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 ICD9CM 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 with melanoma 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