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**Background** Type 1 diabetes mellitus (T1DM) is a rare but serious immune-related adverse event (irAE) of immune checkpoint inhibitors (ICIs). Our goal was to characterize treatment outcomes with ICI-induced T1DM through analysis of clinical and immunological data.

**Methods** This was a single-center case series of patients with solid tumors at Huntsman Cancer Institute (HCI) who received ICIs and subsequently had a new diagnosis of T1DM. The enterprise data warehouse at the University of Utah used ICD codes (ICD-10-CM E10 and ICD9-CM 250.01) to identify patients for chart review to confirm ICI-induced T1DM. Serial blood specimens were studied for proteomic and immunophenotypic changes.

**Results** Between April 14, 2011 and July 15, 2021, 37 of 2745 patients who received ICIs at HCI had a T1DM diagnosis after the first cycle. 8 were confirmed to have ICI-induced T1DM (0.3%), including 3 with melanoma. An additional 5 cases with melanoma were identified by chart review only (table 1). Average age at onset was 54.5 years. 10 of 13 patients received anti-PD1 monotherapy (6 pembrolizumab, 4 nivolumab), 2 received pembrolizumab plus chemotherapy or enzalutamide, and 1 received ipilimumab plus nivolumab. Only 1 received prior ICI (ipilimumab). Median time to onset was 6.4 months (range 0.7-13.7). 10 patients presented with diabetic ketoacidosis (77%) (table 2). Of 6 patients who had autoantibodies tested at onset, only one had elevated anti-glutamic acid decarboxylase. At median follow-up of 24.3 months (range 13.1-66.4), no melanoma patients had progressed nor died, including 6 who received adjuvant and 2 who received active treatments (1 complete response, 1 partial response). Median progression free survival and overall survival were not reached. The 5 patients with other cancers received active treatments (1 partial response, 2 stable disease and 2 disease progression), and 3 died. All patients became permanently insulin-dependent. Further analysis by Olink and CyTOF of serial blood (baseline, pre-irAE, peak-irAE) from 3 ICI-induced T1DM patients, and baseline blood from 6 patients who received anti-PD1 but did not develop irAE, is ongoing and will be presented. Preliminary data suggest lower IL6 and OSMR (in IL-6 signaling) in baseline samples from patients who developed T1DM, among other changes.

**Conclusions** Despite ICI-induced T1DM, patients with melanoma displayed excellent clinical response and survival. All cases were treated with anti-PD1 antibodies, highlighting the importance of PD-1 blockade in the pathogenesis of ICI-induced T1DM. Most of these patients had negative autoantibodies, suggesting a distinct mechanism of this irAE.2

**REFERENCES**
