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Paper Poster Session VI

New data on new cephalosporin/beta-lactamase inhibitor combinations

Antimicrobial resistance patterns of ceftazidime-avibactam and comparators against intra-abdominal Gram-negative pathogens from Europe: international network for optimal resistance monitoring (INFORM) global surveillance study 2013

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Background: Avibactam (AVI), a novel non-β-lactam β-lactamase inhibitor, can inhibit a variety of b-lactamases, such as extended-spectrum β-lactamases (ESBL), class C β-lactamases, serine carbapenemases, and some class D b-lactamases. These enzymes are an increasing problem in Gram-negative pathogens, including those causing intra-abdominal infections (IAI). AVI in combination with ceftazidime (CAZ) may therefore represent a new treatment option for IAI. This report presents the *in vitro* activity of CAZ-AVI and comparators against Gram-negative IAI pathogens collected in selected countries of the European Union in 2013.

Methods: 63 sites in 17 countries (Austria, Belgium, Czech Republic, Denmark, France, Germany, Greece, Hungary, Ireland, Italy, Netherlands, Poland, Portugal, Romania, Spain, Sweden, United Kingdom) collected 991 clinically relevant Gram-negative isolates from patients with IAI in 2013. Only one strain per patient infection episode was included. Susceptibility was determined using the current CLSI broth microdilution method and EUCAST breakpoints. Isolates phenotypically positive for ESBL or non-susceptible to a carbapenem were analysed for the presence of β-lactamases via multiplex PCR, followed by sequencing.

Results: The MIC_{90} values (mg/L) of CAZ-AVI and comparators against selected Gram-negative species and genera (including molecularly characterized ESBL+ subsets and CAZ-non-susceptible phenotypes) are shown below.

79% of CAZ-non-susceptible *P. aeruginosa* had CAZ-AVI MICs ≤8 mg/L (used as reference value for comparative purposes in the absence of a CAZ-AVI breakpoint), compared to 50% susceptible to meropenem and 43% to levofloxacin. The MIC_{90} values for 11 *A. baumannii* isolates were 64 and 128 mg/L for CAZ-AVI and CAZ, respectively. The most common ESBLs found among the molecularly characterized CAZ-non-susceptible *Enterobacteriaceae* isolates included in this report were CTX-M-15 (n=60), SHV-12 (n=9), and CTX-M-27 (n=6).

Conclusions:

- With the exception of *A. baumannii*, CAZ-AVI shows very promising activity against Gram-negative pathogens isolated from IAI.
- MIC_{90} values of CAZ-AVI were reduced at least 32-fold for *Enterobacteriaceae* and 4-fold for *P. aeruginosa* compared to CAZ alone.
- A sizable proportion of *E. coli* (11%) and *Klebsiella* spp. (13%) isolated from patients with IAI were ESBL-positive (mostly CTX-M-15); the *in vitro* activity of CAZ-AVI was excellent against these ESBL-positive strains (MIC_{90} ≤1 mg/L).
- The addition of avibactam resulted in a vastly improved *in vitro* activity of CAZ against CAZ-non-susceptible *Enterobacteriaceae*. CAZ-AVI could be considered as a potential treatment option against this subset of strains that have MIC_{90} values in the resistant range for most other agents, and for which treatment options are limited.