Table

Species/phenotypes	n	% Susceptible[a] C/T	P/T	FEP	CAZ	ATM	MEM	LVX	AMK
All Enterobacterales	909	92.5	88.7	90.8	84.2	84.7	98.1	80.8	98.9
K. pneumoniae	184	89.7	82.1	78.3	75.0	77.2	95.1	76.6	98.4
E. coli	170	98.2	92.9	89.4	85.9	85.3	100	65.9	99.4
P. aeruginosa	621	96.6	70.5	76.5	76.8	64.4	74.2	65.4	96.5
Enterobacterales + *P. aeruginosa*	1530	94.2	81.3	85.0	81.2	76.5	88.4	74.6	97.9
CAZ-NS	288	69.4	24.3	32.3	0.0	9.0	69.1	44.4	93.1
FEP-NS	230	76.1	22.6	0.0	15.2	6.1	56.5	30.4	90.0
MEM-NS	177	83.1	35.6	43.5	49.7	26.6	0.0	32.2	89.8
P/T-NS	286	71.0	0.0	37.8	23.8	15.4	60.1	46.5	92.7

[a]Results for colistin are not shown because Enterobacterales and *P. aeruginosa* are no longer considered susceptible to colistin per CLSI 2020 guidelines, as clinical and PK/PD data demonstrated limited clinical efficacy.
C/T, ceftolozane/tazobactam; P/T, piperacillin/tazobactam; FEP, cefepime; CAZ, ceftazidime; ATM, aztreonam; MEM, meropenem; LVX, levofloxacin; AMK, amikacin

Conclusion. With its broad coverage of Enterobacterales and *P. aeruginosa*, C/T can provide an important empiric therapy option for patients with LRTI in the US.

Disclosures. Sibylle Lob, PhD, IHMA (Employee)Pfizer, Inc. (Consultant) Daryl DePestel, PharmD, BCPS-ID, Merck & Co, Inc (Employee) Katherine Young, MS, Merck & Co., Inc. (Employee, Shareholder)Merck & Co., Inc. (Employee, Shareholder) Mary Motyl, PhD, Merck & Co, Inc (Employee, Shareholder) Daniel F. Sahm, PhD, IHMA (Employee)Pfizer, Inc. (Consultant)Shionogi & Co., Ltd. (Independent Contractor)

1588. Activity of Imipenem/Relebactam Against Clinical Isolates of *P. aeruginosa* and *K. pneumoniae* Collected in Asia/Pacific Countries – SMART 2016-2018

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Relebactam (REL) inhibits class A and C β-lactamases and was approved in the USA in combination with imipenem (IMI) and cilastatin for the treatment of complicated intraabdominal and urinary tract infections. We evaluated the activity of IMI/REL against clinical isolates collected in Asia/Pacific as part of the global SMART surveillance program.

Methods. In 2016-2018, 56 clinical laboratories each collected up to 250 consecutive, aerobic and facultative gram-negative pathogens from various infection sources per year. Susceptibility was determined using CLSI broth microdilution and CLSI breakpoints. IMI-nonsusceptible isolates (except from India) were screened for β-lactamase genes.

Results. Among 5501 *K. pneumoniae* and 4362 *P. aeruginosa* isolates, 46.6% and 65.3%, respectively, were collected from patients with lower respiratory tract infections, 25.6% and 17.1% from intraabdominal infections, 19.9% and 13.9% from urinary tract infections, and 7.2 and 2.9% from bloodstream infections. No infection source was specified for 0.7% of isolates from either species. 90.7% of collected *K. pneumoniae* isolates were IMI/REL-susceptible, ranging from 56.8% in India and ~80% in Thailand and Vietnam (~16% MBL-positive) to ≥97% in 7 countries (0-2% MBL-positive). 28.6% (202/707) of IMI-nonsusceptible *K. pneumoniae* were IMI/REL-susceptible. Of the 425 molecularly characterized IMI-nonsusceptible *K. pneumoniae*, 187 (44.0%) were MBL/OXA-48-like negative and 83.4% of these (156/187) were IMI/REL-susceptible; 82 isolates (19.3%) were KPC-positive and 91.5% of these (75/82) were IMI/REL-susceptible.

The table shows percent susceptible and percent MBL-positive among all collected *P. aeruginosa* isolates. 74.3% of IMI-nonsusceptible *P. aeruginosa* (n=1236) were IMI/REL-susceptible.

Table

Country[b]	n	% Susceptible[a] IMI/REL	IMI	FEP	ATM	P/T	LVX	AMK	% MBL+
Australia	753	96.3	80.2	87.5	77.7	82.5	78.1	97.2	0.1
Hong Kong	94	88.3	66.0	75.5	60.6	68.1	69.2	98.9	0.0
India	389	60.4	38.6	52.2	42.9	47.0	42.2	61.7	--
South Korea	394	88.6	68.0	70.8	60.7	60.2	51.5	94.7	1.8
Malaysia	344	92.7	78.5	83.1	69.5	75.0	81.7	95.1	4.7
New Zealand	399	98.0	83.5	87.0	79.2	88.2	74.4	97.7	0.0
Philippines	173	89.6	77.5	80.4	65.3	76.3	65.3	96.5	4.0
Taiwan	1152	96.9	79.5	82.6	67.5	74.1	71.0	99.0	0.2
Thailand	446	81.2	62.8	69.7	56.1	62.8	61.9	88.3	11.0
Vietnam	182	59.9	42.9	45.1	39.6	51.1	36.3	61.5	41.2
Asia/Pacific	4362	88.9	71.7	77.0	65.2	71.1	66.5	91.8	4.0[c]

[a]Results for colistin are not shown because *P. aeruginosa* isolates are no longer considered susceptible to colistin per 2020 CLSI guidelines.
[b]Showing countries with ≥2 sites; Singapore not shown
[c]Excludes India
FEP, cefepime; ATM, aztreonam; P/T, piperacillin-tazobactam; LVX, levofloxacin; AMK, amikacin

Conclusion. IMI/REL was active against 91% of *K. pneumoniae* and 89% of *P. aeruginosa* isolates collected in Asia/Pacific overall, with higher activity in countries with lower MBL-positive rates. IMI/REL promises to be an important treatment option for IMI-nonsusceptible MBL-negative isolates, including KPC-producing *K. pneumoniae*.

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1589. Activity of Meropenem-Vaborbactam and Comparators against Globally Disseminated *Klebsiella pneumoniae* Sequence Type 258

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Meropenem-vaborbactam (MVB) is a combination of a carbapenem and a b-lactamase inhibitor active against β-lactamases including serine carbapenemases. MVB recently was approved in the US and Europe for the treatment of complicated UTIs, including acute pyelonephritis, and is approved in Europe for treatment of complicated intra-abdominal infections, hospital-acquired bacterial pneumonia, ventilator-associated pneumonia, and bacteremia. Carbapenemase-producing *Enterobacterales* (ENT) isolates, particularly *Klebsiella pneumoniae* (KPN), have disseminated worldwide and are considered endemic in various countries. Carbapenem-resistant (CR) KPN outbreaks have been associated with KPN sequence-type 258 (ST258). Globally, 60-70% of KPC-producing KPN belong to ST258. In this study, we examined the susceptibilities of ST258 isolates collected as a part of the SENTRY global surveillance program.

Methods. KPN isolates from 2016-2019 were susceptibility tested by reference broth microdilution methods. The results were interpreted using CLSI 2020 breakpoints. The sequence type and presence of carbapenemases were determined by whole genome sequencing and analysis.

Results. 130 KPN ST258 isolates were identified in 6 countries. All isolates were extremely drug resistant (XDR, susceptible to < = 1 agent in 2 or fewer drug classes). 76.2% were CR, and 71 isolates contained bla_{KPC-2}, 25 bla_{KPC-3} and 1 bla_{KPC-12}. One isolate contained bla_{NDM-1}. The US had the most ST258 isolates (n=56), of which 22 produced KPC-2 and 19 produced KPC-3. Greece had 32 isolates, with 17 KPC-2 and 5 KPC-3. Brazil had 22 isolates, 17 with KPC-2. The single NDM-1 producing isolate was from Argentina. Susceptibilities to MVB and comparators by country are shown in the table. MVB inhibited 99.2% of the isolates and was the most active agent overall, only 23.1% were meropenem susceptible. Tigecycline was the most active comparator with 98.5% susceptible.

Conclusion. These results demonstrate MVB has potent activity against the internationally disseminated KPN clone ST258 including those producing KPC. MVB may be useful for the treatment of infections caused by XDR *K. pneumoniae*.

Table 1

Organisms by country of origin (n)	% susceptible using CLSI/FDA breakpoints[a] Meropenem-vaborbactam	Meropenem	Amikacin	Piperacillin-tazobactam	Tigecycline	Colistin
All (130)	99.2	23.1	30.8	6.9	98.5	67.4
US (56)	100.0	25.0	41.1	8.9	98.2	81.8
Greece (32)	100.0	28.1	18.8	12.5	100.0	62.5
Brazil (22)	100.0	18.2	27.3	0.0	100.0	36.4
Argentina (15)	93.3	20.0	20.0	0.0	93.3	73.3
Italy (3)	100.0	0.0	0.0	0.0	100.0	33.7
Romania (2)	100.0	0.0	100.0	0.0	100.0	0.0

[a] CLSI M100 (2020). FDA breakpoints are shown for tigecycline. For colistin, %I is shown, no S category is defined by CLSI.

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