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.

	Drug (% susceptible)					
Species/phenotype (n)	**CAZ-AVI**	**CAZ**	**MEM**	**AMK**	**CST**	**TGC**
All *Enterobacteriaceae* (5381)	99.3	70.5	94.4	96.7	82.7	97.3
MDR (1426)	97.3	11.4	79.1	88.3	88.1	97.3
All *E. coli* (1848)	99.95	71.2	99.2	98.4	99.1	99.9
MDR (547)	99.8	13.5	97.4	95.2	98.5	100
All *K. pneumoniae* (1499)	98.7	54.2	84.7	93.1	94.7	97.5
MDR (622)	97.1	4.8	63.3	84.6	88.9	96.1
All *E. cloacae* (356)	97.8	61.8	93.8	95.5	94.4	97.8
MDR (101)	92.1	2.0	79.2	84.2	95.0	96.0
All *P. aeruginosa* (1347)	87.2	69.9	66.1	82.4	99.6	NA
MDR (462)	62.8	22.3	17.1	51.9	99.6	NA

CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; MEM, meropenem; AMK, amikacin; CST, colistin; TGC, tigecycline; NA, not applicable

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

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

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Background. Currently available polymyxins are limited by toxicity and poor efficacy at tolerated doses. 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. *Rat studies*. For the rat lung infection model, Sprague-Dawley rats were infected with ~10^7 CFU/lung. QPX9003 and PMB were administered IV every 4 hours starting 2 hours post-infection and continued over 24 hours. *Bacteria*. For both infection models, animals were infected with *A. baumannii* AB1016 (QPX9003 MIC of 0.5 mg/L and PMB MIC of 1.0 mg/L). Untreated control groups were sacrificed at the start of treatment and both untreated and treated groups were sacrificed 24 hours after the start of treatment, infected tissues harvested, homogenized, and plated to determine colony counts.

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 National Institutes of Allergy and Infectious Diseases [R01AI098771], and the Department of Health and Human Services; Office of the Assistant Secretary for Preparedness and Response; Biomedical Advanced Research and Development Authority (BARDA), under OTA number HHSO100201600026C).

Compounds	Mouse: Single Dose MLD IV (mg/kg)	Mouse: Kidney Changes (10 mg/kg IP x 6 doses)	Rat Lung Model: 24h AUC for 1-log bacterial killing vs. *A. baumannii*
PMB	7.5	Minimal to Severe Nephrosis	>160
QPX9003	20	No change	46

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708. *In Vitro* 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 pyelonephritis. 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 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.

S, susceptible; NS, nonsusceptible; ESBL, extended-spectrum β-lactamase; MDR, multidrug-resistant (NS to antimicrobials from three or more classes); n.d., not defined.

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

Organism/Phenotype (Number tested)	PLZ		Gentamicin		Meropenem	
	$MIC_{50/90}$	%S	$MIC_{50/90}$	%S	$MIC_{50/90}$	%S
Escherichia coli						
ALL (4793)	0.5/1	99.4	≤0.5/2	90.4	≤0.03/≤0.03	99.9
Gentamicin NS (458)	0.5/1	98.9	32/>32	0.0	≤0.03/≤0.03	99.6
Tobramycin NS (405)	0.5/1	98.8	32/>32	31.6	≤0.03/≤0.03	99.5
ESBL-positive (489)	0.5/1	99.8	1/>32	66.5	≤0.03/0.06	99.8
MDR (570)	0.5/1	99.1	2/>32	50.4	≤0.03/0.06	99.6
Klebsiella pneumoniae						
All (1627)	0.25/0.5	99.8	≤0.5/≤0.5	96.5	≤0.03/0.06	99.3
Gentamicin NS (57)	0.25/1	96.5	32/>32	0.0	≤0.03/1	91.2
Tobramycin NS (78)	0.25/0.5	97.4	32/>32	38.5	0.06/2	89.7
ESBL-positive (104)	0.25/0.5	98.1	≤0.5/>32	53.9	≤0.03/1	91.4
MDR (116)	0.25/0.5	97.4	1/>32	53.4	≤0.03/1	90.5
***Klebsiella aerogenes* (174)**	0.5/0.5	99.4	≤0.5/≤0.5	99.4	0.06/0.12	98.9
***Klebsiella oxytoca* (447)**	0.25/0.5	99.8	≤0.5/≤0.5	98.2	≤0.03/0.06	100.0
***Enterobacter cloacae* (736)**	0.25/0.5	99.6	≤0.5/≤0.5	97.2	≤0.03/0.12	99.2
***Morganella morganii* (90)**	2/4	73.3	≤0.5/2	92.2	0.06/0.25	100.0
***Proteus mirabilis* (357)**	4/8	43.1	≤0.5/2	93.3	0.06/0.12	100.0
***Serratia marcsesens* (419)**	0.5/1	97.9	≤0.5/1	99.3	0.06/0.06	99.5
***Pseudomonas aeruginosa* (2665)**	4/16	n.d.	1/8	88.7	0.5/8	79.4

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

709. *In Vitro* Antibacterial 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. Sulbactam (SUL) is an Ambler Class A β-lactamase inhibitor with intrinsic antibacterial activity against a limited number of species, including *Acinetobacter* spp. SUL-DUR 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 × 10^4 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 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 $MIC_{50/90}$ from 8/16 to 0.25/0.5 mg/L vs. *B. pseudomallei* and from 8/8 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.

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

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

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