MHT. Modified Hodge Test, APB: boronic acid synergy; EDTA: EDTA synergy; Pos: positive; Neg: negative. KPC (Klebsiella pneumoniae Carbapenemase), VIM (Verona integron-mediated metallo- β-lactamase), NDM (New Delhi metallo-β-lactamase), OXA (oxacillinase-48-like carbapenemase (OXA-48))

Conclusion. Conventional phenotypic synergy tests with boronic acid and EDTA used for detecting carbapenemases are suboptimal and their routine use should be reconsidered. They depend on the degree of enzyme expression and the distance between disks. Lateral flow immunoassay tests are a rapid and cost-effective tool to detect and differentiate carbapenemases, improving clinical outcomes through targeted therapy and promoting infection prevention measures.

Disclosures. **Diego Josa, Msc**, **ALIFAX** (Speaker's Bureau) **German Esparza, n/a**, **Biomerieux** (Consultant)**Pfizer** (Speaker's Bureau) **Luis Reyes, n/a**, **MSD** (Speaker's Bureau)

1252. *In Vitro* Activity of Aztreonam-Avibactam and Comparator Agents Against Enterobacterales from Patients with Bloodstream Infections collected during the ATLAS Global Surveillance Program, 2015-2019

Sibylle Lob, PhD[1]; Krystyna Kazmierczak, PhD[1]; Francis Arhin, PhD[2]; Daniel F. Sahm, PhD[1]; [1]IHMA, Inc., Schaumburg, IL; [2]Pfizer Canada, Kirkland, Quebec, Canada

Session: P-72. Resistance Mechanisms

Background. Treatment options for β-lactamase-producing Enterobacterales are limited, particularly for infections caused by metallo-β-lactamase (MBL)-producing strains. The β-lactam/non-β-lactam β-lactamase inhibitor combination aztreonam-avibactam (ATM-AVI) is active *in vitro* against Enterobacterales isolates carrying MBLs, including those co-producing β-lactamases of Class A, C, and some class D enzymes. This study evaluated the *in vitro* activity of ATM-AVI and comparators against Enterobacterales isolates collected in 2015-2019 from patients with bloodstream infections (BSI) as part of the ATLAS program.

Methods. Non-duplicate clinical isolates were collected in 53 countries in Europe, Latin America, Asia/Pacific (excluding mainland China and India), and Middle East/Africa. Susceptibility testing was performed by CLSI broth microdilution and interpreted using CLSI 2021 and FDA (tigecycline) breakpoints. ATM-AVI was tested at a fixed concentration of 4 μg/mL AVI. MDR was defined as resistant (R) to ≥3 of 7 sentinel drugs: amikacin, aztreonam, cefepime, colistin, levofloxacin, meropenem, and piperacillin-tazobactam. PCR and sequencing were used to determine the β-lactamase genes present in all isolates with meropenem MIC >1 μg/mL, and *Escherichia coli*, *Klebsiella* spp. and *Proteus mirabilis* phenotypically positive for ESBL activity (2015) or with aztreonam or ceftazidime MIC >1 μg/mL (2016-2019).

Results. ATM-AVI was active *in vitro* against Enterobacterales isolates from BSI (MIC_{90}, 0.12 μg/mL), with 99.97% of isolates inhibited by ≤8 μg/mL of ATM-AVI, including 100% of isolates that produced MBLs. ATM-AVI tested with MIC_{90} values of 0.5 μg/mL against subsets of cefepime-nonsusceptible (NS), meropenem-NS, amikacin-NS, colistin-resistant, and MBL-positive Enterobacterales (Table). The tested β-lactam comparators showed susceptibility of < 79% against these subsets of resistant isolates.

Results Table

	MIC50 [μg/mL] / % Susceptible											
	ATM-AVI		ATM		FEP		MEM		AMK		TGC	
Phenotype (n)	MIC90	%S	MIC90	%S	MIC90	%S	MIC90	%S	MIC90	%S	MIC90	%S
All (11416)	0.12	NA	128	71.0	>16	73.1	0.12	94.0	8	96.6	1	97.5
FEP-NS (3069)	0.5	NA	>128	6.2	>16	0.0	>8	78.4	32	88.6	2	96.2
MEM-NS (689)	0.5	NA	>128	8.6	>16	3.9	>8	0.0	>32	66.5	2	92.3
AMK-NS (390)	0.5	NA	>128	14.1	>16	10.5	>8	40.8	>32	0.0	2	92.6
CST-R (307)[a]	0.5	NA	>128	40.1	>16	46.6	>8	63.2	32	85.3	2	95.8
MDR (2028)	0.5	NA	>128	4.2	>16	2.5	>8	67.4	>32	82.6	2	94.9
MBL-positive (177)	0.5	NA	>128	14.7	>16	0.6	>8	3.4	>32	57.6	4	88.1

ATM-AVI, aztreonam-avibactam; ATM, aztreonam, FEP, cefepime; MEM, meropenem; AMK, amikacin; TGC, tigecycline; CST, colistin; S, susceptible; NS, susceptible; NA, no breakpoint available; MBL, metallo-β-lactamase.
[a]Excluded *Morganellaceae* and *Serratia* spp. with intrinsic resistance to colistin.

Conclusion. Based on MIC_{90} values, ATM-AVI was the most potent agent tested against drug-resistant and MBL-positive subsets of Enterobacterales collected from BSI. The promising *in vitro* activity of ATM-AVI warrants further development of this combination for treatment of BSI caused by drug-resistant Enterobacterales.

Disclosures. **Sibylle Lob, PhD**, **IHMA** (Employee)**Pfizer, Inc.** (Independent Contractor) **Krystyna Kazmierczak, PhD**, **IHMA** (Employee)**Pfizer, Inc.** (Independent Contractor) **Francis Arhin, PhD**, **Pfizer, Inc.** (Employee) **Daniel F. Sahm, PhD**, **IHMA** (Employee)**Pfizer, Inc.** (Independent Contractor)

1253. Antimicrobial Activity of Cefepime in Combination with Taniborbactam Against Clinical Isolates of Enterobacterales from 2018-2020 Global Surveillance

Meredith Hackel, PhD MPH[1]; Mark G G. Wise, PhD[2]; Daniel F. Sahm, PhD[1]; [1]IHMA, Inc., Schaumburg, Illinois; [2]IHMA, Schaumburg, Illinois

Session: P-72. Resistance Mechanisms

Background. Taniborbactam (formerly VNRX-5133) is a novel cyclic boronate-based broad-spectrum β-lactamase inhibitor with potent and selective direct inhibitory activity against both serine- and metallo-β-lactamases (Ambler Classes A, B, C and D). Taniborbactam restores the activity of cefepime against many difficult to treat organisms, including cephalosporin- and carbapenem-resistant Enterobacterales and *Pseudomonas aeruginosa*. The activity of the investigational combination cefepime-taniborbactam (FTB) and comparator agents was evaluated against clinical isolates of Enterobacterales from a 2018-2020 global surveillance study.

Methods. MICs of cefepime with taniborbactam fixed at 4 μg/mL and comparators were determined following CLSI M07-A11 guidelines against 10,543 Enterobacterales. Isolates were from community and hospital infections collected from 259 sites in 56 countries in 2018-2020. Resistant phenotypes were based on 2021 CLSI breakpoints. A set of 827 isolates with meropenem MIC ≥4 μg/mL (n=421) or with cefepime and/or ceftazidime MIC ≥2 μg/mL (n=406) was evaluated for the presence of MBLs, KPC, ESBLs, and OXA-48 group genes via PCR and sequencing. Forty-eight isolates with FTB MIC values of 16 μg/mL or greater were interrogated by WGS.

Results. Overall, 23.0% and 15.9% of isolates were nonsusceptible (NS) to cefepime and piperacillin-tazobactam (TZP), respectively (Table). FTB had potent activity against all Enterobacterales, with $MIC_{50/90}$ values of 0.06/0.25 μg/mL and 99.5% inhibited at ≤8 μg/mL. FTB maintained activity against MBL-, KPC-, OXA-48 group, and ESBL-positive isolates (MIC_{90} range, 1 to >16 μg/mL; 80.5% to 100% inhibited at ≤8 μg/mL). Isolates with elevated FTB MICs had IMP-type enzymes, variation in the cefepime target (penicillin binding protein 3), permeability defects in combination with acquired β-lactamases, and/or possible up-regulated efflux.

Results Table

Resistance Phenotype/ Genotype	N (%)	MIC90 (μg/mL)/Percent susceptible					
		FTB	FEP	CZA	CT	MEV	TZP
All	10543 (100%)	0.25/99.5[a]	> 16/77.0	0.5/98.0	8/86.8	0.12/97.6	128/84.1
FEP NS	2430 (23.0%)	2/98.0[a]	> 16/0	4/91.4	> 8/57.6	8/89.6	> 128/54.9
TZP NS	1680 (15.9%)	2/97.3[a]	> 16/34.7	> 16/87.9	> 8/28.2	16/84.6	> 128/0
MEM NS	527 (5.0%)	8/92.4[a]	> 16/5.1	> 16/64.1	> 8/2.7	> 16/51.0	> 128/1.3
MEV NS	258 (2.4%)	16/85.3[a]	> 16/1.6	> 16/37.2	> 8/0.4	> 16/0	> 128/0
CZA NS	212 (2.0%)	> 16/81.1[a]	> 16/1.9	> 16/0	> 8/0.5	> 16/23.6	> 128/4.3
ESBL-positive[b]	356 (40.7% [e])	1/99.2[a]	> 16/7.0	1/99.2	>8/77.5	0.12/99.4	>128/77.4
KPC-positive[c]	166 (19.0%[e])	2/100[a]	> 16/1.2	4/97.0	> 8/0.6	2/95.8	> 128/0
OXA-48-like-positive[c]	120 (13.7%[e])	4/97.5[a]	> 16/10.0	2/100	> 8/3.3	> 16/26.7	> 128/0
MBL-positive (VIM or NDM)[d]	174 (19.9%[e])	> 16/80.5[a]	>16/0.6	>16/0.6	>8/0	>16/9.2	> 128/0

FTB, cefepime with taniborbactam fixed at 4 mg/L; FEP, cefepime; CZA, ceftazidime-avibactam; CT, ceftolozane-tazobactam; MEM, meropenem; MEV, meropenem-vaborbactam; TZP, piperacillin-tazobactam; NS, nonsusceptible based on 2021 CLSI breakpoints.
[a]Corresponds to cefepime susceptible, dose-dependent breakpoint against Enterobacterales (≤8 μg/mL), for comparative purposes only
[b]Organisms could also possess AmpC-type enzymes, or OSBLs (original-spectrum β-lactamases, e.g., TEM-1, SHV-1)
[c]Note organisms could also possess ESBLs, AmpC-type enzymes, or OSBLs, but no other carbapenemase
[d]Includes NDM (n=158) and VIM (n=16). Note organisms could also possess serine carbapenemases, ESBLs, AmpC-type enzymes, or OSBLs
[e]Percent based on total of 875 molecularly characterized isolates

Conclusion. Taniborbactam significantly restored the *in vitro* activity of cefepime against Enterobacterales, including isolates nonsusceptible to recently-approved BL/BLI combinations and expressing serine and metallo-β-lactamases. This support the continued development of FTB as a potential new treatment option for challenging infections due to resistant Gram-negative pathogens.

Disclosures. **Meredith Hackel, PhD MPH**, **IHMA** (Employee)**Pfizer, Inc.** (Independent Contractor) **Mark G G. Wise, PhD**, **IHMA** (Employee)**Pfizer, Inc.** (Independent Contractor) **Daniel F. Sahm, PhD**, **IHMA** (Employee)**Pfizer, Inc.** (Independent Contractor)

1254. Molecular Epidemiology of *Escherichia coli* Causing Urinary Tract Infections in United States and *in vitro* Activity of Tebipenem, Including Against Strain Lineage and Resistant subsets (2018-2020)

Rodrigo E. Mendes, PhD[1]; Timothy B. Doyle[1]; Ian A. Critchley, Ph.D.[2]; Nicole Cotroneo[2]; Jennifer M. Streit, BS[1]; Mariana Castanheira, PhD[1]; Mariana Castanheira, PhD[1]; [1]JMI Laboratories, North Liberty, Iowa; [2]Spero Therapeutics, Cambridge, Massachusetts

Session: P-72. Resistance Mechanisms

Background. Tebipenem (TBP) is an oral carbapenem in clinical development for treating complicated urinary tract infections (UTIs), including pyelonephritis. This study investigates the epidemiology of *E. coli* (EC) causing UTI in U.S. patients and the activity of TBP and comparators against various subsets.

Methods. A total of 2,395 EC recovered from urine samples during the 2018-2020 STEWARD Surveillance Program were included. Isolates were collected from medical centers in all 9 US Census Regions and centrally tested by reference broth microdilution method. MIC interpretation was based on CLSI criteria. Isolates that met MIC criteria were subjected to genome sequencing, followed by screening of extended-spectrum β-lactamase (ESBL) genes and epidemiology typing (MLST).

Results. A total of 16.1%, 15.4% and 14.6% of EC met the ESBL screening criteria in 2018, 2019 and 2020, respectively. 269/360 (74.7%) carried bla_{CTX-M} and 2/360 (0.6%) had bla_{SHV-12}. bla_{CMY} (33/360; 9.2%) was the most common cephalosporinase, followed by bla_{DHA} (7/360; 1.9%). A CRE phenotype was noted in 1 isolate from New York, which carried bla_{KPC-2}. Acquired genes were not detected in 56 strains. 50 ST types were noted in isolates that met the ESBL criteria screening,