CLINICAL AND DEMOGRAPHIC FACTORS ASSOCIATED WITH IMMUNE RELATED ADVERSE EVENTS AMONG THOSE TREATED WITH IMMUNE CHECKPOINT INHIBITORS

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**Background** Immune-checkpoint inhibitors including monoclonal antibodies targeting CTLA-4, PD-1, and PD-L1, enhance intrinsic antitumor immunity and improve survival in various malignancies. Despite their effectiveness, these promising new treatments have led to a spectrum of immune-related adverse events (irAE) with severity ranging from benign to even deadly. This study aimed to explore the association between clinical and demographic factors and the severity of irAEs.

**Methods** We retrospectively identified 252 cancer patients who received immune-checkpoint inhibitors between April 2011 and September 2020 at the University of Colorado Cancer Center. Patient data were de-identified and stored in a REDCap database. irAEs were graded using NCI CTCAE (version 4.0). Demographic, clinical, and treatment characteristics were stratified by irAE occurrence. Statistical tests, including Wilcoxon rank sum and Fisher’s exact test, assessed continuous and categorical variables, respectively. Logistic regression analyzed irAE rates, adjusting for demographic and clinical covariates. Chi-squared tests evaluated the association between AE grades and key variables. Ordinal logistic regression analyzed the relationship between treatment characteristics and the worst AE grades.

**Results** Among the 252 patients, 92 (37.4%) developed an irAE. Age, sex, and race did not exhibit significant confounding effects (table 1), thus they were not considered as covariates to be adjusted in the multivariate analysis (MVA). Overweight patients (BMI >30) had higher odds of irAE development compared to underweight patients (OR 4.88, 95% CI [1.15–26.59], p=0.04). When compared with skin cancers, patients with neuroendocrine tumors had higher odds of irAE development (OR 5.57, 95% CI [1.50–22.04], p=0.01) and patients with hematologic malignancies showed a trend toward increased odds of irAEs (OR 0.96–28.47), p=0.05), while those with pulmonary cancers showed a trend toward decreased odds of irAE development (OR 0.21, 95% CI [0.03–0.91], p=0.06). Previous chemotherapy treatment reduced the odds of subsequent irAE compared to no prior chemotherapy (OR 0.38, 95% CI [0.16–0.85], p = 0.02). Previous targeted therapy reduced the odds of developing more severe AEs (p=0.01), but this effect was not significant after adjusting for immunotherapy regimen (OR 0.41, 95% CI [0.14–1.12], p=0.08). As expected, patients who received immunotherapy without CTLA-4 had lower odds of developing irAEs than those receiving CTLA-4 (OR 0.22, 95% CI [0.10–0.46], p<0.01), and lower odds of developing more severe AEs (OR 0.34, 95% CI [0.13–0.80], p=0.01).

**Conclusions** Patient body mass index category and neuroendocrine tumor type may identify patients at increased risk of irAE development, while prior chemotherapy may correlate with reduced risk.