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 (43.7%) 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 the 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 114 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.

**Disclosures.** Pablo C. Okhuyzen, MD, FACP, FIDSA, Deinove Pharmaceuticals (Grant/Research Support)Ferring Pharmaceuticals (Consultant)Medinta Therapeutics (Grant/Research Support)Merck & Co. (Grant/Research Support)Napo Pharmaceuticals (Consultant, Scientific Research Study Investigator, Research Grant or Support)Summit Therapeutics (Consultant, Summit Therapeutics)Immunotherapeutics (Advisor or Review Panel member)Gilead Sciences (Consultant, Grant/Research Support, Other Financial or Material Support, Honoraria)

1410. Isoniazid Therapy for Latent Tuberculosis Infection in Patients with Cancer Treated with Checkpoint Inhibitors Immunotherapy
Alexandre Malek, MD, Patrick Chaftari, MD, Pablo C. Okhuyzen, MD, FACP, FIDSA; Hiba Dagher, MD; Harrys A. Torres, MD; Ray Y. Hachem, MD; Anne-Marie Chaftari, MD; George Viola, MD, MPH; Dimitrios P. Kontoyiannis, MD; Victor E. Mukanovich, MD; Issam I. Raad, MD; UT MD Anderson Cancer Center, Houston, Texas; UT MD Anderson Cancer Center, Houston, TX; The University of Texas MD Anderson Cancer Center, Houston, Texas; UT MD Anderson Cancer Center, Houston, TX; The University of Texas MD Anderson Cancer Center, Houston, TX; The University of Texas MD Anderson Cancer Center, Houston, TX; University of Texas MD Anderson Cancer Center, Houston, TX

**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 (43.7%) 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 the 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 114 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.

**Disclosures.** All Authors: No reported disclosures
undergoes identical PK and metabolism in vivo. Dynamic 18F-pretomanid PET/CT imaging was performed in preclinical models of tuberculosis following intra-venous administration of 18F-pretomanid. (B) PET signal was quantified in multiple compartments to generate time activity curves (TACs) used to calculate area under the curve (AUC) over 0–60 minutes. A subset of animals also underwent PET/CT imaging of 18F-py-albumin to assess vascular supply to lung and brain lesions, with 18F-FDG to confirm the presence of neuroinflammation in the mouse and rabbit models of TB meningitis. Tissue resection post-mortem was used to visualize the intralesional retention of 18F-pretomanid using high-resolution (10 µm) autoradiography. The efficacy of the BPaL regimen in TB meningitis was compared to that of standard treatment with rifampin, isoniazid, and pyrazinamide in the mouse model. Mass spectrometry was performed following oral administration of BPaL to determine brain drug levels. (C) These data provide multicompartimental PK analysis, intralvesional levels of pretomanid, and insights into the mechanism that govern pretomanid tissue distribution.

**Results.** 18F-Pretomanid PET provided detailed concentration-time profiles in infected tissues demonstrating excellent lung and brain tissue penetration (AUC ratio to plasma > 1) in both animal species, which was spatially compartmentalized, likely due to differential vascular supply (18F-py-albumin PET) (Figure 2). Brain lesions (identified by 18F-py-FDG PET) demonstrated localized leakiness on 18F-py-albumin PET. Autoradiography and mass spectrometry corroborated the imaging findings. The efficacy of the BPaL regimen in TB meningitis was substantially lower than standard TB treatment (Figure 3), likely due to restricted penetration of bedaquiline and linezolid into the brain parenchyma.

**Figure 2.** Spatial heterogeneity of 18F-Pretomanid penetration and vascular supply to pulmonary TB lesions.

(A) A novel synthetic was devised to obtain 18F-pretomanid, which is chemically identical to pretomanid. (B) Maximum intensity projection (MIP) of 18F-Pretomanid PET/CT in Mtb-infected mice over 3 hrs shows hepatobiliary and renal excretion, high uptake into brown fat, brain, and lungs. (C) Resection of infected lungs 30 minutes post intravenous administration of 18F-pretomanid shows heterogeneous distribution of 18F-pretomanid into the lungs visible by high resolution autoradiography. Areas of pneumonia are identifiable by hematoyxlin and eosin (H&E) staining of the same tissue section used for autoradiography. (D) Time-activity curves of 18F-Pretomanid in infected mouse lung (0–3 hours) and derived area under the curve (AUC) ratios to plasma (E) in infected mouse lung. Representative MIP of 18F-pretomanid (F) and 18F-py-albumin (H) PET/CT in a rabbit with cavitary TB and quantification of the AUC ratios to plasma show heterogeneous penetration of 18F-pretomanid into infected brain lesions in the mouse. (D) 18F-pretomanid AUC ratios of tissue to plasma in mouse brain before (day 0) and two weeks into treatment show a reduction in penetration at week 2. (E) Pretomanid concentrations (µg/mL) in mouse plasma and brain, at day 0 and two 1 days into treatment, measured by mass spectrometry and derived concentration ratios of brain to plasma (F) suggest drug accumulation due to the long half-life. (G) While 18F-py-albumin and 18F-FDG PET/CT show vascular leakage and neuroinflammation in the rabbit model, 18F-pretomanid is heterogeneous and reduced at the lesion site (indicated by white arrow). (H) Quantification of the PET signal shows variability within the same animal. Data are represented as median ± interquartile range, n=3–5 group.

**Figure 4.** Evaluation of a pretomanid-containing regimen in TB meningitis.

(A) Experimental timeline used to assess the penetration of pretomanid into infected mouse brain before and during treatment with antimicrobials bedaquiline (B), pretomanid (Pa), and linezolid (L), and corticosteroid dexamethasone (D). (B) Representative three-dimensional MIP of 18F-pretomanid PET/CT in the CNS-TB model, 10 min post-injection, and transverse section showing high and heterogeneous brain uptake. (C) High-resolution autoradiography was pretomanid confirm heterogeneous penetration of 18F-pretomanid into infected brain lesions in the mouse. (D) 8F-pretomanid AUC ratios of tissue to plasma in mouse brain before (day 0) and two weeks into treatment show a reduction in penetration at week 2. (E) Pretomanid concentrations (µg/mL) in mouse plasma and brain, at day 0 and two 1 days into treatment, measured by mass spectrometry and derived concentration ratios of brain to plasma (F) suggest drug accumulation due to the long half-life. (G) While 18F-py-albumin and 18F-FDG PET/CT show vascular leakage and neuroinflammation in the rabbit model, 18F-pretomanid is heterogeneous and reduced at the lesion site (indicated by white arrow). (H) Quantification of the PET signal shows variability within the same animal. Data are represented as median ± interquartile range, n=3–5 group.

**Conclusion.** Dynamic 18F-Pretomanid PET provided holistic data on pretomanid exposures showing excellent penetration into infected lung and brain tissues. The BPaL regimen was inferior to standard TB treatment for TB meningitis. Thus, new pretomanid-containing regimens need to be developed for the treatment of MDR-TB meningitis.

**Disclosures.** Charles A. Peloquin, Pharm.D. Nothing to disclose Alvaro A. Ordonez, MD, Cubresa (Consultant)/Fujirebio Diagnostics (Research Grant or Support) Sanjay K. Jain, MD, Fujirebio Diagnostics, Inc., USA (Research Grant or Support) Novobiotic LLC, USA (Research Grant or Support) T3 Pharma, Switzerland (Research Grant or Support) Sanjay K. Jain, MD, Fujirebio Diagnostics, Inc., USA (Individual(s) Involved: Self): Research Grant or Support; Novobiotic LLC, USA (Individual(s) Involved: Self): Research Grant or Support; T3 Pharma, Switzerland (Individual(s) Involved: Self): Research Grant or Support

1412. Clinical Epidemiology and Characteristics of Pulmonary Nontuberculous Mycobacterial Isolates from a Large Academic Military Treatment Facility

Mary B. Ford, MD; Jason Okulicz, MD; Jesse Salinas, n/a; John Kiley, MD; Brooke Army Medical Center, JBSA Fort Sam Houston, TX, San Antonio, Texas

**Session:** P-80. Tuberculosis and other Mycobacterial Infections

**Background.** Nontuberculous mycobacteria (NTM) are ubiquitous in the environment and include pathogenic and nonpathogenic species. Although prevalence appears to be increasing in the US, diagnosis and treatment can be challenging. This study describes the epidemiology and clinical characteristics of pulmonary NTM (pNTM) isolates at Brooke Army Medical Center (BAMC).

**Methods.** BAMC pulmonary NTM isolates from 2012-2020 were included. Corresponding electronic health records were reviewed for epidemiologic, microbiologic, and clinical data. Pulmonary NTM infection (pNTM) was defined using 2020 NTM guidelines and patients were divided into 2 groups based on whether guideline criteria for pNTM were met. Demographic, microbiologic, and clinical characteristics were compared between groups.

**Results.** A total of 815 isolates from 225 patients were analyzed (median 2 [IQR 1-4] isolates per patient). Approximately half (49.7%) were female with a median age of 71 years (IQR 62-79, Table 1), and the majority were current or former smokers (57.3%). Compared to those not meeting criteria (n=116; 51.6%), pNTM patients (n=109; 48.4%) more commonly had bronchiectasis (27.6% vs 27.6%; p=0.002) but were less likely to have solid organ malignancy (11.9% vs 23.3%; p=0.036). A higher proportion of pNTM patients were female (58% vs 42%; p=0.005) and had lower median Body Mass Index (BMI, 22.6 vs 25.1; p=0.001). M. avium complex (MAC) was more common among pNTM patients (75.2% vs 35.3%; p=0.001). In contrast, M. simiae and M. gordoniae were more likely to be isolated from those not meeting criteria (35.3% vs 12.3%; p=0.003 and 16.7% vs 1.8%; p=0.001 and 0.001, respectively). Among pNTM patients, 60 (55%) were offered therapy and were more likely to be younger (70 [IQR 63-76] vs 73 [IQR 65-82]; p=0.049), have chronic obstructive pulmonary disease (COPD; 51.7% vs 24.5%; p=0.006) and MAC (88.3% vs 59.2%; p=0.001) compared to untreated patients (Table 2).

**Table 1.** Characteristics of Pulmonary Nontuberculous Mycobacterial Isolates from a Large Academic Military Treatment Facility

| Characteristic                | pNTM Patients (n=109) | No Criteria Patients (n=116) | p-value |
|------------------------------|-----------------------|-----------------------------|---------|
| Gender (Female)              | 60 (55%)              | 49 (42%)                    | 0.001   |
| Age (Median)                 | 70 [IQR 63-76]        | 73 [IQR 65-82]              | 0.049   |
| BMI (Median)                 | 22.6                  | 25.1                        | 0.001   |
| COPD                         | 35 (32%)              | 24 (21%)                    | 0.006   |
| MAC                          | 75 (70%)              | 35 (30%)                    | 0.001   |
| Isolates per Patient         | 2 (IQR 1-4)           | 1 (IQR 1-3)                 | 0.003   |
| History of Smoking           | 57 (55%)              | 42 (40%)                    | 0.005   |
| History of Alcohol Use       | 45 (41%)              | 30 (26%)                    | 0.004   |
| HIV                          | 10 (9%)               | 6 (5%)                      | 0.16    |
| CD4 Count (Median)           | 400 (IQR 100-1600)    | 300 (IQR 100-1500)          | 0.13    |
| CD8 Count (Median)           | 1500 (IQR 700-3500)   | 1000 (IQR 700-2500)         | 0.011   |
| CD8/CD4 Ratio (Median)       | 1.0                   | 1.0                         | 0.25    |