Session: P-80. Tuberculosis and other Mycobacterial Infections

Background. Data on the efficacy and tolerability of latent tuberculosis infection (LTBI) treatment in cancer patients receiving checkpoint inhibitor immunotherapy (CPI) is limited. We sought to assess LTBI therapy and its adverse events and outcomes in patients treated with CPI.

Methods. We performed a retrospective cohort study at MD Anderson Cancer Center of adult patients, between April 2016 and May 2021, who were receiving CPI and were diagnosed with LTBI based on positive T-SPOT TB test. We then compared those patients treated with isoniazid (INH) 3mg/kg daily versus those that did not receive INH therapy.

Results. We identified 35 patients treated with CPI who had a diagnosis of LTBI. Patients were divided into 2 groups: CPI alone (23 patients, 65.7%) and CPI+INH (12 patients, 34.3%). The majority of patients in both groups had renal cell carcinoma (34.3%) and melanoma (17.1%). Nivolumab as monotherapy was the most commonly used CPI agent in both groups (37.1%), whereas nivolumab and ipilimumab combination was mainly used in the CPI group (34.7%) compared to CPI+INH group (8.3%). In the CPI+INH group, 7 patients (58.3%) developed moderate to severe hepatotoxicity that led to discontinuation of INH and CPI therapy versus none in the CPI group (p=0.001). There was no statistically significant difference in the alanine aminotransferase (ALT) at baseline between both groups (p=0.117), whereas the median ALT level was significantly higher during CPI+INH therapy compared to CPI alone (135 U/L vs 24 U/L respectively, p=0.025. Furthermore, immune-related adverse events were reported in a total of 12 of 35 patients (34.2%). None of the patients in either group developed tuberculosis reactivation during a follow up period of up to 1148 days.

Conclusion. Our data suggest that latent tuberculosis reactivation is rare in cancer patients on CPI immunotherapy. Hepatotoxicity remains a concern in this patient population with LTBI treated with CPI and INH. With the widespread use of CPI, close laboratory and clinical monitoring is required to avoid life threatening drug induced liver injury and interruption of LTBI therapy and immunotherapy. Further clinical studies are warranted to determine the optimal management of LTBI during CPI therapy.

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1410. Isoniazid Therapy for Latent Tuberculosis Infection in Patients with Cancer Treated with Checkpoint Inhibitors Immunotherapy

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Conclusion. In N3C, the PNTMI cohort has a lower proportion of COVID-19 infection than the general population, and it was not a cause of mortality. Further analysis to study impact of comorbidities, and differences in race and geographical location are warranted. N3C is a powerful research platform to study the impact of COVID-19 in special populations with low prevalence, and it can be used to study other populations of interest.

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1411. Noninvasive Assessment of Intraleisional Antimicrobial Concentration-Time Profiles in Pulmonary and Central Nervous System Tuberculosis using Dynamic 18F-Pretomanid Positron Emission Tomography

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Background. Pretomanid is used in combination with bedaquiline and linezolid (BPaL regimen) in the treatment of multidrug-resistant tuberculosis (MDR-TB). However, the penetration of pretomanid in privileged sites remain unknown. Antimicrobial pharmacokinetic (PK) parameters are traditionally derived from clinical samples (blood and cerebrospinal fluid), which may not accurately represent the intraleisional tissue PK, affected by drug properties, vascular supply, barrier permeability, and the microenvironment.

Methods. We developed 18F-pretomanid (chemically identical to pretomanid) for in vivo multi-compartment PK by positron emission tomography (PET). Dynamic 18F-pretomanid PET was used to obtain cross species pretomanid concentration-time profiles in animal models of TB (mice and rabbits) to quantify penetration into pulmonary and brain lesions. A subset of animals underwent PET/CT imaging with 18F-py-albumin and 18F-FDG to assess vascular supply and inflammation. Postmortem 18F-pretomanid autoradiography (high-resolution) and mass spectrometry were performed on infected tissues. A mouse model of TB meningitis was used to evaluate the bactericidal activity of the BPaL regimen (Figure 1).

Figure 1. Experimental schematics.

(A) A new synthetic approach was developed to obtain radiofluorinated preto- manid (18F-pretomanid), which is chemically identical to pretomanid and therefore