30.5% susceptible to CAZ-AVI) and (2) NS to all drugs except colistin and amikacin (n = 97, 21% of all MDR isolates; 70.1% susceptible to CAZ-AVI).

**Conclusion.** These in vitro data suggest that CAZ-AVI can be an effective treatment option for infections caused by MDR Enterobacteriaceae and P. aeruginosa collected in Latin America.

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

### 707. QPX9003: Pharmacology of a Novel Polymyxin in Mice and Rats

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**Session:** 68. Novel Antimicrobials and Approaches Against Resistant Bugs

**Thursday, October 3, 2019: 12:15 PM**

**Background.** Currently available polymyxins are limited by toxicity and poor efficacy. We have developed a new series of polymyxin derivatives with improved safety profiles and in vitro potency against major MDR bacteria. The following describes studies on the in vivo antimicrobial activity and toxicity of QPX9003 in mice and rats.

**Methods.** Mouse studies. The minimum lethal dose (MLD) by IV bolus and nephrotoxicity (6 IP doses administered 2 hours apart) of QPX9003 and polymyxin B (PMB) were determined in Swiss mice. For the neutropenic mouse thigh infection using *A. baumannii*, Swiss mice were infected with −10^6 CFU/thigh. Doses were administered IP at various intervals starting 2-hour post-infection and continued over 24 hours. For the neutropenic mouse thigh infection model, animals were infected with −0.41 vs. +0.83 log CFU/lung. QPX9003 and PMB were administered IV every 4 hours starting 2 hours post-infection and continued for 24 hours. *B. cepacia* was treated using *E. coli* B (PMB) were determined in Swiss mice. For the neutropenic mouse thigh infection model, animals were infected with −0.41 vs. +0.83 log CFU/lung. QPX9003 and PMB were administered IV every 4 hours starting 2 hours post-infection and continued for 24 hours. *B. cepacia* was treated using *E. coli* B (PMB) were determined in Swiss mice. For the neutropenic mouse thigh infection model, animals were infected with −0.41 vs. +0.83 log CFU/lung. QPX9003 and PMB were administered IV every 4 hours starting 2 hours post-infection and continued for 24 hours.

**Results.** QPX9003 had reduced acute toxicity and nephrotoxicity compared with PMB in mice. QPX9003 showed better bacterial killing of *A. baumannii* than PMB at similar plasma exposures in both the mouse thigh model (−0.41 vs. −0.83 log CFU/thigh) and rat lung infection model (−1.10 vs. −1.44 log CFU/lung).

**Conclusion.** QPX9003 was less acutely toxic, less nephrotoxic, and was more efficacious in mouse and rat infection models compared with PMB. QPX9003 is a promising new polymyxin. (This work was supported in part by federal funds from the Biomedical Advanced Research and Development Authority (BARDA), under OTA number HHSO100201600026C.)

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### 709. In Vitro Antibacterial Activity and In Vivo Efficacy of Sulbactum–Durlobactam (ETX2514SUL) Against Pathogenic Burkholderia Species

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**Session:** 68. Novel Antimicrobials and Approaches Against Resistant Bugs

**Thursday, October 3, 2019: 12:15 PM**

**Background.** The genus *Burkholderia* contains several pathogenic species with distinct etiologies, including *Burkholderia pseudomallei* the biothreat pathogen responsible for melioidosis and *Burkholderia mallei* which causes glanders. β-Lactams, such as ceftazidime and meropenem, are important therapeutic options for these infections. However, clinical resistance to β-lactams, which is primarily mediated by multiple types of β-lactamases, is a growing concern.

**Methods.** The antibacterial activity of SUL alone or in combination with DUR fixed at 4 mg/L against *B. pseudomallei* (n = 30) and *B. mallei* (n = 28) was determined following CLSI guidelines. In vivo efficacy was tested in an acute murine model of melioidosis in which 4 x 10^5 cfu *B. pseudomallei* (SUL-DUR MIC = 1 mg/L) was administrated intranasally to BalB/c mice. SUL-DUR (200/200 or 400/200 mg/kg) was administered q4h subcutaneously 4 hours post-challenge for 6 days and murine survival was monitored for 45 days. Doxycycline (DOX) and ciprofloxacin (CIP) were dosed as positive controls at 40 mg/kg q12 h for 6 days.

**Results.** The addition of DUR effectively lowered the SUL MIC from 8/16 to 0.25/0.5 mg/L vs. *B. pseudomallei* and from 8/18 to 1/2 mg/L for *B. mallei*. All untreated mice in the melioidosis model succumbed to infection within 3 days of challenge. 60% survival was observed for both dose arms of SUL-DUR as compared with 40% survival observed for both CIP and DOX.

**Conclusion.** Preliminary preclinical data demonstrating robust in vitro and in vivo antibacterial activity of SUL-DUR against *Burkholderia spp.* suggests this combination may be an effective new therapy for the treatment of these challenging pathogens.

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### 710. In Vitro Activity and Performance of Available Susceptibility Testing Methods for Eravacunin Against Carbapenem-Resistant Enterobacteriaceae (CRE)

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**Session:** 71. In Vitro Activity and Performance of Available Susceptibility Testing Methods for Eravacunin Against Carbapenem-Resistant Enterobacteriaceae (CRE)

**Thursday, October 3, 2019: 12:15 PM**

**Background.** Eravacunin (PLZ) is a next-generation aminoglycoside currently approved by the US FDA for the treatment of complicated urinary tract infections, including prostatitis. The purpose of this study was to evaluate the in vitro activity of PLZ against a large collection of Gram-negative bacilli obtained from patients attending Canadian hospitals.

**Methods.** Annualy from 2011 to 2018, sentinel hospitals across Canada submitted blood, respiratory, urine, and wound isolates from patients attending ERs, medical and surgical wards, hospital clinics, and ICUs (CANWARD). Susceptibility testing was performed using broth microdilution (and breakpoints) as described by CLSI (FDA breakpoints used for PLZ).

**Results.** See table. PLZ demonstrated excellent in vitro activity against E. coli and *K. pneumoniae* clinical isolates, including aminoglycoside NS, ESBL-positive, and MDR subsets.

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