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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Novel single-agent immunotherapies

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

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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.

Abstracts

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

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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 endocrinopathies. 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 ≥ 126 or hemoglobin A1c (HbA1c) ≥ 6.5, random blood glucose ≥ 200 mg/dL with symptoms or 2-hour blood glucose ≥ 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 treatment 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 STUDY00001278/BDR 129520.

Consent exempt

REFERENCES

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