Results. N/A

Diagnosis. lepromatous leprosy with pre-treatment immune reaction. This is potentially the first case of autochthonous leprosy in Missouri. Providers should include Hansen's disease in the differential diagnosis of patients with dermal eruption and cutaneous neurological symptoms to avoid delays in diagnosis/care.

Disclosures. **All Authors**: No reported disclosures

1395. Epidemiology of Non-Tuberculous Mycobacteria Infection Among Immunocompromised Children: A Single Center Experience

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Session: P-80. Tuberculosis and other Mycobacterial Infections

Background. Nontuberculous mycobacteria (NTM) infection is associated with high rates of morbidity and mortality among immunocompromised adults. However, sparse data exists regarding clinical outcomes among immunocompromised (IC) children with NTM infection. We sought to characterize clinical features and outcomes among IC children at our institution with microbiologically confirmed NTM disease.

Methods. Retrospective review of cases of microbiologically confirmed NTM infection among IC children between January 2017 and December 2020. Children (≤21y.o) with microbiologically confirmed NTM disease and known primary or secondary immunodeficiency diagnosed between January 1, 2017 and December 20, 2020 were included in the study. All subjects with a positive NTM microbiologic stain or culture but no subsequent treatment for NTM infection were excluded. Demographic and clinical characteristics were assessed and risk factors for mortality were evaluated.

Results. Of 147 mycobacterial cultures sent during the study period, 72 subjects had a positive microbiologically confirmed NTM species, with 10 subjects meeting all inclusion and no exclusion criteria. Median age was 16 years old, with 40 percent being female and 50 percent of Hispanic ethnicity. NTM disease was distributed among patients with primary immunodeficiency (30%), solid organ transplantation (20%), hematopoietic stem cell transplant (20%), rheumatologic disease on immunosuppressive therapy (10%), and hematologic malignancy (10%). Bacteremia was common, with blood cultures positive in 70% of cases, and *M. abscessus (50%) and M. avium complex (30%)* the most frequently implicated pathogens. Hospital acquired infection was common (60%). 2 year mortality following invasive NTM infection was high at 40%.

Conclusion. While rare, NTM infections are associated with significant morbidity and mortality among immunocompromised children. Additional investigations are needed to assess for risk factors associated with NTM and severe NTM disease.

Disclosures. **Laura Filkins, PhD**, **Avsana Labs** (Board Member, Scientific advisory board member)**Biofire Diagnostics** (Grant/Research Support)

1396. The Incremental Hospitalization Burden Associated with Nontuberculous Mycobacterial Lung Disease(NTMLD) among Patients with Chronic Obstructive Pulmonary Disease (COPD) in Japan

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Session: P-80. Tuberculosis and other Mycobacterial Infections

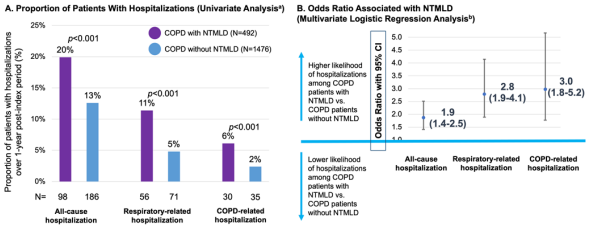
Background. NTMLD is a life-threatening pulmonary infection with increasing incidence and prevalence in Japan. It is associated with progressive lung damage and increased healthcare use. Many patients with NTMLD have comorbid respiratory conditions such as COPD. Treatment of NTMLD in patients with COPD is difficult, however there is limited data on the incremental burden that NTMLD adds to underlying COPD. We assessed the incremental burden associated with NTMLD in Japanese patients with COPD by comparing their hospitalizations to matched COPD patients without NTMLD.

Methods. A retrospective cohort study was conducted using claims data provided by the Japan Medical Data Center (2015-2020). COPD patients with NTMLD were matched 1:3 to COPD patients without NTMLD (controls). Hospitalizations (all-cause, respiratory-related, and COPD-related) were accrued over a 1-year follow-up period after NTMLD diagnosis (index). Incremental burden of NTMLD was assessed by comparing hospitalizations between COPD patients with NTMLD and controls with univariate and multivariate analyses adjusting for comorbidities during 1-year pre-index period.

Results. A total of 492 COPD patients with NTMLD were matched by age and sex to 1476 controls. Mean (SD) age on index date was 56.6 (10.3) years and 61.4% were females. Compared to controls, NTMLD patients had higher prevalence of some pulmonary symptoms and comorbidities such as hemoptysis (11% vs 2%), dyspnea (1.6% vs 0.6%) and lung cancer (7% vs 4%). In univariate analyses, a higher percent of COPD patients with NTMLD had hospitalizations compared to controls (Fig 1A); the unadjusted annual hospitalization rates were also higher among patients with NTMLD (Fig 2A). Multivariate regressions after adjusting for pre-index comorbidities showed COPD patients with NTMLD were 1.9 times more likely to have an all-cause hospitalization, 2.8 times more likely to have a respiratory hospitalization, and 3.0 times more likely to have a COPD-related hospitalization (Fig 1B).

Conclusion. COPD patients with NTMLD had a higher burden of hospitalization than COPD patients without NTMLD. The statistically significantly incremental burden associated with NTMLD in patients with COPD highlights the acute need for appropriate management of NTMLD in Japan.

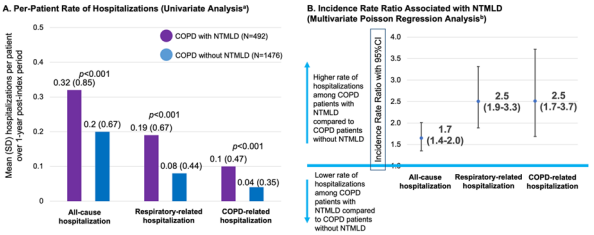
Figure 1: Proportion of patients (A) and odds ratio associated with NTMLD after multivariate logistic regression analysis of hospitalizations over 1-year post-index follow-up period among COPD patients with NTMLD vs matched COPD patients without NTMLD in Japan



[a]p-value based on McNemar's test; [b]Odds ratio (OR) derived from the logistic regression analysis controlling for comorbidities during the 1-year pre-index period.

Comorbidities controlled for in the multivariate regression analysis were diabetes mellitus; high blood pressure; overweight and obesity; chronic kidney disease; total cardiovascular diseases; cancer, excluding lung; dementia; gastroesophageal reflux disease; asthma; idiopathic pulmonary fibrosis; and idiopathic interstitial lung disease.

Figure 2: Per patient rate (A) and incidence rate ratio associated with NTMLD after multivariate Poisson regression analysis (B) of hospitalizations over 1-year post-index follow-up period among COPD patients with NTMLD vs matched COPD patients without NTMLD in Japan



[a]p-value based on Wilcoxon signed-rank test; [b]Incidence rate ratios (IRR) derived from Poisson regression analysis controlling for comorbidities during the 1-year pre-index period. IRR is a ratio of incidence rate between the two groups being compared.

Comorbidities controlled for in the multivariate regression analysis were diabetes mellitus; high blood pressure; overweight and obesity; chronic kidney disease; total cardiovascular diseases; cancer, excluding lung; dementia; gastroesophageal reflux disease; asthma; idiopathic pulmonary fibrosis; and idiopathic interstitial lung disease.

Disclosures. **Naoki Hasegawa, MD, PhD**, **Insmed Incorporated** (Consultant, Scientific Research Study Investigator)**Janssen Pharmaceuticals Inc** (Consultant, Scientific Research Study Investigator) **Kozo Morimoto, MD**, **Insmed Incorporated** (Consultant) **Ping Wang, PhD**, **Insmed Incorporated** (Employee) **Lu Zhang, PhD**, **Panalgo** (Employee, Other Financial or Material Support, Lu Zhang is an employee of Panalgo which provides the analytic platform Instant Health Data that is used by Insmed) **Mariam Hassan, PhD, B. Pharm**, **Insmed Incorporated** (Employee) **Anjan Chatterjee, MD, MPH**, **Insmed Incorporated** (Employee)

1397. Modern Lineages of *Mycobacterium tuberculosis* Were Recently Introduced in Western India and Demonstrate Increased Transmissibility

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Session: P-80. Tuberculosis and other Mycobacterial Infections

Background. *Mycobacterium tuberculosis* (*Mtb*) transmissibility may vary between lineages (or variants) and this may contribute to the slow decline of tuberculosis incidence. The objective of our study was to compare transmissibility across four major lineages (L1-4) of *Mtb* in Pune, India.

Methods. We performed whole-genome sequencing (WGS) of *Mtb* isolated from sputum culture of adult patients with pulmonary TB. We performed genotypic susceptibility testing for both first- and second-line drugs using a previously validated random forest predictor. We identified single nucleotide polymorphisms and generated a multiple sequence alignment excluding drug resistance conferring mutations to avoid skewing the phylogeny due to convergent evolution in these regions. We used Bayesian molecular dating to generate phylogenies and compared tree characteristics using a two-sample Kolmogorov-Smirnov (KS) test.

Results. Of the 642 isolates from distinct study participants that underwent WGS, 612 met quality criteria. The median age of participants was 31 years (range 18-74), the majority were male (64.7%) and sputum smear-positive (83.3%), and 6.7% had co-infection with HIV (Table 1). There was no significant difference in baseline characteristics between lineages. The majority of isolates belonged to L3 (44.6%). The majority (61.1%) of multidrug-resistant (MDR, resistant to isoniazid and rifampin) isolates belonged to L2. In phylogenetic analysis, we found evidence of higher transmissibility of L2 as indicated by shorter branch lengths (i.e., less time had elapsed between transmission and sampling) and more genetic similarity (smaller pairwise single nucleotide polymorphism [SNP] distances) among L2 isolates as compared to other lineages

(Figure 1). Branching times for L2 and L4 were smaller than L1 and L3 indicating recent introduction into the region ($p < 0.001$ [KS test]).

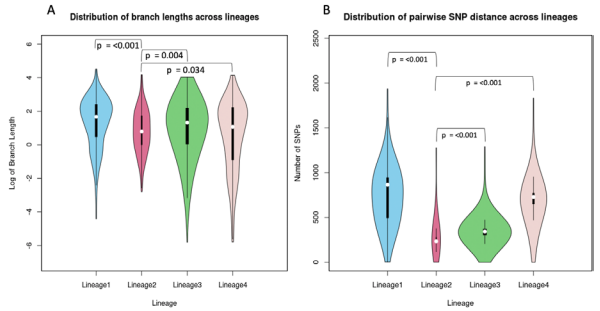

Figure 1: Lineage-wise distribution of A) phylogenetic tree branch lengths (log) and B) pairwise single nucleotide polymorphism (SNP) distance, using 612 tuberculosis isolates from Pune, India. P values calculated using two-sample Kolmogorov-Smirnov test.

	Lineage 1 (n=162)	Lineage 2 (n=45)	Lineage 3 (n=273)	Lineage 4 (n=132)	Total (n=612)
Female Gender	59 (36.4%)	13 (28.9%)	103 (37.7%)	41 (31.1%)	216 (35.3%)
Median Age (Range)	32 (18-74)	29 (18-57)	31 (18-70)	30 (18-65)	31 (18-74)
Smear Positive	138 (85.2%)	40 (88.9%)	222 (81.3%)	110 (83.3%)	510 (83.3%)
HIV Positive	6 (3.7%)	1 (2.2%)	17 (6.2%)	14 (10.6%)	38 (6.2%)
Known Diabetes Mellitus	21 (13%)	3 (6.7%)	38 (13.9%)	18 (13.6%)	80 (13.1%)

Table 1: Demographic characteristics of study participants included in the study, by lineage.

Conclusion. Modern *Mtb* lineages (L2 and L4) were relatively recently introduced in western India, as compared to older lineages (L1 and L3), with the more drug-resistant L2 showing higher transmissibility. These findings highlight the need for early detection and treatment initiation to interrupt transmission with important implications for antimicrobial stewardship and heightened surveillance of TB resistance rates.

Disclosures. **All Authors**: No reported disclosures

1398. Gland Tuberculosis: A Rare Localization of Tuberculosis

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Session: P-80. Tuberculosis and other Mycobacterial Infections

Background. Tuberculosis (TB) is a multisystem disease that might affect all organs. Gland TB is characterized with a misleading clinical presentation which often mimic a neoplastic process. The aim of our work was to study the clinical, therapeutic and evolutionary features of gland TB.

Methods. We conducted a retrospective study including all patients hospitalized for gland TB in the infectious disease department between 1999 and 2020.

Results. We encountered 28 cases among which 24 were females (85.7%). The mean age was 39±14 years. A rural origin was noted in 15 cases (53.5%). Two patients were previously treated for TB (7.1%). Systemic symptoms of TB included fever (60.7%), asthenia (53.5%), loss of appetite (46.4%) and weight loss (25%). There were 18 cases of breast TB (64.3%), 4 cases of salivary gland TB (14.3%) and 3 cases of ovarian TB (10.7%). Two cases of pituitary TB (7.1%) and one case of adrenal TB (3.6%) were noted. Multifocal TB was noted in 7 cases (25%). Lymph node (17.8%), pulmonary (14.2%) and peritoneal (7.1%) TB were associated with gland TB. Tuberculin skin test was positive in 19 cases (67.8%). The diagnosis was based on histopathological proof in 23 cases (82.1%), microbiological proof in 4 cases (14.3%) and clinically confirmed in one case (3.6%). The median duration of antitubercular therapy was 10 [9-15] months. Patients received fixed-dose combination in 11 cases (39.2%). Adverse effects of antitubercular therapy were noted in 10 cases (35.7%) represented by gastrointestinal symptoms (14.3%), increase in hepatic enzyme levels (14.3%) and skin reactions (7.1%). The disease evolution was favorable in 26 cases (92.9%). Relapse was noted in two cases (7.1%).

Conclusion. Gland TB included different sites. The presence of systemic symptoms of TB and the diagnosis of TB elsewhere in the body helped through the diagnosis process which requires high index of suspicion. It was mainly based on histological evidence.

Disclosures. **All Authors**: No reported disclosures

1399. Clarithromycin–Rifampin-based Treatment for Non-tuberculous Mycobacterial Infections in Immunocompromised Patients Who Require Concomitant CYP-Metabolized Medications

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Session: P-80. Tuberculosis and other Mycobacterial Infections

Background. Non-tuberculous mycobacteria (NTM) are causes of pulmonary and extrapulmonary disease that frequently affect immunocompromised hosts (ICH). Current treatment guidelines recommend a macrolide-based, multi-drug regimen that includes rifampin. Rifampin is a potent cytochrome P450 (CYP) 3A inducer, which often results in drug-drug interactions in ICH receiving multiple CYP substrates. One way to mitigate rifampin's CYP induction is to utilize clarithromycin, a CYP inhibitor, as the accompanying macrolide. We evaluated the incidence of NTM treatment-related adverse events (AEs) in patients who received a clarithromycin-based regimen compared to patients who received an azithromycin-based regimen.

Methods. We conducted a retrospective review of NTM infection in 30 immunocompromised adults. All participants had a positive culture for a NTM and had received a rifamycin (rifampin or rifabutin) with a macrolide (azithromycin or clarithromycin) for treatment at Brigham and Women's Hospital between 01/01/2011-10/18/2020 or Dana-Farber Cancer Institute between 06/03/2015-07/01/2020. The primary outcome was the incidence of NTM treatment-related AEs in patients who received a clarithromycin-based regimen compared to those who received an azithromycin-based regimen.

Results. There were no significant differences in the reasons for discontinuation of NTM treatment or 90-day mortality between groups. The number of AEs possibly related to NTM treatment were similar in patients who received a clarithromycin-based regimen and those who received an azithromycin-based one (10/13 vs. 14/17; p=0.73). The most common AE was liver function test abnormalities (Table 1). Additionally, the proportion of patients requiring dose adjustments for interacting medications and patients with out-of-range tacrolimus levels were similar between the two groups (23.1% vs. 29.4%; p=0.76 and 8.0% vs. 6.0%; p=1.00, respectively).

Table 1: Adverse events

Adverse event	Clarithromycin-based regimen (n = 13)				Azithromycin-based regimen (n = 17)					p-value
	Any Grade	Grade 1	Grade 2	Grade 3	Any grade	Grade 1	Grade 2	Grade 3	Grade 4	
LFT abnormalities	7	5	1	1	4	3	1	-	-	0.13
QTc prolongation	5	4	1	-	6	3	2	1	-	1
Gastrointestinal (nausea, vomiting, diarrhea, constipation)	3	2	-	-	7	4	1	2	-	0.13
Worsening baseline condition	2	1	1	-	8	4	4	1	-	0.11
Visual alterations	1	-	1	-	1	-	-	-	1	1
Tinnitus	0	-	-	-	2	-	2	-	-	0.49
Hearing loss	0				4	4	-	-	-	0.11

Conclusion. A clarithromycin-based regimen for NTM treatment was safe and well tolerated in our patient population. This combination provides a good alternative for patients requiring medications that are CYP substrates, or those who cannot tolerate azithromycin.

Disclosures. **Matthew Cheng, MD**, **GEn1E Lifesciences** (Advisor or Review Panel member)**Kanvas Biosciences** (Board Member, Shareholder)**nplex biosciences** (Advisor or Review Panel member)

1400. Pretomanid in the Treatment of Patients with Tuberculosis in the United States: the Bedaquiline, Pretomanid and Linezolid (BPaL) Accelerated Monitoring (BAM) Project

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Session: P-80. Tuberculosis and other Mycobacterial Infections

Background. In August 2019 the U.S. FDA approved pretomanid as part of a 6-month all-oral BPaL (bedaquiline, pretomanid, and linezolid) regimen for treating pulmonary extensively drug-resistant (XDR) or treatment-intolerant or nonresponsive multidrug-resistant (MDR) tuberculosis (TB). In the study supporting approval, 89% of patients had a favorable outcome, and all reported ≥ 1 adverse event. We describe the reported use of BPaL in the United States.

Methods. Using the 2020 CDC Report of a Verified Case of Tuberculosis (RVCT) MDR TB supplemental form, TB programs and providers submitted data for patients who began taking BPaL between Aug 1, 2019 and May 1, 2020, for retrospective descriptive analysis.

Results. Programs and providers reported 17 TB patients aged a mean of 41 years (range 23–76) who received BPaL: 11 (65%) were male; 15 (88%) were non-U.S. born; 15