Background Checkpoint inhibitors (CPIs) targeting PD-1/PD-L1 and CTLA-4 have dramatically improved outcomes for a range of solid malignancies. irAEs from CPIs affect a wide range of tissues, vary in severity, and are difficult to predict. Multiple studies have reported on incidence of irAEs by immunotherapy type, but few have examined the association of irAEs with tumor histology or with sites of metastasis. This study aims to investigate the association between type and incidence of irAEs with type of solid tumor histology, as well as with sites of cancer metastasis.

Methods We performed a retrospective analysis of all patients with genitourinary (GU), melanoma, gastrointestinal (GI), and lung malignancies treated with CPI monotherapy at the University of California, Irvine using an outpatient oncology pharmacy database. Data was collected from 1/1/2020 to 6/30/2021. Patients were aged 18 years and older. Patients must have received at least one dose of a CPI agent. Patients who received CPI-containing combination therapy with chemotherapy or targeted therapy were excluded.

Results Of 423 patients on unique treatment lines in our data set, 268 patients received CPI monotherapy. irAEs were documented in 133 patients (49.6%). 71 patients (62.8%) required treatment with oral or intravenous steroids, and 42 patients (37.2%) received treatment with other supportive therapy. The incidence of irAEs based on tumor type is listed in table 1. Most common irAEs per tumor type were rash in GU malignancies (26.0%), colitis in melanoma (25.4%), rash in GI malignancies (29.3%), and pneumonitis in lung malignancies (60.0%). In patients with irAEs, 102 (76.7%) had metastatic disease and of those, 18 (17.6%) had an irAE involving a metastatic site (p<0.0001). In patients with irAEs involving the primary site of malignancy, 2 patients (4.7%) with renal cell carcinoma had nephritis, 12 patients (37.5%) with melanoma had dermatitis, and 2 patients (50%) with a lung malignancy had pneumonitis.

Conclusions This study examines the differences in type and incidence of irAEs across GU, melanoma, GI, and lung cancers treated with CPI monotherapy. We found differences in the incidence of irAEs as relevant to tumor histology. Further, there was a statistically significant increased incidence of irAEs involving a metastatic site. Additional studies are needed, including those with a larger sample, combination immunotherapy and chemotherapy, as well as with additional tumor histologies.

Ethics Approval Application #16536 for HS #2021-6843 titled, "Primary Cancer Histology and Sites of Metastatic Disease Correlate with Tissues Affected by Immune-Related Adverse Events" obtained approval by the University of California, Irvine Institutional Review Board. A waiver of consent was obtained as this study involved no more than minimal risk as it was a retrospective chart review.