P0111
Poster Session I
Animal models: treatment

TP-271, A NOVEL FLUOROCYCLINE, IS EFFICACIOUS IN A TREATMENT MODEL OF AEROSOLIZED FRANCISELLA TULARENSIS INFECTION IN BALB/C MICE

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Objective: The threat of genetically engineered biological weapons requires the development of novel antibiotics with activity against drug-resistant bacteria. *Francisella tularensis* (*Ft*) is a biothreat of concern as it can be weaponized for use in an aerosolized mass attack. TP-271, a fully synthetic tetracycline with potent broad spectrum antibacterial activity, was tested in a mouse tularemia treatment model. **Methods:** The minimal inhibitory concentration (MIC) for *Ft* SchuS4 was determined as per CLSI guidelines. BALB/c mice (6 - 8 weeks old; n=18 - 19, treated group; n=9, untreated group) were exposed by nose-only aerosol to 1.05 x 10^3 colony forming units (CFUs)/mouse (91 LD_{50}) of *Ft* SchuS4. At 72 hrs post-infection, TP-271 was dosed intraperitoneally (IP), once-daily, at 3, 6, 12 or 18 mg/kg for 21 days. Doxycycline (doxy) was given IP twice-daily at 40 mg/kg for 21 days as a positive control. Bacteremia was assessed in 6 mice at the time of treatment initiation. On day 22, half of each group was sacrificed for bacterial burden enumeration, and survival of the remaining half was monitored for 14-days. **Results:** TP-271 and doxy MIC values for *Ft* SchuS4 were 0.03 and 0.06 µg/mL, respectively. At the time of treatment initiation, all 6 sacrificed animals were bacteremic. The mean time to death for the untreated group was 4.8 days. Survival at the end of dosing in the 3, 6, 12 and 18 mg/kg TP-271 groups was 89%, 100%, 100%, and 100%, respectively, and 100% in the doxy group. Of the mice that were sacrificed on day 24, after the last dose, none showed any evidence of bioburden in liver, lungs, spleen or blood. During the relapse period, deaths occurred in the following groups: 6 mg/kg TP-271 (1 of 9 mice) and doxy (7 of 9 mice); no relapse occurred in the 3, 12 and 18 mg/kg TP-271 groups. **Conclusions:** TP-271 showed excellent efficacy and potency in an aerosolized mouse tularemia treatment model when dosing was initiated when the mice were bacteremic. Mice treated with TP-271 showed little to no relapse following end of dosing, whereas doxycycline showed a high rate of relapse (88%). TP-271 continues to show promise as a novel countermeasure for use in the event of an aerosolized exposure to *Ft*.