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

In vitro: When combined with other aminoglycosides or carbapenems, 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 bacterial 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 Ceftriaxone Against Pathogens Collected Globally from the AWARE Surveillance Program, 2016
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Background. Ceftriaxone, the active metabolite of ceftriaxone fosamil, is a cephalosporin developed for treating infections caused by β-hemolytic streptococci, Streptococcus pneumoniae, β-hemolytic streptococci, and some Gram-negative pathogens. This study reports the in vitro activity of ceftriaxone against clinically relevant isolates collected in 2016 from the AWARE Surveillance Program.

Methods. 22,752 non-duplicate mecillinam-sensitive S. aureus (MRSA), Streptococcus pneumoniae, β-hemolytic streptococci, and some Gram-negative pathogens. This study reports the in vitro activity of ceftriaxone against clinically relevant isolates collected in 2016 from the AWARE Surveillance Program.

Results. Ceftriaxone activity, based on % susceptibility (%S) and MIC comparisons, is shown in the table. Ceftriaxone 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
MSSA (3,678) 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 0 0.008 0.015
Enterobacteriaceae (9,647) 91.7 3.7 4.6 0.12 0.5
ESBL-Negative (9,647) 99.7 0.3 ≤0.015 0.03

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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1242. Activity of Ceftazidine–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 ceftazidine–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 (Ebs) and Pseudomonas aeruginosa (Paer) 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 (US FDA and colistin (EUCAST; Ebohuly). 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) (CST-R) and MDR subsets (>93% S). CAZ-AVI showed potent activity against meropenem-non-susceptible (MEM-NS) Ebs (89.7% S) was reduced due to production of metallo-β-lactamas (MBL); MEM-NS MBL-negative isolates were 100% S. CAZ-AVI showed greater activity in vitro against Paer 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 Paer subsets (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 Paer resistant to commonly used and last-line agents.

Funding. This study was sponsored by AstraZeneca. The AstraZeneca product ceftaroline fosamil was acquired by Pfizer in December 2016.

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