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### Cancer care access in northwestern Ontario—a population-based study using administrative data

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**Background** Despite universal access to health care in Canada, disparities relating to social determinants of health contribute to discrepancies in cancer incidence and outcomes between rural and urban areas. Given that Canada has one of the highest-quality national population-based cancer registry systems in the world and little information is available about cancer statistics specific to northwestern Ontario, the purpose of this study was to estimate the percentage of cancer patients without documentation of a specialist consultation (medical or radiation oncology consultation) and to determine factors that affect access to specialist consultation in northwestern Ontario.
**Methods** This population-based retrospective study used administrative data obtained through the Ontario Cancer Data Linkage Project. For each index case, a timeline was constructed of all Ontario Health Insurance Plan billing codes and associated service dates, starting with the primary cancer diagnosis and ending with death. Specific factors affecting access to specialist consultation were assessed.
**Results** Within the 6-year study period (2010–2016), 2583 index cases were identified. Most ($n$=2007, 78%) received a specialist consultation. Factors associated with not receiving a specialist consultation included older age [$p$<0.0001; odds ratio (OR): 0.29; 95% confidence interval (CI): 0.19 to 0.44] and rural residence ($p$<0.0001; OR: 0.48; 95% CI: 0.48 to 0.72). Factors associated with receiving a specialist consultation included increased duration of disease ($p$<0.0001; OR: 1.32; 95% CI: 1.19 to 1.46), a diagnosis of breast cancer ($p$<0.0001; OR: 2.51; 95% CI: 1.43 to 4.42), and a diagnosis of lung cancer ($p$<0.0001; OR: 1.77; 95% CI: 1.38 to 2.26).
**Conclusions** This study is the first to look at care access in northwestern Ontario. The complexity and multidisciplinary nature of cancer care make the provision of appropriate care a challenge; a one-size-fits-all disease prevention and treatment strategy might not be appropriate.

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### Practice patterns of medical oncologists: a survey of advance care planning in the outpatient setting

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**Objective** Advance care planning (ACP) is an important part of cancer care. We determined the ACP practice patterns of medical oncologists at our tertiary academic cancer centre in Canada.
**Methods** Medical oncologists at our centre were invited to participate in a paper-based questionnaire in August 2019. Questions were validated by a local survey expert. Eleven multiple choice questions were included.
**Results** From among 23 eligible oncologists, 17 responses were obtained (74% response rate). Of respondents, 64% were male, and 76% had been in practice less than 16 years. Tumours commonly treated by respondents included breast (53%), lung (24%), gastrointestinal (24%), and genitourinary (24%) cancers.

Oncologists thought that components of ACP included designating a substitute decision-maker (100%), determining goals of care (100%), making decisions about cardiopulmonary resuscitation (94%), and determining disposition of property or finances (88%). They discuss ACP with patients having curable and incurable disease 6% and 93% of the time respectively. Although 88% of oncologists felt that it would be desirable to initiate ACP discussions in the first 3 visits, only 29% reported discussing ACP in the incurable setting during visits 1–3. Patient characteristics that prompt oncologists to discuss ACP in the first 3 visits in the curative and incurable settings include advanced age (23% and 59%), poor performance status (47% and 88%), and short prognosis (47% and 88%). Oncologists thought that the most appropriate time to discuss ACP in the curative setting was at the time the patient initiates the discussion (35%) and during visits 2–3 in the incurable setting (41%). The most common barriers to discussing ACP included insufficient time (71%), too much information for the patient (71%), and too emotionally difficult for the patient (41%).
**Conclusions** Although medical oncologists believe that discussing ACP with patients with cancer in the first few outpatient visits is important, such discussion seldom occurs because of several barriers. Resources facilitating ACP discussions should be developed.

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### Exploitation of treatment-induced tumour lysis to enhance sensitivity of ctDNA analysis: a first-in-human pilot study

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**Objective** Limitations in sensitivity remain a barrier to replacing tissue -based testing with testing for circulating tumour DNA (ctDNA). There is a paucity of data about the optimal time to measure ctDNA—specifically, the dynamics of ctDNA levels in the hours to days after the start of a new and effective treatment. We hypothesize that chemotherapy or radiation will yield an increased abundance of ctDNA in plasma by inducing tumour lysis, allowing for the detection of genetic alterations that were occult in baseline testing.
**Methods** Two prospective cohorts of 20 patients (pts) with stage III/IV non-small-cell lung cancer (NSCLC) were enrolled. Cohort 1 (C1) contained pts starting the 1st cycle of platinum doublet chemoradiation (C1a, $n$=10) or the 1st cycle of platinum doublet cytotoxic chemotherapy with or without immunotherapy (C1b, $n$=10). Cohort 2 (C2) contained pts receiving palliative radiation. Consenting pts provided 2 baseline samples. In C1, subsequent samples were collected 2–3, 4–6, 18–72, and 42–96 hours after initiation of chemotherapy. Pts in C2 had samples collected immediately before radiotherapy fractions 2, 3, and 4. Using the 36-gene amplicon-based next-generation sequencing InVisionFirst–Lung assay (Inivata, Research Triangle Park, NC, U.S.A.), samples were analyzed for ctDNA.
**Results** Complete results are available for the first 28 of 40 enrolled pts: C1a, 8 pts; C1b, 8 pts; C2, 12 pts. Detectable ctDNA was present at baseline in 21 pts (75%), 4 additional pts (14.3%) had detectable ctDNA in posttreatment samples (C1a, 2 pts; C1b, 1 pt; C2, 1 pt). Of the patients with detectable ctDNA at baseline, 3 (10.7%) had new genetic alterations detected in posttreatment samples. New genetic alterations were detected in the posttreatment samples from 7 of 28 pts (25%). Mutant molecule numbers increased with treatment in 19 of 25 pts with detectable ctDNA (76%): C1, 11 of 15 pts (73.3%); and C2, 8 of 10 pts (80%). Levels of ctDNA peaked a median of 2.2 hours after the initiation of chemotherapy [25%–75% interquartile range (IQR): 1.5–2.9 hours] and a median of 1 day (IQR: 1–2 days) after radiation commenced. The percentage increase in ctDNA was a median of 39.3% (IQR: –20.5% to 112.8%) in C1, with median increases of 22.0% and 39.3% in C1a and C1b respectively. The median increase in C2 was 81.9% (IQR: 0%–161.5%).
**Conclusions** In the hours to days after starting a new treatment, ctDNA increased. Testing for ctDNA in the acute posttreatment phase can yield results not evident in pretreatment testing. Application of this principle could improve the utility of ctDNA as an alternative to tissue-based testing or the sensitivity of the test for the detection of treatment-resistant clones, or both.

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## Current trends and clinical outcomes in patients with locally advanced muscle-invasive bladder cancer undergoing radical treatment in British Columbia, Canada

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**Objectives** This study compares current trends and clinical outcomes in patients with muscle-invasive bladder cancer (MIBC) receiving radical therapy, including neoadjuvant chemotherapy before radical cystectomy (NAC), radical cystectomy alone (RC), adjuvant chemotherapy after radical cystectomy (AC), radiotherapy (RT), and chemoradiotherapy (CRT). Another trend that was investigated was whether increasing the number of pelvic lymph nodes dissected (PLNDs) during cystectomy leads to improved outcomes for patients.
**Methods** We conducted a retrospective study of 290 patients with MIBC from Sep 2014 to Dec 2016. Median and 3-year overall survival (OS) and progression-free survival (PFS) were determined using the Kaplan–Meier method and Cox proportional hazards models.
**Results** The radical treatments received by patients in this study were: RC (35%), NAC (29%), AC (8%), CRT (7%), and RT (21%). Those percentages did not vary from year to year ($p$=0.808). When compared with RC alone, NAC, AC and CRT were associated with a significant increase in 3-year OS. Furthermore, compared with RC, all modalities (including NAC, AC, CRT, and RT) were associated with a significantly longer 3-year PFS (Table). In patients undergoing surgery, 37% had fewer than 9 PLNDs, 10% had 9–12, 23% had 13–20, and 30% had more than 20. The number of PLNDs was not associated with a significant difference in median OS ($p$=0.501). On multivariate analysis, intermediate- ($p$=0.013) and high-grade ($p$=0.014) histology, and lymphovascular invasion ($p$=0.014), were identified as predictors of worse median OS.
**Conclusions** This study provides real-world data in support of NAC in the treatment of MIBC; only 29% of eligible patients received NAC, consistent with the literature. Despite the improved outcomes associated with AC and CRT compared with RC, it remains unclear whether either option can be recommended as comparable standard of care. A greater number of PLNDs might not be associated with improved median OS.

**TABLE** Survival outcomes with each radical treatment modality

| Treatment and outcome | Median months (range) | 3-Year % (range) | HR (95% CI) | *p* Value |
|---|---|---|---|---|
| *Overall survival* | | | | |
| RC | 19.1 (15.3–24.0) | 28.4 (19.7–37.2) | Reference | — |
| NAC | NE (NE–NE) | 71.4 (61.8–81.1) | 0.26 (0.16 to 0.41) | ≤0.001 |
| AC | 38.5 (22.0–NE) | 58.3 (38.6–78.0) | 0.41 (0.21 to 0.79) | 0.008 |
| CRT | NE (23.9–NE) | 57.1 (36.0–78.3) | 0.44 (0.22 to 0.88) | 0.019 |
| RT | 19.1 (13.3–38.1) | 37.3 (25.0–49.6) | 0.86 (0.58 to 1.28) | 0.469 |
| *Progression-free survival* | | | | |
| RC | 9.5 (8.5–13.8) | 27.5 (18.9–36.0) | Reference | — |
| NAC | NE (NE–NE) | 67.9 (58.4–77.3) | 0.24 (0.15 to 0.37) | ≤0.001 |
| AC | 38.5 (15.3–NE) | 54.2 (35.2–73.2) | 0.38 (0.20 to 0.72) | 0.003 |
| CRT | NE (22.5–NE) | 57.1 (36.0–78.3) | 0.33 (0.17 to 0.67) | 0.002 |
| RT | 16.4 (11.6–30.1) | 33.9 (22.1–45.7) | 0.66 (0.44 to 0.97) | 0.034 |

HR = hazard ratio; CI = confidence interval; RC = radical cystectomy alone; NAC = neoadjuvant chemotherapy before radical cystectomy; AC = adjuvant chemotherapy after radical cystectomy; CRT = chemoradiotherapy; RT = radiotherapy.

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## Impact of value frameworks on the magnitude of clinical benefit: evaluating a decade of randomized trials for systemic therapy in solid malignancies

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**Objective** In the era of rapid development of new, expensive cancer therapies, value frameworks were developed to quantify clinical benefit. In this study, we assessed how the magnitude of clinical benefit has evolved since the 2015 introduction of the American Society of Clinical Oncology and the European Society for Medical Oncology value frameworks.
**Methods** Randomized phase II and III clinical trials assessing new cancer treatments for solid malignancies from Jan 2010 to Jul 2019 were evaluated. Study characteristics were recorded, and magnitude of clinical benefit (Δ) was calculated for the endpoints of overall survival (OS), progression-free survival (PFS), response rate (RR), and quality of life (QOL). Multivariable analyses compared ΔOS, ΔPFS, and ΔRR in the 2010–2014 period [pre–value frameworks (PRE)] with those in the 2015–2019 period [post–value frameworks (POST)].
**Results** Of the 290 studies analyzed [60 (21%) PRE and 230 (79%) POST], the most common primary endpoint was PFS (46%), followed by OS (20%), RR (16%), and QOL (8%), with no significant difference for PRE and POST. In the POST era, studies evaluating immunotherapy and treatment in the palliative setting increased significantly (Table). Studies reporting QOL improvement doubled POST, although that finding was not statistically significant. Median ΔOS was significantly greater POST ($n$=140 evaluable studies, 1.3 months vs. –0.2 months, Wilcoxon $p$=0.005), but no significant difference in median ΔPFS or ΔRR was observed. Multivariable analyses revealed significant improvement in ΔOS in the POST era ($p$=0.018) after adjusting for drug mechanism of action, line of therapy, disease setting, and primary endpoint.
**Conclusions** After the development of value frameworks, median OS improved very minimally. The introduction of immunotherapy likely contributed to that advance. No substantial improvements in other endpoints shown to affect value, such as QOL, were observed.

**TABLE** Analysis of study characteristics in relation to value frameworks

| Variable | Value frameworks era | | *p* Value |
|---|---|---|---|
| | Pre (2010–2014) | Post (2015–2019) | |
| Studies [$n$[a] (%[b])] | 60 (21) | 230 (79) | |
| Primary endpoint [$n$ (%[b])] | | | |
| Overall survival | 9 (15) | 50 (22) | 0.07[c] |
| Progression-free survival | 27 (45) | 107 (47) | |
| Response rate | 16 (27) | 28 (12) | |
| Quality of life | 2 (3) | 19 (8) | |
| Other | 6 (10) | 26 (11) | |
| Quality of life | | | |
| Not reported | 45 (75) | 159 (69) | 0.56[c] |
| No improvement | 12 (20) | 49 (21) | |
| Improved | 3 (5) | 22 (10) | |
| Experimental drug mechanism of action | | | |
| Cytotoxic therapy | 21 (35) | 68 (30) | |
| Targeted therapy or antibody | 36 (60) | 113 (49) | 0.0008[c] |
| Immunotherapy | 0 | 39 (17) | |
| Other | 3 (5) | 10 (4) | |
| Line of therapy | | | |
| 1 | 27 (45) | 118 (51) | 0.07[c] |
| 2 | 32 (53) | 93 (40) | |
| >2 | 1 (2) | 19 (8) | |
| Disease setting | | | |
| Curative | 35 (58) | 88 (38) | 0.005[d] |
| Palliative | 25 (42) | 142 (62) | |

[a] If a trial had more than 1 experimental arm, each experimental arm was counted as a separate study (28 trials has more than 1 experimental arm).
[b] Rounded up to the nearest whole number.
[c] Fisher exact test.
[d] Chi-square test.

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### Early-onset pancreatic ductal adenocarcinomas are characterized by a distinct mutational landscape

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**Objectives** The incidence of early-onset (≤55 years) pancreatic cancer (EOPC) is rising, but reports of treatment and survival outcomes in EOPC remain limited. We characterized the genomic and transcriptomic landscapes of EOPC, while also leveraging provincial health data to investigate survival outcomes in advanced EOPC in a separate dataset.

**Methods** We used RNA-seq data and matched clinical metadata to generate a comprehensive and integrative dataset for 402 patients with pancreatic ductal adenocarcinoma, encompassing both resectable (International Cancer Genome Consortium, The Cancer Genome Atlas) and advanced (Personalized OncoGenomics and COMPASS) disease. Patients were stratified into EOPC ($n$=96), average-onset pancreatic cancer [AOPC (≥70 years, $n$=121)], and intermediate-onset pancreatic cancer [IOPC (>55 to <70 years, $n$=185)] groups.

Survival analysis in a separate dataset was conducted using 578 patients who received systemic therapy between Jan 2012 and Dec 2015 in British Columbia.

**Results** *CDKN2A* single nucleotide variant (SNV)/indels were identified in 22% and 26% of patients with IOPC and AOPC respectively, and in only 7% of patients with EOPC ($p$<0.01). SNV/indels in epigenetic modifiers *KMT2C/D* trended toward lower frequency in EOPC (4% and 5% respectively) compared with IOPC (13% and 13%) and AOPC (13% and 13%), although those observations did not pass multiple-test correction ($p$=0.09, 0.20). Differential expression and gene-set enrichment analysis revealed EOPC-specific upregulation of genes in synaptic signal transduction pathways. In a separate analysis of provincial data, Kaplan–Meier survival analysis revealed that survival was similar in the EOPC, AOPC, and IOPC groups.

**Conclusions** Using an extensive pancreatic ductal adenocarcinoma (PDAC) sequencing dataset, we highlight a novel association between *CDKN2A* SNV/indel frequency and EOPC. Those data indicate potential age-specific differences in the mutational and developmental trajectories of PDAC and generate novel hypotheses for further study of EOPC.

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### Interaction of aging, comorbidities, and polypharmacy on cancer treatment

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**Objective** Evaluate the interaction between age, comorbidity, and polypharmacy on cancer treatment.

**Methods** Our retrospective cohort analysis included patients 18 years of age and older diagnosed with multiple myeloma; non-Hodgkin lymphoma; or breast, lung, colorectal, prostate, or ovarian cancer from 2004 to 2015. Stages were included where the standard of care included chemotherapy (CTx). Information collected included demographics, oncologic characteristics and treatment history, resource utilization band (RUB), and number of prescribed medications. The RUB is used to assess comorbidity severity. A descriptive analysis and multivariable logistic regression analysis were completed to determine impact of cancer variables on likelihood of receiving CTx.

**Results** 18,187 Patients were diagnosed within the 12-year period, 52% being male—29% colorectal cancer, 28% lung cancer, 13% prostate cancer, 12% breast cancer, 10% non-Hodgkin lymphoma, 5% multiple myeloma, and 4% ovarian cancer. Of those patients, 24% were less than 60 years of age, 26% were between 60 and 69, 26% were between 70 and 79, 19% were between 80 and 89, and 5% were 90 years or age or older. As age increased, proportionally fewer patients received all treatment modalities. In patients between 80 and 89 years of age, CTx or hormonal therapy (HT) was administered in 7% and 16% respectively, and of patients 90 years of age and older, 0.2% received CTx and 3%, HT. 44% of patients were prescribed 6 or more medications, of whom 36% received CTx; 63% of patients receiving fewer than 6 medications received CTx. Patients with high RUB scores were less likely to receive CTx. Multivariable analysis found an interaction of age and type of cancer, age and stage of cancer, and age and number of prescribed medications with the likelihood of receiving CTx or HT.

**Conclusions** Older age, polypharmacy, and high comorbidity decrease the chance of receiving HT or CTx. Chronologic age interacts with cancer type, stage, and polypharmacy, showing variance in relationships over the range of those variables. Consideration of age in systemic therapy decisions is complex.

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### The impact of early palliative care on the quality of life of patients with advanced pancreatic cancer: the IMPERATIVE study

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**Objectives** The primary objective is to use the Functional Assessment of Cancer Therapy–Hepatobiliary (FACIT.org, Elmhurst, IL, U.S.A.) to test for change in quality of life (QOL) between baseline (BL) and 16 weeks. Secondary objectives are to test for change between BL and 16 weeks in symptom control (Edmonton Symptom Assessment System–revised) and in depression and anxiety (Hospital Anxiety and Depression Scale and Patient Health Questionnaire-9).

**Methods** This ongoing prospective case crossover study is looking at the impact of an early palliative care (EPC) approach in patients with advanced pancreatic cancer (PANC). The EPC is provided by a palliative care physician and a clinical nurse specialist shortly after diagnosis with PANC. Symptom control, QOL, depression, and anxiety are assessed at BL before initial EPC assessment, and then every 4 weeks until week 16. A generalized linear model will test for statistically significant change in scores between BL and week 16; chemotherapy (yes/no) will be included as a confounding covariate, and model fit will be assessed. A sample size of 20 patients provides 80% power after controlling for covariate effects. To account for missing data, 40 patients will be enrolled. During 15 months, 31 patients have enrolled, and 27 have completed the 16-week intervention, with an overall enrolment rate of 72%.

**Significance** The benefit of EPC for patients with PANC is not known; however, EPC is increasingly recognized internationally by patients and stakeholders as a critical intervention that might improve both QOL and satisfaction with care. The report from the Canadian Partnership Against Cancer about the patient experience states that "the best possible patient experience means all people with cancer have equitable access to high-quality person-centered palliative care." This study offers access to EPC and provides an environment in which the benefit of an integrated approach is evaluated.

Preliminary results are expected to be available by the time of presentation, with full analysis to be completed by September 2020.

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### Eligibility for second-line therapy in patients with advanced hepatocellular carcinoma—a BC Cancer population-based study

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**Objective** Evidence supporting second-line therapies has become available for advanced hepatocellular carcinoma (AHCC), including regorafenib, cabozantinib, ramucirumab, and nivolumab. The optimal second-line treatment regimen is unknown, and real-world data about the eligibility of patients for second-line therapies in AHCC are limited. We aimed to characterize the real-world eligibility and use of second-line therapies after sorafenib.

**Methods** We identified all patients with AHCC who received 1 or more cycles of first-line sorafenib between 1 Jan 2014 and 31 Dec 2017 across 6 centres in British Columbia. All patients were required to be classified as Child–Pugh A for initiation of sorafenib. Baseline characteristics and clinical outcomes were reviewed. Eligibility for second-line therapy was determined using the RESORCE and CELESTIAL study entry criteria.

**Results** Of 144 patients with AHCC who received 1 or more cycles of first-line sorafenib, median age was 65.3 years (range: 32.2–83.4 years), and 85% were men. Median duration of sorafenib was 2.6 months, with 12 patients (8%) going on to receive second-line treatment.

37 Patients (26%) were deemed eligible for second-line systemic therapy. Primary reasons for ineligibility included an Eastern Cooperative Oncology Group performance status of 2 or greater (58%) and deterioration to Child–Pugh B status (28%). On Cox regression, improved survival was associated with better performance status and recurrent disease (Table).

Kaplan–Meier analysis demonstrated that eligibility for second-line treatment was associated with improved median overall survival from end of first-line treatment (8.5 months vs. 5.1 months, $p<0.01$).

**Conclusions** Only a minority of real-world patients with aHCC were eligible for second-line therapies based on second-line trial criteria. Given the high rate of attrition, improved first-line treatment options are urgently needed.

**TABLE** Cox regression results

| Variable | HR | 95% CI | *p* Value |
|---|---|---|---|
| Age | 0.51 | 0.97 to 1.01 | 0.51 |
| Baseline ECOG PS | 1.81 | 1.35 to 2.42 | < 0.01 |
| Number of metastatic sites | 1.11 | 0.88 to 1.40 | 0.39 |
| Child-Pugh score (B vs. A) | 1.83 | 0.88 to 3.80 | 0.11 |
| Recurrent disease (vs. *de novo*) | 0.42 | 0.27 to 0.64 | <0.01 |

HR = hazard ratio; CI = confidence interval; ECOG PS = Eastern Cooperative Oncology Group performance status.

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## Implementing changes to a residency program curriculum before competency-based medical education: a survey of Canadian medical oncology program directors

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**Background** Postgraduate medical education is undergoing a paradigm shift in many universities worldwide, transitioning from a time-based model to competency-based medical education (CBME). Residency programs might have to alter clinical rotations, educational curricula, assessment methods, and faculty involvement in preparation for CBME, a process not yet characterized in the literature. The main objective of this study was to gain an understanding of the changes made within Canadian medical oncology residency programs in preparation for implementation of CBME.

**Methods** We conducted a cross-sectional survey of Canadian medical oncology program directors. Questions addressed 5 themes: planned structural and curricular rotation changes, orientation of incoming residents and faculty to CBME, changes to learning resources for residents, changes to methods of teaching and assessment of trainees, and new educational roles for faculty members.

**Results** Before implementing CBME, all program directors had made changes to at least 1 clinical rotation, most commonly changing the malignant hematology rotation (74%) from a mixed inpatient and outpatient rotation to one that was entirely outpatient, and eliminating the radiation oncology rotation (64%). Introductory rotations were altered to focus on common tumour sites, while rotations closer to the end of training were changed to increase learner autonomy. Most program directors planned to enhance resident learning with the addition of electronic teaching modules (79%), inclusion of new training experiences (71%), and changing the academic half-day curriculum (50%). Most program directors (64%) planned to change assessment methods to be entirely based on entrustable professional activities and milestones. All programs had developed a competence committee to review learner progress and most (86%) had integrated academic coaches.

**Conclusions** Transitioning to CBME led to major structural and curricular changes within medical oncology training programs. Awareness of commonly implemented changes might help other programs who have yet to transition to CBME.

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## High-dose chemotherapy with autologous stem-cell transplantation for relapsed metastatic germ-cell tumours—the Alberta experience from 2001 to 2018

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**Objectives** High-dose chemotherapy with autologous stem-cell transplantation (HDC-ASCT) is a standard therapy for patients (pts) with metastatic germ-cell tumours (mGCTs) whose disease progresses on or after conventional-dose chemotherapy. We conducted a retrospective review of HDC-ASCT in pts with relapsed mGCT in Alberta over the past two decades.

**Methods** Pts with mGCTs who received HDC-ASCT at 2 provincial referral cancer centres in Alberta from 2001 to 2018 were identified. Baseline clinical and treatment characteristics were collected, as were overall survival (OS) and disease-free survival (DFS). Relevant prognostic variables were analyzed.

**Results** For the 43 pts identified, median age was 28 years (range: 19–56 years). Most (95%) had non-seminoma histology and a testis/retroperitoneal primary (84%). In 20 pts (47%) disease was poor-risk (per the International Germ Cell Consensus Classification) at the start of first-line chemotherapy. HDC-ASCT was used as second-line therapy in 65%, and 58% received tandem HDC-ASCT. Median follow-up from ASCT was 22 months (range: 2–181 months). At last follow-up, 42% of pts were alive without disease, including 3 of 7 pts (43%) with primary mediastinal disease. The 2-year and 5-year DFS and OS were 44% and 51%, and 41% and 43% respectively. Median OS and DFS for all pts were 27.9 months (10.2 months to not reached) and 9.3 months (4.2–124 months) respectively.

**Conclusions** We found that HDC-ASCT is an effective salvage therapy in mGCT, consistent with existing literature. Pts appeared to benefit regardless of primary site. Though limited by a small sample size, we found a numeric difference in DFS and OS between second- and third-line HDC-ASCT and single compared with tandem ASCT (Table).

**TABLE** Variables prognostic for disease-free survival (DFS)

| Variable | DFS [*n/N* (%)] | *p* Value | HR | 95% CI |
|---|---|---|---|---|
| *ASCT* | | | | |
| At second-line | 13/28 (46.4) | | 1.00 | |
| At third-line or later | 4/15 (26.7) | 0.06 | 2.15 | 0.97 to 4.76 |
| Single | 8/18 (44.4) | | 1.00 | |
| Tandem | 9/25 (36.0) | 0.62 | 0.82 | 0.37 to 1.83 |
| *Primary* | | | | |
| Mediastinal | 3/7 (42.9) | | 1.00 | |
| Testis/retroperitoneal | 14/36 (36.1) | 0.75 | 1.19 | 0.41 to 3.47 |

HR = hazard ratio; CI = confidence interval; ASCT = autologous stem-cell transplantation.

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## Impact of surveillance among patients with resected pancreatic cancer after adjuvant chemotherapy

Selina K. Wong, Lovedeep Gondara, Daniel J. Renouf, Howard Lim, Sharlene Gill

**Background** Pancreatic adenocarcinoma carries a poor prognosis and a high risk of recurrence even after surgery and adjuvant chemotherapy (aCTx). Guidelines recommend against routine surveillance imaging because of a lack of evidence supporting a survival benefit. With current first-line chemotherapy options, it is unclear whether surveillance allows for early detection of asymptomatic disease and therefore an opportunity to offer chemotherapy to fit patients. We describe the patterns of surveillance at a Canadian provincial cancer agency and determine whether routine imaging after aCTx is associated with receipt of palliative chemotherapy (pCTx).

**Methods** A retrospective review identified patients treated at BC Cancer centres between 1 Jan 2010 and 31 Dec 2016 who had undergone curative-intent resection and received at least 1 cycle of aCTx. Baseline characteristics, number of scans done after aCTx completion to recurrence, and pCTx were collected. Logistic regression analysis was performed.

**Results** Of 151 patients identified, those who recurred within 28 days after aCTx were excluded, leaving 142 patients, of whom 115 experienced recurrence. We defined 2 cohorts based on number of scans done between aCTx completion and recurrence: patients with 0–1 scans were "symptomatic" recurrences (22 patients, median age 68 years, 64% female, and 91% node-positive), and those with more than 1 scan were "surveillance" recurrences (93 patients, median age 64 years, 43% female, and 81% node-positive). Patients who underwent surveillance scans were more likely to receive pCTx at time of recurrence, though statistical significance was not reached (odds ratio: 2.11; 95% confidence interval: 0.75 to 6.58; $p=0.17$).

**Conclusions** Despite guidelines, most patients treated in British Columbia underwent surveillance imaging. Within the limits of our sample size, we demonstrated a trend toward increased likelihood of receipt of pCTx in patients who received surveillance scans. With efficacious pCTx options, studies to determine whether receipt of pCTx in asymptomatic recurrences translates into improved survival or quality of life, or both, are warranted.

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## Neoadjuvant systemic therapy utilization and outcomes in breast cancer

Marya Hussain,* Caleb Braun,† Alireza Sabouri,† Sunil Verma,‡[a] Omar F. Khan§

**Objective** This study identified changes in breast cancer (BCa) neoadjuvant therapy (NT) utilization trends and patient outcomes over time in Alberta.
**Methods** Patients with BCa treated with NT in Alberta during 2008–2016 were identified from electronic medical records. Provincial cancer registry data were used to determine NT utilization. Kaplan–Meier curves with log-rank tests were used to analyze recurrence-free survival (RFS) and overall survival (OS). Detailed analysis was performed on a subset of patients to identify rates and factors associated with pathologic response [complete response (pCR), partial response, or no response (pNR)].
**Results** 1866 Patients were identified, and 455 patients were included in the detailed subset. Utilization of NT steadily increased from 2008 to 2016 (Table I), most prominently in the HER2-positive subtype. Rates of response varied by receptor subtype (Table II). The RFS did not differ by receptor subtype after NT ($p$=0.096), but was significantly higher after pCR (Figure 1). Of patients with pNR after NT, those with hormone receptor–positive (HR+) disease had longer RFS than other groups ($p$=0.002). OS was similar in patients treated during 2008–2011 and in those treated in 2012 and later ($p$=0.20). OS was longer in HR+ BCa than in HER2-positive or triple-negative BCa ($p$<0.001).
**Conclusions** NT utilization is increasing in early-stage BCa, especially for HER2-positive disease. Our results confirm previously reported pCR rates with NT in a real-world setting. Based on our results, we plan to create a predictive model estimating the relationship of variables known before NT start with pathologic response. In future, such a model (supplemented with imaging or other data, such as circulating tumour DNA) could be used to evaluate a patient's candidacy for neoadjuvant chemotherapy.

**TABLE I** Proportion of patients with breast cancer receiving neoadjuvant therapy, by receptor subtype

| Year | Received neoadjuvant therapy (%) | | | |
|---|---|---|---|---|
| | HR-positive | HER2-positive[a] | Triple-negative | Overall |
| 2008 | 3.8 | 5.4 | 7.4 | 5.0 |
| 2009 | 4.3 | 1.3 | 5.5 | 4.8 |
| 2010 | 7.9 | 12.7 | 4.1 | 7.7 |
| 2011 | 8.6 | 14.2 | 6.8 | 8.5 |
| 2012 | 9.9 | 18.2 | 8.4 | 10.5 |
| 2013 | 11.1 | 17.7 | 8.7 | 11.6 |
| 2014 | 12.4 | 19.5 | 15.6 | 14.2 |
| 2015 | 12.2 | 14.5 | 13.0 | 13.5 |
| 2016 | 12.9 | 17.4 | 13.3 | 14.4 |

[a] HER2 testing was not reported routinely during 2008 and 2009, resulting in lower proportions of HER2-positive patients.
HR = hormone receptor.

**TABLE II** Proportion of 455 patients with breast cancer receiving neoadjuvant therapy who achieved no pathologic response (pNR) or a pathologic partial (pPR) or complete response (pCR) at time of surgery

| Receptor status | Response type (%) | | |
|---|---|---|---|
| | pNR | pPR | pCR |
| HR+ | 13.7 | 74.8 | 11.5 |
| HER2+ and HR+ | 3.7 | 58.5 | 37.8 |
| HER2+ and HR– | 5.9 | 35.3 | 58.8 |
| Triple-negative | 12.9 | 51.6 | 35.5 |

HR = hormone receptor.

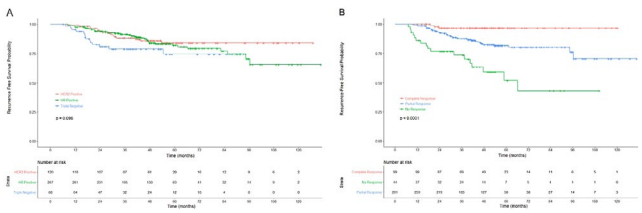


**FIGURE 1** Recurrence-free survival for patients with breast cancer by (A) receptor subtype and (B) pathologic response to neoadjuvant therapy.

[a] Dr. Verma's contribution to this project occurred entirely while he was a member of the Department of Oncology at the Tom Baker Cancer Centre. No contribution has occurred since he moved to AstraZeneca in August 2019.

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## The incidence of brain metastases among patients with HER2-positive or triple-negative metastatic breast cancer: a systematic review and meta-analysis

Markus Kuksis, William Tran, Christianne Hoey, Yizhuo Gao, Aman Dhaliwal, Kelvin Chan, Katarzyna Jerzak

**Objective** To evaluate the possible benefit of a brain metastases screening program for patients with metastatic breast cancer (mBCa), we conducted a meta-analysis to determine the incidence of brain metastases among patients with triple negative or HER2-positive (HER2+) mBCa who are at high risk of central nervous system disease involvement.
**Methods** Using MeSH terms related to breast cancer, brain metastasis, and incidence, research articles were extracted from the MEDLINE and EMBASE databases and the Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews. After removal of duplicates, abstracts of all 818 articles were screened by 2 reviewers, and full texts were examined by a 3rd reviewer. The cumulative incidence of brain metastases was extracted from studies for patients with HER2+, triple-negative, and undifferentiated mBCa; using a random effects model, a pooled estimate for incidence, with its 95% confidence interval, was calculated. Publication bias was assessed using the Egger test.
**Results** The incidence of brain metastases in patients with HER2+, triple-negative, and undifferentiated mBCa was reported in seventeen, five, and ten studies respectively. For the HER2+ subgroup, the pooled incidence of brain metastases was 0.29 (95% CI: 0.22 to 0.36), with a median follow-up that ranged from 5.8 months to 53.6 months. The incidence of brain metastases was 0.26 (95% CI: 0.16 to 0.36) for patients with triple-negative mBCa, with a median follow-up that ranged from 12.0 months to 48.1 months. In the studies that reported the incidence of mBCa without distinguishing subtype ("undifferentiated mBCa"), the pooled incidence of brain metastases was 0.15 (95% CI: 0.09 to 0.20), with a range in median follow-up of 12.0 months to 137.0 months. Publication bias was detected in the triple-negative ($p$=0.062) and undifferentiated mBCa ($p$=0.097) study subsets, but not the HER2+ study subset.
**Conclusions** There is a high cumulative incidence of brain metastases in patients with HER2+ and triple-negative mBCa; the utility of a brain metastasis screening program warrants investigation in this patient population.

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## Patient-reported outcomes in patients with colorectal cancer near end of life

Atul Batra,*† Colleen Cuthbert,‡ Rodrigo Rigo,*† Lin Yang,§ Devon Boyne,|| Andrew Harper,§ Winson Cheung*†

**Objective** Data concerning patient-reported outcomes near end of life (EOL) in patients with colorectal cancer (CRC) are limited. This study aimed to use the Edmonton Symptom Assessment System (ESAS) to assess the burden of symptoms near EOL in a real-world cohort.
**Methods** Patients with CRC who completed an ESAS questionnaire within 6 months of death from 2016 to 2019 in a large Canadian province were identified. The symptom scores were categorized as mild (0–3), moderate (4–6), and severe (7–10), and subsequently grouped into physical, psychological, and total scores. The severity of symptoms was further analyzed by logistic regression for any associations with age, sex, time to death (TTD), and primary tumour site (colon vs. rectum).

**Results** We identified 315 patients for the present analysis, of which 63% were men, and whose median age was 67 years. Overall, physical and psychological symptoms were severe in, respectively, 11% and 9% of patients with CRC (Table). Within the psychological domain, anxiety and depression were reported at similar frequencies. However, severe tiredness and loss of appetite were more common than other physical symptoms. There were no associations of symptom severity with age, sex, and primary tumour site. However, pain score was more likely to be rated severe in patients with rectal cancer than in those with colon cancer ($p$=0.02). In logistic regression, TTD was associated with the total ($p$=0.005) and physical ($p$=0.002) symptom scores, but not with the psychological score ($p$=0.14).
**Conclusions** In the real-world setting, unique symptom trajectories can emerge for patients with CRC near EOL. Intensifying the collection of patient-reported outcomes and increasing interval symptom monitoring might highlight at-risk patients who could benefit from targeted palliative interventions to improve quality of life.

**TABLE** Severity of symptoms in patients with colorectal cancer near end of life

| Domain | Responses [*n* (%)] | | |
|---|---|---|---|
| | Mild | Moderate | Severe |
| Physical | 137 (44) | 144 (46) | 34 (11) |
| Pain | 178 (57) | 82 (26) | 51 (16) |
| Tiredness | 97 (31) | 95 (30) | 123 (39) |
| Drowsiness | 156 (50) | 89 (29) | 66 (21) |
| Nausea | 255 (82) | 36 (12) | 20 (6) |
| Loss of appetite | 144 (46) | 79 (25) | 88 (28) |
| Shortness of breath | 205 (65) | 73 (23) | 36 (12) |
| Psychological | 223 (71) | 64 (20) | 28 (9) |
| Depression | 229 (73) | 54 (17) | 30 (10) |
| Anxiety | 215 (69) | 64 (20) | 34 (11) |
| Other | | | |
| Well-being | 120 (40) | 115 (38) | 64 (21) |
| TOTAL | 152 (48) | 137 (44) | 26 (8) |

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## Comparison of patient and physician attitudes regarding precision oncology

Navdeep Dehar,* Tasnima Abedin,† Patricia Tang,‡ Gwyn Bebb,‡ Winson Y. Cheung‡

**Objective** In the era of precision oncology, the number and frequency of biomarker tests that are offered to patients are increasing. To determine stakeholder understanding of the impact of those tests, we compared the expectations of patients and cancer physicians toward testing.
**Methods** Two separate, complementary, self-administered questionnaires for cancer patients and their physicians were collected in Calgary, Alberta. Survey responses from patients were subsequently matched with those of their corresponding oncologists to form patient–oncologist dyads. An analysis was performed to identify concordance rates between patients and their oncologists.
**Results** From Jul to Sep 2019, 113 patients and 12 physicians participated in the survey. Almost 80% of patients demonstrated good understanding of general cancer biology and diagnostic processes associated with precision oncology. A large proportion of patients (70%) were willing to undergo minor procedures and also to participate in research involving precision oncology testing. Approximately 65% reported the potential for biomarker testing to guide treatment. Those views from patients were largely shared by their oncologists (concordance of 64%). However, knowledge and expectations about the application of test results with respect to diagnosis and prognosis were grossly discrepant between patients and their oncologists (concordance of 26% and 36% respectively).
**Conclusions** Patients and cancer physicians do not consistently agree about the roles and applications of precision oncology testing, which could result in misplaced expectations. Strategies to improve education and communication are needed to align those expectations and to improve the quality of clinical decision-making.

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## Eligibility of real-world patients with stage II/III colorectal cancer in adjuvant chemotherapy trials

Atul Batra,*† Rodrigo Rigo,*† Shiying Kong,‡ Winson Cheung*†

**Objective** The results of adjuvant chemotherapy (ACTx) trials in stage II/III colorectal cancer (CRC) are often generalized to real-world patients. However, clinical trials have stringent inclusion and exclusion criteria, which can potentially lead to poor generalizability of results and slow accrual. This study was conducted to determine the proportion of real-world patients with stage II/III CRC who would be eligible for ACTx trials based on common eligibility criteria and to compare outcomes in trial-eligible and -ineligible patients.
**Methods** We identified all patients in the Alberta Cancer Registry diagnosed with stage II/III CRC during 2004–2015. Patients meeting any 1 of the following criteria were considered ineligible: age greater than 75 years, anemia, comorbid conditions (heart disease, uncontrolled diabetes, kidney disease, liver disease), and history of a prior malignancy or immunosuppression. Logistic regression was used to describe the likelihood of receiving ACTx, and Cox regression models were constructed to determine overall survival (OS).
**Results** Of 7841 patients with stage II/III CRC identified, 52% were men, and the median age at diagnosis was 71 years (25%–75% interquartile range: 61–79 years). Approximately 59% of patients were deemed trial-ineligible, and the most common reasons for ineligibility were advanced age (36%), renal dysfunction (27%), and cardiac disease (17%). In the real-world sample, 54% of eligible patients and 23% of ineligible patients received ACTx (odds ratio: 3.89; 95% confidence interval: 3.53 to 4.28; $p$<0.0001). The 5-year OS was significantly better in trial-ineligible patients who received ACTx than in those treated with surgery alone (Table).
**Conclusions** Most real-world patients with stage II/III CRC are unable to participate in ACTx trials because of strict exclusion criteria, but a fair proportion of those patients still derive some benefit from ACTx. The eligibility criteria for ACTx trials in CRC should be broadened to be more representative of real-world patients.

**TABLE** Survival of trial-eligible and -ineligible patients

| Group | 5-Year OS (%) | HR | 95% CI | *p* Value |
|---|---|---|---|---|
| Ineligible | | | | |
| Received aCTx | 56.3 | — | — | — |
| Did not receive aCTx | 74.4 | 0.48 | 0.42–0.54 | <0.001 |
| Eligible | 83.1 | 0.54 | 0.48–0.61 | <0.001 |

OS = overall survival; HR = hazard ratio; CI = confidence interval; aCTx = adjuvant chemotherapy.

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## Outcomes of neoadjuvant chemoradiation with or without surgery using the CROSS trial regimen and definitive chemoradiation with carboplatin and paclitaxel in esophageal and gastroesophageal junction cancer in Canada

Sidra Khalid,* Wilma Hopman,† Anna Tomiak,* Kiran Virik*

**Background** Trimodality therapy using the CROSS trial protocol is an accepted standard of care for locally advanced esophageal and gastroesophageal junction cancer. For medically inoperable patients (pts), chemoradiation (CRT) is standard. This single-institution review aimed to assess the real-world application of the CROSS trial protocol.
**Methods** A retrospective review of 83 pts who underwent CRT with carboplatin and paclitaxel with trimodality or upfront definitive intent was undertaken between Jun 2012 and Jun 2018. Pt demographics and clinical, pathologic, treatment, and surgical characteristics were assessed. Those factors and outcomes were analyzed in exploratory analyses.
**Results** Of the 83 pts, 65 received neoadjuvant CRT (nCRT); 40 had surgery. Another 18 received definitive CRT (dCRT). For the 83 pts, median age was 69 years (range: 48–82 years), and 80% were male; 77% had adenocarcinoma, median tumour length was 5 cm, and 80% were classified as Siewert I. The median RT dose was 50.4 Gy, median chemotherapy doses were 5, median time from diagnosis to CRT was 69 days, and median time from CRT to surgery was 62 days. Based on surgical eligibility for pts 75 years of age or older, 5 (23%) received nCRT, and 13 (72%) received dCRT. Of those pts, 49% and 33% respectively had no interruption to CRT. Pts who underwent surgery were younger ($p$=0.04) and weighed more ($p$=0.05). For the nCRT and surgery, nCRT only, and dCRT groups respectively, median overall survival was 35.5, 12.1, and 17.1 months (log-rank $p$=0.008) and progression-free survival was

32.2, 10, and 9.6 months (log-rank $p$=0.001). Further correlative outcomes data will be presented.

**Conclusions** Despite broadening of the CROSS trial eligibility criteria in our real-world data, survival benefit is maintained with trimodality therapy. The use of carboplatin and paclitaxel in dCRT has to be further evaluated.

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## Upfront neoadjuvant chemotherapy versus chemoradiation in high-risk locally advanced rectal cancer: a case for systemic control

Conley Kriegler,* Tahir Abbas,*† Vijayananda Kundapur*†

**Objective** Does stage III locally advanced rectal cancer (CRC) treated with upfront aggressive neoadjuvant chemotherapy followed by chemoradiation (TNT) have less incurable systemic failure than is seen with the standard of care: upfront chemoradiation (CRT)?

**Methods** Retrospectively examined recurrence rates in stage III CRC ($n$=24) treated with conventional CRT ("standard group") and stage III/IV CRC ($n$=14) treated with upfront aggressive chemotherapy ("high-risk group").

**Results** Systemic failure was less frequent in the high-risk group treated with TNT (28.6%) than in the standard group treated with CRT (33.3%), but not statistically significantly so (chi-square: 0.0928; $p$=0.7607; Table). Furthermore, unresectable systemic failure to organs excluding the liver was also less with TNT (14.3%) than with CRT (29.2%), although not significantly so (chi-square: 1.233; $p$=0.267).

**Conclusions** Findings in our study suggest that TNT would decrease systemic failure in this high-risk CRC group.

**Future Directions** The conclusion is based on a small group of patents. A larger risk-stratified randomized study could answer this question so that a treatment can be tailored to individual patients based on risk.

**TABLE** Outcomes in stage III colorectal cancer, by treatment group

| Treatment group | Pts ($n$) | N2 pts [$n$ (%)][a] | Remissions [$n$ (%)] | Systemic failures [$n$ (%)] | | Derived stage ($n$) |
|---|---|---|---|---|---|---|
| | | | | Overall | Excluding liver | |
| TNT | 14 | 7 (50) | 10 (71.4) | 4 (28.6) | 2 (14.3) | 0, IIIA; 1, IIIB; 2, IIIC; 0, IIINOS; 11, IVA |
| | | | | *Locations:* 2, liver; 0, lung only; 2, lung and liver; 0, peritoneum and omentum; 0, bone and distant lymph nodes | | |
| CRT | 24 | 21 (87.5) | 16 (66.7) | 8 (33.3) | 7 (29.2) | 1, IIIA; 8, IIIB; 8, IIIC; 7, IIINOS; 0, IVA |
| | | | | *Locations:* 1 liver; 2 lung; 2 lung and liver; 2 peritoneum and omentum; 1 bone and distant lymph nodes | | |

[a] Having 4 or fewer positive lymph nodes.

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## Sequence decision-making for cabazitaxel versus abiraterone or enzalutamide post docetaxel in a publicly funded health care system

Alexander S. Watson, Richard Gagnon, Eugene Batuyong, Nimira Alimohamed, Richard Lee-Ying

**Objective** Recent data suggest that earlier cabazitaxel chemotherapy might provide benefit in metastatic castrate-resistant prostate cancer (M1-CRPC) after docetaxel. Because our centre funds access to docetaxel, cabazitaxel, enzalutamide, and abiraterone in this setting, we sought to quantify the use of cabazitaxel at our institution and outcomes post docetaxel.

**Methods** We included all patients with M1-CRPC who received docetaxel at our tertiary referral centre from Oct 2012 (provincial cabazitaxel approval) to 31 Dec 2017. We assessed cabazitaxel eligibility per the TROPIC trial criteria, tracked therapies received, and documented objective and subjective reasoning for therapeutic decisions. Overall survival was measured using the Kaplan–Meier method, and the log-rank test was used to compare outcomes.

**Results** 158 Patients with M1-CRPC received docetaxel over the study period, including 37 (23.4%) for castrate-sensitive disease, and 151 patients progressed radiographically or biochemically, or both. The agent most commonly used immediately post docetaxel was enzalutamide ($n$=65, 41.1%), followed by abiraterone ($n$=48, 30.4%). At docetaxel progression, 50 patients (33.1%) were ineligible for cabazitaxel per the TROPIC trial criteria, most commonly because of docetaxel intolerance (<225 mg/m$^2$ received, 8.9%), performance status (8.6%), or neuropathy (5.3%). An additional 21 patients (13.9%) had clinical or patient factors that led to avoidance of cabazitaxel, and 39 (25.8%) lacked a documented consideration of cabazitaxel. 52 Patients (34.4%) received cabazitaxel, but only 15 (9.5%) immediately post docetaxel. The median overall survival in patients who received any cabazitaxel was 14.0 months (compared with 10.1 months), log-rank $p$=0.685.

**Discussion** Many patients who are potential cabazitaxel candidates might not be receiving it because of concerns about tolerability or clinical preference, particularly immediately post progression on docetaxel. Optimal M1-CRPC treatment sequencing remains unclear; however, given data pointing to improved outcomes with cabazitaxel, it is important to address barriers to its use. Ongoing data collection from additional centres will permit more robust statistical comparisons of outcomes.

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## Safety of cycles of chemotherapy with platinum–pemetrexed administered with neutrophils of 1.0 to 1.49 compared with 1.5 or greater

Sulaiman Al Saadi,* Tinghua Zhang,† Stephanie Brule,* Glen Goss,* Garth Nicholas,* M. Neil Reaume,* David Stewart,* Paul Wheatley-Price,* Scott Laurie*

**Background** The Canadian product monograph for pemetrexed states that treatment should be administered only once the absolute neutrophil count (ANC) is 1.5 or greater, but at our centre, patients are routinely treated provided ANC is 1.0 or greater.

**Objectives** To evaluate the risk of febrile neutropenia (FN) in patients who received platinum–pemetrexed chemotherapy with a pretreatment ANC less than 1.5 compared with 1.5 or greater.

**Methods** With institutional research ethics board approval, a retrospective chart review of the medical records of patients who received first-line platinum–pemetrexed between 1 Jan 2014 and 30 Jun 2018 was performed. Data collected included baseline demographics, rates of hospitalization and FN, and overall survival. Univariate and multivariate analyses to determine factors associated with FN and survival were performed.

**Results** Pretreatment ANC levels for all cycles were available for 459 of 466 patients identified. Baseline characteristics: median age 66; 50% women; 60% carboplatin, 40% cisplatin; 6% mesothelioma, 94% non-small-cell lung cancer. 74 Patients received at least 1 cycle with ANC 1.0–1.49. In 1656 cycles, 20 FN events occurred (1.21%; 95% confidence interval: 0.61% to 1.81%). There was no significant difference in FN between patients who received chemotherapy with pretreatment neutrophils less than 1.5 or with pretreatment neutrophils 1.5 or greater (0.97% vs. 1.22% respectively, $p$=0.92), and the difference remained nonsignificant in multivariate analysis controlling for platinum type and age ($p$=0.88). Median overall survival was 14 months for the whole cohort, but median overall survival was significantly higher in patients with pretreatment neutrophils less than 1.5 than 1.5 or greater (21 months vs. 12 months respectively, $p$=0.0066). This retrospective study did not find a significant difference in the risk of FN in patients who received platinum and pemetrexed with a pretreatment ANC less than 1.5 compared with 1.5 or greater.

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## Treatment patterns and outcomes of women with breast cancer brain metastasis: a single-centre retrospective study

Yizhuo Kelly Gao,* Markus Kuksis,† William Tran,‡ Katarzyna Jerzak*‡

**Objective** To assess the treatment patterns and outcomes of women with breast cancer (BCa) brain metastasis (BrM) in the modern era of stereotactic radiosurgery (SRS).

**Methods** We conducted a retrospective analysis of women with metastatic BCa (mBCa) who were treated with whole-brain radiotherapy (WBRT) or SRS to the brain at the Sunnybrook Odette Cancer Centre, Toronto, between 2008 and 2013. Eligible patients were identified using the hospital's MOSAIQ online system. Patients with a history of other malignancies and those with an uncertain date of diagnosis of BrM were excluded. Descriptive statistics were generated, and survival analyses were performed, with subgroup analyses by BCa subtype.

**Results** Of 683 eligible patients, 153 (22.4%) had triple-negative BCa (TNBC), 188 (27.5%) had HER2-positive (HER2+) BCa, 246 (36.0%) had hormone receptor–positive (HR+) HER2-negative (HER2–) BCa, and 61 (13.3%) had mBCa of unknown subtype. Most patients were treated with SRS ($n$=126, 18.4%) or WBRT ($n$=459, 67.2%) as first-line local therapy, with 57 (45.2%) and 71 (15.5%) respectively receiving radiation re-treatment. Compared with patients who were asymptomatic, those who presented with neurologic symptoms at the time of BrM diagnosis ($n$=529, 77.5%) were more likely to

require surgery (relative risk: 2.74; 95% CI: 1.13 to 6.67; $p$=0.0261). In total, 115 of 683 patients (16.8%) died at a median follow-up of 5.1 months. Patients with HER2+ BrM lived the longest (median overall survival: 8.1 months); those with TNBC and BrM had the shortest survival (median: 2.6 months). Age greater than 60 years, presence of neurologic symptoms at BrM diagnosis, TNBC or HR+ HER2– subtype (as opposed to HER2+), and first-line surgical treatment were independently prognostic for shorter overall survival.

**Discussion** Despite the use of SRS, outcomes for patients with BCa BrM remain poor—particularly for those who present with symptomatic disease. Strategies for early detection of BrM before the development of symptoms, might warrant further investigation.

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## Implementing at-home patient-reported outcomes to improve care for patients with gastrointestinal cancer

Sondra Chen,* Zhen Fan,* Colleen Fox,† Charmaine Lynden,* Alexandra Wills,* Charles Lim*

**Objective** To assess the feasibility of daily, online, at-home patient-reported outcome (PRO) completion and impacts on overall PRO completion at a community cancer centre.

**Methods** Retrospective kiosk submission data between 2018 and 2019 were reviewed to establish baseline comparisons. Patients gastrointestinal cancer starting chemoradiation were asked to submit daily at-home Edmonton Symptom Assessment System (ESAS) scores during and up to 4 weeks after treatment. As a standard of care, all patients receiving chemoradiation attend a weekly nurse practitioner–led symptom management clinic, where they submit kiosk ESAS scores. Home scores of 7/10 or greater triggered e-mail notifications to clinicians who provided follow-up care. Feasibility was defined as more than 80% of patients reporting more than 80% of the time. Baseline and posttreatment questionnaires assessed attitudes toward remote symptom management (RSM).

**Results** The median age for study patients ($n$=11) was 61 years. At baseline, 10 patients indicated that RSM is important, and 9 believed that RSM should be available throughout treatment. Mean at-home PRO submission rates were 39% on treatment and 22% post treatment, with 2 and 0 patients respectively reporting more than 80% of the time. Two patients were lost to follow-up. Three patients triggered 6 total notifications, with 34-minute median clinician response time. Post treatment ($n$=9), 7 patients reported satisfaction with daily reporting, and 5 said RSM improved their treatment.

For retrospective analysis, 88 eligible patients were included. Their mean in-person PRO completion rate was 71%. In the study cohort, the completion rate was 87%.

**Conclusions** There is interest in RSM, but feasibility targets for daily at-home PRO reporting were unmet. Providing this opportunity might improve in-person and overall PRO reporting. Strategies to improve adherence and to address barriers to at-home PRO reporting are needed.

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## Population-based *ROS1* testing in advanced non-small-cell lung cancer

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**Background** *ROS1* gene rearrangements are found in 1%–2% of all non-small-cell lung cancer (NSCLC). Reflex testing is recommended in all patients at diagnosis, but public funding is unavailable. This study models the most efficient *ROS1* diagnostic testing strategy to maximize detection of true positive (TP) cases, while minimizing costs and turnaround time (TAT).

**Methods** A decision model was developed for population-based *ROS1* diagnostic testing from a Canadian (Ontario) public health care system perspective. Eight diagnostic strategies examined the use of immunohistochemistry (IHC) and next-generation sequencing (NGS) compared with fluorescence *in situ* hybridization (FISH, the "gold standard") in a molecular or clinician-selected (never-smokers) setting, using blood- compared with tissue-based testing. Model inputs were obtained from existing literature and expert opinion. Direct testing costs and TAT were analyzed from the Ontario public perspective [University Health Network, Ontario Health (Cancer Care Ontario)].

**Results** Reflex testing with IHC and subsequent FISH confirmation identified a high proportion of TP cases within a relatively short TAT. Compared with upfront FISH, screening by IHC saves CA$233 per case and, among all testing strategies, captured the highest proportion of TP cases (88% vs. 92% for FISH). The most costly reflex strategy was NGS, with a greater proportion of missed TP and a long TAT. Clinician-initiated strategies had the longest time to result. One-way sensitivity analysis demonstrated that cost estimates are most sensitive to specificity of the IHC assay.

**Conclusions** *ROS1* IHC screening with FISH confirmation was the least costly strategy, but still allowed a high proportion of TP cases to be detected with the shortest TAT. Clinician-initiated testing significantly lengthened TAT, and selecting for never-smokers missed a large proportion of TP cases in which patients would benefit from targeted therapy.

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## Real-world utilization and safety of ipilimumab plus nivolumab in patients with metastatic renal cell carcinoma: results from the Canadian Kidney Cancer Information System

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**Objective** To determine the amount and tolerability of ipilimumab plus nivolumab (I+N), including discontinuation rates, reasons for discontinuation, and outcomes for patients with treatment-naïve metastatic renal cell carcinoma (MRCC) in the Canadian Kidney Cancer Information System (CKCis) database.

**Methods** Patients in CKCis who received first-line I+N were included. The number of doses of I+N, number of patients who received maintenance single-agent nivolumab, and duration of maintenance nivolumab were identified. Reasons for treatment discontinuation, including details of toxicities, were determined. Efficacy outcomes included overall response rate (ORR), time to treatment failure (TTF), progression-free survival (PFS), and overall survival (OS).

**Results** The cohort included 196 patients; 12% on a clinical trial. Median follow-up was 10.4 months. Median age was 63 years; 71% had clear-cell histology; International Metastatic RCC Database Consortium good 13%, intermediate 54%, and poor risk 33%. All 4 I+N doses were received by 91 patients (46%), of whom, 76 (84%) received maintenance nivolumab. Fewer than 4 doses of I+N were received by 105 patients (54%), of whom, 38 (36%) received maintenance nivolumab. 76 Patients (39%) are still on treatment. Median time on maintenance nivolumab was 4.6 months. Of 67 toxicity events, the most common were colitis (49%), pneumonitis (19%), and hepatitis (10%), with no toxicity-related deaths. Therapy was discontinued in 21% of patients because of toxicity. The ORR was 34% (4.3% complete responses). Median TTF was 4.1 months; PFS was 11.4 months. Median OS was not reached (41 events to date). Second-line treatment was received by 34% of patients, sunitinib being the most common agent.

**Conclusions** In this real-world cohort, most patients with MRCC did not receive all 4 doses of I+N, contrasting with clinical trial reporting; and yet many still received maintenance nivolumab. In 21% of patients, treatment was discontinued because of toxicity. Further data will be presented, including outcomes stratified by the number of cycles of I+N received.

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## Immune-related adverse events in the emergency department: analysis of frequencies and management at Kingston General Hospital

Ryan Holstead, Baskoro Kartolo, Tara Baetz

**Objectives** Immune-related adverse events (irAEs) are known complications of immune checkpoint inhibitors (ICIs) with significant variation of presenting symptoms. Early identification and management lead to improved morbidity and mortality. Research on the identification and management of irAEs in the emergency department (ED) is limited.

**Methods** We performed a single-centre retrospective chart review of all patients (pts) treated with ICIs in 2018. Pts were stratified by site of primary malignancy, and all diagnoses of irAEs were recorded. For all pts who

presented to the ED within 3 months of receiving an ICI, we assessed whether the presenting symptoms were eventually diagnosed as an irAE. We assessed disposition, time to initiation of corticosteroids, and outcomes in those pts.
**Results** In 2018, 174 pts were treated with an ICI, most for melanoma (32.2%) and lung cancer (48.8%). An irAE of any grade was diagnosed in 47 pts (27%). In 2018, 59 pts (33.9%) had at least 1 presentation to the ED, 9 of whom presented with symptoms attributable to a new irAE, including pneumonitis ($n$=2), arthritis ($n$=2), hypophysitis ($n$=3), colitis ($n$=1), and adrenalitis ($n$=1). Those pts had received ICI therapy for a range of 1–20 months before presentation and 6 of the 9 (66.7%) had grade 3 or greater toxicity. Of those 6 pts, 4 were admitted at that encounter, and 2 were admitted within 48 hours because of related symptoms. All 9 pts eventually received oral corticosteroids, and only 2 received further ICI therapy. For the 4 directly admitted patients, an order for a corticosteroid was placed 4–43 hours (mean: 21.2 hours) after ED triage.
**Conclusions** We found that, for a notable proportion of irAEs at our centre, pts first present at the ED. A standardized approach at the time of presentation might lead to improved identification and management of those patients.

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### An opportunistic Nordic pole-walking group intervention for cancer patients residing temporarily in Kelowna for multi-week radiotherapy: a pilot project

Kirsten Allen,* Sarah Lucas,† Sheri Simson,‡ Barb Mangold,‡ Madison Huggins,* Susan Ellard§

**Objective** To provide information to out-of-town patients with cancer about the value of physical activity (PA) and to offer an engaging, safe, inexpensive, accessible, and sustainable group activity that they can engage in during multi-week radiotherapy.
**Methods** Out-of-town patients who must reside temporarily in Kelowna for multi-week radiation are eligible if they are capable of walking comfortably and are able to understand the English language. Patients complete 3 questionnaires about PA activities before, immediately after, and 6–9 months after radiation. They are also given information in support of regular PA generally and during cancer treatment. Patients optionally can participate in a group Nordic pole-walking (NPW) clinic offered twice weekly in Kelowna. Participants receive 30 minutes of instruction on the methods and benefits of NPW and can both walk with the group and sign out poles to use between group sessions.
**Results and Conclusions** From Sep 2019 through Jan 2020, 53 patients were referred. 10 Patients are pending starting treatment and 20 patients have consented to participate. Average patient age is 70 years (range: 56–81 years). Most frequent cancer types are breast, lung, and prostate.

Of the referred patients, 57% attended 3 or more group walks; 29%, 1–2 group walks; and 14%, no group walks. Outside organized groups, 65% reported using poles.

Feedback has been positive. On a 1–5 scale, 50% reported high enjoyment (score: 5), 22% (score: 4), 7% (score: 3), and 21% gave no response or "not applicable." Some patients have reported improved mental health, self-image, and relaxation, or relief of treatment-related symptoms including nausea and arm weakness. None felt that NPW worsened their cancer or treatment symptoms.

Participation rates are encouraging despite the program launching in fall and winter. For many, NPW is feasible, beneficial, and engaging during radiation therapy in a variety of cancer types and situations. Longer-term follow-up using questionnaires will compare PA minutes per week against baseline to determine if reported short-term increases in PA are sustained.

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### A real-world comparison of cisplatin versus cetuximab used concurrently with radiation in the treatment of locally advanced oropharyngeal carcinoma: updated results

Andrea S. Fung,* Arfan Afzal,† Robyn Banerjee,‡§ Brock Debenham,‖ Desiree Hao‡§

**Objective** In clinical practice, patients might be ineligible for cisplatin because of age, performance status, or comorbidities, and real-world evidence is needed to help guide treatment of such patients, who are not well represented in randomized trials. This population-based study compares the efficacy of cisplatin versus cetuximab with concurrent radiation as definitive treatment in patients with oropharyngeal carcinoma (OPC) using real-world data.
**Methods** A retrospective analysis of patients with stages III–IVB (AJCC 6th edition) OPC treated with cisplatin plus radiation (cis-RT) or cetuximab plus radiation (cetux-RT) during 2006–2016 at 2 tertiary cancer centres in Alberta was completed. Using the Kaplan–Meier method, median overall survival (MOS) and disease-free survival (DFS) were compared between treatment groups. Multivariable analysis with a Cox proportional hazards model was completed.
**Results** Of 546 patients with OPC identified, 431 (78.9%) received cis-RT, and 115 (21.1%), cetux-RT. Median age was 58 years; 86% were men; 30% were never-smokers; and 72% had HPV-positive disease. Patients who received cis-RT were younger than those who received cetux-RT and included a larger proportion of patients with a lower score on the Charlson comorbidity index (CCI). Compared with patients receiving cis-RT, those treated with cetux-RT were more likely to develop a recurrence after treatment (25% vs. 15%, $p$=0.01). Regardless of HPV status, MOS was longer in patients treated with cis-RT than in those treated with cetux-RT (32 months vs. 16.5 months in HPV-negative disease, $p$=0.003, and 51 months vs. 35 months in HPV-positive disease, $p$<0.001). On multivariable analysis, current smoking, HPV-negative status, higher CCI score, and T stage also independently predicted for worse OS and DFS. On multivariable analysis, treatment with cetux-RT (compared with cis-RT) was predictive of worse DFS (hazard ratio: 2.15; $p$<0.001) and OS (hazard ratio: 1.96; $p$=0.003).
**Conclusions** Real-world patients treated with cis-RT tended to be younger, with fewer comorbidities. Consistent with results from recent randomized studies, better survival outcomes were associated with cis-RT than with cetux-RT in a real-world population.

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### Trends in the Canadian medical oncology workforce and trainees, 1990–2019

Adam Fundytus,* Shaun Loewen,* Steven Yip,* Jacob Easaw,*† Desiree Hao*

**Introduction** Canadian cancer incidence rates have steadily risen over the last three decades, but it is unclear whether the medical oncology workforce has kept pace. The objective of this study is to characterize national trends in the medical oncology workforce and trainees between 1990 and 2019, and to explore their relationship with cancer incidence as a surrogate demand marker.
**Methods** We used publicly available databases from the Canadian Medical Association subspecialty reports (1994–2019) in conjunction with records from the Canadian Institute for Health Information database (1990–2018) to estimate number, age, and gender demographics, and regional distribution of medical oncologists (MOs) in practice in Canada. Cancer incidence by province was obtained from Statistics Canada for 1990–2016, except for Quebec, where data were available only for 1990–2010. Cancer incidence among adult patients was projected for all provinces to 2019 by age–period–cohort modelling using Canadian population statistics from Statistics Canada. Ratios of the annual cancer incidence to MO provider were generated to estimate the demand for, and supply of, medical oncology services. In addition, 1990–2019 Canadian Post-M.D. Education Registry data were used to characterize MO-in-training programs.
**Results** Between 1990 and 2019, the annual number of cancer cases in adults rose to 218,574 from 102,780 (113%), while the number of MOs increased to 625 from 88 over the same timeframe (a 610% increase). The ratio of cancer incidence to MO provider dropped to 350 cases per MO in 2019 from 1168 cases per MO in 1990. Overall, the Canadian MO workforce is aging, with an average age of 48.0 in 2018 compared with 39.3 in 1990. In 1990, only 6% of MO providers were 50 years of age or older, and none were more than 65 years of age, compared with 42% and 11% respectively in 2018. Nationally, the MO workforce has nearly reached gender parity, being 53% male in 2019 compared with 76% in 1990. Trends in Canadian MO trainees have largely mirrored those in practice, with a 341% increase in the annual trainee cohort to 119 in 2019 from 27 in 1990. In 1990, 80.6% of trainees were male compared with 42.9% in 2019. Although Ontario has the largest proportion of MOs (38% in 2019) and MO trainees (45%), those proportions have fallen over time relative to Quebec, Western Canada, and Atlantic Canada.
**Conclusions** The MO workforce has shown considerable growth, and between 1990 and 2019, the ratio of incident cancer cases to MOs has fallen in all regions across Canada. In addition, with higher proportions of MO providers nearing retirement age, those exiting the workforce could influence future workforce trends. Our study is limited because it does not take into consideration the increasing number and complexity of systemic therapies or referral patterns for new and existing cancer patients. Continued monitoring of human resource levels in medical oncology and of cancer incidence data are therefore crucial to ensure that training programs continue to meet future demands in cancer care.

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### Clinical utilization of the Oncotype DX genomic assay tool by Canadian medical oncologists in systemic treatment decision-making for patients with early-stage breast cancer

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**Objective** Evidence suggests that medical oncologists differ on how they use the Oncotype DX [ODX (Genomic Health, Redwood City, CA, U.S.A.)] genomic assay as a tool for making decisions about systemic therapy in patients with breast cancer. Given the recent emergence of clinical trial data supporting the use of ODX in both node-negative and node-positive disease, it is important to survey medical oncologists in Canada to assess their current use and perception of the ODX assay.

**Methods** A 34-item survey was distributed to Canadian medical oncologists through the Canadian Association of Medical Oncologists. Data were collected about physician demographics, current ODX usage patterns, and physician perception of the impact of various clinical and pathologic characteristics on their decision to use ODX. The survey also included case scenarios to assess ODX use under various clinical settings. A validated questionnaire was also included to measure tolerance of the participants for uncertainty in clinical decision-making.

**Results** Response rate was 20.6%, with 47 responses received from 228 surveys sent. There were 45 responses eligible for analysis. Overall, 62% of respondents (28 of 45) predominantly treated breast cancer, and 60% (27 of 45) had been in practice for at least 10 years. The most commonly cited reason for using ODX was to avoid giving patients unnecessary chemotherapy (64%, 29 of 45). Most oncologists (67%, 30 of 45) deferred making treatment decisions until ODX testing was completed. Factors most strongly affecting use of ODX included patient request, medical comorbidities, and tumour grade. In clinical scenarios, ODX was more frequently selected for patients 40–65 years of age (vs. <40 years or >65 years, $p<0.001$), grade 2 tumours (vs. grade 1 or 3, $p<0.001$), and a Ki-67 index of 10%–20% (vs. <10% or >20%, $p<0.001$). There was no significant correlation between physician tolerance of uncertainty and ODX use ($p=0.362$).

**Conclusions** This survey demonstrated that Canadian medical oncologists prefer to use ODX as a means of avoiding unnecessary chemotherapy. The ODX is used mainly in patients with intermediate clinical and pathologic features, which reflects the subgroup of patients with early breast cancer for whom additional predictive tools might offer guidance for optimal adjuvant treatment decision-making.

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### An exercise rehabilitation program for patients with breast cancer at a single institution

Rashida Haq,*† Sivakumar Gulasingam,†‡ Gerilyn Danischewsky,‡ Pauline Gulasingam*

**Objective** To determine the feasibility of an onsite exercise rehabilitation program (ERP) for patients with breast cancer (BCa).

**Methods** Medical oncologists referred patients with BCa at various phases of chemotherapy to the ERP held monthly in collaboration with a physiatrist and an exercise supervisor from a Cardiac Rehabilitation Centre. After baseline assessment, patients were given the option to enrol in the home exercise program (HEP) or the structured exercise program (SEP) at the Cardiac Rehabilitation Centre. Patients rerolled in HEP received a personalized exercise prescription, exercise diary, monthly telephone calls, and a repeat assessment at 12 weeks. The outcomes were assessed using the Functional Assessment of Cancer Therapy–Breast (FACT-B: FACIT.org, Elmhurst, IL, U.S.A.) and Center for Epidemiologic Studies Depression Scale (CES-D) questionnaires, resting pulse rate (RPR), and body mass index (BMI) at baseline and at 12 weeks. A patient satisfaction questionnaire was completed at 12 weeks.

**Results** During the 6 sessions, 32 eligible patients were referred to the program, with 85% consenting and attending the initial session. Of those 32 patients, 20 enrolled in HEP, 5 in SEP, and 2 in community programs. Of the patients rerolled in HEP, 70% continued to exercise at 12 weeks (only 14% maintained the diaries). Their BMI and RPR were similar, and no differences were observed in FACT-B and CES-D outcomes. In responses to the satisfaction questionnaire, 85.7% agreed that the exercise prescription was tailored; 78.5% felt that the program helped them to exercise regularly; and 64% indicated that they needed more support to adhere to the program.

**Conclusions** An onsite tailored ERP is feasible. Patients with BCa have a higher rate of exercise uptake, regardless of phase of chemotherapy, when referred by their oncologists. A HEP that incorporates an exercise prescription, education, and frequent follow-up might help patients with BCa to increase exercise and adherence. Integrating exercise into standard BCa care requires a collaborative approach from clinicians, allied health professionals, and stakeholders at institutions.

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### Antibiotic exposure among patients on ipilimumab and nivolumab for metastatic melanoma or renal cell carcinoma at the Nova Scotia Cancer Centre

Ceilidh MacPhail, Jennifer Melvin, Robyn Macfarlane

**Objective** A quality improvement project to describe the use of antibiotics preceding and during 4 cycles of dual immunotherapy in patients with metastatic melanoma or renal cell carcinoma.

**Methods** Retrospective chart review for patients with metastatic melanoma or renal cell carcinoma started on ipilimumab and nivolumab between Jul 2018 and Aug 2019.

**Results and Conclusions** Of 45 patients identified for chart review, 27 (60%) were exposed to antibiotics during the 6 months before immunotherapy start or during the course of 4 cycles of dual immunotherapy. Antibiotics were received by 51% of patients in the 6 months before therapy start.

Of patients receiving antibiotics pre-immunotherapy, 37% progressed radiologically after 4 cycles, and 52% had a complete or mixed response. Of patients with no antibiotic exposure, 28% progressed radiologically after 4 cycles of immunotherapy, and 50% had either a mixed or complete response.

To identify trends in antibiotic use before and after immunotherapy, indications for prescription and location of assessment are described. Post-immunotherapy antibiotics were most commonly prescribed for a suspected gastrointestinal infection in the emergency department.

Patients with metastatic melanoma and renal cell carcinoma appear to have high a prevalence of antibiotic use in the 6 months preceding and during immunotherapy. There is emerging evidence that antibiotics might influence outcomes with immunotherapy. Although our sample is small, a tend toward higher rates of progression was observed in patients who received antibiotics.

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### The pancreas and the peritoneum: disease characteristics and clinical outcomes

Mehrnoosh Pauls,* Abdul Aziz Al Shareef,* Winson Cheung,† Rachel Goodwin,* Michael Vickers*

**Objective** To compare clinical outcomes for patients with pancreatic adenocarcinoma with and without peritoneal metastasis (PMets) in the context of modern chemotherapy regimens.

**Methods** Using a retrospective cohort design, medical records from all adult patients diagnosed with metastatic pancreatic cancer across 5 cancer centres in Canada from 2014 to 2019 were reviewed. Prognostic variables including age, Charlson comorbidity index, Eastern Cooperative Oncology Group performance status (ECOG PS), cigarette smoking, nodal status, sites of metastasis, and first-line chemotherapy were collected. A Cox proportional hazards model (multivariable analysis) was used to examine the association between peritoneal involvement and survival, adjusted for measured confounders. Analyses were completed using the SAS software application (SAS Institute, Cary, NC, U.S.A.), with alpha of 0.05 defined as the level of significance.

**Results** The 1161 participants included in the study were predominantly male (53%) and had a median age of 71 years. Metastatic sites included peritoneum ($n=170$, 14.6%), lung ($n=145$, 12.5%), and liver ($n=563$, 48.5%). Patients with PMets received first-line FOLFIRINOX ($n=31$), gemcitabine–nab-paclitaxel ($n=20$), gemcitabine ($n=18$), and no treatment ($n=97$). In univariable analysis, worse ECOG PS, presence of lymph node metastasis, and presence of lung metastasis were associated with PMets. Most patients died (1030 of 1161, 88.7%), with the median OS being 3 months for patients with PMets and 7 months for patients without PMets ($p<0.001$). In multivariable analysis, presence of PMets; advancing age; male sex; ECOG PS 3 or 4; treatment with gemcitabine (vs. FOLFIRINOX); and lymph node, liver, or lung metastasis were associated with worse survival.

**Conclusions** In the setting of modern-day chemotherapy, prognosis continues to be poor for patients with PMets compared with those without, which might be attributable to the impact of PMets on PS and the inability to administer palliative chemotherapy.

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## The impact of primary pancreatic tumour location on clinical outcomes in advanced disease

Abdul Aziz Al Shareef,* Mehrnoosh Pauls,* Winson Cheung,† Rachel Goodwin,* Michael Vickers*

**Objective** To determine whether there is an association between location of the primary pancreatic adenocarcinoma and spread to the peritoneum. The impact of location of the primary tumour within the pancreas (head or neck vs. body vs. tail) on overall survival.
**Methods** A retrospective cohort design was used to identify cases of advanced pancreatic cancer and to assess disease- and treatment-related characteristics. Medical records from all adult patients diagnosed with metastatic pancreatic cancer across 5 cancer centres in Canada from 2014 to 2019 were reviewed using a national Research Electronic Data Capture database. Prognostic variables including age, Charlson comorbidity index, Eastern Cooperative Oncology Group performance status, cigarette smoking, nodal status, sites of metastasis, and type of first-line chemotherapy were considered. A Cox proportional hazards model was used to examine the association between peritoneal involvement and survival, adjusted for measured confounders. Analyses were completed using the SAS software application (SAS Institute, Cary, NC, U.S.A.), with an alpha of 0.05 defined as the level of significance.
**Results** The 1161 participants with metastatic pancreas cancer were predominantly male (53%) and had a median age of 71 years. The primary tumour origin was the head or neck in 602 patients (51.8%), the tail in 235 (20.2%), and the body in 184 (15.8%). Metastatic sites included peritoneum ($n$=170, 14.6%), lung ($n$=145, 12.5%), and liver ($n$=563, 48.5%). Most patients who developed peritoneal metastasis had tumours originating from the pancreas body (16.8%) or tail (21%); peritoneal metastasis originating from a primary of the head or neck occurred at a lower frequency (9.1%, $p$<0.001). On multivariate analysis, primary tumour location was not significantly associated with overall survival.
**Conclusions** The primary location of a pancreatic tumour (body, neck, tail, or head) does not have significant clinical relevance to overall survival in patients with advanced metastatic pancreatic cancer. That observation is contradictory to findings in prior studies that have shown worse overall survival in patients with a primary originating in the pancreatic tail.

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## The use of peptide receptor radionucleotide therapy in patients with neuroendocrine tumour cardiac metastases

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**Purpose** Peptide receptor radionucleotide therapy (PRRT) is approved for the treatment of somatostatin receptor–positive gastroenteropancreatic neuroendocrine tumours (NETs). The heart is an infrequent site of metastasis, and safety concerns exist regarding cardiac integrity and function in response to PRRT in this setting. Our objectives are to characterize patients with cardiac metastases in NETs diagnosed by $^{68}$Ga DOTATATE integrated positron-emission tomography–computed tomography (PET/CT), and to describe safety and outcomes with PRRT.
**Methods** Sequential patients who underwent $^{68}$Ga DOTATATE PET/CT imaging and received 1 or more doses of PRRT were included. Retrospective chart review was performed to identify those with cardiac metastases. Clinical, laboratory, and radiographic information was obtained and summarized.
**Results** Of 123 sequential patients who received $^{68}$Ga DOTATATE PET/CT imaging, 3 (2.4%) had cardiac metastases detected, and all subsequently received 1 or more doses of PRRT. All 3 patients had midgut grade 1 tumours that were functional and had a high burden of metastasis to at least 5 different distant sites (Table). Mean duration of follow-up was 46 weeks. Sites of cardiac involvement were the interatrial septum ($n$=1) and ventricular wall ($n$=2); cardiac function was normal. In 2 of 3 patients, the cardiac lesions were not detected on transthoracic echocardiogram, but were visualized on $^{68}$Ga DOTATATE PET/CT imaging. Two patients received 4 doses of PRRT, and the third patient has completed 3 doses. All have demonstrated tolerance to treatment, with no reports of cardiorespiratory concerns or heart failure.
**Conclusions** Cardiac metastases from NETs were documented in patients with midgut grade 1 tumours with a high burden of metastases, and the use of PRRT was safe. Follow-up is required to determine the efficacy and long-term safety of PRRT in this unique population.

**TABLE** Characteristics of 3 patients with midgut neuroendocrine tumours (NETs) and cardiac metastases

| Characteristic | Patient | | |
|---|---|---|---|
| | A | B | C |
| Primary tumour location | Small bowel | Small bowel (terminal ileum) | Midgut |
| Stage at diagnosis | pT3N2M1 | pT3N0M1 | pTxNxM1 |
| Histology | | | |
| Differentiation | Well-differentiated | Well-differentiated | Well-differentiated |
| Ki-67 index | <2% | 1%–2% | NA |
| Mitotic rate | NA | NA | 0 |
| Grade | 1 | 1 | 1 |
| Tumour functional status | Functional | Functional | Functional |
| Chromogranin A[a] (ng/mL) | 152 | 356 | 7748 |
| Sites of metastasis[b] | Lymph nodes, liver, peritoneum, bone, heart | Lymph nodes, lung, liver, bone, heart | Lymph nodes, chest wall/pleura, liver, bone, heart ±pancreas |
| Cardiac metastases | | | |
| Location | Left ventricle in myometrium | Interatrial septum | Left ventricular inferior wall, right ventricular wall, left ventricular anterior wall |
| Visualization on other imaging modalities | Not visualized on CT (×2) or on transthoracic echocardiogram | Not visualized on transthoracic echocardiogram | Of 3 lesions, 2 visualized on CT and on transthoracic echocardiogram |
| Other echocardiogram findings | | | |
| LVEF | 50%–55% | 65% | 57% |
| Valvular abnormality | None | None | Thickened and calcified tricuspid valve<br>Mild-to-moderate tricuspid regurgitation |
| Use of PRRT | | | |
| Dose (mCi) | 585.6 | 792.5 | 695.6 |
| Doses received *(n)* | 3 | 4 | 4 |
| Duration of follow-up (weeks) | 42 | 49 | 48 |

[a] Upper limit of normal: <93 ng/mL.
[b] Seen on $^{68}$Ga DOTATATE integrated positron-emission tomography–computed tomography.

NA = not available; CT = computed tomography; LVEF = left ventricular ejection fraction; PRRT = peptide receptor radionucleotide therapy.

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## Comparison of patient-related outcomes and efficacy between FOLFIRINOX and nab-paclitaxel–gemcitabine in first-line treatment of advanced pancreatic ductal adenocarcinoma

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**Background** FOLFIRINOX and nab-paclitaxel–gemcitabine (nabPGem) are standard therapies for advanced pancreatic ductal adenocarcinoma (APDAC). Our objective was to compare patient-related outcomes [PROs: Edmonton Symptom Assessment System–revised (ESASr)] and survival for those regimens.
**Methods** This was a retrospective cohort study of patients in Alberta (2015–2017) who had treatment-naïve APDAC and who subsequently completed at least 3 cycles of FOLFIRINOX or nabPGem. Change in the mean PRO score (Δ) from baseline for each ESASr symptom was compared for the two regimens at 1 and 3 months by $t$-test. Cut-offs established by Hui *et al.* (>1)

were considered the minimally clinically important difference for each symptom. Survival was analyzed in a multivariate Cox regression model.
**Results** PROs were available for 88 patients (33 FOLFIRINOX, 55 nabPGem; 60% male) whose median age was 64 years (range: 31–78 years). For each symptom, no differences in score were observed at baseline or at 1 month. At 3 months, change in the mean well-being score was significantly less for patients who received nabPGem than for those who received FOLFIRINOX (Δ: 0.29 vs. 2.05; $p$=0.02). The minimally clinically important difference was not observed for the total distress score at any time point. No statistically significant difference was observed in median progression-free survival (5.1 months with FOLFIRINOX vs. 4.5 months with nabPGem, $p$=0.28) or overall survival (11.6 months with FOLFIRINOX vs. 10.9 months with nabPGem, $p$=0.53).
**Conclusions** In this real-world cohort, survival and quality of life, as assessed by the ESASr, were similar for patients treated with FOLFIRINOX or with nabPGem. In the absence of a randomized comparison of the two regimens, our findings should inform clinical decision-making for APDAC.

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## Impact of sequence order of anthracyclines and taxanes in neoadjuvant chemotherapy for breast cancer: results from a prospective institutional database

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**Background** There has been growing interest in the optimal sequencing of anthracyclines and taxanes in neoadjuvant chemotherapy (NACT) for breast cancer. However, data comparing the efficacy of administering taxanes before anthracyclines as opposed to the opposite sequence remain limited and inconsistent. The objective of our study was to assess the impact of sequence order on pathologic and clinical outcomes in a real-world setting.
**Methods** A prospective institutional database was analyzed to identify all patients with HER2-negative breast cancer treated with NACT from 2012 to 2019. Rates of pathologic complete response (pCR), downstaging, and breast-conserving surgery were compared for patients who received anthracyclines followed by taxanes (AC-T) and for those who received taxanes followed by anthracyclines (T-AC). Chi-square and independent-sample nonparametric tests were used to test for associations between variables and outcomes.
**Results** Of the 270 patients who met eligibility criteria, 175 (65%) received AC-T and 95 (35%) received T-AC. Median age was 55 years [25%–75% interquartile range (IQR): 24–86 years]. Overall, 83% of patients had stage IIB or greater tumours, 40% had grade 3 histology, and 36% had triple-negative disease. Characteristics were balanced between the AC-T and T-AC groups (all $p$<0.05). Median duration of treatment with NACT was 102 days (IQR: 29–203 days). Rates of pCR (19% vs. 21%, $p$=0.750), downstaging (68% vs. 61%, $p$=0.188), and conversion to breast-conserving surgery (26% vs. 20%, $p$=0.314) were, respectively, similar for AC-T and T-AC. A higher pCR rate was observed in triple-negative compared with hormone-positive cases (33% vs. 13%, $p$<0.001).
**Conclusions** In this small population-based cohort, sequence order of anthracyclines and taxanes did not demonstrate statistically significant differences in evaluated outcomes from NACT for breast cancer. This finding supports the current variation in prescribing practice and highlights the need for further studies in this area.

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## Disease registries and real-world evidence

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**Objective** To explore the use of disease registries as a source of real-world evidence (RWE).
**Methods** RWE is generated by analyzing data gathered in routine clinical practice. This work focuses on the disease registry as a vehicle for collecting real-world data (RWD) from patients. Based on the experience of a Canadian technology company specializing in RWE health informatics and analytics, a review of cancer registries developed and in development was undertaken.
**Results** The results of this review highlight current challenges in incorporating RWE into routine clinical practice, solutions to overcome those barriers, and how the data collected can help shape and inform decision-making in cancer care in Canada to benefit clinicians and their patients. Further, the results point to unique opportunities to incorporate disease registry data, particularly in terms of patient-reported outcomes, throughout the health technology lifecycle, providing insights into areas including health economic value and real-world impact. At each stage of RWE generation, the quality and representativeness of the RWD were identified as being critical to the impact that the resulting RWE can have on health care decisions.
**Conclusions** The role of RWE in drug development, regulatory, and health care decision-making is rapidly expanding as stakeholders gain a greater appreciation of the value of RWE and seek to explore ways to make use of these evidence sources for policy development. This situation is attributable in part to the potential for RWE to provide a better understanding of the real-world patient experience, creating a more complete description of a patient's journey, and the real-world benefit of available therapies. In that regard, disease registries have the potential to play a role as an evidence source.

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