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1724. Murine Efficacy Studies of Sulopenem Against Bacillus anthracis
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Background. Sulopenem is a thiopenem β-lactam antibiotic being developed for the treatment of infections caused by multi-drug resistant bacteria. Sulopenem is available as intravenous and oral pro-drug formulations, and its activity aligns with the most urgent drug-resistant antimicrobial threats defined by the CDC. Sulopenem possesses potent activity against species of the Enterobacterales that encode ESBLs or AmpC-type β-lactamases that confer resistance to third generation cephalosporins. It has also demonstrated good in vitro microbiological activity against a range of bacterial pathogens including penicillin resistant S. pneumoniae, β-lactamase-producing H. influenza, and M. catarrhalis. Sulopenem is also active in vitro against a number of bio-threat pathogens at concentrations likely to be achieved after oral dosing in humans and meets criteria to be tested in the murine models of Bacillus anthracis, Yersinia pestis, Burkholderia mallei, and Burkholderia pseudomallei. The development of novel medical countermeasures (MCMs) is critical to biodefense preparedness for both military and public health.

Methods. Female BALB/c mice were challenged with B. anthracis Ames spores by whole-body aerosol, with an average challenge of 15 x LD₅₀ and randomly divided into cohorts of 10 mice per group. At 24h post-exposure prophylaxis (PEP), which represents therapy before onset of clinical symptoms, mice were treated q8h for 14 days with vehicle (saline, IP), ciprofloxacin (30mg/kg, IP) or sulopenem etzadroxil (50, 25, or 12.5 mg/kg, PO). Mice were monitored for a total of 30 days and data analyzed to determine the effects of sulopenem etzadroxil on survival as compared to the positive treatment control, ciprofloxacin, using Log-Ranks tests for the pair wise comparisons with SAS software.

Results.

Figure 1:
Conclusion. Sulopenem is active in vivo in the murine model of *B. anthracis*. Survival in the sulopenem treated groups was not statistically inferior to the ciprofloxacin positive control, a standard-of-care for PEP of *B. anthracis*. These results support further development of sulopenem for treating *B. anthracis* as a novel broad-spectrum and orally available MCM.

Disclosures. Sailaja Puttagunta, MD, Iterum Therapeutics: Stocks/Bonds
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