Fine and Gray competing risks analyses was used to identify predictors of cancer-specific mortality (CSM) and Cox proportional hazard models was performed to evaluate overall survival (OS).
Results: A total of 12 124 patients with UTUC were identified. Of these, there were 10 638 (87.7%) Caucasians, 793 (6.5%) Asian, 578 (4.8%) Black, and 115 (1%) patients of other races. A total of 1193 (9.8%) patients had metastasis at diagnosis and 10 539 (86.9%) had non-metastatic disease. The rate of Caucasian and Asian patients who presented with metastatic disease at diagnosis was 9.5% and 12.6%, respectively. Compared to Caucasian patients, Asians were 38% (odds ratio 1.38; 95% confidence interal [CI] 1.09–1.74) more likely to present with metastatic disease and were 27% more likely to die of UTUC (hazard ratio 1.27; 95% CI 1.10–1.45). There were no differences in surgical management or OS between Caucasians and Asians (Table 1).
Conclusions: Asian patients with UTUC are more likely to present with metastatic disease at diagnosis and have worse CSM compared to Caucasian patients. Further research should be conducted to evaluate the underlying reason for these findings in order to improve the outcomes for Asian patients with UTUC.

POS-2.2

Contemporary survival rates for muscle-invasive bladder cancer treated with definitive or non-definitive therapy in the pre-immunotherapy era

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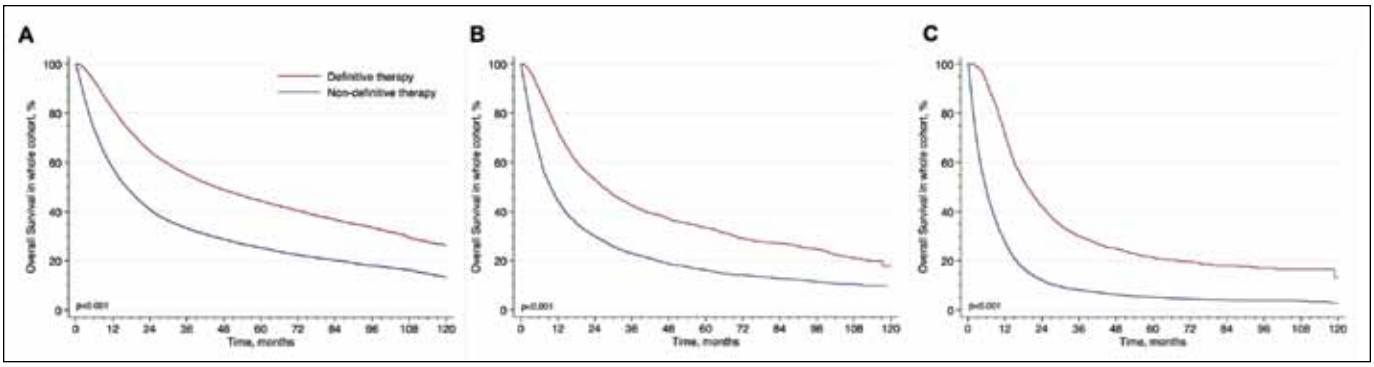
Introduction: Definitive, curatively intended therapy for muscle-invasive bladder cancer can be associated with significant morbidity and

POS-2.1. Table 1. Clinical characteristics of patients with UTUC

Characteristic	Total n (%)	Caucasian n (%)	Asian n (%)	Black n (%)	Unknown n (%)	p
Sample size	12 124	10 638 (87.74)	793 (4.77)	578 (4.77)	115 (0.95)	
Age at diagnosis, years						<0.0001
20–44	1450 (1.2)	114 (1.07)	14 (1.77)	14 (2.42)	3 (2.61)	
45–64	2570 (21.2)	2199 (20.67)	165 (20.81)	172 (29.73)	34 (29.57)	
>64	9409 (77.61)	8325 (78.26)	614 (77.73)	392 (67.82)	78 (67.83)	
Gender						<0.0001
Male	7192 (59.32)	6408 (60.24)	414 (52.21)	297 (51.38)	73 (63.48)	
Female	4932 (40.68)	4230 (39.76)	379 (47.79)	281 (48.62)	42 (36.52)	
Primary site						0.0003
Kidney and renal	7552 (62.29)	6619 (62.22)	459 (57.88)	390 (67.47)	84 (73.04)	
Pelvis	4572 (37.71)	4019 (37.78)	334 (42.12)	188 (32.53)	31 (26.96)	
Ureter						
Laterality						0.83
Left	6130 (50.56)	5363 (50.41)	410 (51.70)	296 (51.21)	61 (53.04)	
Right	5994 (49.44)	5275 (49.59)	383 (48.30)	282 (48.79)	54 (46.96)	
Grade						<0.0001
Well-differentiated	547 (4.51)	483 (5.54)	34 (4.29)	25 (4.33)	5 (4.35)	
Moderately differentiated	1635 (13.49)	1466 (13.78)	75 (9.46)	80 (13.84)	14 (12.17)	
Poorly differentiated	3136 (25.87)	2785 (26.18)	204 (25.73)	120 (20.76)	27 (23.48)	
Undifferentiated	4894 (40.37)	4249 (39.94)	375 (47.29)	223 (38.58)	47 (40.87)	
Unknown	1912 (15.77)	1655 (15.56)	105 (13.24)	130 (22.49)	22 (19.13)	
T stage						0.0106
1	4066 (33.54)	3606 (33.9)	243 (30.64)	178 (30.80)	39 (33.91)	
2	2002 (16.51)	1753 (16.48)	133 (16.77)	96 (16.61)	20 (17.39)	
3	4051 (33.41)	3547 (33.34)	179 (35.18)	181 (31.31)	44 (38.26)	
4	1141 (9.41)	992 (9.33)	86 (10.84)	58 (10.03)	5 (4.35)	
Unknown	864 (7.13)	740 (6.96)	53 (6.56)	65 (11.25)	7 (6.09)	
Metastasis at diagnosis						0.0023
No	10 539 (86.93)	9299 (87.41)	664 (83.73)	478 (82.70)	98 (85.22)	
Yes	1193 (9.84)	1009 (9.48)	100 (12.61)	71 (12.28)	13 (11.30)	
Unknown	392 (3.23)	330 (3.10)	29 (3.66)	29 (5.02)	4 (3.48)	
Surgery						
No surgery	1883 (15.53)	1611 (15.14)	126 (15.89)	134 (23.18)	12 (10.43)	<0.0001
Endoscopic	684 (5.64)	619 (5.82)	37 (4.67)	23 (3.98)	5 (4.35)	
Partial	1224 (10.10)	1056 (9.93)	106 (13.37)	49 (8.48)	13 (11.30)	
Radical	8254 (68.08)	7280 (68.43)	519 (65.45)	370 (64.01)	85 (73.91)	
Unknown	79 (0.65)	72 (0.68)	5 (0.35)	2 (0.35)	0 (0.0)	
Insurance status						<0.0001
Uninsured	108 (0.89)	91 (0.86)	10 (1.26)	4 (0.69)	3 (2.61)	
Insured	6365 (52.50)	5718 (53.75)	328 (41.36)	266 (46.02)	53 (46.09)	
Any Medicaid	708 (5.84)	492 (4.62)	146 (18.41)	58 (10.03)	12 (10.43)	
Insured, no specifics	1542 (12.72)	1320 (12.41)	111 (14.0)	88 (15.22)	23 (20.0)	
Unknown	3401 (28.05)	3017 (28.36)	198 (24.97)	162 (28.03)	24 (20.87)	
Marital status						<0.0001
Divorced/separated/ widowed/single	4501 (37.12)	3879 (36.46)	269 (33.92)	306 (40.87)	47 (40.87)	
Married/with partner	7072 (58.33)	6275 (58.99)	490 (61.79)	244 (42.21)	63 (54.78)	
Unknown	551 (4.54)	484 (4.55)	34 (4.29)	28 (4.84)	5 (4.35)	

UTUC: upper tract urothelial carcinoma.



POS-2.2. Fig.1.

adverse effects on quality of life, leaving patients reluctant to opt for these interventions.
Methods: To provide perspective, we examined stage-by-stage overall survival of definitive therapy (DT, either radical cystectomy in conjunction with neoadjuvant chemotherapy or trimodal therapy) vs. non-definitive therapy (nDT, including palliative transurethral resection, chemotherapy, and radiation treatment) among 42 144 patients within the National Cancer Database (2004–2012).
Results: Median overall survival stratified by receipt of DT vs. nDT was 45.3 vs.16.4 months, 26.7 vs. 9.6 months, and 21.2 vs. 7.5 months in AJCC stages II, III, and IV, respectively (Fig 1A, 1B, 1C, respectively, for each stage). In multivariable Cox regression analysis, DT conferred a significant survival benefit in all stages, most pronounced in AJCC stage IV (hazard ratio 0.46; 95% confidence interval CI 0.43–0.49; p<0.001).
Conclusions: Despite potentially significant morbidity and adverse effects on quality of life, DT is associated with a significant survival benefit.
Quoc-Dien Trinh is supported by an unrestricted educational grant from the Vattikuti Urology Institute, a Clay Hamlin Young Investigator Award from the Prostate Cancer Foundation, and a Genentech BioOncology Career Development Award from the Conquer Cancer Foundation of the American Society of Clinical Oncology.. David-Dan Nguyen is supported by a Herbert Brendler, MD Fund - AUA Summer Medical Student Fellowship Award.

POS-2.3

The association between patient body mass index and perioperative outcomes following radical cystectomy: An analysis using the American College of Surgeons National Surgical Quality Improvement Program

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Introduction: While radical cystectomy is currently the gold standard for the treatment of muscle-invasive bladder cancer, it is a highly morbid procedure, with 30-day perioperative complication rates approaching 50%. We aimed to determine the effect of patients' body mass index (BMI) on perioperative outcomes following radical cystectomy for bladder cancer.
Methods: We identified 3930 eligible patients who underwent radical cystectomy for non-metastatic bladder cancer using the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database. Patients with missing data on relevant covariates and those with disseminated disease were excluded. The primary exposure was preoperative BMI, categorically operationalized in four strata according to the World Health Organization criteria: <18.5 kg/m^2, 18.5–25 kg/m^2, 25–30 kg/m^2, and >30 kg/m^2. Our primary outcome was major perioperative complication comprising mortality, reoperation, cardiac event, or neurological event. Secondary outcomes included pulmonary and infectious complications, venous thromboembolism, bleeding requiring transfusion, and prolonged length of stay (>7 days).
Results: BMI was significantly associated with patient age, gender, comorbidity as assessed using American Society of Anesthesiologists (ASA) score, history of diabetes, history of chronic obstructive pulmonary disease (COPD), active smoking, functional status, and urinary diversion type (p<0.0001–0.007). BMI was significantly associated with rates of major complications: major complications were experienced by 17.0% of patients with BMI <18.5 kg/m^2, 7.8% of patients with BMI 18.5–25 kg/m^2, 7.9% of patients with BMI 25–30 kg/m^2, and 10.8% of patient with BMI >30 kg/m^2 (p=0.003, p-value for trend=0.06). Following multivariable adjustment for relevant patient demographics, comorbidities and treatment details, compared to patients with BMI 18.5–25 kg/m^2, patients with BMI <18.5 kg/m^2 (odds ratio [OR] 2.28; 95% confidence interval [CI] 1.07–4.78) and BMI >30 kg/m^2 (OR1.59; 95% CI 1.17–2.16) were significantly more likely to experience a major complication in the 30 days following cystectomy. Among the secondary outcomes, significant differences were identified in rates of pulmonary complications (p=0.003), infectious complications (p≤0.001), bleeding requiring transfusion (p=0.01), and prolonged length of stay (p=0.001). There was no difference in venous thromboembolism (p=0.37).
Conclusions: Patients who are outside of a normal BMI range are more likely to experience major complications, as well as pulmonary complications, infection, bleeding requiring transfusion, and prolonged length of stay. While this database has rich patient and comorbidity data, the strength of these conclusions is limited by sample size, selection bias inherent in observational data, and lack of specific oncological detail.

POS-2.4

The utility of the ACS NSQIP surgical risk calculator in patients undergoing radical cystectomy: Open and robotic techniques

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Introduction: Radical cystectomy (RC) is a major operation that carries significant risk for morbidity. The American College of Surgeons (ACS) has developed a preoperative risk calculator to assist surgeons in their preoperative clinical decision-making and patient counselling. The objective of this study was to assess the utility of the ACS risk calculator in patients undergoing open or robotic RC at our institution.
Methods: Preoperative variables were collected from a prospectively maintained dataset of patients undergoing RC (open or robotic) at our

institution from 2015–2017. These variables were entered into the online ACS risk calculator to generate predicted risks of complications within the first 30 days following RC. The predictive performance of the risk assessment tool was assessed using Wilcoxon rank sum tests and Brier scores.
Results: Of the 302 RC cases reviewed, 148 were open and 154 were robotic. Median age was 68 years (range 41–90 and 42–87 for the open and robotic cohorts, respectively). In the open cohort, 45 (30.2%) patients experienced a NSQIP-related complication compared with 40 (21.6%) in the robotic cohort. The overall 30-day complication rate was identical between the two surgical approaches at 57%. The most common complications were hospital readmission, urinary tract infection, and surgical site infection. Median length of stay was five days for both the open and robotic cohorts. The ACS calculator demonstrated poor predictive performance for early postoperative complications in both the open and robotic cohorts (area under the curve 0.55 for any complication).
Conclusions: Complication rates and length of stay appear similar between patients undergoing open or robotic RC at our institution. The ACS preoperative risk assessment tool does not appear useful in predicting early postoperative complications in patients undergoing either open or robotic RC at a high-volume centre.

POS-2.5

DNA damage repair gene mutations and associated tumour immune landscape as biomarkers of response to immunotherapy in muscle-invasive urothelial cancer

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Introduction: Molecular subtyping of urothelial cancer (UC) has significantly advanced the understanding of bladder tumour heterogeneity and development of prognostic and predictive biomarkers. Evolving evidence across cancers strongly suggests that tumour immunoediting has a profound impact on the behaviour of cancer cells and their adaptation to the co-evolving microenvironment and response to treatment. In alignment with this concept, recent immune checkpoint blockade (ICB) therapies in UC have demonstrated the predictive potential of mutations in the DNA damage repair (DDR). A comprehensive understanding of DDR mutation-associated expression of immune regulatory genes could thus aid in expansion of current immunotherapies and predictive biomarkers for the design of patient-tailored combination treatments.
Methods: We thus investigated the pre-treatment tumour transcriptomic profiles of the five recently described molecular subtypes of muscle-invasive urothelial cancer (MIUC; n=408) from the Genomic Data Commons, to determine subtype specific immune cell abundance, expression of 67 immune regulatory genes, and association with DDR gene mutation profiles.
Results: Analysis using CIBERSORT immune cell abundance determination tool showed significant differences in immune cell profiles and abundance between MIUC subtypes. Expression patterns of a selected panel of 67 genes, including both immune stimulatory and inhibitory genes, showed significant associations with subtypes and DDR mutation status.
Conclusions: Findings from our study provide compelling evidence for co-expression of multiple immune checkpoint genes, including PD-1, PD-L1, IDO1, TIGIT, TIM-3, TGFB1, LAG3, and others, that potentially contribute to compensatory immune evasion in bladder tumours. Our findings also emphasize on the urgent need for biomarker discovery approaches that combine molecular subtype, DDR gene mutation status, tumour immune landscape classification, and immune checkpoint gene expression to increase the number of patients responding to immunotherapies.

POS-2.6

Malignant Leydig cell tumour of the testis presenting as a hydrocele

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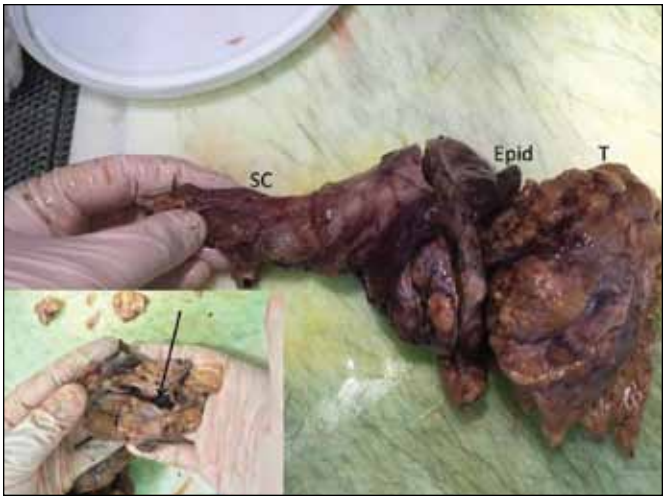
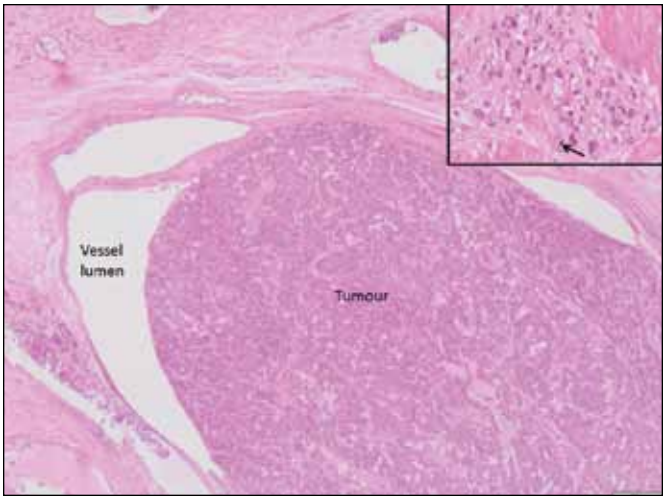
Introduction: Hydrocele of the scrotum is relatively common, but Leydig cell tumours (LCTs) are less common. The majority of LCTs are benign, but malignant cases are well-recognized. Some cases are identified incidentally, but they may present with testicular changes or with features of hormone imbalance, such as gynecomastia. Tumour presentation is either an incidental finding or gynecomastia, which is the result of hormonal imbalance.
Case report: An 80-year-old non-Caucasian, sexually active male presented to the urology clinic with a two-year history of right testicular swelling. Clinical examination was unremarkable apart from scrotal examination, which showed atrophy of the left testis and swelling of the right scrotum with positive trans-illumination test compatible with hydrocele. Ultrasound of the testes showed a large right hydrocele 28 mm in diameter. No focal abnormality of the right testicle or epididymis could be visualized and there was no varicocele. The patient was followed up with repeated outpatient ultrasound scans. Two years after the initial diagnosis of hydrocele, he complained of new discomfort within the right



POS-2.6. Fig. 1. Orchidectomy specimen.



POS-2.6. Fig. 2. Microscopic look at the tumour.

testicle. Preoperative tumour marker serology was negative (LDH, HCG, AFP). However, during elective hydrocele repair, a testicular tumour was identified involving the hydrocele cavity and right radical orchidectomy was performed.
The orchidectomy specimen (Fig. 1) included a disrupted, multinodular, friable tumour with a light tan cut surface. The tumour had replaced the entire testis and macroscopically involved the paratesticular tissue, hydrocele wall, and spermatic cord. On microscopic examination, there were typical morphological and immunohistochemical features of LCT. However, there were also widespread features associated with aggressive behaviour (Fig. 2). The pathological features were considered to be those of a malignant LCT.
Postoperative testosterone levels were normal; postoperative imaging revealed no evidence of metastatic disease and the patient remains well at one year followup, including serum testosterone and interval imaging.
Conclusions: Hydrocele is a common disorder that is usually benign and easily managed. However, some patients with significant pathology can present with a hydrocele. This is an unusual case of unexpected malignant LCT identified during hydrocele repair.

POS-2.7

Early experience with chemotherapy intensification for poor prognosis metastatic non-seminomatous germ cell cancer (mNSGCT) and unfavourable tumour marker decline (UTMD)

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Introduction: Despite results of the GETUG 13 randomized trial suggesting clinical benefit, chemotherapy intensification in men with poor prognosis metastatic non-seminomatous germ cell cancer (mNSGCT) and unfavourable tumour marker decline (UTMD) after one cycle of bleomycin, etoposide, and cisplatin (BEP) chemotherapy has not been widely adopted. We began offering the GETUG 13 approach to suitable patients and report our experience.
Methods: Men with poor prognosis mNSGCT defined by the International Germ Cell Consensus Classification (IGCCC) criteria treated at London Health Sciences Centre October 2013 to September 2017 were eligible. Patients were identified from a database with outcome data extracted retrospectively. Survival was calculated from the initiation of chemotherapy. Predicted time to normalization of tumour markers (TTN) was calculated from baseline and day 22 alpha-fetoprotein (AFP) and/or human chorionic gonadotropin (HCG) values as previously described (Fizazi 2004). Patients with a rise in tumour markers at day 22 or TTN greater than nine weeks for AFP or six weeks for HCG were classified as having UTMD and offered chemotherapy intensification starting at cycle 2. Based on GETUG 13, this consisted of paclitaxel (T)-BEP x 3 cycles plus etoposide, ifosfamide, and cisplatin (VIP) x 1 cycle, or T-BEP x 2 plus TIP x 1 plus VIP x 1 with prophylactic G-CSF and postoperative resection of residual masses (Fizazi 2014).
Results: Nine men with poor prognosis mNSGCT were identified, and seven were evaluable for tumour marker decline. Six had UTMD and received intensified chemotherapy. There were no toxic deaths. Five of these pts underwent post-chemotherapy retroperitoneal lymph node dissection (RPLND), with one patient also having right hepatic lobectomy and one patient having orchiectomy. Two had residual mature teratoma. One patient died of synchronously diagnosed metastatic adenocarcinoma ex teratoma. The other five patients are alive with no evidence of disease (NED) at median of 51 months (range 31–59). Long-term effects included one patient with grade 3 neuropathy and one unable to work due to neuropsychological dysfunction. Of three patients who received standard chemotherapy, two had post-chemotherapy surgery: RPLND plus right hepatic lobectomy, and RPLND plus orchiectomy. One of these patients has died of disease and the other two are NED at 38.6 and 38.8 months.
Conclusions: To date, our experience with intensified chemotherapy for men with poor prognosis mNSGCT and UTMD shows that it is feasible, safe, and appears to provide results similar to those reported in GETUG 13.

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POS-2.8

Oncocytic adrenocortical carcinoma – A rare tumour variant

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Introduction: Oncocytic adrenal neoplasms (OANs) are a unique subtype of adrenal masses that can be a diagnostic challenge. As they are difficult to distinguish preoperatively from traditional adrenocortical carcinomas yet present as large adrenal masses, surgical treatment is often necessary and histopathology is required for diagnosis. OANs typically present as large, non-functional benign masses discovered on incidental imaging.
Case report: We present a case of a 55-year-old female with an OAN, classified as a carcinoma using Lin-Weiss-Bisceglia criteria. Oncocytic adrenocortical carcinomas are quite rare, with 36 documented cases in the literature, and represent a distinct clinical entity from conventional adrenocortical carcinomas. Oncocytic adrenocortical carcinomas can carry a more favourable prognosis than conventional adrenocortical carcinomas, and should be considered in the workup of large, incidentally discovered adrenal masses (Figs. 1–4).

POS-2.9

Association between PD-L1 status and immune checkpoint inhibitor response in advanced malignancies according to patient sex: A systematic review and meta-analysis of overall survival data.

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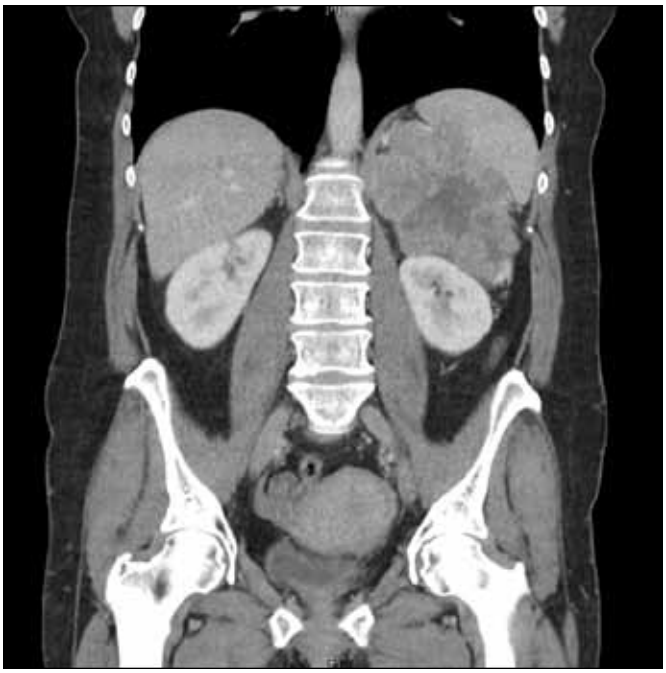
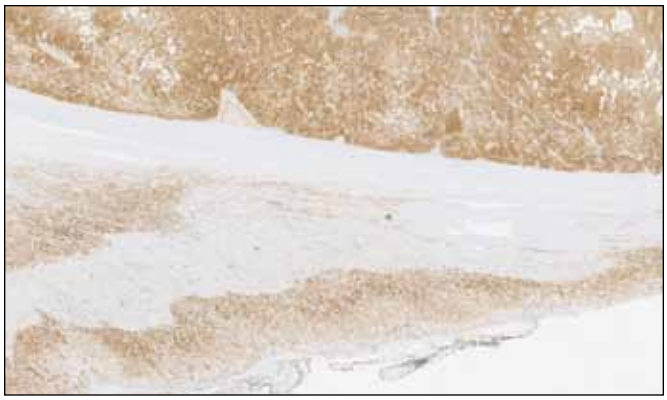
Introduction: Immune checkpoint inhibitors, including those targeting the programmed death ligand 1 (PD-L1) pathway, have emerged as standard of care for many advanced malignancies in the past few years. Owing to their mechanism of action, it has been postulated that PD-L1 expression may be predictive of response. However, data thus far are lacking. We performed a systematic review with stratified meta-analysis to assess the hypothesis that patients with high PD-L1 levels would experience a greater benefit from immunotherapy (IO), compared with standard of care systemic therapy, than patients with low PD-L1 levels.
Methods: We performed a systematic review as of June 16, 2018 for randomized clinical trials assessing immune checkpoint inhibitors on overall survival (OS) in advanced cancers, compared to standard systemic therapy, with data stratified by PD-L1 status. We used PD-L1 expression



POS-2.8. Fig. 1. Cervical staging CT displaying incidental adrenal mass.

levels as determined by the original investigators and operationalized these using cutoffs of 1%, 5%, 10%, and 50%. The primary analysis used a 1% threshold while the remainder formed secondary analyses. Pooled hazard ratios (HR) and 95% confidence intervals (CI) were calculated among patients with high and low PD-L1 levels using random-effects models, and heterogeneity was assessed between the two estimates using a test for interaction.

Results: Twenty eligible trials reporting on 12 193 patients were included. Ten studies reported stratified outcomes using a 1% threshold, three used a 5% threshold, four used a 10% threshold, and two used a 50% threshold. Using the 1% threshold, there was a significant OS benefit of IO therapy for patients with both low (HR 0.79; 95% CI 0.71–0.89) and high (HR 0.62; 95% CI 0.55–0.70) PD-L1 expression. There was a significant OS benefit of immunotherapy for patients in all strata, except patients with PD-L1 expression <5% (HR 0.79; 95% CI 0.56–1.11). Despite differences in PD-L1 assay, there was no significant heterogeneity in IO benefit within each strata we examined. In each analysis, patients with high PD-L1 expression had a greater benefit from IO therapy; using thresholds of 1%,



POS-2.8. Fig. 2. Calretinin (+) within lesion and adrenal cortex.

5%, and 10%, the test for subgroup differences was significant (p=0.003, 0.02, 0.007, respectively). Due to lack of power, subgroup differences were not significant using a 50% threshold (p=0.09).

Conclusions: Stratified meta-analysis demonstrates that PD-L1 levels have important predictive value in determining the response to IO therapy. However, patients with low PD-L1 levels still experience improved survival with IO compared to standard of care systemic therapy.

POD-3.1

Do elderly men (>75 years) harbour more aggressive prostate cancer? Comparison of Decipher and PAM50 tests among different age groups

Hanan Goldberg[1], Jaime Omar Herrera Cáceres[1], Maria Santiago-Jiminez[3], Nick Fishbane[3], Elai Davicioni[3], Zachary Klaassen[1], Thenappan Chandrasekar[1], Christopher J.D. Wallis[1], Dixon T.S. Woon[1], Robert J. Hamilton[1], Girish S. Kulkarni[1], Alejandro Berlin[2], Neil E. Fleshner[1]

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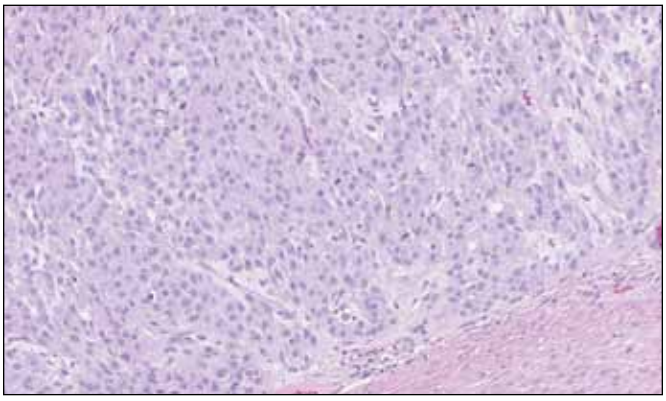
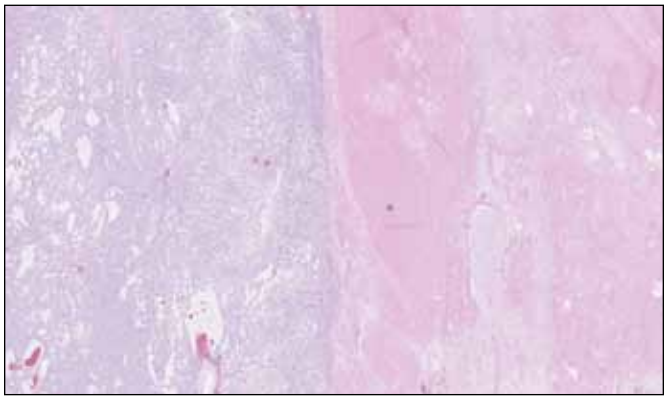
Introduction: Age is an important prognostic factor in decision-making in oncology. Over 20% of men diagnosed with prostate cancer (PCa) are ≥75 years old. In the growing elderly population, objective methods for predicting outcomes beyond chronological age are necessary in order to minimize the likelihood of withholding curative treatment when warranted. Herein, we describe and analyze age-related differences in clinical-genomic prognostic indices of aggressiveness in localized PCa.



POS-2.8. Fig. 3. Mitotically active lesion cells. Mitotic rate 20 per high-powered field with atypical mitoses.



POS-2.8. Fig. 4. Section of lesion with adjacent necrosis.

POD-3.1. Table 1. Clinical characteristics of prospective biopsy cohort by age group

Variables	<55 years	55–65 years	65–70 years	70–75 years	75–80 years	≥80 years
No. of patients (%)	560 (6.7)	2427 (29.0)	2001 (23.9)	1794 (21.5)	1032 (12.4)	541 (6.5)
PSA at diagnosis (ng/mL)						
<10	392 (70.0)	1693 (69.8)	1270 (63.5)	1180 (65.8)	590 (57.2)	237 (43.8)
10–20	40 (7.1)	245 (10.1)	263 (13.1)	244 (13.6)	159 (15.4)	113 (20.9)
>20	27 (4.8)	107 (4.4)	98 (4.9)	89 (5.0)	69 (6.7)	74 (13.7)
Unavailable	101 (18.0)	382 (15.7)	370 (18.5)	281 (15.7)	214 (20.7)	117 (21.6)
Gleason grade group (Bx)						
1	263 (47.0)	982 (40.5)	692 (34.6)	510 (28.4)	218 (21.1)	79 (14.6)
2	171 (30.5)	813 (33.5)	701 (35.0)	579 (32.3)	350 (33.9)	150 (27.7)
3	73 (13.0)	372 (15.3)	323 (16.1)	371 (20.7)	232 (22.5)	128 (23.7)
4	27 (4.8)	166 (6.8)	170 (8.5)	202 (11.3)	121 (11.7)	99 (18.3)
5	25 (4.5)	93 (3.8)	115 (5.7)	132 (7.4)	111 (10.8)	85 (15.7)
Unavailable	1 (0.2)	1 (0.0)				
Clinical stage						
T1	278 (49.6)	1213 (50.0)	1034 (51.7)	888 (49.5)	471 (45.6)	255 (47.1)
T2a	40 (7.1)	201 (8.3)	167 (8.3)	160 (8.9)	93 (9.0)	50 (9.2)
T2b/c	33 (5.9)	149 (6.1)	127 (6.3)	149 (8.3)	97 (9.4)	50 (9.2)
T3/4	7 (1.2)	27 (1.1)	17 (0.8)	26 (1.4)	12 (1.2)	3 (0.6)
Unavailable	202 (36.1)	837 (34.5)	656 (32.8)	571 (31.8)	359 (34.8)	183 (33.8)
Percent of positive Bx cores						
<50	368 (65.7)	1588 (65.4)	1297 (64.8)	1178 (65.7)	654 (63.4)	294 (54.3)
≥50	192 (34.3)	836 (34.4)	698 (34.9)	609 (33.9)	375 (36.3)	245 (45.3)
Unavailable		3 (0.1)	6 (0.3)	7 (0.4)	3 (0.3)	2 (0.4)
NCCN risk group						
Low	156 (27.9)	538 (22.2)	347 (17.3)	251 (14.0)	89 (8.6)	32 (5.9)
Int-fav	64 (11.4)	312 (12.9)	273 (13.6)	221 (12.3)	119 (11.5)	48 (8.9)
Int-unfav	81 (14.5)	430 (17.7)	411 (20.5)	404 (22.5)	218 (21.1)	119 (22.0)
High/very high	66 (11.8)	328 (13.5)	350 (17.5)	388 (21.6)	278 (26.9)	212 (39.2)
Unavailable	193 (34.5)	819 (33.7)	620 (31.0)	530 (29.5)	328 (31.8)	130 (24.0)
Decipher risk group						
Low	276 (49.3)	1123 (46.3)	826 (41.3)	671 (37.4)	345 (33.4)	149 (27.5)
Intermediate	131 (23.4)	598 (24.6)	523 (26.1)	455 (25.4)	243 (23.5)	112 (20.7)
High	153 (27.3)	706 (29.1)	652 (32.6)	668 (37.2)	444 (43.0)	280 (51.8)

Bx: biopsy; NCCN: National Comprehensive Cancer Network; PSA: prostate-specific antigen.

Methods: Clinical and genomic data for 8355 patients from the Decipher Genomic Resource Information Database (GRID; NCT02609269) was obtained. Conventional and genomic prognostic indices, including Decipher GC scores, PAM50 molecular subtypes (e.g., luminal A/B or basal) NCCN risk groups, and Gleason groups (GG), were stratified by age using multivariable logistic regression analyses (MLRA).
Results: Table 1 demonstrates the clinical characteristics and biopsy results of the cohort. With increasing decile of age, we observed a higher proportion of high GG and higher Decipher scores. There was a statistically significant increase in the proportion of patients with high Decipher scores with increasing age among GG1 and GG2 (<55: 10.2%, 30.7%; 55–60: 15.4%, 25.6%; 60–65: 15.9%, 29.7%; 65–70: 16.9%, 28.2%; 70–75: 17.9%, 30%; and >75: 20.3%, 37.3%, respectively). Furthermore, the prevalence of the PAM50 luminal B subtype (associated with worse prognosis) increased with age among GG1 and GG2 (<60: 22.2%, 40%; 60–65: 29.1%, 41.7%; 65–70: 28.2%, 39.2%; 70–75: 30%, 43.4%; 75–80: 33.5%, 44.3%; >80: 34.2%, 52%, respectively). Among higher-grade tumours (GG 3–5), no statistically significant differences between the different age groups were observed. MLRA demonstrated that in addition to higher T stage, prostate-specific antigen and GG, each age decile entailed a 20% increased risk for a high Decipher score (odds ratio 1.2; 95% confidence interval 1.11–1.3; p<0.001).
Conclusions: Older men with lower-grade tumours, as opposed to higher-grade tumours, harboured worse disease based on genomic risk models. The accepted paradigm of elderly PCa patients being treated conservatively based solely on chronological age needs to be changed. We provide evidence suggesting the utility of clinical-genomic characterization for better treatment-individualization decisions.

POD-3.2

Improving quality of prostate cancer surgery by providing feedback to surgeons: The Surgical Report card (SuRep) study

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Introduction: Prostate cancer is often cured by surgical removal of the prostate. Cancer Care Ontario has emphasized reducing positive surgical margins during radical prostatectomy (RP). Unfortunately, this well-intentioned initiative may encourage surgeons to perform more aggressive surgery, resulting in worse postoperative quality of life for patients. We believe that surgeons should strive to achieve optimal cancer control while maximizing postoperative quality of life. However, achieving this goal may be difficult without standardized performance assessment. In this Surgical Report card (SuRep) study, we aimed to closely monitor cancer, urinary, and sexual outcomes and provide surgeons with report cards assessing their performance

Methods: Prospective RP patients at the Ottawa Hospital were consented for participation in SuRep. All nine prostate cancer surgeons at the Ottawa Hospital also consented for participation. Surgery was performed using an open or robotic-assisted technique. Feasibility goals for the study were 95% patient enrollment, with 80% patient participation at six-month followup, and 70% patient participation at 12-month followup. At enrollment and followup, patients were assessed using validated questionnaires (EPIC and EQ-5D). Patients were defined as potent if they had no erectile dysfunction and continent if they had no incontinence. The patient data was analyzed and report cards were provided to surgeons every four months starting approximately one year after the first patient was enrolled.

Results: During the study period, 422 of 436 (97%) RP patients participated. Followup data was available for 358 (84.4%) patients at six months and 356 (86.4%) patients at 12 months following surgery. Overall case volumes per surgeon ranged from 14–116. Two-hundred and ten (50%) patients were included in the first year (pre-report card) and 212 (50%) patients were included in the second year (post-report card). Baseline patient and tumour characteristics were similar in the pre- and post-report card cohorts. Almost all patients were continent (404; 98%) and the majority of patients were potent (61%) prior to surgery. Nerve-sparing surgery increased from 148 (70%) pre-report card to 173 (82%) post-report card. Overall, there was a non-statistically significant increase in the proportion of patients with a positive surgical margin post-report card (64;32% pre-report card vs.80;39% post-report card; p=0.09). There was no difference in postoperative erectile function for patients with any form of nerve spare (19;24% pre-report card vs. 25;26% post report card; p=0.69) and a decrease in continence (124; 76% pre-report card vs. 110; 63.2% post report card; p=0.01).

Conclusions: Given the high enrollment and followup, a surgical report card program is feasible. With one year of feedback, overall patient outcomes did not improve. Specific initiatives and longer duration of feedback are needed for positive change to occur.

POD-3.3

Expression of ERBB family members demonstrates a potential to predict prostate cancer progression

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Introduction: Prostate cancer (PCa) is the most frequently diagnosed cancer in men and the third leading cause of cancer-related mortality among men in Canada. Because PCa patient management varies widely, there is a need for reliable biomarkers to identify patients with poor prognosis and to accurately stratify PCa for optimal treatment. Members of the ERBB family are involved in epithelium cancers and represent potential biomarkers for PCa. Our objective was to evaluate these proteins, separate or combined, and correlate their expression with patient clinical data.

Methods: Immunofluorescence was performed on tissue microarrays (TMAs) composed of radical prostatectomy specimens (285 patients). The TMAs included two cores of benign tissue and two cores of tumour from each patient. Quantification of biomarker expression was semi-automated using the VisiomorphDP software. Correlation with patient clinical outcome was determined using SPSS V25 and R V1.1.383 softwares.

Results: Within benign epithelial cells, Kaplan-Meier analysis showed significant association between high expression of EGFR or ERBB2 and an increased risk of developing a biochemical recurrence (BCR) (p=0.009 and p=0.022, respectively). Patients expressing high levels of both EGFR and ERBB2 had the worst prognosis (p=0.004). Based on a multivariate Cox regression model, these proteins were strong predictive biomarkers of BCR. Within tumour cores, Kaplan-Meier analysis showed significant association between low ERBB2 or ERBB3 expression and the development of bone metastasis (p=0.003 and p=0.036, respectively). The combined effect of low ERBB2 and ERBB3 expression in patients was also associated with bone metastasis development (p=0.002).

Conclusions: Our results show that the expression levels of ERBB family members may predict patient prognosis. Indeed, two different combinations of these proteins are associated with poor patient outcome when using BCR or bone metastasis development as an endpoint.

Molecular Pathology core facility of CRCHUM. Movember foundation.

POD-3.4

Personalized medicine tool to characterize treatment response in ex-vivo tumour-derived prostate cancer samples

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Introduction: Among the several therapeutic options available to treat castrate-resistant prostate cancer (CRPC), choosing the most suitable option for an individual patient remains a clinical challenge. For this, our group has developed a novel ex-vivo model based on patient-derived micro-dissected tissues (MDT) cultivated in microfluidic devicesto determine patient sensitivity profile in the presence of therapeutic agents.

Methods: MDTs (~400 µm in diameter) derived from prostate cancer cell line xenografts (DU145 and LnCaP) were exposed to docetaxel (10 nM for 12 hours) or enzalutamide (10 µM for 24 hours) and analyzed after a 12-hour recovery period or immediately after exposure time. Cell fate was measured using flow cytometry techniques (Annexin V for apoptotic cells and DRAQ7 for dead cells) and by a technique based on formalin fixed paraffin embedding of MDTs within a microfluidic device creating a high-density MDT-array (MDTA). Using MDTA we can monitor MDT viability (cleaved caspase-3), proliferation (Ki-67), and epithelial composition (CK 8/18) by immunohistochemistry (IHC) and immunofluorescence (IF). MDTs were also separately treated with TNF-α at a concentration of 10 ng/mL for 30 minutes and analyzed by MDTA.

Results: We show that the microfluidic device does not affect the viability (>85% by flow cytometry) or proliferative capacity (60% by IHC) of the MDTs during a culture period of 15 days in prostate cancer cell line xenograft models (n=3 for LNCaP, n=2 for DU145). Pharmacological responses to docetaxel showed 50% increase in caspase-3 activity by IF and 20% increase in cell death by flow cytometry compared to control MDTs. Enzalutamide response was dependent on the cells 2D hormone sensitivity profile. The nuclear translocation of p65 was also monitored in 80% of MDTs treated with TNF-α.

Conclusions: Within less than 5five days, we can obtain treatment response analysis using our ex-vivo drug response model, appropriate for clinical decision-making, The precise techniques developed within our lab allows the characterization of molecular responses of cancerous cells in the presence of various therapeutic agents while conserving the natural tumour microenvironment.

POD-3.5

After low-dose-rate brachytherapy monotherapy, biochemical progression-free survival is strongly influenced by the number of adverse prognostic features: An analysis of 4150 consecutive implants

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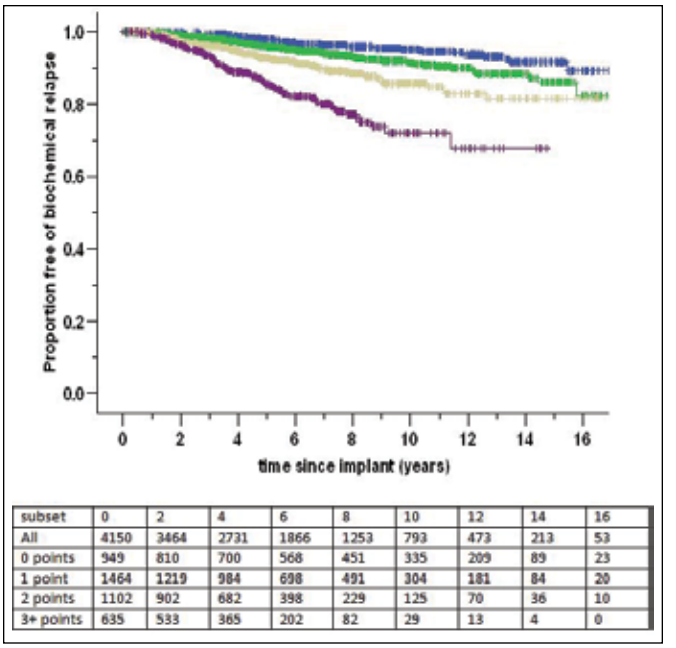
Introduction: A consecutive cohort of 4150 Iodine-125 low-dose-rate prostate brachytherapy (LDR-PB) monotherapy patients (i.e., no supplemental external irradiation) with implant dates from August 1998 to October 2013, was used to analyze the effect of prognostic variables on biochemical progression-free survival (b-PFS).

Methods: The cohort consists of 1365 NCCN low-risk (LR) and 2785 intermediate-risk (IR) patients. Six months of androgen-deprivation therapy (ADT) was given to 42%. The median followup was 5.4 years; 19% have been followed for at least 10 years. The nadir +2 ng/mL threshold was used to define b-PFS. Based on a multivariable Cox model, the cohort was split into prognostic substrata derived from points accumulated as follows: 1 point for pre-treatment prostate-specific antigen (iPSA) above the median value (7 ng/mL), 1 point for clinical T-stage (CS) of T2b-c, and 1 point for Gleason grade group (GG) 2/5 (3+4=7); 2 points were awarded for GG 3/5 (4+3=7). Of the 4150 men in the cohort, 949 (23%) had 0 points, 1465 (35%) had 1 point, 1100 (27%) had 2 points, and 635 (15%) had 3 or 4 points.

Results: In multivariable analysis, iPSA, CS, and GG were each highly significant predictors of b-PFS ($p<0.001$). The use of ADT improved b-PFS (hazard ratio [HR] 0.48; $p=0.005$), but the magnitude was small (~2% at five years). Rounded to the nearest whole number, the five- and 10-year Kaplan-Meier b-PFS estimates were 98% and 95%, respectively, for the substratum with 0 points, 95% and 91% for 1 point, 93% and 85% for 2 points, and 86% and 70% for 3+ points (Fig 1).

Conclusions: Along with a small contribution from ADT, the three principal prognostic variables (iPSA, CS, and GG) accounted for virtually all the variance seen in this dataset. Based on b-PFS for those with 3+ points, LDR-PB monotherapy significantly underperformed the LDR-PB boost arm of ASCENDE-RT,[1] despite the latter consisting of mainly (68%) NCCN high-risk patients. This implies that LDR-PB monotherapy may constitute undertreatment for IR patients with multiple adverse features.



subset	0	2	4	6	8	10	12	14	16
All	4150	3464	2731	1866	1253	793	473	213	53
0 points	949	810	700	568	451	335	209	89	23
1 point	1464	1219	984	698	491	304	181	84	20
2 points	1102	902	682	398	229	125	70	36	10
3+ points	635	533	365	202	82	29	13	4	0

POD-3.5. Fig. 1. Kaplan-Meier b-PFS estimates.

Reference:

1. Morris WJ, Tyldesley S, Rodda S, et al. Androgen suppression combined with elective nodal and dose-escalated radiation therapy (the ASCENDE-RT trial): An analysis of survival endpoints for a randomized trial comparing a low-dose-rate brachytherapy boost to a dose-escalated external beam boost for high- and intermediate-risk prostate cancer. *Int J Radiat Oncol Biol Phys* 2017;98:275-85. https://doi.org/10.1016/j.ijrobp.2016.11.026

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