2594 **Poster Session**

Cancer PD1/PD-L1 inhibitor efficacy as stratified by smoking status: A population large database study.

Zachary D. Urdang, SoHye Park, Ramez Philips, Hee-Soon Juon, Jennifer Maria Johnson, Ubaldo E. Martinez-Outschoorn, Joseph M. Curry; Departments of Otolaryngology and Clinical/Experimental Pharmacology - Thomas Jefferson University, Philadelphia, PA; Department of Medical Oncology Division of Population Health, Thomas Jefferson University, Philadelphia, PA; Department of Otolaryngology,Thomas Jefferson University, Philadelphia, PA; Department of Medical Oncology Division of Population Science, Thomas Jefferson University, Philadelphia, PA; Department of Medical Oncology, Thomas Jefferson University, Philadelphia, PA; Department of Otolaryngology, Thomas Jefferson University, Philadelphia, PA

Background: Delineating clinical factors that predict immune checkpoint inhibitor (ICI) cancer therapy response is a pressing need and smoking is a known factor. In this study we leveraged a large international (heavily US) database to perform the largest study to date for all cancers and major cancer subsites/types. **Methods:** Utilizing the TriNetX electronic health records database with 84.3M patients we tested the hypotheses that ICI response stratifies based on smoking, and continued smoking after ICI. Queries were constructed using billing codes for all cancer types treated with an ICI with and without smoking. The smoking cohort was subsequently sub-stratified for continuing vs cessation of smoking after ICI. Next, using ICI therapy as the index event, odds ratios (OR) with 95% confidence intervals for death, and treatment related secondary outcomes were calculated between 0.5-5 years after ICI treatment. Statistics were calculated using TriNetX's integrated statistical platform before and after 1:1 propensity score matching (PSM) for smoking related co-morbidities. **Results:** The OR for death after ICI therapy for smokers (*n* 13336) vs non-smokers (*n* 38973) for any cancer type was 1.27(1.21-1.34) and decreased to 1.11(1.04-1.19) after PSM. Further sub-stratifying the smoking cohort for continued vs cessation of smoking yielded ORs of 1.13(1.03-1.24) and 1.12(1.01-1.24) before and after PSM respectively. Secondary outcomes included ablative surgery, chemotherapy, radiation, and secondary neoplasm. ORs for receiving chemotherapy, and developing secondary neoplasm were most consistently statistically significant across comparisons. **Conclusions:** Smoking adversely potentiates cancer outcomes after ICI therapy. PSM for smoking related comorbid conditions decreased the magnitude of this association although the findings remained clinically and statistically significant. This highlights the key role in smoking related co-morbid conditions as prognostic clinical characteristics. Furthermore, this suggests that smoking affects ICI on a mechanistic/biological level beyond increasing burden of medical comorbidities. Lastly, as smoking cessation also improved outcomes after PSM this further suggests that washout of smoke toxins has a mechanistic/biological effect on ICI activity.
Research Sponsor: None.

Propensity score matching corrected	Alive	Deceased (between 0.5-5yrs after ICI)
Smoker	9,379	2,754
Non-Smoker	9,337	2,540

Odds ratio = 1.11(1.04-1.19)