lineages and sub lineages, relationship between strains, underline mutations conferring drug-resistant TB, which may not be shown by molecular and phenotypic tests. As far as we know this is the first study that describes genetic diversity of *M. tuberculosis* strains causing DR-TB and using WGS in central region of Mozambique.We aim to describe genetic diversity of *M. tuberculosis* strains causing DR-TB in central Mozambique.

Methods. A total of 35 strains from Beira Mozambique were evaluated with genotypic tests (Genotype MTBDRplus™, and MTBDRsl™); phenotypic (MGIT-SIRE™) and DST. All isolates resistant to isoniazid (H) or rifampicin (R) or both were submitted to WGS Illumina HiSeq 2000 and analyzed with TB profiler database and phylogenetic tree was done using Figtree tool. This was a descriptive cross-sectional study.

Results. WGS shown that strains analyzed, belongs to three of six major lineages, with Lineage 4: 25(71.4%); Lineage 1: 5(14.3%); and Lineage 2 Beijing family: 5(14.3%)]. All pre-XDR strains 3(8.6%) were from lineage 4.3. By WGS, all 35 strains had any mutations conferring DR-TB while in one strain, mutation was not shown by genotypic neither phenotypic DST. Compared with genotypic tests, WGS had best performance in showing mutation conferring resistance to etambutol 12/35 (34.3%) and 7/35 (20%).

Conclusion. The DR-TB disease in Beira Mozambique is mainly caused by *M. tuberculosis* strains of Lineage 4, sub-lineage 3 although lineage 1 and 2 are also present. WGS shows underline mutations causing DR–TB that are not detected by genotypic and phenotypic DST test.

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800. Drug-Resistant TB: An Experience From Qatar

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Background. Drug-resistant tuberculosis (DR-TB) is an important issue for public health. This study was conducted to evaluate the characteristics, treatment outcome, and risk factors associated with 223 DR-TB cases in the State of Qatar.

Methods. A descriptive records-based retrospective study was conducted on patients registered at Communicable Disease Centre (CDC), Qatar to all consecutive microbiologically confirmed tuberculosis cases for the period January 2010–March 2015. Demographic and clinical data extracted included: patient's age, sex, and country of origin; disease site (pulmonary or extra-pulmonary); presence of comorbidities, HIV/AIDS status, previous chemoprophylaxis and/or previous treatment for TB, and anti-TB drug resistance the resistance pattern of isolated mycobacteria. The sputum culture conversion rate and treatment outcome was assessed for the patient who completed their treatment in Qatar

Results. Of 3,301 patients with positive *M. tuberculosis* culture were analyzed; 223 (6.7%) were resistant to one or more first-line drugs, to isoniazid in 3.1% (n = 102), streptomycin in 1.2% (n = 41), rifampicin in 0.2% (n = 6), ethambutol in 0.15% (n = 5), and multi-drug resistance in 1.2% (n = 38) of patients. Among the resistant TB patients, more common demographic characteristics were former resident of Indian subcontinent (64.1%). A history of anti-TB treatment was not a risk factor with drug resistance in our cohort. Only 111 (49.7%) patients were tested for HIV antibodies and the results were all negative. There was significant correlation between the type of drug-resistance and CXR finding (23.3% had cavity—P = 0.019). Sputum culture conversion to negative at 2 month of therapy was 94% (n = 101), whereas 122 cases lost follow-up. The outcome of treatment was assessed for 85 resistant cases with follow-up after completion of treatment, show cure rate of 97.6%, and relapse of 2.4%. However, 137 cases (61.4% from total) they left the country before completion of therapy.

Conclusion. Drug-resistant TB in Qatar is influenced by migration, especially from the Indian subcontinent, where the patients were probably infected. Rapid sputum sampling performed in the early stages of the disease, patient isolation, and drug susceptibility testing should be the standard of care to avoid further transmission and improve TB control.

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

801. Emergence of Multi-Drug Resistance Tuberculosis During the Treatment Course of Pan-Susceptible TB: A Case Series

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Background. Successful treatment of tuberculosis (TB) requires monitoring for clinical, radiographic, and microbiologic improvement. Even after negative cultures are obtained, there should be continued monitoring of sputa. If cultures become positive during treatment of drug susceptible TB (DS-TB), there should be concern for multi-drug-resistant tuberculosis (MDR-TB). We present two cases diagnosed with DS-TB who developed MDR-TB during treatment. Case Report: Case 1 is a 33-year-old male who was incarcerated in Peru. During incarceration in 2008, three of his cellmates had MDR-TB and he was diagnosed with DS-TB and treated with directly observed therapy (DOT) for 7 months. In Texas in 2015 he was diagnosed with DS-TB and was initiated on rifampin, isoniazid, pyrazinamide, and ethambutol (RIPE). Five months into DOT, his sputa became culture positive with molecular detection of drug resistance (MDDR) and drug susceptibility testing (DST) revealing resistance to all of RIPE. Repeat MDDR and DST of the 2015 isolate showed no resistance. Genotyping of the two isolates were identical by mycobacterial interspersed repetitive units (MIRU) and spoligotyping. However, whole genome sequencing showed two different isolates. Case 2 is a 63-year-old female diagnosed with DS-TB in Saipan and started on RIPE in April 2017. She was on DOT until July when she moved to Texas and was lost to follow-up until September. She claims adherence with rifampin and isoniazid during this time. All sputa collected between diagnosis and September were smear and culture negative. Six months into therapy, she had sputa that was culture positive with MDDR and DST showing MDR-TB. Her isolates from Saipan and Texas were sent for genotyping. The MIRU and spoligotyping showed two different isolates.

Conclusion. These cases show the importance of following cultures throughout treatment. Traditionally, MDR-TB is thought to be due to poor adherence. However, in high prevalence areas, heterogeneous infection with two different strains is an important consideration for the cause of MDR-TB. Concomitant infection of DS and MDR-TB can occur with MDR-TB not being detected until far into therapy. These cases represent heterogeneous exogenous infection of DS and MDR-TB—only discovered after meticulous culture monitoring.

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

802. Use of *N*-Acetylcysteine for Prevention and Treatment of Isoniazid Induced Liver Injury During Treatment of Mycobacterial Infections

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Background. Hepatotoxicity secondary to therapy for *Mycobacterium tuberculosis* (MTB) is a common complication that may lead to treatment interruption. *N*-Acetylcysteine (NAC) exerts a hepatoprotective effect by repleting glutathione stores and enhancing the cellular antioxidant defense mechanism. NAC has been found to be protective against liver toxicity in animals treated for MTB infection. Randomized controlled trials have shown that its use in humans also decreases the risk of hepatotoxicity associated with anti-MTB treatment but there is minimal data regarding its utility for treatment of liver toxicity.

Methods. Patients who received NAC from January 2012 to March 2018 for prophylaxis and treatment of increasing liver function tests (LFTs) while on isoniazid (INH) were included. A retrospective review of the medical record system was performed.

Results. Nineteen patients were included. Eight received NAC for treatment. The average age was 49 years. Seventy percent of patients were male. The mean BMI was 25. Five patients had underlying liver cirrhosis and two had hepatic steatosis. Eleven patients had Hepatitis C (HCV) and one had active Hepatitis B infection. Ten patients had MTB pulmonary infection, thee had latent TB infection, two meningitis, and three had disseminated disease. One patient was treated for atypical mycobacterial infection. The dose of NAC used was 600 mg oral twice daily and the duration was variable.

The prophylaxis group had stable LFTs during treatment, except for two patients whose enzymes increased more than three times the upper limit of normal. These two patients had underlying HCV and liver cirrhosis. Only one required discontinuation of INH. This group received NAC for an average of 47 days. The treatment group had a favorable trend of liver enzymes after NAC initiation, with levels significantly improving by day 14 (Figures 1 and 2). Three patients did not require discontinuation of antibiotics. INH was stopped prior to NAC initiation in four patients. No side effects of NAC were documented in any patient.

Conclusion. NAC is a safe and effective measure to prevent and treat hepatotoxicity secondary to INH therapy. More studies are needed to determine its optimal dose and duration for this indication.

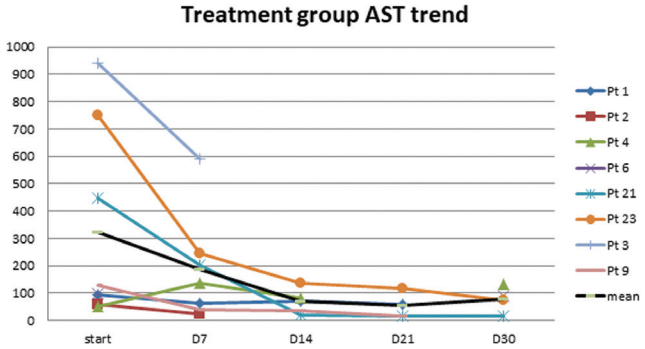

Figure 1.

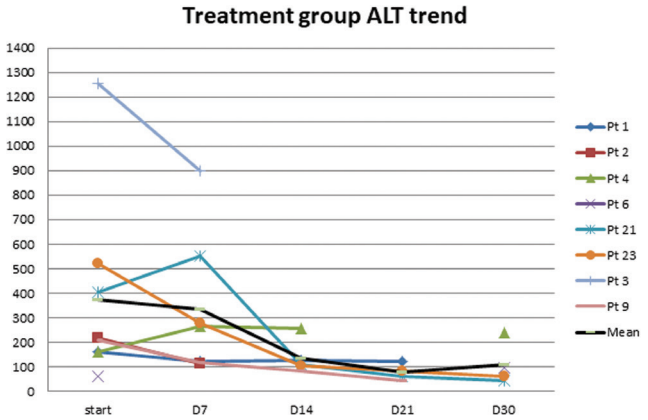

Figure 2.

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803. Overcoming β-Lactam Resistance in *Mycobacterium abscessus*

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Background. *Mycobacterium abscessus* (*Mab*) is an environmentally acquired nontuberculous mycobacterium (NTM) that causes severe pulmonary infections in patients with chronic lung disease, such as cystic fibrosis (CF). The incidence of drug-resistant *Mab* infections in CF patients in the United States is steadily rising, making it increasingly difficult to manage these often chronic and incurable infections. *Mab* requires two enzyme classes, L,D- and D,D-transpeptidases, to synthesize peptidoglycan (PG); an integral component of the bacterial cell wall. Each enzyme class is uniquely susceptible to different classes of β-lactam antibiotics. We hypothesize that a combination of two β-lactams, each specific for an enzyme class, will optimally inhibit PG synthesis and swiftly kill *Mab*, with potential to overcome drug-resistance.

Methods. Paired antibiotic combinations were tested *in vitro* for synergy against the *Mab* reference strain ATCC 19977 at 10^6 CFU/mL, per CLSI guidelines. Combinations included two β-lactams, a β-lactam and a β-lactamase inhibitor, or a β-lactam and a rifamycin. The minimum inhibitory concentration (MIC) of each drug was initially confirmed via broth microdilution assay. A validated checkerboard assay was used to determine the fractional inhibitory concentration index (FICI) for each combination to identify pairs that exhibit synergistic activity against *Mab*.

Results. Of the initial 227 combinations screened, 18 pairs exhibited a high level of synergy (FICI ≤ 0.5). Half of these were combinations of two β-lactams. The average reduction in MIC for each drug in combination was at least fourfold, with 8/18 combinations exhibiting reductions greater than eightfold. Although MIC breakpoints against *Mab* have not been established for all of the antibiotics tested in this study, the MICs of at least seven combinations were within the therapeutic range.

Conclusion. Comprehensive inhibition of essential enzymes involved in PG synthesis requires more than one β-lactam antibiotic, and this phenomenon is hypothesized to be the basis for observed synergy between β-lactams. Some of the combinations reduced MICs to within therapeutically achievable levels, potentially leading to vital new treatment options against drug-resistant *Mab.*

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

804. Impact of Azithromycin Prophylaxis in Lung Transplant Recipients on the Risk of Nontuberculous Mycobacterial Infections

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Background. Azithromycin has been shown to improve FEV1 in lung transplant recipients (LTR) with bronchiolitis obliterans syndrome (BOS). The impact of azithromycin use on the incidence of infections due to *Mycobacterium avium* complex (MAC) and *M. abscessus* in LTR is currently unknown.

Methods. We conducted a nested case–control study of a retrospective cohort of adult LTR transplanted between 2007 and 2017. Cases were defined as LTR with nontuberculous mycobacterial (NTM) infections due to MAC and/or *M. abscessus.* Controls were defined as LTR without NTM infections. NTM infection was defined by presence of pulmonary symptoms and radiographic changes (clinical criteria) in addition to positive cultures from ≥2 sputa or ≥1 bronchial specimens (microbiological criteria) according to the IDSA/ATS criteria. LTR who meet microbiological, but not clinical criteria were considered colonized and not included for analysis. Azithromycin use was defined as ≥90 days for BOS treatment.

Results. Among 538 LTR, 60% (321/538) were male and 81% (434/538) received double LTs. Indication for LT was idiopathic pulmonary fibrosis (28% [152/538]), chronic obstructive pulmonary disease (23% [121/538]), cystic fibrosis [CF] (13% [68/538]), and other (37% [197/538]). The overall incidence of NTM infections was 4.3% (23/538); of which 65.2% (15/23), 17.4% (4/23), and 17.4% (4/23) were due to MAC, *M. abscessus* and polymicrobial infections, respectively. Thirty-one percent (165/538) of LTR received azithromycin. LTR who received azithromycin prophylaxis had 0.21 times the odds of developing NTM infections compared with LTR who did not receive azithromycin prophylaxis (OR: 0.21, 95% CI: 0.02 – 0.86, $P = 0.02$). Age ($P = 0.88$), type of LT ($P = 0.81$), pretransplant NTM colonization ($P = 0.46$), and CF ($P = 0.22$) were evaluated as possible risk factors, but were not associated with increased risk of developing NTM infections in bivariable analyses. In a multivariable logistic regression model, azithromycin prophylaxis was independently associated with decreased risk of NTM infections after adjusting for CF and pretransplant NTM colonization (aOR: 0.20, 95% CI: 0.05–0.88, $P = 0.01$).

Conclusion. Azithromycin use was associated with lower risk of NTM infections due to *M. abscessus* and MAC in our LTR.

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

805. Amikacin Liposome Inhalation Suspension (ALIS) Add-on Therapy for Refractory *Mycobacterium avium* Complex (MAC) Lung Disease: Effect of *In Vitro* Amikacin Susceptibility on Sputum Culture Conversion

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Background. ALIS (590 mg amikacin base) is liposome-encapsulated amikacin for inhalation, which delivers amikacin directly to the lung and limits systemic exposure. In the CONVERT phase 3 trial, significantly more adults with treatment-refractory MAC lung disease receiving ALIS plus guideline-based therapy (GBT) vs. GBT alone achieved sputum culture conversion by month 6 (29.0% vs. 8.9%, $P < 0.0001$). Amikacin treatment failure has previously been reported in patients with amikacin minimum inhibitory concentrations (MIC) >64 μg/mL. We analyzed the impact of amikacin MIC on culture conversion during treatment with add-on ALIS.

Methods. In CONVERT, patients were randomly assigned (2:1) to receive once daily ALIS+GBT ($n = 224$) or GBT alone ($n = 112$). Patients with amikacin-resistant MAC isolates (MICs >64 μg/mL by broth microdilution) were excluded prior to randomization. The primary endpoint was culture conversion, defined as 3 consecutive monthly MAC-negative sputum cultures by month 6. Amikacin MICs were correlated with culture conversion rates.

Results. Amikacin MIC distributions at baseline (day 1) were similar in both groups (Figure 1). Conversion rates in the ALIS+GBT arm were 28.6–34.5% for MAC with amikacin MICs of 8–64 μg/mL (Figure 2). Overall, 28 patients developed post-screening amikacin MIC >64 μg/mL, 4/112 in the GBT alone arm (post-baseline), and 24/224 in the ALIS+GBT arm (1 at baseline and 23 post-baseline after adding ALIS). Most of these (18/24) had MAC isolates with persistent amikacin MIC >64 μg/mL. Only 1/24 patients in the ALIS+GBT arm with amikacin MIC >64 μg/mL achieved culture conversion. No patient with both macrolide resistance and persistent amikacin MIC >64 μg/mL (8/24) converted.

Conclusion. In the ALIS+GBT arm of CONVERT, culture conversion rates were similar for amikacin MICs ranging from 8–64 μg/mL at baseline. Amikacin MIC >64 μg/mL emerged in 10.3% of patients after initiation of add-on ALIS treatment, and 3.6% in the GBT alone arm. Emergent amikacin MIC >64 μg/mL was associated with failure to convert, particularly with concurrent macrolide resistance. Determining amikacin susceptibility at both treatment initiation and during treatment may have utility for guiding treatment decisions.

1. Amikacin MIC Distribution at Baseline, All MAC isolates (ITT Population)