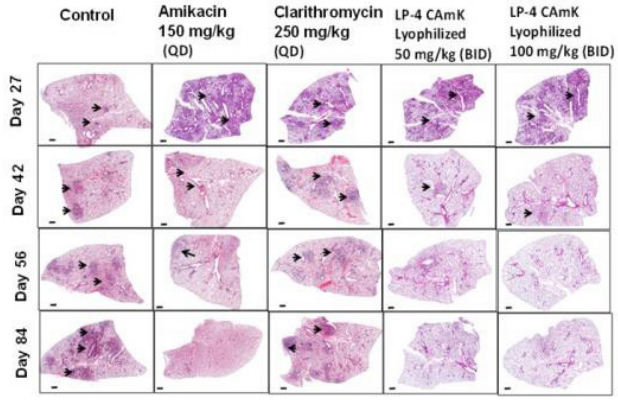
Lung Pathology

Lung pathology in cystic fibrosis mice infected with a macrolide resistant strain of *M. abscessus* subspecies *abscessus* 1513. Sections of Formalin-fixed and paraffin-embedded lung tissue on days 27, 42, 56 and 84 after drug treatment were compared. Lesions (arrow) were more numerous and larger in infected mice that were treated with clarithromycin, and amikacin compared to the smaller lesions after treatment with **oral** LP-4 CAmK Lyophilized 50 mg/kg and **oral** LP-4 CAmK Lyophilized 100 mg/kg.



Conclusion: Conclusions

Oral administration of amikacin-LNCs safely and effectively treats macrolide resistant mycobacterial infections in a mouse model of Cystic Fibrosis.

Disclosures. Ruying Lu, n/a, Matinas BioPharma Inc. (Employee)Matinas BioPharma Inc. (Employee, Shareholder) Raphael J. Mannino, n/a, Matinas BioPharma Inc. (Employee, Shareholder)

1636. Risk of Latent Tuberculosis Reactivation in Patients Treated with Checkpoint Inhibitors Immunotherapy Compared to Other Anti-Cancer Therapies including Hematopoietic Cell Transplantation

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Session: P-72. Tuberculosis and other Mycobacterial Infections

Background. The risk of latent tuberculosis infection (LTBI) reactivation in cancer patients during checkpoint inhibitor immunotherapy (CPI) remains largely unknown. We sought to evaluate LTBI therapy and outcomes between cancer patients receiving CPI versus conventional chemotherapy (CC) and hematopoietic cell transplantation (HCT) recipients.

Methods. We conducted a retrospective cohort study of adult patients with LTBI (positive T-SPOT TB test) at MD Anderson Cancer Center between April 2016 and May 2020, who received CPI or combined with other conventional chemotherapy. Thereafter we compared each group to patients treated with other anti-cancer therapies including CC alone or HCT.

Results. We identified 106 patients with LTBI, who were analyzed into 3 distinct groups: CPI (32 patients, 30%) CC alone (37 patients, 35%), and HCT (37 patients, 35% (7 autologous versus 30 allogeneic). The majority of patients in the CPI group (97%) had solid tumors compared to 54% in the CC group. Nivolumab was the most commonly used CPI agent in 13 patients (40%), followed by pembrolizumab 10 pts (31%). In the CPI group, 20 pts (62%) received LTBI therapy that included Isoniazid (INH), versus 18 patients (49%) in the HCT group and 16 patients (43%) in the CC group (p=0.26). Only 3 patients (CC group) had TB reactivations (8%; p=0.11). None of these 3 patients had received LTBI therapy or corticosteroids prior to the diagnosis. Immune-related adverse effect (IrAEs) were reported in 11 pts (34%) patients, and 9 (82%) of them received corticosteroids. Out of 20 of CPI patients whom received INH, 4 (20%) developed possible INH-induced liver toxicities leading to interruption of medication versus 1 (6%) patient which had mild hepatitis in CC group versus none of HCT patients (p=0.09).

Conclusion. Our data suggest that latent tuberculosis reactivation remains rare, especially in the severely immunocompromised patients on CPI, CC and steroids. However, hepatotoxicity is relatively common in patients treated with CPI and INH. Therefore, caution and close laboratory and clinical monitoring is required to avoid significant hepatic injury and interruption of LTBI therapy and lifesaving oncological therapy.

Disclosures. **Issam I. Raad, MD**, **Citius** (Other Financial or Material Support, Ownership interest)**Cook Medical** (Grant/Research Support)**Inventive Protocol** (Other Financial or Material Support, Ownership interest)**Novel Anti-Infective Technologies** (Shareholder, Other Financial or Material Support, Ownership interest)

1637. SPR720, A Novel Benzamidazole Gyrase Inhibitor, Demonstrates Potent Efficacy Against Mycobacterium avium ATCC 700898 in a Chronic C3HeBFeJ Mouse Infection Model

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Session: P-72. Tuberculosis and other Mycobacterial Infections

Background. SPR719 (the active metabolite of phosphate prodrug SPR720) belongs to a novel class which targets the ATPase subunits of gyrase by a mechanism distinct from fluoroquinolones. SPR719 has potent antibacterial activity against nontuberculous mycobacteria strains (NTM), including *Mycobacterium avium*, and is under development for treatment of NTM pulmonary disease. Oral efficacy of SPR720 was evaluated alone and in combination treatment in the C3HeBFeJ chronic mouse infection model which produces necrotic granulomas, similar to humans.

Methods. Mice were infected with a pulmonary aerosol of $1x10^{8.5}$ CFU of *M. avium* ATCC 700898, (SPR719 MIC = 2 mg/mL). Treatment started on day 28 for 8 weeks with: saline, clarithromycin 250 mg/kg (CLR) QD, SPR720 at 10, 30 and 100 mg/kg QD, or SPR720 at 50 mg/kg BID. SPR720 at 30 mg/kg QD was also combined with CLR +/- ethambutol at 100 mg/kg (EMB), or CLR + rifabutin at 100 mg/kg (RFB) +/- EMB. Mice were evaluated for bacterial burden (CFU) on days 1, 27 and 60 after infection by plating serial dilutions of organ homogenates on nutrient 7H11 and charcoal agar plates. Lung pathology was evaluated by assessing prevalence and size of pulmonary lesions.

Results. CLR treatment for 28 days showed a significant reduction in the bacterial burden in the lung, spleen, and liver compared to the untreated control. SPR720 demonstrated a dose dependent reduction in bacterial burden, including at 100 mg/kg which showed a statistically significant reduction in the bacterial burden in the lung, spleen, and liver. CLR + EMB + SPR720 at 30 mg/kg reduction in the bacterial burden in the lung, spleen, and liver. RFB when added to the treatment regimen did not demonstrate enhanced efficacy compared the additive effect of EMB + CLR +/- SPR720. Lung pathology showed that lesions were less numerous and smaller in infected mice treated with all regimens.

Conclusion. Oral administration of SPR720 demonstrated a statistically significant reduction in the bacterial burden in all tissues with concomitant improvement in lung pathology, both alone and in combination with standard of care agents. These results support the continued development of SPR720 for treatment of NTM pulmonary infections.

Disclosures. Nicole S. Cotroneo, BS, Spero Therapeutics (Employee, Shareholder) Suzanne Stokes, PhD, Spero Therapeutics (Employee, Shareholder)

1638. Synchronous Video Observed Therapy for Monitoring Treatment of Tuberculosis: Experience in a Cases Series from Cali, Colombia, 2019

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Session: P-72. Tuberculosis and other Mycobacterial Infections

Background. In Directly Observed Treatment (DOT) monitoring strategy for the treatment of tuberculosis (TB), the patient has to travel daily to the health institution to take the TB medication. Although has been usefulness, this strategy increases the catastrophic costs of the disease, rising the probability of rejection, abandonment, and failure to treatment. Therefore, a monitoring strategy was implemented through video calls phone known as Synchronous Video Observed Therapy (S-VOT), to document the experience and its results in a series of patients from a low-middle income country.

Methods. A prospective case series study was conducted involving 23 TB patients managed with standard treatment, who were supervised through daily video call phone, during 2019, Cali-Colombia. Adherence to VOT strategy and treatment were evaluated, as well as patient characteristics, adverse drug effects, perception and