30.5% susceptible to CAZ-AV1 (2) and (2) NS to all drugs except colistin and amikacin (n = 97, 21% of all MDR isolates; 70.1% susceptible to CAZ-AV1).

**Conclusion.** These in vitro data suggest that CAZ-AV1 can be an effective treatment option for infections caused by MDR Enterobacteriaceae and P. aeruginosa collected in Latin America.

**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 in select dosed states. We have developed a new series of polymyxins 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 minimal 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 neutrophilic mouse thigh infection using A. baumannii, Swiss mice were infected with 10⁵ CFU/thigh. Doses were administered IP at various intervals starting 2-hour post-infection and continued over 24 hours. Rat studies. For the rat lung infection model, Sprague-Dawley rats were administered IP at various intervals starting 2-hour post-infection and continued over 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 USCAST, San Diego, California; Monash University, Clayton, Victoria, Australia; Qpx Biopharma/United States Committee on Antimicrobial Susceptibility Testing (USCAST), San Diego, California)

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708. In Vivo Activity of Plazomicin vs. Clinical Isolates of Gram-Negative Bacilli, Including Aminoglycoside Nonsusceptible and Multidrug-Resistant Subsets, Recovered from Patients Across Canada as Part of the CANWARD study, 2011–2018

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**Background.** Plazomicin (PLZ) is a next-generation aminoglycoside currently approved by the US FDA for the treatment of complicated urinary tract infections, including prenephritis. 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.** Annually from 2011 to 2018, sentinel hospitals across Canada submitted blood, respiratory, urine, and wound isolates from patients attending EDs, 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 activity in vitro against E. coli and K. pneumoniae clinical isolates, including aminoglycoside NS, ESBL-positive, and MDR subsets.

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709. In Vitro Antimicrobial Activity and In Vivo Efficacy of Sulbactam–Durlobactam (ETX2514SUL) Against Pathogenic Burkholderia Species

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**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 in these species, is a growing concern. Durlobactam (ETX2514, DUR) is a novel β-lactamase inhibitor with broad-spectrum activity against Ambler class A, C, and D β-lactamases. Burkholderia (SUL) is an Ambler Class A β-lactamase inhibitor with intrinsic antibacterial activity against a limited number of species, including Acinetobacter spp. Sulbactam (SUL) is currently in Phase 3 clinical testing for the treatment of carbapenem-resistant infections caused by Acinetobacter spp. In this study, SUL-DUR was tested for in vitro antibacterial activity against B. pseudomallei and B. mallei as well as for in vivo efficacy in a preclinical model of melioidosis.

**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 10⁶ cfu Bp K96423 (SUL-DUR MIC = 1 mg/L) was administered intranasally to BalbC mice. SUL-DUR (100/200 or 400/200 mg/kg) was administered q12h 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 q12h for 6 days.

**Results.** The addition of DUR effectively lower the SUL MIC₉₀ from 8/16 to 0.25/0.5 mg/L. B. pseudomallei and from 8/11 to 0.12/0.25 mg/L. 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 Eravacycline Against Carbapenem-Resistant Enterobacteriaceae (CRE)

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**Background.** The current era of antimicrobial resistance (AMR) presents a major threat to human health. Carbapenem-resistant Enterobacteriaceae (CRE) are emerging as a major threat. Eravacycline (ERV) is a novel, glycylpropionyl-tetrazinyl-tricyclic-spiro[isoxazolidine-piperazine]-dione (TET) class antimicrobial. ERV acts by targeting the bacterial deoxyribonucleic acid (DNA) gyrase and topoisomerase IV enzymes. We evaluated the performance of commercially available susceptibility testing methods for ERV against a collection of CRE isolated from cases of CRE bloodstream infections (BSIs) as well as against a single isolate of Burkholderia pseudomallei, which is related to CRE and to which ERV is active.

**Methods.** In vitro testing was performed using broth microdilution (and breakpoints) as described by CLSI. The CLSI broth microdilution panel contained 26 CRE isolates, 1 B. pseudomallei isolate, and 1 B. mallei isolate. The isolates represent a range of CRE serotypes and were collected from the United States, Europe, and Asia. The CRE panel included 11 KPC-3, 2 KPC-2, 11 IMP, 1 VIM-1, and 1 NDM-1 strains. Additionally, 1 isolate each of KPC-2 and IMP-1 was collected from Central and South America. The B. pseudomallei isolate was collected from a patient in Thailand.

**Results.** All methods were tested in a blinded fashion. Overall, in vitro MIC results were comparable across all methods; however, the majority of susceptibility results were different for B. pseudomallei. The most consistent method was the CLSI broth microdilution panel, followed by NCCLS broth microdilution and CLSI agar dilution. The Vitek 2 system produced discrepant results for B. pseudomallei. For B. mallei, all methods resulted in an MIC₉₀ ≤ 0.06 μg/mL.

**Conclusion.** CRE are emerging as a major threat to human health. Eravacycline is a promising new agent active against CRE. In vitro methods vary in their performance, with the most consistent results produced by the CLSI broth microdilution panel. Further, in vitro methods consistently underestimates the in vivo activity of ERV against CRE and B. pseudomallei.

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