and AmpC), and aztreonam (ATM) is a monobactam stable to hydrolysis by metallo-β-lactamases (MBL).

Methods. A total of 10,451 *Enterobacteriaceae*(ENT) consecutively collected from 84 United States (US) medical centers and 250 carbapenem-resistant ENT (CRE) collected from 38 centers in 25 other countries (ex-US) were tested for susceptibility (S) by reference broth microdilution methods in a central monitoring laboratory (JMI Laboratories). CRE strains were screened for the presence of carbapenemase (CBP)-encoding genes using whole genome sequencing analysis.

Results. All ENT isolates from US ($MIC_{50/90}$, ≤0.03/0.12 µg/mL), except for 1 *Escherichia coli* strain with an ATM-AVI MIC of 8 µg/mL, and all ex-US CRE isolates ($MIC_{50/90}$, 0.25/0.5 µg/mL) were inhibited at ATM-AVI MIC of ≤4 µg/mL (CLSI S breakpoint for ATM). Among US isolates, ATM-AVI was also very active against CRE (n = 120; $MIC_{50/90}$, 0.12/0.5 µg/mL; highest MIC, 4 µg/mL), multidrug-resistant (MDR; n = 876; $MIC_{50/90}$, 0.06/0.25 µg/mL), extensively drug-resistant (XDR; n = 111; $MIC_{50/90}$, 0.12/0.5 µg/mL), pan-drug resistant (n = 2; MICs ≤0.03 and 0.12 µg/mL), and ceftazidime-non-S *Enterobacter cloacae* ($MIC_{50/90}$, 0.25/1 µg/mL) isolates. Meropenem was very active against US ENT overall ($MIC_{50/90}$, 0.03/0.06 µg/mL; 98.8%S per CLSI), but showed limited activity against MDR (86.2%S) and XDR (30.6%S) isolates. Amikacin and colistin were active against 74.2% and 81.7% of US CRE, 93.4% and 58.3% US MDR, 65.8% and 57.7% of US XDR, and 58.0% and 79.2% of ex-US CRE isolates, respectively. A total of 106 CBPs were detected in 106 US CRE isolates, including 102 KPC-like, 2 SME-4, 1 NDM-1, and 1 IMP-27. Also, 248 CBPs were identified on 241 ex-US CRE isolates, including 124 KPC-like, 64 OXA-like, 50 NDM-like, 7 VIM-1, 2 IMP-4, and 1 SME-4. All CRE isolates, including all CBP-producing ENT (US and ex-US), were inhibited at ATM-AVI MIC of ≤4 µg/mL.

Conclusion. ATM-AVI demonstrated potent *in vitro* activity against a large collection of contemporary (2016) ENT isolated from patients in US hospitals and CRE isolates collected worldwide, including NDM, KPC, OXA, VIM, and SME producers.

Disclosures. **H. S. Sader**, Allergan: Research Contractor, Research grant; **R. E. Mendes**, Allergan: Research Contractor, Research grant; **D. Shortridge**, Allergan: Research Contractor, Research grant; **R. K. Flamm**, Allergan: Research Contractor, Research grant; **M. Castanheira**, Allergan: Research Contractor, Research grant

1234. Activity of Meropenem-Vaborbactam Against *Enterobacteriaceae* Isolates Carrying bla_{KPC} Collected Worldwide

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Background. Meropenem-vaborbactam (MER-VAB) is a carbapenem-β-lactamase inhibitor combination with enhanced activity against KPC-producing *Enterobacteriaceae* recently evaluated in a phase 3 clinical trials for cUTIs and infections due to CRE. We analyzed the activity of MER-VAB against 517 isolates carrying bla_{KPC} collected worldwide during 2014–16.

Methods. *Enterobacteriaceae* isolates (n = 34,069) from 34 countries were susceptibility (S) tested by reference broth microdilution method for MER-VAB (at fixed 8 µg/mL) and comparators. Carbapenem-resistant *Enterobacteriaceae* (CRE; CLSI criteria) were submitted to PCR/Sanger sequencing or next-generation sequencing for bla_{KPC} screening.

Results. A total of 517 (1.5%) carried bla_{KPC} and 6 variants were observed: 293 bla_{KPC-3}, 218 bla_{KPC-2}, 2 bla_{KPC-4}, 2 bla_{KPC-17}, and 1 each of bla_{KPC-2}-like and bla_{KPC-12}. Isolates were mainly *K. pneumoniae* (437), but also 32 *E. cloacae*, 13 *K. oxytoca*, 12 *E. coli*, 12 *S. marcescens*, and 4 other species. Isolates carrying bla_{KPC} were detected in 17 countries. The occurrence ranged from <0.1% to 11.3%, being higher in Brazil, Italy (9.3%), Poland (5.6%), and Argentina (5.2%). MER-VAB inhibited 514/517 (99.4%) isolates carrying bla_{KPC} at ≤8 µg/mL and this compound was the most active agent tested against these isolates ($MIC_{50/90}$, 0.12/1 µg/mL). Three isolates displaying elevated MER-VAB MIC values (>8 µg/mL) co-harbored bla_{NDM-1} or bla_{OXA-48}-like in addition to bla_{KPC} or had a missense mutation on OmpK35. MER alone ($MIC_{50/90}$, 32/>32 µg/mL), imipenem ($MIC_{50/90}$, >8/>8 µg/mL), and doripenem ($MIC_{50/90}$, >4/>4 µg/mL) were not active against isolates harboring bla_{KPC}. Amikacin ($MIC_{50/90}$, 16/>32 µg/mL) and gentamicin ($MIC_{50/90}$, 2/>8) µg/mL inhibited only 54.9% and 57.3% of the isolates (CLSI breakpoint). Colistin ($MIC_{50/90}$, ≤0.5/>8 µg/mL; 70.4% S/EUCAST breakpoint) and tigecycline ($MIC_{50/90}$, 0.5/1 µg/mL; 99.4% S/US FDA criteria) were the most active comparators.

Conclusion. The occurrence of bla_{KPC} is still low overall, but can be as high as 5–10% in a few countries and occur in species other than *Klebsiella*. KPC-producers are highly resistant to available antimicrobial agents and MER-VAB will be a useful alternative to treat infections caused by these organisms.

Disclosures. **M. Castanheira**, Rempex, a wholly owned subsidiary of The Medicines Company: Research Contractor, Research grant; **R. E. Mendes**, Rempex, a wholly owned subsidiary of The Medicines Company: Research Contractor, Research grant; **L. R. Duncan**, Rempex, a wholly owned subsidiary of The Medicines Company: Research Contractor, Research grant; **L. N. Woosley**, Rempex, a wholly owned subsidiary of The Medicines Company: Research Contractor, Research grant; **R. K. Flamm**, Rempex, a wholly owned subsidiary of The Medicines Company: Research Contractor, Research grant

1235. Activity of Plazomicin against *Enterobacteriaceae* Isolates Collected in the United States Including Isolates Carrying Aminoglycoside-Modifying Enzymes Detected by Whole Genome Sequencing

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Session: 147. Expanded Spectrum – New Antimicrobial Susceptibility Testing
Friday, October 6, 2017: 12:30 PM

Background. Plazomicin (PLZ) is a next-generation aminoglycoside (AMG) stable against aminoglycoside-modifying enzymes (AME) that completed Phase 3 studies for complicated urinary tract infections and serious infections due to carbapenem-resistant *Enterobacteriaceae* (ENT). We evaluated the activity of PLZ and AMGs against ENT collected in US hospitals during 2016.

Methods. A total of 2,097 ENT were susceptibility (S) tested by CLSI reference broth microdilution methods. *E. coli*, *Klebsiella* spp. *Enterobacter* spp., and *P. mirabilis* isolates displaying non-S MICs (CLSI criteria) for gentamicin (GEN), amikacin (AMK), and/or tobramycin (TOB) were submitted to WGS, *de novo* assembly and screening for AME genes.

Results. Against ENT, PLZ was more active than all 3 clinically available AMGs (Table). PLZ and AMK activities were stable regardless of the infection type; however, differences were observed for GEN and TOB. Bloodstream isolates displayed higher GEN MICs when compared with the other infection sites. TOB activity varied 4-fold, being higher for bloodstream and pneumonia infections and lower for skin/soft tissue and other/unknown specimens. Against 198 isolates carrying 1 or more AME-encoding genes detected among 208 AMG-non-S isolates, the activity of PLZ was 8- to 16-fold greater when compared with the activity of AMK and at least 16-fold higher than the activity of GEN or TOB.

Conclusion. PLZ was active against ENT isolates from US hospitals regardless of infection type. PLZ displayed activity against isolates carrying AME genes that represent 12.0% of selected species. AME-carrying isolates were considerably more resistant to AMK, GEN, and TOB, highlighting the potential value of PLZ to treat infections caused by these organisms.

This project has been funded under BARDA Contract No. HHSO100201000046C.

	$MIC_{50/90}$ (µg/mL)			
Organism group/infection type (no. tested)	Plazomicin	Amikacin	Gentamicin	Tobramycin
Enterobacteriaceae (2,097)	0.5/1	2/4	0.5/4	0.5/4
Urinary tract infection (587)	0.5/1	2/4	0.5/2	0.5/4
Bloodstream infection (572)	0.5/1	2/4	0.5/>8	0.5/8
Pneumonia in hospitalized patients (451)	0.25/1	2/4	0.5/4	0.5/8
Skin/soft tissue infection (298)	0.5/2	2/4	0.5/1	0.5/2
Intra-abdominal infection (152)	0.5/1	2/4	0.5/4	0.5/4
Other sites (37)	0.25/1	1/2	0.5/1	0.5/2
Isolates carrying AME genes (198)	0.5/1	4/16	>8/>8	>8/>8

Disclosures. **M. Castanheira**, Achaogen: Research Contractor, Research grant; **L. M. Deshpande**, Achaogen: Research Contractor, Research grant; **C. M. Hubler**, Achaogen: Research Contractor, Research grant; **R. E. Mendes**, Achaogen: Research Contractor, Research grant; **A. W. Serio**, Achaogen: Employee, Salary; **K. M. Krause**, Achaogen: Employee, Salary; **R. K. Flamm**, Achaogen: Research Contractor, Research grant

1236. *In Vivo* Efficacy of Tigecycline-based Therapy Against *Vibrio vulnificus* Sepsis: Comparison with pre-Existing Regimens

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Session: 147. Expanded Spectrum – New Antimicrobial Susceptibility Testing
Friday, October 6, 2017: 12:30 PM

Background. The mortality of *Vibrio vulnificus* sepsis is still high, despite the application of various antibiotic regimens. *In-vivo* efficacy of tigecycline against *V. vulnificus* has not been examined.

Methods. Time-kill assay was performed to evaluate the presence of *in-vitro* antibiotic synergism. The cytotoxicity of *V. vulnificus* was measured by using the lactate dehydrogenase assay, and rtxA1 toxin gene transcription was measured by β-galactosidase assay. Subcutaneous injection of *V. vulnificus* was performed with 1×10^8 CFU on iron-overloaded female BALB/c mouse, then intraperitoneal antibiotic therapy was initiated 2 hours after bacterial inoculation.

Results. In vitro time-kill assay reveals synergism between tigecycline and ciprofloxacin. Inhibitory effects of tigecycline on rtx A1 transcription (66%) and cytotoxicity (59%) were comparable to those of ciprofloxacin (64% and 53%), but superior to those of minocycline (76% and 69%) or cefotaxime (86% and 83%; $P < 0.05$, each). Survival of tigecycline-treated mice were significantly higher than those of mice treated by current regimens ($P < 0.05$, each; Table). At *Vibrio vulnificus* sepsis mice inoculating 1×10^9 CFU, survival rate for tigecycline-plus-ciprofloxacin was significantly higher than that of tigecycline (0%; 0/19) or tigecycline-plus-cefotaxime (0%; 0/19) ($P < 0.05$, each; Table).

	10^8 CFU, 96hr survival (%)	10^9 CFU, 96hr survival (%)
control	0/24 (0%)	0/13 (0%)
ciprofloxacin	14/25 (56%)	N.A
cefotaxime-minocycline	16/25 (64%)	N.A
tigecycline	22/25 (88%)	0/19 (0%)
tigecycline-cefotaxime	21/25 (84%)	0/19 (0%)
tigecycline-ciprofloxacin	21/25 (84%)	7/19 (37%)