(5,448/49.5%), Latin America (1,805/16.4%), MidEast/Africa (861/7.8%), and North America (1,145/10.4%).

Results. Ceftaroline and comparator agent activities are summarized in the following table.

Table

Organism (n)*	MIC_{90} (µg/mL)/%Susceptible				
	CPT	CRO	LZD	DAP	ERY
Staphylococcus aureus, MRSA (2,454)	1/91.4	>64/na	2/100	1/99.8	>8/33.8
Staphylococcus aureus, MSSA (2,692)	0.25/99.9	4/na	2/100	0.5/100	8/77.3
Staphylococcus epidermidis (1,978)	0.5/98.0	>32/na	2/98.7	1/99.9	>8/30.1
Streptococcus pneumoniae (2,421)	0.12/99.9	0.5/97.4	1/100	0.5/0	8/76.0
Beta-hemolytic streptococci (1,453)†	0.015/100	0.12/99.9	1/100	0.5/100	>1/80.5

* n refers to number of isolates tested against ceftaroline; numbers may vary for comparators (range 1031-5785); †includes *S. agalactiae* (n=342), *S. dysgalactiae* (n=305), and *S. pyogenes* n=806).
CPT, ceftaroline; CRO, ceftriaxone; LZD, linezolid; DAP, daptomycin; ERY; erythromycin; na, no MIC breakpoints available.

Conclusion. Greater than 98% of *S. pneumoniae, S. epidermidis,* beta-hemolytic streptococci and MSSA isolates included in a 2012-2018 collection of gram-positive blood stream pathogens were susceptible to ceftaroline. 91.4% of MRSA were susceptible, and 8.6% isolates categorized as susceptible-dose dependent (MIC, 2-4 ug/mL); two isolates (one each from Thailand and S. Korea) were resistant to ceftaroline (MIC >4 ug/mL). Ceftaroline continues to demonstrate potent *in vitro* activity against clinically relevant pathogens associated with BSI.

Disclosures. **Greg Stone, PhD**, **AztraZeneca** (Shareholder, Former Employee)**Pfizer, Inc.** (Employee) **Daniel F. Sahm, PhD**, **IHMA** (Employee)**Pfizer, Inc.** (Consultant)**Shionogi & Co., Ltd.** (Independent Contractor)

1567. *In Vitro* Activity of Aztreonam-Avibactam and Comparator Agents Against Multidrug-Resistant Enterobacterales Collected Globally as Part of the ATLAS Surveillance Program, 2016-2018

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Avibactam (AVI) is a serine-β-lactamase inhibitor in development with aztreonam (ATM) for treatment of infections caused by drug-resistant Enterobacterales (Ent), especially carbapenem-resistant isolates co-producing serine- and metallo-β-lactamases (MBL), which are often resistant to agents from multiple drug classes. This study evaluated the *in vitro* activity of ATM-AVI and comparators against Ent collected globally as part of the Antimicrobial Testing Leadership and Surveillance (ATLAS) program.

Methods. 44,671 non-duplicate clinical isolates were collected in 2016-2018 in 52 countries in Europe, Asia/Pacific (excluding China and India), Middle East/Africa, and Latin America. Susceptibility testing was performed by CLSI broth microdilution and interpreted using CLSI 2020 and FDA (tigecycline) breakpoints. ATM-AVI was tested at a fixed concentration of 4 µg/mL AVI. Drug-resistant phenotypes were defined as: multidrug resistant (MDR), resistant (R) to ≥3 of 7 sentinel agents (amikacin [AMK], ATM, cefepime [FEP], colistin [CST], levofloxacin [LVX], meropenem [MEM], piperacillin-tazobactam [TZP]); extensively drug resistant (XDR), susceptible to ≤2 sentinel agents; and pandrug resistant (PDR), non-susceptible to all sentinel agents. Isolates with MEM MIC >1 µg/mL were screened for β-lactamase genes by PCR and sequencing.

Results. 14.9%, 4.3%, 3.7%, 1.3%, and 0.3% of Ent collected globally were MDR, XDR, MEM-R, MBL-positive, and PDR, respectively. ATM-AVI tested with MIC_{90} values of 0.12 µg/mL against all Ent and 0.5 µg/mL against subsets of resistant isolates (Table). On the regional level, similar values were observed against all (MIC_{90}, 0.12 µg/mL) and resistant isolates (MIC_{90}, 0.25-1 µg/mL) (not shown). The tested comparators, excluding TGC, showed percentages of susceptibility < 90% against regional and global subsets of resistant isolates. 99.97% (44658 of 44671) Ent, including all MBL-positive and PDR isolates, were inhibited by ≤8 µg/mL of ATM-AVI.

Table

	Drug (MIC_{90} [µg/mL]/ % Susceptible)									
	ATM-AVI		ATM		MEM		AMK		TGC	
Phenotype (n)	MIC_{90}	% S	MIC_{90}	% S	MIC_{90}	% S	MIC_{90}	% S	MIC_{90}	% S
All Enterobacterales (44671)	0.12	NA	64	74.2	0.12	95.7	8	97.4	1	97.0
MEM-R (1645)	0.5	NA	>128	10.7	>8	0.0	>32	64.1	2	91.9
MDR (6662)	0.5	NA	>128	4.8	>8	73.0	>32	84.4	2	94.2
XDR (1936)	0.5	NA	>128	4.0	>8	16.8	>32	55.7	2	91.0
PDR (151)	0.5	NA	>128	0.0	>8	0.0	>32	0.0	4	75.5
MBL+ (582)	0.5	NA	>128	19.6	>8	5.2	>32	59.1	4	87.1

ATM-AVI, aztreonam-avibactam; ATM, aztreonam; MEM, meropenem; AMK, amikacin; TGC, tigecycline; R, resistant; MDR, multidrug resistant (R to ≥3 of 7 sentinel agents [ATM, MEM, AMK, cefepime, colistin, levofloxacin, piperacillin-tazobactam]); XDR, extensively drug resistant (susceptible (S) to ≤2 sentinel agents); PDR, pandrug resistant (S to 0 sentinel agents); MBL+, metallo-β-lactamase-positive (a gene encoding an MBL was detected by PCR); NA, no breakpoints available. % Susceptible was determined using CLSI 2020 breakpoints for all agents except TGC. TGC MICs were interpreted using U.S. FDA breakpoints.

Conclusion. Based on MIC_{90} values, ATM-AVI demonstrated potent *in vitro* activity against resistant and MBL-positive subsets of Ent collected globally. ATM-AVI could be an effective therapy for difficult-to-treat infections caused by drug-resistant Ent.

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1568. *In Vitro* Activity of Ceftazidime-Avibactam and Comparator Agents Against Enterobacterales and *Pseudomonas aeruginosa* Collected < 48 Hours and ≥48 Hours Post-Admission from Pediatric Patients, ATLAS Surveillance Program 2015-2018

Krystyna Kazmierczak, PhD[1]; Greg Stone, PhD[2]; Daniel F. Sahm, PhD[1]; [1]IHMA, Inc., Schaumburg, IL; [2]Pfizer, Inc., Groton, Connecticut

Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Ceftazidime-avibactam (CAZ-AVI) is a β-lactam/non-β-lactam β-lactamase inhibitor combination with *in vitro* activity against Enterobacterales (Ent) and *Pseudomonas aeruginosa* (*Psa*) carrying Class A, C and some Class D β-lactamases. We examined the *in vitro* activity of CAZ-AVI and comparators against presumed community-acquired (CA; cultured < 48 h after hospital admission) and hospital-acquired (HA; cultured ≥48 h post-admission) isolates collected from pediatric patients as part of the ATLAS surveillance program.

Methods. 6023 non-duplicate isolates were collected in 50 countries in Europe (n=3122), Latin America (n=1220), Middle East/Africa (n=1007), and Asia/Pacific (excluding China; n=674) from patients (newborn to 17 y) with lower respiratory tract (LRTI; n=1641), urinary tract (UTI; n=1595), skin and soft tissue (SSTI; n=1027), intra-abdominal (IAI; n=949), and bloodstream (BSI; n=811) infections. Susceptibility testing was performed by CLSI broth microdilution and values were interpreted using CLSI 2020 breakpoints. CAZ-AVI was tested at a fixed concentration of 4 µg/mL AVI. Isolates with CAZ or aztreonam MICs ≥2 µg/mL (*Escherichia coli*, *Klebsiella* spp., *Proteus mirabilis*) or meropenem MICs ≥2 µg/mL (all Ent species) or ≥4 µg/mL (*Psa*) were screened for β-lactamase genes.

Results. The *in vitro* activity of CAZ-AVI exceeded that of meropenem and other tested β-lactams against Ent (98.5% susceptible (S)) and *Psa* (93.1% S) collected globally from pediatric patients (Table). Percentages of susceptibility to CAZ-AVI ranged from 96.8-99.3% among CA Ent from different infection types and were reduced 0.4-1.0% among HA isolates from SSTI, IAI and BSI. Susceptibility to CAZ-AVI was also similar (92.7-95.4% S) among CA *Psa* from different infection types and was reduced 0.1-4.4% among HA isolates. For both Ent and *Psa*, the lowest percentages of susceptibility to the tested β-lactams were observed among isolates from BSI, which included a higher proportion of isolates carrying extended-spectrum β-lactamases and/or carbapenemases than isolates from other infection types.

Table

Organism (n, % of total)/ Drug	All Sources	% Susceptible (Infection Source/Length of Hospitalization)									
		LRTI		UTI		SSTI		IAI		BSI	
		<48 h	≥48 h	<48 h	≥48 h	<48 h	≥48 h	<48 h	≥48 h	<48 h	≥48 h
Enterobacterales	4692 (100)	331 (32.2)	698 (67.8)	838 (59.9)	561 (40.1)	324 (42.0)	447 (58.0)	447 (55.9)	353 (44.1)	216 (31.2)	477 (68.8)
CAZ-AVI	98.5	98.2	99.1	99.3	99.3	98.8	97.8	99.3	98.3	96.8	96.4
CAZ	75.3	76.7	71.9	79.5	71.8	84.6	77.4	87.0	77.3	67.6	58.9
MEM	97.0	96.4	97.9	98.2	97.1	96.9	96.2	98.9	97.7	94.4	93.9
TZP	85.2	82.2	82.7	87.8	83.4	92.0	82.8	94.2	85.0	82.4	79.2
P. aeruginosa	1331 (100)	230 (37.6)	382 (62.4)	86 (43.9)	110 (56.1)	108 (42.2)	148 (57.8)	95 (63.8)	54 (36.2)	41 (34.7)	77 (65.3)
CAZ-AVI	93.1	94.8	91.4	93.0	92.7	95.4	95.3	94.7	92.6	92.7	88.3
CAZ	82.0	81.3	79.6	87.2	83.6	80.6	84.5	89.5	83.3	82.9	75.3
MEM	78.1	77.8	72.8	91.9	79.1	79.6	81.1	90.5	79.6	70.7	67.5
TZP	78.3	78.7	74.9	82.6	76.4	78.7	79.1	86.3	85.2	78.0	75.3

LRTI, lower respiratory tract infection; UTI, urinary tract infection; SSTI, skin and soft tissue infection; IAI, intra-abdominal infection; BSI, bloodstream infection; CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; MEM, meropenem; TZP, piperacillin-tazobactam. Isolates for which data regarding infection source and length of hospitalization were not available were excluded from analysis.

Conclusion. CAZ-AVI could provide a valuable therapeutic option for treatment of CA and HA infections caused by Ent and *Psa* in pediatric patients.

Disclosures. Krystyna Kazmierczak, PhD, IHMA (Employee)Pfizer, Inc. (Consultant) Greg Stone, PhD, AztraZeneca (Shareholder, Former Employee)Pfizer, Inc. (Employee) Daniel F. Sahm, PhD, IHMA (Employee)Pfizer, Inc. (Consultant) Shionogi & Co., Ltd. (Independent Contractor)

1569. *In Vitro* Activity of Ceftazidime-avibactam and Comparator Agents against Enterobacterales and *Pseudomonas aeruginosa* Collected from Patients with Bloodstream Infections as Part of the ATLAS Global Surveillance Program, 2015-2018

Krystyna Kazmierczak, PhD[1]; Sibylle Lob, PhD[1]; Greg Stone, PhD[2]; Daniel F. Sahm, PhD[1]; [1]IHMA, Inc., Schaumburg, IL; [2]Pfizer, Inc., Groton, Connecticut

Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Avibactam (AVI) is a β-lactamase inhibitor with potent inhibitory activity against Class A, Class C, and some Class D serine β-lactamases. The combination of ceftazidime (CAZ) with AVI has been approved in Europe and in the United States for several indications. This study evaluated the *in vitro* activity of CAZ-AVI and comparators against Enterobacterales (*Eba*) and *Pseudomonas aeruginosa* (*Pae*) isolates collected from patients with bloodstream infections as part of the ATLAS surveillance program in 2015-2018.

Methods. A total of 57048 *Eba* and 15813 *Pae* non-duplicate clinically significant isolates, including 7720 *Eba* and 1286 *Pae* isolated from bloodstream infections, were collected in 52 countries in Europe, Latin America, Asia/Pacific (excluding mainland China), and the Middle East/Africa region. Susceptibility testing was performed by CLSI broth microdilution. CAZ-AVI was tested at a fixed concentration of 4 µg/ml AVI. Meropenem-nonsusceptible (MEM-NS) *Eba* and *Pae* isolates were screened for the presence of β-lactamase genes.

Results. Susceptibility data are shown in the Table. Percentages of susceptibility (% S) to the tested agents were 0.3-2.9% lower among *Eba* and *Pae* from bloodstream infections compared to isolates from combined sources in most cases. CAZ-AVI showed potent *in vitro* activity against all *Eba* bloodstream isolates and the CAZ-NS subset (MIC_{90}, 0.5-2 µg/ml, 93.4-98.1% S). Reduced activity against MEM-NS *Eba* was attributable to carriage of class B metallo-β-lactamases (MBLs) because 99% of MEM-NS MBL-negative isolates were susceptible to CAZ-AVI. None of the tested comparators exceeded the activity of CAZ-AVI. CAZ-AVI also showed good *in vitro* activity against the majority of *Pae* bloodstream isolates (MIC_{90}, 16 µg/ml, 89.4% S). Activity was reduced against CAZ-NS and MEM-NS subsets (54.2-63.8% S), which included isolates carrying MBLs, but exceeded the activity of CAZ and MEM against these subsets by 26-31 percentage points. Amikacin was the only tested comparator that demonstrated comparable activity against *Pae* bloodstream isolates.

Table

		CAZ-AVI		CAZ		MEM		TZP		AMK	
Source	Organism/Phenotype (n)	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S
All	Enterobacterales, All (57048)	0.5	98.6	64	74.5	0.12	95.6	> 64	84.0	8	97.0
Blood	All (7720)	0.5	98.1	64	71.6	0.12	94.2	> 64	83.7	8	96.6
	CAZ-NS (2192)	2	93.4	> 128	0.0	> 8	81.0	> 128	52.8	32	89.7
	MEM-NS (445)	> 128	69.4	> 128	6.5	> 16	0.0	> 128	1.1	> 64	62.9
	MEM-NS, MBL-negative (312)	4	99.0	> 128	9.3	> 16	0.0	> 128	1.0	> 64	69.6
All	*P. aeruginosa*, All (15813)	8	90.9	64	76.5	> 8	73.2	128	72.2	32	89.9
Blood	All (1286)	16	89.4	64	76.9	> 8	71.6	> 64	73.9	> 32	87.0
	CAZ-NS (297)	128	54.2	> 128	0.0	> 16	23.6	> 128	7.7	> 64	53.5
	MEM-NS (365)	128	63.8	> 128	37.8	> 16	0.0	> 128	31.5	> 64	58.1
	MEM-NS, MBL-negative (288)	32	80.2	> 128	47.2	16	0.0	> 128	38.2	64	69.8

CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; MEM, meropenem; TZP, piperacillin-tazobactam; AMK, amikacin; NS, non-susceptible; MBL, metallo-β-lactamase. % Susceptible was determined using CLSI 2020 breakpoints.

Conclusion. CAZ-AVI provides a valuable therapeutic option for treating bloodstream infections caused by MBL-negative *Eba* and *Pae* isolates.

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1570. *In Vitro* Activity of Ceftazidime-Avibactam and Comparator Agents Against Enterobacterales from ICU and Non-ICU Wards Collected in Latin America and Globally as part of the ATLAS Surveillance Program 2017-2018

Sibylle Lob, PhD[1]; Krystyna Kazmierczak, PhD[1]; Greg Stone, PhD[2]; Daniel F. Sahm, PhD[1]; [1]IHMA, Inc., Schaumburg, IL; [2]Pfizer, Inc., Groton, Connecticut

Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Ceftazidime-avibactam (CAZ-AVI) is a β-lactam/non-β-lactam β-lactamase inhibitor combination with activity against Enterobacterales producing class A, C and some class D β-lactamases. Resistance caused by these β-lactamases is especially high in ICUs. This study evaluated the *in vitro* activity of CAZ-AVI and comparators against Enterobacterales isolates from patients in ICU and non-ICU wards.

Methods. Non-duplicate clinical isolates were collected in 2017-2018 from patients in Asia/Pacific, Europe, Latin America, and Middle East/Africa. Susceptibility testing was performed using CLSI broth microdilution and interpreted using CLSI 2020 and FDA (tigecycline) breakpoints. PCR and sequencing were used to determine the β-lactamase genes present in all isolates with meropenem (MEM) MIC >1 µg/ml, and *Escherichia coli*, *Klebsiella* spp. and *Proteus mirabilis* with aztreonam or ceftazidime MIC >1 µg/ml.

Results. The activity of CAZ-AVI and comparators is shown in the table. Susceptibility rates among global Enterobacterales were generally lower for isolates from patients in ICU than non-ICU wards, but this difference was small for CAZ-AVI, which inhibited ≥97% of isolates from both ward types. Among MEM-nonsusceptible (NS) isolates, CAZ-AVI was active against 66.5% and 68.1% of ICU and non-ICU isolates, respectively (of which 31.8% and 30.8%, respectively, carried metallo-β-lactamases [MBLs]). CAZ-AVI inhibited >97% of MEM-NS MBL-negative isolates collected globally. Antimicrobial activity against all Enterobacterales from both ICU and non-ICU wards in Latin America (LA) was generally similar to the global average. Among MEM-NS isolates, antimicrobial activity of CAZ-AVI and TGC was higher in LA than the global average among isolates from both ward types, at least partly because of a lower proportion of MBL-positive isolates in this subset (15.8% and 17.9% in ICU and non-ICUs, respectively). CAZ-AVI inhibited 100% of MEM-NS MBL-negative isolates from LA.

Table

		Drug (% Susceptible)					
Region/phenotype	**Ward type (n)**	**CAZ-AVI**	**CAZ**	**MEM**	**TZP**	**AMK**	**TGC**
Global[a]							
All Enterobacterales	ICU (6896)	97.0	66.6	91.5	77.7	94.5	97.0
	Non-ICU (19259)	98.6	75.0	96.1	85.8	97.6	96.7
MEM-NS	ICU (585)	66.5	6.8	0.0	1.9	58.0	93.0
	Non-ICU (759)	68.1	8.0	0.0	4.5	68.8	90.5
MEM-NS MBL-negative	ICU (399)	97.5	10.0	0.0	2.3	66.4	93.5
	Non-ICU (525)	97.9	11.6	0.0	5.5	74.7	93.9
Latin America							
All Enterobacterales	ICU (1166)	98.2	61.7	89.7	78.0	94.5	97.0
	Non-ICU (3101)	99.1	70.0	95.7	84.9	97.0	97.2
MEM-NS	ICU (120)	84.2	2.5	0.0	0.8	70.0	97.5
	Non-ICU (134)	82.8	9.0	0.0	3.7	67.9	95.5
MEM-NS MBL-negative	ICU (101)	100	3.0	0.0	1.0	75.3	97.0
	Non-ICU (110)	100	10.9	0.0	2.7	72.7	98.2

[a]Includes isolates from Asia/Pacific (excluding mainland China), Europe, Latin America, and Middle East/Africa
CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; MEM, meropenem; TZP, piperacillin-tazobactam; AMK, amikacin; TGC, tigecycline; NS, non-susceptible; MBL, metallo-β-lactamase

Conclusion. CAZ-AVI provides a valuable treatment option for infections caused by Enterobacterales that do not carry MBLs, including those among patients in ICU wards, where antimicrobial resistance is typically higher.

Disclosures. Sibylle Lob, PhD, IHMA (Employee)Pfizer, Inc. (Consultant) Krystyna Kazmierczak, PhD, IHMA (Employee)Pfizer, Inc. (Consultant) Greg Stone, PhD, AztraZeneca (Shareholder, Former Employee)Pfizer, Inc. (Employee) Daniel F. Sahm, PhD, IHMA (Employee)Pfizer, Inc. (Consultant)Shionogi & Co., Ltd. (Independent Contractor)

1571. *In Vitro* Activity of Ceftazidime-Avibactam and Comparator Agents Against MDR Enterobacterales and *Pseudomonas aeruginosa* Collected in Latin America During the ATLAS Global Surveillance Program 2017-2018

Krystyna Kazmierczak, PhD[1]; Sibylle Lob, PhD[1]; Greg Stone, PhD[2]; Daniel F. Sahm, PhD[1]; [1]IHMA, Inc., Schaumburg, IL; [2]Pfizer, Inc., Groton, Connecticut

Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Ceftazidime-avibactam (CAZ-AVI) is a β-lactam/non-β-lactam β-lactamase inhibitor combination that can inhibit class A, C and some class D β-lactamases. Resistance caused by these β-lactamases often results in multidrug-resistance (MDR). This study evaluated the *in vitro* activity of CAZ-AVI and comparators against MDR Enterobacterales and *Pseudomonas aeruginosa* isolates collected from patients in Latin America.

Methods. Non-duplicate clinical isolates were collected in 2017-2018 in 10 countries in Latin America. Susceptibility testing was performed using CLSI broth microdilution and interpreted using CLSI 2020 and FDA (tigecycline) breakpoints. MDR was defined as resistant (R) to ≥3 of 7 sentinel drugs: amikacin (AMK), aztreonam (ATM), cefepime (FEP), colistin (CST), levofloxacin (LVX), meropenem (MEM), and piperacillin-tazobactam (TZP).

Results. The activity of CAZ-AVI and comparators against all isolates and MDR subsets is shown in the table. MDR rates for the studied species ranged from 17.6% among *E. cloacae* to 31.0% among *K. pneumoniae*. CAZ-AVI was active against 99% of Enterobacterales isolates and maintained activity against 85-99% of MDR isolates of the examined species. Only tigecycline showed comparable or higher activity. Among *P. aeruginosa*, CAZ-AVI was active against 86% of all isolates and 45% of MDR isolates; no other studied drug was more active. The three most common MDR phenotypes among Enterobacterales were 1) R to ATM, FEP, and LVX (n=538, 50% of all MDR Enterobacterales; 100% susceptible (S) to CAZ-AVI), 2) R to all sentinel drugs except AMK and CST (n=112, 10% of all MDR isolates; 88% S to CAZ-AVI), and 3) R to ATM, FEP, LVX, and TZP (n=111, 10% of all MDR Enterobacterales; 100% S to CAZ-AVI). The three most common MDR phenotypes among *P. aeruginosa* were 1) R to all sentinel drugs except CST (n=70, 22% of all MDR isolates; 20% S to CAZ-AVI), 2) R to AMK, LVX, and MEM (n=33, 10% of all MDR isolates; 33% S to CAZ-AVI), and 3) R to all sentinel drugs except AMK and CST (n=30, 9% of all MDR isolates; 70% S to CAZ-AVI).