Background Immune-related adverse events (irAEs) are serious side effects of immune checkpoint inhibitors (ICIs) for patients with advanced cancer. Understanding the epidemiology and risk factors for severe irAEs would be beneficial for patients and clinicians.

Methods We performed a retrospective review of cancer patients treated with ICIs using un-identifiable claims data from a nationwide US health insurance plan from January 3rd, 2011 to December 31st, 2019. Patients with an identified primary cancer and at least one administration of an ICI were included in the study. We defined severe irAE as any inpatient hospitalization with new immunosuppression within 2 years after initiation of ICI. The main outcomes were incidence of severe irAE in ICI therapy and factors associated with severe irAE occurrence. Multivariable logistic regression, including Charlson comorbidity index, age, gender, primary cancer, region, and zip code average income and unemployment, was used to model risk factors for severe irAE (table 1).

Results There were 14,378 patients followed over 19,177 patient-years identified with a primary cancer and at least 1 administration of ICI. 504 (3.5%) patients developed a severe irAE. The incidence of severe irAEs per patient ICI treatment year was 2.6%, rising from 0% (0/71) in 2011 to 3.7% (93/2486) in 2016 (figure 1). Combination immunotherapy (OR: 2.44, p < 0.001) and younger age (OR: 0.77, p < 0.001) were associated with increased odds of developing severe irAEs, whereas patients with non-lung cancer were associated with decreased odds of irAEs (melanoma OR: 0.70, p = 0.01, renal cell carcinoma OR: 0.71, p = 0.03, other cancers OR: 0.50, p < 0.001; figure 1). Sex, region, zip code income, and zip-code imputed unemployment were not associated with severe irAE incidence. Prednisone (72%) and methylprednisone (25%) were the most common immunosuppressive treatments identified in irAE hospitalizations.

Conclusions We found that 3.5% of patients initiating ICI therapy experienced severe irAEs requiring hospitalization and immunosuppression. The odds of severe irAEs were higher with younger age, treatment with combination ICI therapy (CTLA-4 and PD-1 or PD-L1), and lower for other cancers compared with patients on PD-1 or PD-L1 inhibitors with lung cancer. This evidence from the first nationwide study of severe irAEs in the US identified the real-world epidemiology, risk factors, and treatment patterns of severe irAEs in the US which may guide treatment selection and decisions for patients and clinicians.

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CUTANEOUS ADVERSE EVENTS OF IMMUNE CHECKPOINT INHIBITOR THERAPY: INCIDENCE AND TYPES OF REACTIVE DERMATOSES

Thomas Le*, Subhi Kaul, Shannon Wongrubulil, Laura Cappelli, Jarushka Naidoo, Yevgeniy Semenov, Shawn Kwatra.
Johns Hopkins University School of Medicine, Baltimore, MD, USA; Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University, Baltimore, MD, USA; Harvard Medical School, Cambridge, MA, USA

Background Cutaneous toxicities are a common and potentially serious complication of programmed cell death receptor PD-1 immune checkpoint inhibitor (anti-PD-1 ICI) therapy. These cutaneous immune-related adverse events (irAEs) have been reported in up to one-third of treated patients, and are usually the first adverse event to occur with immune checkpoint inhibitor use. Due to non-specific reporting in many anti-PD-1 clinical trials, little data is available on the real-world incidence and morphology of cutaneous irAEs. Understanding the spectrum of cutaneous adverse events in real-world clinical environments is necessary to support clinical awareness, diagnosis, and management when undergoing anti-PD-1 therapy. We aimed to describe the incidence of a known spectrum of skin dermatoses in the setting of ICI, and also identify the risk of these adverse events compared with the general population.

Methods This was a cross-sectional study of anti-PD-1 (pembrolizumab or nivolumab) treated patients at a tertiary healthcare institution from September 2014 to November 2018. Inflammatory dermatoses occurring in the setting of anti-PD-1 therapy (pembrolizumab or nivolumab) was compiled using our institutional experience with ICIs and case studies and...
reports on PUBMED. Selected dermatologic events following immunotherapy were identified in the electronic medical record. Unadjusted odds ratios (OR) for the development of a given cutaneous event was calculated by comparison to the non-ICI general population.

Results Of the 1,857 patients treated with anti-PD-1 ICIs, there were 1,079 patients treated with nivolumab, 821 patients treated with pembrolizumab, and 43 patients treated with both pembrolizumab and nivolumab. There were 254/1857 (13.7%) patients that developed one of the 28 different dermatoses identified from review of the anti-PD-1 ICIs. Compared with the general population, patients treated with anti-PD-1 had a greater risk for development of mucositis (OR 65.7, 95% CI 35.0-123.3), xerostomia (OR 11.3, 95% CI 8.4-16.8), pruritus (11.3, 95% CI 8.9-14.3), and lichen planus/lichenoid dermatitis (OR 10.7, 95% CI 5.6-20.7) compared to the control group.

Conclusions We report the frequency of dermatoses encountered in the setting of ICI therapy, both commonly (pruritus, rash, vitiligo) and more rarely reported (scleroderma, urticaria). As nivolumab and pembrolizumab currently make up the bulk of approvals for ICI therapy, this analysis of real-world irAE incidence will be of use to treatment teams to improve quality of life and ensure ICI therapy adherence. Furthermore, this analysis sets the stage for future in-depth investigation of these cutaneous toxicities, including dose-response relationships, prognostic information from cutaneous events, and optimal treatment strategies.

Ethics Approval This study did not require IRB approval, due to the use of anonymized and de-identified aggregate-level data.

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PRELIMINARY REVIEW OF DIABETES MELLITUS INCIDENCE IN PATIENTS TREATED WITH IMMUNE CHECKPOINT INHIBITORS (ICI) THERAPY – ROSWELL PARK COMPREHENSIVE CANCER CENTER (RPCCC) EXPERIENCE

1Zhen Zhang*, 1Grazyna Riebandt, 1Rajeev Sharma, 1Lamya Hamad, 2Jordan Scott, 3Laurie Plexinski, 1Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; 4Ysouville School of Pharmacy, Buffalo, NY, USA; 5University at Buffalo, Buffalo, NY, USA

Background Immune checkpoint inhibitor (ICI) therapy has revolutionized cancer treatment and has become a standard of care. There are now numerous FDA approved indications for ICIs and an increasing number of patients receiving these treatments, which has led to an increase in the risk of immune-related adverse events (irAEs) including endocrinopaties. Diabetes mellitus is a rare irAE of ICI therapy with an approximate incidence of 1-2%. There is paucity of data in literature about incidence, characteristics and possible predictive factors of ICI-induced diabetes mellitus. Due to limited data on ICI-induced diabetes, we conducted a retrospective review of patients who received ICI therapy at RPCCC and developed diabetes mellitus. The goal of this study is to report incidence and characteristics of new onset and worsening of diabetes in patients treated with ICI therapy.

Methods We conducted a retrospective chart review of patients who received ICIs treatment from January 1st, 2010 to May 15th, 2020. We identified patients with newly diagnosed diabetes and worsening of preexisting diabetes. Newly diagnosed diabetes was defined as fasting blood glucose \( \geq 126 \) or hemoglobin A1c (HbA1c) \( \geq 6.5 \), random blood glucose \( \geq 200 \) mg/dL with symptoms or 2-hour blood glucose \( \geq 200 \) mg/dL on oral glucose tolerance test. Worsening of preexisting diabetes, defined as more than 0.5% increase in absolute HbA1c value in preceding 3-6 months or need for insulin in stable patients with diabetes on oral hypoglycemic agents. Subjects with pre-existing type 1 diabetes mellitus or on systemic corticosteroids for more than 1-week duration prior to diagnosis of diabetes mellitus were excluded.

Results Among 2,382 reviewed patients who received one or multiple ICIs, 15 patients developed new onset of diabetes and 12 patients experienced worsening of pre-existing Type 2 diabetes. In these 27 patients, 8 presented with diabetic ketoacidosis. Median time to new onset diabetes or worsening diabetes from ICI therapy initiation was 19 weeks, ranging from 2 to 320 weeks. Positive autoantibodies were found in 3 patients, among who 2 patients with positive Glutamic Acid Decarboxylase (GAD65) antibodies and one patient with positive insulin autoantibodies (IAA).

Conclusions The incidence of new onset diabetes and worsening diabetes in patients treated with ICI therapy was 1.1%.

Ethics Approval The study was approved by Roswell Park Comprehensive Cancer Center’s Ethics Board, IRB ID STUDY0001278/BDR 129520.

Consent exempt

REFERENCES

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Novel single-agent immunotherapies

LAMP1 TARGETING OF THE LARGE T ANTIGEN OF MERKEL CELL POLYOMAVIRUS ELICITS POTENT CD4+ T CELL RESPONSES AND PREVENTS TUMOR GROWTH

1Claire Bucht Rosean*, 1Claire Bucht Rosean, 1Pratima Sinha, 2David Koelle, 3Paul Nghiem, 1Teri Helland. 1Immunomic Therapeutics, Inc, Rockville, MD, USA; 2University of Washington, Seattle, WA, USA

Background The majority of Merkel cell carcinomas (MCC), a rare and highly-aggressive type of neuroendocrine skin cancer, are associated with Merkel cell polyomavirus (MCPyV) infection. MCPyV integrates into the host genome, resulting in expression of a truncated form of the viral large T antigen (LT) in infected cells, and making LT an attractive target for therapeutic cancer vaccines. While induction of tumor-reactive CD8+ T cells is a major goal of cancer therapy, CD4+ T cells provide essential support to CD8+ T cells by promoting their expression of cytotoxic effector molecules and increasing their migratory capacity. Cytokines secreted by CD4+ T cells, such as IFNγ, can also exert desirable effects on the tumor microenvironment. Therefore, we set out to design a cancer vaccine that promotes potent, antigen-specific CD4+ T cell responses to MCPyV-LT.

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