1240. In Vitro and In Vivo Activity of Single and Dual Antimicrobial Agents Against KPC-producing Klebsiella pneumoniae
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Session: 147. Expanded Spectrum - New Antimicrobial Susceptibility Testing
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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 extended concentrations, time-kill experiments and the Galleria mellonella model of infection were used to examine the activity of polymyxin B, ceftazidime-avibactam, meropenem, rIFAPm, 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 ceftazi- dime-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
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Background. Ceftaroline, the active metabolite of ceftaroline fosamil, is a cepha- losporin developed for treating infections caused by β-lactamase-producing Enterobacteriaceae, 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 meticillin-sensitive S. aureus (MSSA), MRSA, S. pneumoniae, β-hemolytic streptococci (S. pyogenes, S. agalactiae, S. dysgalac- tiae) and 91.7% of ESBL-negative Enterobacteriaceae were collected from 107% 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 (a%) complicated intraabdominal (2,126/9.9%), complicated urinary tract (3,029/13.3%), complicated skin and soft tissue (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 MIC50, 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.

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. I. 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
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Background. The 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, sta- bly derepressed AmpC, and serine carbapenemases. This study evaluated the in vitro activity of CAZ-AVI and comparators against respiratory isolates of Enterobacteriaceae (Ebs) 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 respira- tory 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; Ebonly)). 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 Ebs isolates (MIC90 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) Ebs (89.7% S) was reduced due to production of metallo-β-lactama- ses (MBL); MEM-NS MBL-negative isolates were 100% S. CAZ-AVI showed greater in vitro activity against Pae isolates (MIC90 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 were (50.1–92.6% 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 Ebs and Par 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
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Session: 147. Expanded Spectrum - New Antimicrobial Susceptibility Testing
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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 carbapenem- emases, and the chromosomal AmpC of Pseudomonas aeruginosa (Pae). This study evaluated the in vitro activity of CAZ-AVI and comparators against Enterobacteriaceae (Ebs) 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 comp- arators. 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 Ebs (MIC90 0.5 µg/mL; 98.0% S) and against ceftazidime-non-susceptible (CAZ-NS), colistin-resistant (CST-R), and MDR isolates, with >91% of these resistant subsets test- ing as susceptible (MIC ≤8 µg/mL). Reduced activity against meropenem-non-susceptible (MEM-NS) Ebs was attributable to the presence of class β 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 (MIC90 ≤8 µg/mL; 92.5% S), as well as CST-R isolates (MIC90 ≤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.
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