Figure 3. Concepts and data sources of pulmonary non-tuberculous Mycobacterium infection phenotype in N3C

Table 1: Baseline Characteristics of Pulmonary non-tuberculous *Mycobacterium* infection cohort

Characteristic	Total (n=555)		COVID-19 Positive (n=24)		COVID-19 Negative (n=531)		p
Age, years							0.1384
Mean (SD)	66.9 (14.2)		65.6 (14.4)		70 (14.2)		
Median (range)	69 (21-89)		65.6 (65-89)		69 (21-89)		
18-29	< 20		< 20		< 20		
30-49	58	10.5%	< 20		56	10.5%	
50-69	223	40.2%	< 20		210	39.5%	
70 and more	266	47.9%	< 20		257	48.4%	
Sex							0.0656
Female	340	61.3%	< 20		321	60.5%	
Male	215	38.7%	< 20		210	39.5%	
Unknown or missing							
Race							0.0218
White	447	80.5%	< 20		428	80.6%	
Black or African American	70	12.6%	< 20		66	12.4%	
Asian	< 20		< 20		< 20		
Native Hawaiian or Other Pacific Islander	< 20		< 20		< 20		
Other	< 20		< 20		< 20		
Unknown or missing	< 20		< 20		< 20		
Ethnicity							0.7582
Not Hispanic or Latino	508	91.5%	23	95.8%	485	91.3%	
Hispanic	30	5.4%	< 20		29	5.5%	
Unknown or missing	< 20		< 20		< 20		
Geographical Location							0.0002
US Northeast	< 20		< 20		< 20		
US Midwest	125	22.5%	< 20		111	20.9%	
US South	114	20.5%	< 20		107	20.2%	
US Mountain	< 20		< 20		< 20		
US West	< 20		< 20		< 20		
Unknown or missing	302	54.4%	< 20		302	56.9%	
Deaths							0.94
No	511	92.1%	22	91.7%	489	92.1%	
Yes	44	7.9%	< 20		42	7.9%	

SD, standard deviation. Geographical locations based on US Census tract regions. Per N3C policy, exact counts that are 20 or less were not reported to protect the privacy of individuals.

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

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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) 5mg/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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1411. Noninvasive Assessment of Intralesional Antimicrobial Concentration-Time Profiles in Pulmonary and Central Nervous System Tuberculosis using Dynamic 18F-Pretomanid Positron Emission Tomography

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Session: P-80. Tuberculosis and other Mycobacterial Infections

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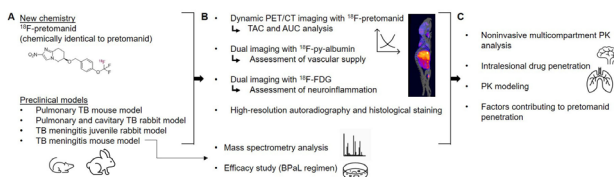
(A) A new synthetic approach was developed to obtain radiofluorinated pretomanid (18F-pretomanid), which is chemically identical to pretomanid and therefore