CAMO 2021 VIRTUAL MEETING

BOOK OF ABSTRACTS

The National CAMO Residents Research Day | **Thursday, April 1, 2021**

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ORAL PRESENTATION

01_CAMO_2021

BARRIERS TO ACCESS OF CONTEMPORARY TREATMENT FOR LETHAL PROSTATE CANCER: AN ONTARIO POPULATION-BASED STUDY

Jennifer Leigh[1], Danial Qureshi[2], Ewa Sucha[3], Colleen Webber[2], Peter Tanuseputro[2,3] and Michael Ong[4].
[1]Department of Medicine, University of Ottawa, Ottawa, Ontario
[2]Ottawa Hospital Research Institute, Ottawa, Ontario
[3]ICES University of Ottawa, Ottawa Hospital Research Institute, Ottawa, Ontario
[4]Department of Medicine, The Ottawa Hospital Cancer Center, Ottawa, Ontario

OBJECTIVE

Our objective was to investigate and describe the factors important to receipt of novel life prolonging therapy (LPT) in patients with lethal castration-resistant prostate cancer in Ontario.

METHODS

Population-based administrative databases from Ontario, Canada were used to identify patients 65 years or older with prostate cancer who were eligible for Ontario Drug Benefit 2002-2018 (n=138,976), received continuous androgen deprivation therapy (ADT, n=37,578), and died of prostate cancer-specific death between 2013-2017 (n=3,575). Baseline and treatment characteristics were analyzed for association with receipt of therapy in a 2-year observation period prior to death.

RESULTS

Only 40.4% were identified to receive LPT in the two years preceding death despite 51.3 % presenting with metastasis. Type of LPT received included abiraterone (66.3%), docetaxel (50.3%), enzalutamide (17.2%), radium-223 (10.0%), and cabazitaxel (3.5%). LPT access increased with cancer centre consultation (yes: 50.2%; no: 22.5%, p<0.0001), and type of oncologist involved (urologist: 39.1%; radiation: 48.3%; medical: 56.5%, p<0.0001). Accessibility decreased with advanced age (65-74 yrs.: 58.8%; 75-84 yrs.: 41.3%; 85+ yrs.: 22.3%, p<0.0001), greater number of chronic conditions (0: 49.4%, 1-4: 41.6%, 5+: 29.2%, p<0.0001), and long-term care registration (yes: 7.8%; no: 41.2%, p<0.0001). Proportion of patients receiving LPT within two years of death significantly increased with decedent year (2013:22.7%, 2014: 31.8%, 2015: 41.8%, 2016: 49.1%, 2017: 57.9%). LPT receipt was not associated with income quartile, rurality index, patient distance to cancer centre, or metastatic status at diagnosis.

CONCLUSION

A high proportion of patients dying of prostate cancer in Ontario never receive LPT, although large increases in LPT by year and new indications for LPT use are poised to address the shortfall. Our provincial health care system did not discriminate on the basis of income, remoteness or rurality for access to LPT. Improving access to cancer centre consultation may be important to further improve delivery.

ORAL PRESENTATION

02_CAMO_2021

A REVIEW OF OBSP SCREENING TRENDS ACROSS THE PROVINCE – A RETROSPECTIVE POPULATION-BASED STUDY USING ADMINISTRATIVE DATA

Michela Febbraro, Gregory Pond, Kathleen Bell, Nidhi Kumar-Tyagi, Sukhbinder Dhesy-Thind
Juravinski Cancer Center, Hamilton, Ontario

BACKGROUND

The Ontario Breast Screening Program (OBSP) was introduced to provide high-quality breast cancer screening services. Despite universal access to OBSP services, screening and diagnosis rates differ across the province. This study sought to identify whether patient factors act synergistically with regional aspects of care and impact OBSP screening.

METHODS

A retrospective population-based study using linked administrative health care data through ICES (formally the Institute for Clinical Evaluative Sciences) was conducted between 2009 and 2016. The study cohort was defined as all screen eligible women (aged 51-74 years) with breast cancer living in Ontario, Canada. The primary outcome was OBSP screening within 730 days prior to diagnosis. Prognostic factors for OBSP use in the screened cohort were identified using logistic regression.

RESULTS

44,732 screen eligible women were diagnosed with breast cancer with 17,800 (39.8%) receiving OBSP screening within 730 days prior to breast cancer diagnosis. 35,844 women (80%) were diagnosed with stage I/II breast cancer. Of these, 43.7% had OBSP screening within 730 days prior to diagnosis. In contrast, 6,878 women had stage III/IV breast cancer, of whom, 25.5% had prior OBSP screening (chi-square p-value < 0.001). In multivariable model, increasing age (odds ratio [OR] 1.29, 95% confidence interval [CI] 1.27-1.31) and rural LHIN location (OR 1.14, 95% CI 0.96-1.36) were more likely to receive OBSP screening. Charlson score (2+ vs 0-1, OR 0.58, 95% CI 0.55-0.60), previous cancer (OR 0.87, 95% CI 0.78-0.98), and higher marginalization index (OR 0.95, 95% CI 0.93-0.96) were less likely to have OBSP screening prior to diagnosis.

CONCLUSION

OBSP screening is associated with lower stage breast cancer. However, regional variations in OBSP screening are dependent upon several factors, the most important being population density and marginalization which need to be addressed independently in order to overcome barriers to care.

ORAL PRESENTATION

03_CAMO_2021

BEYOND BRCA? CLINICAL UTILITY OF HOMOLOGOUS RECOMBINATION DEFICIENCY IN GASTROINTESTINAL CANCERS

Erica S. Tsang[1], Veronika Csizmok[2], Laura M. Williamson[2], Erin Pleasance[2], James Topham[3], Joanna Karasinska[3], Emma Titmuss[2], Intan Schrader[1], Fergus Cafferty[1], Stephen Yip[4], Basile Tessier-Cloutier[2], Karen Mungall[2], Tony Ng[4], Sophie Sun[1], Howard J. Lim[1], Jonathan M. Loree[1], Janessa Laskin[1], Marco A. Marra[2], Steven J.M. Jones[2], David F. Schaeffer[4], Daniel J. Renouf[1]

[1]BC Cancer, Vancouver, Canada
[2]Canada's Michael Smith Genome Sciences Center, Vancouver, Canada
[3]Pancreas Center BC, Vancouver, Canada
[4]Department of Pathology and Laboratory Medicine, Vancouver General Hospital, Vancouver, Canada

BACKGROUND

There is emerging evidence about the predictive role of homologous recombination deficiency (HRD), but the clinical utility is less well defined in gastrointestinal (GI) malignancies.

METHODS

We reviewed the whole genome (WGS) and transcriptomic (RNA-Seq) data of patients with advanced GI cancers between 2012-2018 in the Personalized Oncogenomics trial (NCT02155621). HRD was defined as a score ≥34, and a high mutational signature 3 score was defined as >0.05. Retrospective chart review was conducted to extract treatment and survival outcomes. Overall survival (OS) from initiation of first-line systemic therapy and time to progression on platinum therapy (TTPp) were calculated. Linear and multivariable regression analyses were conducted.

RESULTS

Of 154 patients with GI primaries, 56% were male and 105 (68%) were exposed to a platinum agent in the metastatic setting. Primary sites included upper GI (N=20, 9%), pancreas (N=35, 16%), colorectal (N=74, 33%), and other GI primary (N=25, 11%). Ten patients (6%) had a *BRCA1/2* mutation, 20 (13%) had a high HRD score, and 11 (7%) had a high signature 3 score (>0.05). Six patients had both high HRD and high signature 3 scores.

On linear regression, high HRD scores and mutational signature 3 were independently associated with longer TTPp (β=4.17, 95% CI 0.15-8.19, p=0.04; β=8.03, 95% CI 2.87-13.18, p<0.05, respectively). On multivariable linear regression, after adjusting for HRD score, *BRCA1/2* status, and tumor site, only cases with a mutational signature 3 retained significance (p<0.05). HRD status was not prognostic for OS (HR 1.02, 95% CI 0.65-1.62, p=0.92).

CONCLUSIONS

Within a cohort of patients with GI malignancies, mutational signature 3 was more strongly associated with TTPp compared to HRD score. These data highlight potential predictive implications of Signature 3 to complement HRD and *BRCA* status in identifying patients who may benefit from exposure to platinum therapy.

ORAL PRESENTATION

04_CAMO_2021

DOSING, EFFECTIVENESS AND SAFETY OF LENVATINIB IN THE REAL-WORLD TREATMENT OF HEPATOCELLULAR CARCINOMA: RESULTS FROM A CANADIAN MULTICENTER DATABASE (HCC CHORD)

Carla P. Amaro[1], Michael J Allen[2], Jennifer J. Knox [2], Erica S Tsang [3], Howard J. Lim [3], Richard M. Lee-Ying [1], Kelvin KW Chan[4], Jessica Qian [5], Brandon M. Meyers [5], Alia Thawer [4], Sulaiman M. S. Al-Saadi [6], Tina Hsu [6], Ravi Ramjeesingh [7], Hatim Karachiwala [8], Tasnima Abedin [1], Vincent C. Tam [1]
On behalf of the HCC CHORD Consortium
[1]Tom Baker Cancer Centre, University of Calgary, Calgary, AB, Canada;
[2]Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada;
[3]BC Cancer, Vancouver, BC, Canada;
[4]Sunnybrook Odette Cancer Centre, University of Toronto, Toronto, ON, Canada;
[5]Juravinski Cancer Centre, Hamilton, ON, Canada;
[6]Ottawa Regional Cancer Centre, Ottawa, ON, Canada;
[7]Nova Scotia Cancer Centre, Dalhousie University, Nova Scotia, NS, Canada;
[8]Cross Cancer Institute, Edmonton, AB, Canada.

OBJECTIVE
To assess the real-world effectiveness and safety of lenvatinib in advanced Hepatocellular Carcinoma(HCC).

METHODS
From July 2018 to December 2019, HCC patients treated with lenvatinib from 10 different Canadian cancer centers were included. Overall survival (OS), progression-free survival (PFS) and objective response rate (ORR) were retrospectively analyzed and compared across first- and 2nd/3rd-line use of lenvatinib. In first-line patients, OS was also compared between different mean dose-intensities and starting dose groups.

RESULTS
A total of 220 patients were included. Median follow-up was 4.5 months. A total of 79% patients received lenvatinib as first-line therapy. ORR, PFS and OS results and their comparison between the different lines of therapy are shown in the table. Considering the patients who received lenvatinib first-line, 40% received a mean dose intensity of 67% or less. Median OS for mean dose intensity > 67% and <=67% were 13.7 and 7.7 months (p = 0.009), respectively. Of these first-line patients, 54% started lenvatinib at full dose according to their weight. Median OS for starting lenvatinib at full and reduced dose was 12.3 and 15.8 months (p = 0.75), respectively. Toxicities occurred in 86% of patients and led to drug discontinuation in 24% patients. The most common side effects were fatigue (59%) and hypertension (41%).

CONCLUSIONS

Lenvatinib appears to be effective and safe in real-world practice regardless of the line of therapy, with results in first-line comparable to those demonstrated in the REFLECT trial. For patients who received lenvatinib first-line, treatment mean dose-intensity of >67% may improve survival while starting dose does not appear to affect survival.

	LEN 1st line n=173	LEN 2nd-4th lines n=47	P value
ORR	23%	19%	0.234
Median PFS (95% CI), months	8.0 (6.4 – 9.6)	5.0 (1.3 – 8.7)	0.182
Median OS (95% CI), months	13.0 (9.0 – 17)	15.0 (7.7 – 22.3)	0.891

ORAL PRESENTATION

05_CAMO_2021

THE INFLUENCE OF ADJUVANT CHEMOTHERAPY DOSE INTENSITY ON OVERALL SURVIVAL IN RESECTED COLON CANCER: A MULTICENTRE RETROSPECTIVE ANALYSIS

Suganija Lakkunarajah[1], Daniel Breadner[2], Hanbo Zhang[3], Shiying Kong[4], Winson Chung[4], Jonathan Loree[5], Stephen Welch[2]
1 Department of Medicine, Schulich School of Medicine, London, Ontario, Canada
2 Department of Oncology, Schulich School of Medicine, London, Ontario, Canada
3 Department of Oncology, Cross Cancer Institute, Edmonton, Alberta, Canada
4 Department of Oncology, Arnie Charbonneau Cancer Institute, Calgary, Alberta, Canada
5 Department of Oncology, British Columbia Cancer Agency, Vancouver, British Columbia, Canada

BACKGROUND

Colorectal cancer remains the second leading cause of cancer death in developed countries, despite the implementation of early detection and screening programs. There are many notable trials showing the benefit of using fluorouracil-based chemotherapy in the addition of oxaliplatin such as modified FOLFOX (fluorouracil (5-FU), leucovorin, oxaliplatin) and CAPOX (capecitabine and oxaliplatin). There is evidence that achieving a 5-FU dose intensity (DI) > 70 - 80% in adjuvant colon cancer treatment improves overall survival (OS). The oxaliplatin dose intensity threshold under which survival is inferior is not established.

METHODS

Patients treated with adjuvant chemotherapy between 2006 and 2011 for resected stage III colon cancer (CC) from four academic cancer centres in Canada were retrospectively analysed. Patients that received CAPOX and FOLFOX were examined for the relationship between DI and OS.

RESULTS

625 patients were analysed with resected high risk stage II or stage III CC that received adjuvant chemotherapy. The median age was 63. 34.3% and 31.5% patients had T4 and N2 disease, respectively. Median follow was 38.2 months. The median oxaliplatin DI was 70%. 56.8% of patients had an oxaliplatin DI of > 80%. An oxaliplatin DI of >80% was associated with a significant improvement in survival, HR=0.45 (95%CI 0.24 – 0.86, p<0.01). Achieving a DI of >80% for capecitabine or 5-FU did not improve OS. Other factors associated with inferior OS included T4 (HR=2.9, p=0.05) and N2 (HR=5.15, p=0.0007) subgroups.

CONCLUSIONS

Patients receiving adjuvant chemotherapy with an oxaliplatin DI of >80% for high risk stage II and stage III CC have a superior OS.

ORAL PRESENTATION

06_CAMO_2021
IMPACT OF TAILORX DATA ON CHEMOTHERAPY PRESCRIBING IN BRITISH COLUMBIA

Megan Tesch[1], Caroline Speers[2], Rekha Diocee[2], Alan Nichol[3], Caroline Lohrisch[1]
[1]Department of Medical Oncology, BC Cancer, Vancouver, British Columbia, Canada
[2]Breast Cancer Outcomes Unit, BC Cancer, Vancouver, British Columbia, Canada
[3]Department of Radiation Oncology, BC Cancer, Vancouver, British Columbia, Canada

BACKGROUND
The 21-gene recurrence score assay (RS) reduces adjuvant chemotherapy use in hormone+, HER2-, node- breast cancer, justifying the assay's cost. The TAILORx trial confirmed the predictive value of RS and established thresholds for chemotherapy benefit in younger and older patients. We examined chemotherapy use in BC post-TAILORx publication, as a prelude to exploring age-adjusted cost-effectiveness of the assay.

METHODS
We assembled 3 cohorts of patients with hormone+, HER2-, node- breast cancer: diagnosed before RS funding (cohort 1: January 1, 2013-December 31, 2013), after public funding (cohort 2: July 1, 2015-June 30, 2016), and post-TAILORx (cohort 3: July 1, 2018-June 30, 2019). Patients 18-80 years old (yo) with tumors that were grade 3, grade 2 ≥ T1b, or any T size and grade if ≤ 40 yo were included, matching BC funding criteria. Chemotherapy use was compared between cohorts using univariate analyses.

RESULTS
2,066 patients met inclusion criteria. Chemotherapy use in cohorts 1, 2, and 3 was 21%, 17%, and 13%, respectively. Chemotherapy use declined by 19% after RS funding and by another 23% post-TAILORx (p=0.001). Reduction in chemotherapy use was significant for RS 11-20 tumors (cohort 3 vs. 2, p=0.004). A 7.5% nonsignificant increase in chemotherapy use was seen for RS 26-30 tumors (cohort 2 vs. 3, p=0.55). There was no significant change in chemotherapy use in patients > 50 yo (12% in cohort 2 vs. 10% in cohort 3, p=0.22). Among patients 70-80 yo in cohort 3 with RS, 14% had RS ≥ 26, and of these, 40% had chemotherapy, compared with 92% chemotherapy use for patients ≤ 50 yo with RS ≥ 26.

CONCLUSIONS
Chemotherapy use decreased post-TAILORx, driven primarily by RS 11-20 tumors and patients ≤ 50 yo. Chemotherapy use changed little in patients > 50 yo, suggesting trial results confirmed pre-existing prescribing practices, and increased for RS 26-30 tumors, reflecting acceptance of TAILORx thresholds for chemotherapy benefit. Chemotherapy use was low overall in patients > 50 yo, especially in those 70-80 yo, in part due to the low frequency of high RS tumors. Given these findings, we conclude that cost-effectiveness modelling for publicly funded RS should take age into consideration.

ORAL PRESENTATION

07_CAMO_2021

OPTIMIZING CABAZITAXEL (CBZ) VS NOVEL ANTI-ANDROGENS (NAA) ABIRATERONE (ABI) OR ENZALUTAMIDE (ENZ) POST-DOCETAXEL (DTX) IN METASTATIC CASTRATE RESISTANT PROSTATE CANCER (MCRPC)

Alexander S Watson[1], Richard Gagnon[1], Eugene Batuyong[1], Nimira Alimohamed[1], Richard Lee-Ying[1]
[1]Tom Baker Cancer Centre, University of Calgary, Calgary, Alberta

OBJECTIVE

Treatment sequencing post-Dtx in mCRPC remains uncertain, with Cbz chemotherapy anecdotally underutilized. The recent CARD trial suggested Cbz may have benefit over NAA in patients who had rapid progression within 12 months (RP) on a previous NAA. We sought to characterize real-world Cbz use and factors interacting with clinical outcomes.

METHODS

mCRPC patients in Alberta who received Dtx from October 2012 to December 31st 2017 were assessed. We examined Cbz eligibility per trial criteria, tracked therapies, outcomes, and documented therapy discussions. OS was measured using the Kaplan-Meier method and compared via log-rank test. Agent utilization and outcome interactions were analysed via Chi-Square.

RESULTS

593 mCRPC patients received Dtx over the study period. 338 patients (57%) were Cbz-eligible per TROPIC trial criteria, with ineligibility most often for Dtx intolerance (14%) or comorbidities (14%). Patients with RP on first NAA had poorer OS (12.3 vs 24.8 months, p<0.001). OS was increased among RP patients who received Cbz (16.9 vs 10.3 months, p=0.015), but not improved without RP (17.1 vs 32 months, p=0.084). The most common agents post-Dtx were Abi (280, 47%) and Enz (250, 42%). Significantly fewer patients (177, 30%) received Cbz (p<0.001). Immediately post-Dtx, 398 patients (67%) did not have a documented discussion around Cbz, and in 238 cases (40%) Cbz consideration was never documented. Patient choice against Cbz was recorded in 16% of discussions.

CONCLUSION

In a real-world mCRPC cohort, Cbz was less utilized then NAA post-Dtx. Provider preference was a major factor, with Cbz discussions limited post-Dtx, despite many patients being eligible. Cbz use was associated with improved OS among patients who had RP on first NAA, a subset with worse outcomes overall. These real-world data suggest Cbz use could be optimized by focusing on patients with RP on prior NAA.

ORAL PRESENTATION

08_CAMO_2021

REAL WORLD OUTCOMES OF METASTATIC BREAST CANCER (MBC) PATIENTS WITH BRAIN METASTASES (BRM) TREATED WITH RADIOTHERAPY IN ONTARIO: A POPULATION-BASED STUDY

Xin Y. Wang, MD[1]; Michael Rosen, BSc[3]; Rania Chehade MD[1,2]; Arjun Sahgal, MD[1,2]; Hany Soliman, MD[1,2]; Refik Saskin, MSc[4]; Bo Zhang, MPH, PhD[4]; Kelvin K.W. Chan, MD, MSc, PhD[1,2] Katarzyna J. Jerzak, MSc, MD[1,2]

[1]Department of Medicine, University of Toronto, Toronto, Ontario
[2]Division of Medical Oncology, Sunnybrook Health Sciences Centre, Toronto, Ontario
[3]Faculty of Medicine, University of Ottawa, Ontario
[4]Institute for Clinical Evaluative Sciences (ICES), Sunnybrook Health Sciences Centre, Toronto, Ontario

OBJECTIVES

Identify treatment patterns and outcomes among women treated with radiotherapy for breast cancer BrM in Ontario.

METHODS

We used the Ontario-wide ICES database to identify patients diagnosed with de-novo MBC between January 2009 and December 2018. Primary endpoints included were i) cumulative incidence of radiotherapy for BrM accounting for the competing risk of death (calculated using the Cumulative Incidence Function), and ii) time from MBC diagnosis to treatment with brain radiotherapy. The key secondary endpoint was overall survival (OS). Kaplan-Meier analyses were performed for time-to-event endpoints. Univariable and multivariable logistic regression analyses were used to account for potential confounding variables. Data were censored if patients were alive at last available follow-up with the last cut-off date being March 31, 2019.

RESULTS

3,916 patients with de-novo MBC were identified, among whom 549 (14%) developed BrM requiring radiotherapy; patients with HER2+ (23.0%) and triple negative breast cancer (TNBC) (20.9%) were most likely to require brain radiotherapy.

The median time from MBC diagnosis to treatment for BrM was 15 months, ranging from 7.5 months to 19.8 months for patients with TNBC and HER2+/HR+ MBC, respectively.

The median OS from the time of brain radiotherapy was 5.1 months, ranging from 2.6 months to 9.4 months for TNBC and HER2+/HR- populations, respectively. In a multivariable Cox regression model, HER2-negative status, treatment with whole brain radiotherapy (WBRT), lower income quintile, and age >60 were independently prognostic for shorter OS. Patients treated with stereotactic radiosurgery (SRS) had lower 30-day mortality (6.4% vs. 18.9%, p=0.003) and lower likelihood of hospitalization (9.6% vs. 20.2%, p=0.015) compared to patients treated with WBRT.

CONCLUSION

Approximately 1 in 7 patients with MBC in Ontario will require radiotherapy for BrM. Our data support the use of SRS when indicated and provide insights regarding the time to development of BrM by breast cancer subtype.

ORAL PRESENTATION

09_CAMO_2021

EXAMINATION OF FEBRILE NEUTROPENIA AND THE UTILIZATION OF G-CSF ON HEALTHCARE SYSTEMS

Alec Pencz[1], Morgan Black[1], Scott Strum[2], Meghan Gipson[3], Mark Vincent[1]
1 Department of Oncology, London Regional Cancer Program, London, Ontario, Canada
2 Department of Medicine, Schulich School of Medicine and Dentistry, London, Ontario, Canada
3 Department of Medicine, Royal College of Surgeons in Ireland, Dublin, Ireland

OBJECTIVE

Febrile neutropenia (FN), a hallmark toxicity of myelosuppressive chemotherapy, frequently results in chemotherapy delays, dose decreases, or premature cessation. The utilization of granulocyte colony-stimulating factor (G-CSF) has been prescribed to mitigate this problem and has been widely studied. The biosimilar Grastofil® (a form of G-CSF), provincially funded in December 2016, is a less expensive but high-quality alternative to Neupogen®. Increasing availability of G-CSF to patients might decrease hospitalizations and costs.

METHODS

A retrospective chart review was carried out on 158 patients treated at the London Regional Cancer Program (from 01/Sept/2015–30/June/2018) with non-haematological, solid tumors, whom experienced FN. Patients were arranged into two cohorts: before (01/Sept/2015–30/Nov/2016), and after (01/Apr/2017–30/June/2018), Grastofil® funding. Comparative analyses were completed and Student's T was calculated to determine statistical significance.

RESULTS

After the introduction of Grastofil®, the frequency of FN in all patients with cancer decreased by 29.85% (p=0.0190, pre FN-Rate 7.70%, post FN-rate 5.40%), and the length of hospital stay for each FN patient decreased by 25.87% (p=0.105, Pre: 11.40 days/pt. Post: 8.45 days/pt.). Furthermore, the absolute number of FN patients who received G-CSF support as primary prophylaxis increased by 90.91% (p=0.0714). Finally, comparison of average costs revealed a savings of $42,117.78 for every 200 patients started on cytotoxic chemotherapy (p=0.0116). This data was consistent with the hypothesis that increased availability and usage of G-CSF led to a decrease in FN admissions, length of stay, and costs.

ORAL PRESENTATION

10_CAMO_2021
CURRENT ATTITUDES TOWARD UNFUNDED CANCER THERAPIES AMONG CANADIAN MEDICAL ONCOLOGISTS

Selina K Wong, Lovedeep Gondara, Sharlene Gill
BC Cancer, Vancouver, Canada

OBJECTIVE
To describe the frequency and predictors of discussion of unfunded cancer treatments among Canadian medical oncologists.

METHODS
A REDCap survey with multiple choice and case-based scenarios was distributed in July 2020. Descriptive statistics and multivariate logistic regression were performed.

RESULTS
116 responses were received: BC (35%), ON (27%) and AB (11%), 53% female, 88% from a comprehensive cancer center (CCC), and 47% in practice for >15 years.

48% reported that they would discuss unfunded treatments if recommended in guidelines even if not Health Canada (HC) approved, while 50% would only do so for HC approved treatments. Only 2% of respondents would never discuss unfunded treatments. Per Table 1, respondents in practice >15 years were significantly less likely to discuss treatments that are not HC approved compared to those in practice < 5years: OR 0.14, p=0.002. Other variables were not statistically significant.

Main predictors of increased likelihood of discussing unfunded treatments: availability of a manufacturer compassionate access or co-pay program, patient willingness to pursue self-pay, and if the patient has private insurance. 90% indicated moderate to extreme levels of concern regarding the future of Canadian cancer drug funding.

	OR (95% CI)	p-value
Ontario vs BC	1.53 (0.47-4.97)	0.47
Community vs CCC	0.17 (0.03-0.91)	0.04
Male vs Female	2.35 (0.92-5.97)	0.07
Years in practice >15y vs <5y	0.14 (0.04-0.50)	0.002*
Workload (No/Min vs Mod/Sev)	0.42 (0.15-1.16)	0.09
Institution permits unfunded treatment, no vs yes	0.49 (0.14-1.74)	0.27
Drug access navigator available, no vs yes	2.32 (0.52-10.15)	0.28

Table 1. Likelihood of discussing unfunded, non-HC approved treatments

CONCLUSIONS

Given fiscal limitations within our publicly funded system, an increasing proportion of cancer therapies may not receive approval for public funding. Our survey reveals variability in practice with respect to discussing unfunded therapies, with years in practice as a significant determinant of willingness to discuss.

ORAL PRESENTATION

11_CAMO_2021

PROGNOSTIC PATHOLOGICAL AND CLINICAL FACTORS ASSOCIATED WITH OVERALL SURVIVAL IN METASTATIC MELANOMA UNDERGOING ANTI PD-1 TREATMENT

Kim Koczka[1], Rodrigo Rigo[1], Eugene Batuyong[2], Mohammed Asad[2], Aleksi Suo[1], Edwin Wang[2] and Tina Cheng[1]
1. Department of Oncology, University of Calgary, Calgary Alberta, Canada.
2. Cumming School of Medicine, University of Calgary, Calgary AB, Canada.

BACKGROUND

Anti PD-1 immunotherapy has revolutionized metastatic melanoma treatment, as first line monotherapy or in combination with Ipilimumab. Up to 40% of patients will progress within 3 months, with limited evidence on who derives benefit from immunotherapy. We report clinical and pathological prognostic factors from a multi-institutional cohort.

METHODS

Patients between 2014-2017 treated with Nivolumab and Pembrolizumab were identified from a provincial pharmacy database in Alberta, Canada. All patients had unresectable stage III or IV melanoma. Patient characteristics, investigations, treatment and clinical outcomes were obtained from electronic medical records. We utilized Cox regression and Kaplan-Meier methods to analyze progression free survival (PFS) and overall survival (OS).

RESULTS

143 patients with either cutaneous (114) or primary unknown (29) melanoma were identified. Immunotherapy was median second line treatment and patients received a median of 7 doses. The overall response rate was 33%, with median follow up of 25 months. Ulcerated primary tumors had a lower mOS of 30 months vs. 49 months (p=0.042). Other pathologic factors (including Breslow, tumor infiltrating leukocytes, mitosis) were not associated with PFS or OS. Clinical factors associated with worsened mPFS and mOS were liver metastases, >3 sites of disease, and any visceral disease. Elevated LDH, platelets, neutrophils, and lower hemoglobin, lymphocytes, and a neutrophil/lymphocyte ratio were associated with worse mPFS and mOS. We identified 4 prognostic subgroups using LDH and number of visceral sites (Table 1) which was statistically significant for mPFS and mOS.

CONCLUSION

Ulcerated primary tumors, liver metastasis, and more sites of disease had worse mPFS and mOS. We identified prognostic clinical factors associated with mPFS and mOS, along with 4 subgroups of patients.

TABLE 1

	Normal LDH, < 3 visceral sites	Normal LDH, $\geq$ 3 visceral sites	LDH 1-2x ULN	LDH > 2x ULN
mPFS (months)	32.3	16.9	8.5	4.8
mOS (months)	84.3	40.1	20.0	8.7

ORAL PRESENTATION

EFFICACY OF PERIOPERATIVE CHEMOTHERAPY IN RESECTED COLORECTAL LIVER METASTASES: A SYSTEMATIC REVIEW AND META-ANALYSIS

Nicholas A. Bosma[1, 2], MD MSc, Alysha R. Keehn[3, 4], MD, Richard Lee-Ying[1, 2], MD MPH, Anthony R. MacLean[3], MD, Darren M. Brenner[2, 4], PhD

[1] Department of Medicine, University of Calgary; [2] Department of Oncology, University of Calgary; [3] Department of Surgery, University of Calgary; [4] Department of Community Health Sciences, University of Calgary

BACKGROUND

Nearly half of patients with colorectal cancer develop liver metastases. Radical resection of colorectal liver metastases (CRLM) offers the best chance of cure, significantly improving 5-year survival. Recurrence of metastatic disease is common, occurring in 60% or more of patients. Clinical equipoise exists regarding the role of perioperative chemotherapy in patients with resected CRLM and the optimal regimen and sequencing of chemotherapy remain to be elucidated for this population.

OBJECTIVE

To investigate the efficacy of perioperative chemotherapy in patients that have undergone curative-intent resection of CRLM.

METHODS

A systematic review and meta-analysis was completed of randomized controlled trials (RCTs) comparing perioperative chemotherapy to surgery alone in patients with resected CRLM. MEDLINE (Ovid), EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) databases were searched as well as abstracts published within the last 5 years from the American Society of Clinical Oncology (ASCO) and the European Society for Medical Oncology (ESMO) conferences. A meta-analysis was performed pooling the hazard ratios for disease-free survival (DFS) and overall survival (OS), using a random-effects model.

RESULTS

A total of five, phase 3, open-label RCTs were included, resulting in a pooled analysis of 1,119 of the total 1,146 enrolled patients. 559 patients were randomized to perioperative chemotherapy and 560 to surgery alone. Pooled estimates demonstrated a statistically significant improvement in DFS (HR 0.71, 95% CI: 0.61-0.82; $p<0.001$) but not OS (HR 0.87, 95% CI: 0.73-1.04; $p=0.136$).

CONCLUSION

Perioperative chemotherapy in the setting of resected CRLM was associated with an improvement in DFS, however this did not translate into an OS benefit. Poor compliance to post-hepatectomy oxaliplatin-based chemotherapy regimens was identified. Further investigation into the optimal regimen and sequencing of perioperative chemotherapy is justified.

RAPID FIRE PRESENTATION

13_CAMO_2021

EFFICACY AND TOXICITY OF COMBINED INHIBITION OF EGFR AND VEGFR IN ADVANCED NON-SMALL-CELL LUNG CANCER PATIENTS HARBORING ACTIVATING EGFR MUTATIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Jasna Deluce[1,2,3], David Maj[1,3], Gabriel Boldt[2,3], Daniel Breadner[1,2,3] and Jacques Rapheal[1,2,3]
[1]Schulich School of Medicine and Dentistry, London, Ont.
[2]London Regional Cancer Program, Division of Medical Oncology, London, Ont.
[3]London Health Sciences Centre, London, Ont.

BACKGROUND

Dual inhibition of epidermal growth factor receptor (EGFR) and vascular endothelial growth factor (VEGF) pathways have demonstrated promising results for treatment of advanced non-small cell lung cancer (NSCLC). We conduced a systematic review and meta-analysis to assess the efficacy and toxicity of the combined treatment with EGFR tyrosine kinase inhibitors (TKIs) and VEGF monoclonal antibodies (MABs) for advanced NSCLC patients harboring activating EGFR mutations, in comparison EGFR TKIs alone.

METHODS

The electronic databases PubMed, Cochrane and EMBASE, were searched for relevant randomized trials between 2000 and 2019. The primary endpoints were overall survival (OS) and progression-free survival (PFS). Secondary endpoints included objective response rate (ORR), disease control rate (DCR), and grade 3 or higher adverse events (AEs). Pooled hazard ratios (HR) for OS and PFS and odds ratios (OR) for ORR, DCR and toxicity were meta-analyzed using the generic inverse variance and the Mantel-Haenszel methods. Random-effect models were used to compute pooled estimates. Subgroup analyses compared PFS by gender, age, smoking status, type of EGFR mutation, intra-cranial disease and ECOG status.

RESULTS

A total of 1,246 patients from 6 trials were evaluated for analyses. The combination treatment decreased the risk of disease progression (PFS) (HR=0.64; 95%CI, 0.55-0.75), but had no effect on OS compared to EGFR inhibition alone (HR=0.90; 95%CI, 0.68-1.19). There was a significantly increased number of AEs reported in the dual treatment arm (OR=3.55; 95%CI 2.74-4.59), with proteinuria (OR=14.55; 95%CI 4.47-47.4) and hypertension (OR=7.02; 95%CI 4.73-10.43) being the most significantly increased AEs. Furthermore, no difference in ORR and DCR was found. The PFS benefit was consistent across all subgroups.

CONCLUSIONS

This study suggests combined inhibition of EGFR and VEGF pathways significantly improves PFS, with no interim OS benefit, and increases AEs. Mature OS data are needed to strengthen these results along with results from newer trials exploring this strategy with 3rd generation EGFR-TKIs.

RAPID FIRE PRESENTATION

14_CAMO_2021
PD-L1 EXPRESSION IN BREAST CANCER BRAIN METASTASES

Rania Chehade[1], Maleeha A. Qazi[2], Sharon Nofech-Mozes[3], Katarzyna J. Jerzak[4]
[1] Department of Medical Oncology, Faculty of Medicine, University of Toronto, Toronto, ON
[2] Faculty of Medicine, University of Toronto, Toronto, ON
[3] Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON
[4] Odette Cancer Centre, Sunnybrook Health Sciences Centre, Toronto, ON

BACKGROUND

Brain metastases (BrM) are a major cause of morbidity and mortality in women with breast cancer. Immunotherapy has the potential for intracranial efficacy among patients with breast cancer BrM since intracranial response to immunotherapy has been observed in other solid tumors. The aim of the study is to analyze the immunohistochemical expression of programmed death ligand 1 (PD-L1), a predictive biomarker of response to immunotherapy, in breast cancer BrMs.

METHODS

A retrospective cohort study of consecutive patients with metastatic breast cancer BrM who underwent surgery for BrM at Sunnybrook Health Sciences Centre between July 1999 and June 2013 were identified through the Anatomic Pathology departmental database. A tissue microarray using 1um cores was obtained. PD-L1 expression by immunohistochemistry (IHC) was assessed on BrM samples in triplicate; PD-L1 positive status was defined as PD-L1 expression ≥1% on tumor infiltrating cells as a percentage of tumor area using Ventana SP142 antibody. Estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor (HER2) status was determined using 2018 ASCO/CAP guidelines.

RESULTS

The median patient age at the time of BrM diagnosis was 53 (range 32-85). In our overall cohort, PD-L1 expression was identified in 9 out 61 (14.7%) breast cancer BrM. ER, PR and HER2 status was available for BrM in 60 out of 61 patients. Patients with triple negative breast cancer were most likely (n= 3/12, 25%) and those with HER2+ breast cancer were least likely (n=3/28, 10.7%) to have PD-L1 positive BrM. Among patients with hormone receptor positive/HER2- breast cancer, 15% (n=3/20) of BrM were PD-L1 positive.

CONCLUSION

One in 7 patients in our cohort had PD-L1 positive BrM; this proportion was highest (25%) among those with triple negative disease. Hence, there is rationale to include patients with breast cancer BrM in clinical trials evaluating efficacy of immunotherapy.

RAPID FIRE PRESENTATION

OUTCOMES OF ELDERLY PATIENTS WITH UNRESECTABLE STAGE 3 NSCLC TREATED WITH DEFINITIVE CHEMORADIATION WITH OR WITHOUT DURVALUMAB

Malcolm Ryan, Jessica Weiss, Aline Fusco Fares, Ming Sound Tsao, Geoffrey Liu, Penelope A Bradbury, Natasha B Leighl, Frances A Shepherd, Adrian G Sacher, Sally CM Lau
Princess Margaret Cancer Centre, University Health Network, University of Toronto, ON M5G 2M9

INTRODUCTION

The recent addition of durvalumab after chemoradiation (CRT) in unresectable stage 3 non-small cell lung cancer (NSCLC) significantly improves survival. The benefit of CRT in elderly patients is controversial given its increased toxicity. However, patients cannot receive durvalumab unless CRT was given. We sought to investigate the outcomes of elderly patients treated with CRT.

METHODS

We conducted a review of all stage 3 NSCLC patients treated with CRT between 2018 and 2020. Patients were analyzed based on age: <70 years, ≥70 years. Endpoints evaluated were treatment patterns, toxicity, progression free survival (PFS) and overall survival (OS).

RESULTS

We identified a total of 106 patients: 40 patients ≥70 years (70-89) and 66 patients <70 years (34-69). Patients were fit: ECOG 0-1 (98%/99%), mean Charlson comorbidity index (CCI) (1.3/1.1) in elderly vs young patients; p>0.05. All other baseline characteristics including PD-L1 expression were similar. The chemotherapy regimens and dose intensity were similar. However, patients ≥70 were less likely to receive all planned number of cycles (p=0.05). There were 2 treatment related deaths from CRT in young and none in the elderly patients. At the completion of CRT, 72% of elderly and 70% of young patients received durvalumab. The incidence of grade ≥3 immune-related adverse events was 8% in elderly patients and 5% young patients; p=0.68. Median PFS was similar between elderly and young patients (17.6 vs 10.2 months respectively; p=0.08), even after adjusting for the CCI (HR 0.60; p=0.08). The 12-month OS rates are also similar (p=0.93): 86% in elderly and 83% in young patients.

CONCLUSIONS

Definitive CRT followed by durvalumab is tolerable in elderly patients ≥70 years with a non-significant trend towards better PFS in elderly patients. All patients should undergo comprehensive oncologic assessment to determine if curative intent treatment can be delivered to avoid undertreatment.

RAPID FIRE PRESENTATION

16_CAMO_2021

IMPACT OF SMOKING ON RESPONSE TO IMMUNOTHERAPY IN *KRAS* MUTANT NON-SMALL CELL LUNG CANCER

Kieran Sharma, Shelley Kuang, Ming Sound Tsao, Frances A Shepherd, Penelope A Bradbury, Geoffrey Liu, Natasha B Leighl, Adrian G Sacher, Sally CM Lau
Princess Margaret Cancer Centre, University Health Network, University of Toronto, ON

BACKGROUND

Immune checkpoint inhibitors (ICI) are highly effective in the management of advanced non-small cell lung cancer (NSCLC). Non-smokers appear to derive less benefit from ICI, often attributed to the higher likelihood of a primary driver mutation. However, the variation in responses to ICI cannot be explained by oncogene addiction alone. We sought to investigate the impact of smoking among *KRAS* driven NSCLC.

METHODS

We conducted a review of patients with *KRAS* mutant advanced NSCLC who have received at least one cycle of ICI. Primary outcomes were overall response rates (ORR) and progression free survival (PFS).

RESULTS

We identified 91 patients with *KRAS* mutant NSCLC who were treated with ICI: 23 never/53 former/15 current smokers with similar distributions of age, ethnicity, and tumor histology. There was trend towards a higher proportion of females among never smokers (p=0.09). Smoking history also was associated with a trend (p=0.06) to high PD-L1 expression (≥50%): 27%/53%/62% and significantly higher rates of TP53 co-mutations: 36%/46%/80% (p=0.03) among never/former/current smokers, respectively. Transversion mutations account for 76%/81%/93% of never/former/current smokers; p=0.13. ORR were higher among smokers: 13%/34%/80% among never/former/current smokers (p=0.001) and remained significant even after adjusting for PD-L1 expression. Median PFS was associated with smoking on univariate analysis (2.9 vs. 4.9 vs. 26.8 months in never/former/current smokers; p=0.02), but the association was lost after adjusting for PD-L1 expression.

CONCLUSION

Never smokers with *KRAS* mutant NSCLC appear to derive less benefit from ICI. The differences in PD-L1 expression and rates of TP53 co-mutations, which are surrogate markers of response, suggest that the underlying tumor immune microenvironment (TME) among smokers and non-smokers, even in the presence of the same oncogene, is fundamentally different. Correlative efforts using serial plasma samples are ongoing to help understand the impact of smoking on the TME and response to ICI.

RAPID FIRE PRESENTATION

17_CAMO_2021

OGIVRI VERSUS HERCEPTIN – "REAL WORLD" PCR RATES IN PATIENTS WITH HER2+ BREAST CANCER TREATED WITH NEOADJUVANT CHEMOTHERAPY PLUS TRASTUZUMAB FROM ALBERTA, CANADA

Charlie Yang[1,2], Raida M Khwaja[1,3], Karen King[3], Nancy A Nixon[2], Patricia A. Tang[2], Sasha Lupichuk[2]

[1] Co-first authors

[2] Department of Medical Oncology, University of Calgary, Calgary, Alberta

[3] Department of Medical Oncology, University of Alberta, Edmonton, Alberta

OBJECTIVE

This retrospective study compared the pathological complete response (pCR) rates of trastuzumab-dkst (Ogivri) to Herceptin in the neoadjuvant setting for HER2+ early breast cancer (EBC) in Alberta.

METHODS

Neoadjuvant patients with HER2+ EBC treated with Herceptin from November 2018 -October 2019 and Ogivri from December 2019 - September 2020 were identified. There was no crossover between products. Logistic regression was used to control for variables potentially associated with pCR: trastuzumab product (Ogivri vs Herceptin), age (<40 vs 40+), pre-operative T (T1/2 vs T3/4) and N stage (negative vs positive), grade (I/II vs III), HR status (ER and/or PR positive vs ER/PR negative), HER2 (3+ vs SISH+), chemotherapy (anthracycline containing vs not), and chemotherapy completion (yes vs no).

RESULTS

136 patients were identified (56% Herceptin; 43% Ogivri) and there were no significant differences in baseline characteristics except more patients in the Ogivri group were clinically N negative; 39% vs 14.3% Herceptin (p=0.001). pCR was 35.6% for patients treated with Ogivri versus 40.3% with Herceptin (p =0.598). In the logistic regression model, there was no significant difference in the odds of a pCR for patients treated with Ogivri versus Herceptin after controlling for the variables selected *a priori* (OR 1.1, 95% CI 0.5-2.4, p=0.850). There was a trend for decreased odds of pCR for anthracycline use (OR 0.72 95% CI 0.3-1.6, p=0.417).

CONCLUSIONS

pCR rates were similar for patients treated with Ogivri compared to Herceptin in our real world study of HER2+ neoadjuvant EBC and comparable to pivotal phase 3 trials. For a 65 kg patient, the estimated cost savings of Ogivri therapy is $22,000, and approximately $240-300 for a non-anthracycline chemotherapy backbone.

RAPID FIRE PRESENTATION

18_CAMO_2021

THE EFFECT OF THE COVID-19 PANDEMIC ON THE EVOLUTION OF CANCER CARE IN NOVA SCOTIA

Margaret Sheridan, Bruce Colwell, Arik Drucker, Robyn Macfarlane, Daniel Rayson, Stephanie Snow, Lori Wood, and Ravi Ramjeesingh
Division of Medical Oncology, Dalhousie University, Halifax, Nova Scotia

OBJECTIVE

To review Medical Oncology (MO) workload in a local context and evaluate the impact of COVID-19.

METHODS

All patient encounters (new patient consults, follow-up visits (F/U), telephone toxicity assessments, and chart checks) were identified over a 3-month period (February through April) across a 6-year interval (2014-2019) and extrapolated to derive an estimate of annual workload. This data was then analyzed based on type of encounter and disease site. The same data was collected over one month from mid-March to mid-April 2020, during the province-wide COVID-19 lockdown measures.

RESULTS

In 2014, there were an estimated 2,052 new consults, which increased to 2,484 by 2019 (21.1% increase). The number of F/U increased from 9,312 to 10,532 (13.1%). Virtual care (VC), which includes chart reviews and virtual consults, and telephone toxicities increased by 24.6% and 238.1% respectively over a similar time span.

VC accounted for 41.2% of the care provided in 2018 and 45.2% of the care provided in 2019, which increased to 79.9% in 2020, during a sampled time period during the COVID lockdown. A proportional change was observed amongst different treatment sites.

VC provided by immunotherapy treaters increased from 49.9% in 2018 to 53.8% in 2019 and to 85.3% in 2020. A larger increase was seen in the non-immunotherapy treaters, who provided only 34.1% of VC in 2018, 34.8% in 2019, but 73.5% in 2020, more than doubled what was observed in the previous two years.

CONCLUSIONS

MO workload has increased over time, with more new consults, increasing time spent in follow up and delivery of VC, due to the changing landscape of cancer care and now more poignantly, in the wake of the COVID-19 pandemic. This metric requires recognition in effort to ensure delivery of optimal patient care moving forward.

RAPID FIRE PRESENTATION

19_CAMO_2021

POPULATION-BASED IMPACTS OF NEW THERAPIES ON OUTCOMES FOR STAGE IV NON-SMALL CELL LUNG CANCER

Rebekah Rittberg[1,2], Oliver Bucher[3], Lin Xue[3], Zeb Aurangzeb[3], Shantanu Banerji[1,2,4], David E. Dawe[1,2,4]

1 Department of Internal Medicine, University of Manitoba, Winnipeg, MB, Canada
2 CancerCare Manitoba, Department of Hematology and Medical Oncology, Winnipeg, MB, Canada
3 CancerCare Manitoba, Department of Epidemiology, Winnipeg, MB, Canada
4 Research Institute in Oncology and Hematology at CancerCare Manitoba, Winnipeg, MB, Canada

OBJECTIVE

Evaluate real world, population-based treatment patterns and outcomes of Stage IV non-small cell lung cancer (NSCLC) to assess changes in treatment patterns and survival.

METHODS

A retrospective cohort analysis was completed to evaluate *de novo* Stage IV NSCLC diagnosed in Manitoba from 2006 to 2015. We evaluated treatment received (not seen by specialist, saw a specialist but did not receive therapy, radiation therapy (RT) only, and systemic therapy (mutation unknown and known)) and treatment era of diagnosis (2006-2009, 2010-2013 and 2014-2015). Multivariable logistic regression assessed systemic therapy predictors. Kaplan-Meier curve and Cox proportional hazard models evaluated overall survival (OS).

RESULTS

3,601 patients were diagnosed with Stage IV NSCLC, 53% male. Only 21% received systemic therapy, mean age of 62. Within the cohort, 973 (27%) patients did not see a specialist, 610 (17%) saw a specialist but did not receive therapy, 1248 (35%) only received RT, and 771 (21%) received systemic therapy (17% mutation status unknown and 4% known). Younger patients and those with confirmed histology were more likely to see a specialist and receive treatment, each (p<0.001). Patients who received systemic therapy had lower comorbidity and higher income quintile, each (p<0.001). Median OS did not differ between treatment era with median OS of 3.0, 2.9 and 2.8 months for 2006-2009, 2010-2013 and 2014-2015 respectively, p=0.082. When survival analysis was restricted to patients who received systemic therapy, median OS improved by era to 10.9, 11.2 and 15.6 months respectively, p=0.001. Variables found to be independently associated with survival included treatment type, age, sex and comorbidity.

CONCLUSION

Improved systemic therapy and molecular testing has improved OS for patients who receive systemic therapy. However, due to the large proportion of Stage IV NSCLC patients who never receive systemic therapy we do not see improved survival at a population level between treatment eras.

RAPID FIRE PRESENTATION

20_CAMO_2021

INCREASED SURVIVAL IN PATIENTS WITH MELANOMA WHO DEVELOP IMMUNE RELATED ADVERSE EVENTS: A REAL-WORLD RETROSPECTIVE STUDY

Ryan Holstead[1], Adi Kartolo[1], Wilma Hopman[2], Tara Baetz[1]

[1]Department of Oncology, Queen's University, Kingston, Ontario
[2] Department of Medicine, Queen's University, Kingston, Ontario

Some clinical trials have described improved outcomes in patients who develop immune-related adverse events (irAEs), while receiving immune checkpoint inhibitors for advanced melanoma. It is unknown if this effect would be seen in a real world population.

This is a single-center retrospective analysis of all patients receiving single agent PD -1 inhibitor for unresectable stage III or stage IV melanoma between 2012 and 2018. The majority of patients had cutaneous melanoma and were elderly (put in median and range). 33.3% were BRAF mutated and 22% of patients had brain metastases at presentation. Of the 87 patients included in this analysis, 48 (55%) developed at least one irAE. Dermatologic toxicities were the most common irAE. The median time to develop any irAE was 12 weeks. Only one patient died of immune related toxicity.

Overall survival in the population of patients that had an irAE was significantly greater than those that did not have any toxicity (21.1 vs 7.5 months; p<.001). The development of endocrine toxicity had the strongest correlation with survival.

 A high grade of toxicity (NCI CTC V.5) did not correlate with survival outcome and the greatest correlation was seen in patients with grade I toxicity. The development of multiple toxicities did not correlate with survival. In patients with multiple toxicities the type of irAE that presented initially did not impact the outcome. These findings add to the growing body of literature suggesting an association between immune related toxicity and immune-checkpoint inhibitor efficacy, while suggesting that this benefit may depend on type of toxicity and severity.