1240. *In Vitro* and *In Vivo* Activity of Single and Dual Antimicrobial Agents Against KPC-producing *Klebsiella pneumoniae*

Farzad Moussavi, MD[1]; Sarath Nath, MD[1]; Daniel Abraham, MD[1]; David Landman, MD, FIDSA[2] and John Quale, MD, FIDSA[2]; [1]SUNY Downstate Medical Center, Brooklyn, New York, [2]Medicine, SUNY Downstate Medical Center, Brooklyn, New York

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Background. Options for treatment of infections due to KPC-producing *K. pneumoniae* are limited, and combination therapy is often recommended. In this report, the *in vitro* and *in vivo* activity of potential therapeutic agents and combinations was assessed against four KPC-producing *K. pneumoniae* isolates.

Methods. Using clinically-relevant concentrations, time-kill experiments and the *Galleria mellonella* model of infection were used to examine the activity of polymyxin B, ceftazidime-avibactam, meropenem, rifampin, and amikacin alone and in combination. Four isolates of KPC-producing *K. pneumoniae* were studied, including two isolates that were resistant to polymyxin B and had ceftazidime-avibactam MICs of 8 μg/mL. The other two *K. pneumoniae* isolates were susceptible to polymyxin B and had lower MICs of ceftazidime-avibactam.

Results. Two isolates that were resistant to polymyxin B and with ceftazidime-avibactam MICs of 8 μg/mL were also resistant to amikacin and meropenem. When ceftazidime-avibactam was combined with either amikacin or meropenem, synergy was observed *in vitro*, and these combinations were associated with improved survival with the *in vivo* model. The other two *K. pneumoniae* isolates were susceptible to polymyxin B and had lower MICs of ceftazidime-avibactam. At concentrations four times the MIC, ceftazidime-avibactam had bactericidal activity *in vitro*; at one fourth the MIC, synergy was observed when combined with meropenem. Improved survival rates were observed with therapy with ceftazidime-avibactam, particularly when combined with a second agent for one isolate. In the *in vivo* model, polymyxin B with or without rifampin or meropenem, was ineffective against polymyxin B resistant strains.

Conclusion. Pending clinical studies, combining ceftazidime-avibactam with another agent (e.g., a carbapenem) should be encouraged when treating serious infections due to these pathogens, especially for isolates with ceftazidime-avibactam MICs near the susceptibility breakpoint.

Disclosures. **All authors:** No reported disclosures.

1241. *In vitro* Activity of Ceftaroline Against Pathogens Collected Globally from the AWARE Surveillance Program, 2016

Meredith Hackel, PhD, MPH[1]; Joseph Iaconis, PhD[2] and Dan Sahm, PhD[1]; [1]International Health Management Associates, Inc., Schaumburg, Illinois, [2]AstraZeneca Pharmaceuticals, Waltham, Massachusetts

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Background. Ceftaroline, the active metabolite of ceftaroline fosamil, is a cephalosporin developed for treating infections caused by *Staphylococcus aureus*, including methicillin-resistant *S. aureus* (MRSA), *Streptococcus pneumoniae*, β-hemolytic streptococci, and some Gram-negative pathogens. This study reports the *in vitro* activity of ceftaroline against clinically relevant isolates collected in 2016 from the AWARE Surveillance Program.

Methods. 22,752 non-duplicate methicillin-sensitive *S. aureus* (MSSA), MRSA, *S. pneumoniae,* β-hemolytic streptococci (*S. pyogenes*, *S. agalactiae, S. dysgalactiae*) *Haemophilus influenzae,* and extended spectrum β-lactamase (ESBL)-negative *Enterobacteriaceae* were collected from (n/%) Asia/South Pacific (4,215/18.5%), Europe (12,962/57.0%), Latin America (3,384/14.9%), and Middle East/Africa (2,191/9.6%) during 2016. Isolates were from (n/%) complicated intraabdominal (2,149/9.5%), complicated urinary tract (3,029/13.3%), complicated skin and skin structure (8,271/36.4%), blood stream (2,422/10.6%) and lower respiratory tract infections (6,881/30.2%). MIC values were determined by broth microdilution and interpreted using CLSI breakpoints.

Results. Ceftaroline activity, based on % susceptibility (%S) and MIC_{90}, is shown in the table. Ceftaroline was active *in vitro* against both Gram-positive (100% of MSSA, 93.6% of MRSA and 99.7% of *S. pneumoniae*) and Gram-negative (99.7% of *H. influenzae* and 91.7% of ESBL-negative *Enterobacteriaceae*) isolates.

Organism (N)	% S	% I	% R	MIC50	MIC90
MRSA (5,022)	93.6	6.0	0.5	0.5	1
MSSA (3,675)	100	0	0	0.25	0.25
Streptococcus pneumoniae (2,024)	99.7	–	0.3	0.008	0.12
β-hemolytic streptococci (1,713)	100	–	–	0.008	0.015
Enterobacteriaceae, ESBL-Negative (9,647)	91.7	3.7	4.6	0.12	0.5
Haemophilus influenzae (671)	99.7	–	0.3	≤0.015	0.03

%S, %I, %R- percent susceptible, intermediate, resistant based on CLSI breakpoints; MIC_{50}, MIC_{90} in μg/mL.

Conclusion. Based on these data generated with isolates collected in 2016, ceftaroline exhibited potent *in vitro* activity against clinically relevant isolates, with >91% of all isolates susceptible at their CLSI breakpoints.

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Disclosures. **J. Iaconis**, AstraZeneca: Employee and Shareholder, Salary and Shareholder in AstraZeneca

1242. Activity of Ceftazidime–Avibactam Against Respiratory Isolates of *Enterobacteriaceae* and *Pseudomonas aeruginosa* Collected in Latin America as Part of the INFORM Global Surveillance Program, 2014–2016

Krystyna Kazmierczak, PhD[1]; Mark Estabrook, PhD[1]; Gregory G. Stone, PhD[2] and Dan Sahm, PhD[1]; [1]International Health Management Associates, Inc., Schaumburg, Illinois, [2]Pfizer, Inc., New York, New York

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Background. The β-lactam/non-β-lactam β-lactamase inhibitor combination ceftazidime-avibactam (CAZ-AVI) is active *in vitro* against isolates producing class A, C, and some class D β-lactamases, including extended-spectrum β-lactamases, stably derepressed AmpC, and serine carbapenemases. This study evaluated the *in vitro* activity of CAZ-AVI and comparators against respiratory isolates of *Enterobacteriaceae* (*Eba*) and *Pseudomonas aeruginosa* (*Pae*) collected in Latin America from 2014–2016 as part of the INFORM surveillance program.

Methods. Non-duplicate isolates from hospitalized patients with lower respiratory tract infections were collected from 24 medical centers in Argentina, Brazil, Chile, Colombia, Mexico, and Venezuela. Susceptibility (S) testing was performed by broth microdilution and interpreted using CLSI breakpoints except for CAZ-AVI (U.S. FDA) and colistin (EUCAST; *Eba*only). AVI was tested at a fixed concentration of 4 μg/mL with doubling dilutions of CAZ. Multidrug resistance (MDR) phenotype was defined as resistant by CLSI breakpoints to sentinel agents from ≥3 drug classes. Isolates were screened for β-lactamase genes by PCR and sequencing.

Results. CAZ-AVI showed potent *in vitro* activity against *Eba* isolates (MIC_{90}, 0.5 μg/mL; 99.3% S) and against CAZ-non-susceptible (CAZ-NS), colistin-resistant (CST-R) and MDR subsets (>93% S). CAZ-AVI activity against meropenem-non-susceptible (MEM-NS) *Eba* (89.7% S) was reduced due to production of metallo-β-lactamases (MBL); MEM-NS MBL-negative isolates were 100% S. CAZ-AVI showed greater *in vitro* activity against *Pae* isolates (MIC_{90}, 32 μg/mL; 85.4% S) than CAZ (69.2% S) or MEM (59.9% S). CAZ-AVI activity against CAZ-NS, CST-R, MEM-NS, MEM-NS MBL-negative, and MDR *Pae*isolates (50.4–92.6% S) also exceeded that of CAZ and MEM against these resistant subsets.

Conclusion. CAZ-AVI is a potential treatment option for respiratory infections in Latin America that are caused by *Eba* and *Pae* resistant to commonly used and last-in-line agents.

Funding: This study was sponsored by AstraZeneca. The AstraZeneca product ceftazidime-avibactam was acquired by Pfizer in December 2016.

Disclosures. **G. G. Stone**, Pfizer: Employee, Salary AstraZeneca: Shareholder, Capital Gains

1243. Activity of Ceftazidime–Avibactam Against Respiratory Isolates of *Enterobacteriaceae* and *Pseudomonas aeruginosa* Collected in Asia/Pacific as part of the INFORM Global Surveillance Program, 2014–2016

Krystyna Kazmierczak, PhD[1]; Mark Wise, PhD[2]; Gregory G. Stone, PhD[3] and Dan Sahm, PhD[1]; [1]International Health Management Associates, Inc., Schaumburg, Illinois, [2]IHMA, Inc, Schaumburg, Illinois, [3]Pfizer, Inc., New York, New York

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Background. Avibactam (AVI) is a non-β-lactam β-lactamase inhibitor that restores the *in vitro* activity of ceftazidime (CAZ) against class A, class C, and some class D β-lactamases, including extended-spectrum β-lactamases, serine carbapenemases, and the chromosomal AmpC of *Pseudomonas aeruginosa* (*Pae*). This study evaluated the *in vitro* activity of CAZ-AVI and comparators against *Enterobacteriaceae* (*Eba*) and *Pae* collected from patients with lower respiratory tract infections (LRTI) in Asia/Pacific in 2014–2016 as part of the INFORM surveillance program.

Methods. Non-duplicate isolates from patients with LRTI were collected from 28 medical centers in Australia, Hong Kong, Japan, Malaysia, Philippines, South Korea, Taiwan, and Thailand. Susceptibility (S) testing was performed by broth microdilution and interpreted using FDA breakpoints for CAZ-AVI and CLSI breakpoints for comparators. AVI was tested at a fixed concentration of 4 μg/mL with doubling dilutions of CAZ. Multidrug resistance (MDR) phenotype was defined as resistant by CLSI breakpoints to sentinel agents from ≥3 drug classes.

Results. CAZ-AVI showed potent *in vitro* activity against the overall population of *Eba* (MIC_{90}, 0.5 μg/mL; 98.0% S) and against ceftazidime-nonsusceptible (CAZ-NS), colistin-resistant (CST-R), and MDR isolates, with >91% of these resistant subsets testing as susceptible (MIC ≤8 μg/mL). Reduced activity against meropenem-nonsusceptible (MEM-NS) *Eba* was attributable to the presence of class B metallo-β-lactamases (MBL); 95.7% of MEM-NS, MBL-negative isolates were susceptible to CAZ-AVI. CAZ-AVI also showed good activity against most *Pae* isolates (MIC_{90}, 8 μg/mL; 92.5% S), as well as CST-R isolates (MIC_{90}, 8 μg/mL; 100% S). Activity of CAZ-AVI was reduced against CAZ-NS, MEM-NS, MEM-NS MBL-negative, and MDR *Pae* subsets (46.9–82.3% S) but exceeded the activity of CAZ and MEM.