Table

Table. Antimicrobial activity of CAZ-AVI and comparators tested against AmpC-overproducing *Enterobacterales* and *Pseudomonas aeruginosa* isolates

	CLSI	
Organism and antimicrobial agent (no. of isolates)	**Susceptible, n (%)**	**Nonsusceptible, n (%)***
Enterobacterales, AmpC overproducing (n=77)		
Ceftazidime-avibactam	74 (96.1)	3 (3.9)
Ceftazidime	5 (6.5)	72 (93.5)
Meropenem-vaborbactam	76 (98.7)	1 (1.3)
Meropenem	74 (96.1)	3 (3.9)
Ceftolozane-tazobactam	20 (35.1)	57 (64.9)
Gentamicin	47 (61.0)	30 (39.0)
Levofloxacin	37 (48.1)	40 (51.9)
Amikacin	65 (84.4)	12 (15.6)
P. aeruginosa, AmpC overproducing (n=53)		
Ceftazidime-avibactam	39 (73.6)	14 (26.4)
Ceftazidime	1 (1.9)	52 (98.1)
Meropenem-vaborbactam	No CLSI breakpoints	
Meropenem	20 (37.7)	33 (62.3)
Ceftolozane-tazobactam	31 (58.5)	22 (41.5)
Gentamicin	25 (47.2)	28 (52.8)
Levofloxacin	9 (17.0)	44 (83.0)
Amikacin	37 (69.8)	16 (30.2)

*Nonsusceptible includes intermediate or resistant isolates. CLSI=Clinical & Laboratory Standards Institute

Conclusion. CAZ-AVI was the most active agent against AmpC-overproducing *P. aeruginosa* with higher proportion of clinical cure than controls. CAZ-AVI was also among the most active agents against AmpC-overproducing *Enterobacterales*, with >96% isolates susceptible.

Disclosures. Lynn-Yao Lin, MS, AbbVie (Employee) Dmitri Debabov, PhD, AbbVie (Employee) William Chang, BS, AbbVie (Employee) Urania Rappo, MD, MS, PharmD, Allergan (before its acquisition by AbbVie) (Employee)

1593. Antimicrobial Activity of Ceftazidime-Avibactam and Comparator Agents Against OXA-48 β-lactamase–Producing *Enterobacterales* Collected in International Medical Centers, Including the United States, in 2017–2018

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. OXA-48 is a carbapenemase with low-level hydrolytic activity toward cephalosporins. This study evaluated in vitro activities of ceftazidime-avibactam (CAZ-AVI), meropenem (MEM), meropenem-vaborbactam (MVB), ceftolozane-tazobactam (C/T), and other antimicrobial agents against 113 OXA-48-producing *Enterobacterales* with multiple resistance mechanisms collected in a 2017–2018 global surveillance program.

Methods. Nonduplicate clinical isolates of 113 *Enterobacterales* were collected from medical centers in 25 countries in 2017–2018. In vitro susceptibility tests were performed by broth microdilution with a custom-made panel consisting of CAZ-AVI, ceftazidime (CAZ), MEM, MVB, C/T, colistin (COL), gentamicin (GEN), levofloxacin (LEV), and amikacin (AMK). Whole genome sequencing or quantitative PCR data were used to analyze resistance mechanisms, such as OXA-48, extended-spectrum β-lactamase (ESBL), original-spectrum β-lactamase (OSBL), and AmpC β-lactamase. Clinical and Laboratory Standards Institute breakpoints were applied for susceptibility interpretations.

Results. Of 113 OXA-48–producing clinical isolates, 20 carried OXA-48 alone. The remaining 93 isolates carried additional β-lactamases, including 63 with ESBL (CTX-M-15) + OSBL (SHV, TEM), 15 with AmpC (DHA, AAC, CMY) + ESBL (CTX-M-15), and 15 with OSBL (SHV, TEM). 99.1% (all but 1) of all isolates tested were susceptible to CAZ-AVI, whereas 71.7%, 17.7%, and 14.2% were susceptible to MVB, MEM, and C/T, respectively. Among isolates harboring multiple resistance mechanisms (OXA-48 + ESBL + OSBL; n=63), 98.4%, 69.8%, 11.1%, and 7.9% were susceptible to CAZ-AVI, MVB, MEM, and C/T, respectively. Among isolates carrying OXA-48 + AmpC + ESBL + OSBL (n=15), 100%, 66.7%, 13.3%, and 13.3% were susceptible to CAZ-AVI, MVB, MEM, and C/T, respectively (Table). Aminoglycosides (AMK and GEN) and other β-lactams (eg, CAZ) were 20%–90% active against these isolates. COL was the second most effective comparator, inhibiting 83.2% of these isolates.

Table

Table. In vitro susceptibility of ceftazidime-avibactam and comparators against isolates with OXA-48–producing *Enterobacterales* with multiple resistance mechanisms.

Antimicrobial agent	% Susceptible				
	All OXA-48 (n=113)	OXA-48 alone (n=20)	OXA-48 + OSBL (n=15)	OXA-48 + ESBL + OSBL (n=63)	OXA-48 + AmpC (DHA, AAC, CMY) + ESBL +OSBL (n=15)
CAZ-AVI	99.1	100	100	98.4	100
CAZ	27.4	25	20	23.8	33.3
MVB	71.7	100	46.7	69.8	66.7
MEM	17.7	45	13.3	11.1	13.3
C/T	14.2	25	20	7.9	13.3
GEN	54.9	60	73.3	52.3	53.3
LEV	27.4	55	26.7	20.6	26.7
AMK	79.6	90	80	82.5	86.7
COL	83.2	85	80	79.4	100

AmpC, AmpC β-lactamase; AMK, amikacin; CAZ, ceftazidime; CAZ-AVI, ceftazidime-avibactam; COL, colistin; C/T, ceftolozane-tazobactam; ESBL, extended-spectrum β-lactamase; GEN, gentamicin; LEV, levofloxacin; MEM, meropenem; MVB, meropenem vaborbactam; OSBL, original-spectrum β-lactamase.

Conclusion. CAZ-AVI was the most effective agent in this study compared with other antibiotics, including β-lactams, β-lactam–β-lactamase inhibitor combinations, aminoglycosides, and COL, against OXA-48-producing *Enterobacterales* carrying multiple β-lactamases.

Disclosures. Lynn-Yao Lin, MS, AbbVie (Employee) Dmitri Debabov, PhD, AbbVie (Employee) William Chang, BS, AbbVie (Employee)

1594. Antimicrobial Resistance Monitoring through the ATLAS Global Surveillance Program 2012-2018

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Antimicrobial resistance is an increasingly serious threat to global public health. The Antimicrobial Testing Leadership and Surveillance (ATLAS) program has provided reliable, global, regional and local *in vitro* susceptibility data, including mechanisms of resistance, since 2004. In this analysis, data from the ATLAS program are used to measure the *in vitro* activity of several key gram-negative/gram-positive agents against major global pathogens.

Methods. A total of 251,837 gram-negative and 132,363 gram-positive non-duplicate, clinical isolates were collected from multiple infection sources from 743 unique sites in 74 countries during 2012-2018 in the ATLAS program. Identification was confirmed to the species level using MALDI-TOF spectrometry. Only one clinically relevant causative isolate per patient was accepted into the study. MICs were determined by broth microdilution following CLSI guidelines and interpreted using 2020 CLSI breakpoints. Phenotypic ESBL screening and confirmatory testing were performed using the CLSI M100 method.

Results. The *in vitro* activities of selected antimicrobial agents are provided in the table below. Based on percent susceptibility, ceftazidime-avibactam, amikacin, tigecycline, meropenem, and ceftolozane-tazobactam were the most active agents against most gram-negative isolates. The CRE rate among Enterobacterales isolates was 3.2%, with tigecycline and ceftazidime-avibactam the most active among this resistant subgroup. Ceftazidime-avibactam, ceftolozane-tazobactam, and amikacin were the most active agents against *Pseudomonas aeruginosa*. Ceftaroline, linezolid, tigecycline and vancomycin all showed good activity against gram-positive isolates.