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ABSTRACT

**INTRODUCTION**

- Ceftolozane/tazobactam is a novel extended-spectrum cephalosporin/β-lactamase inhibitor combination, which has shown greater activity against Pseudomonas aeruginosa when compared with ceftazidime and ciprofloxacin.

- Ceftolozane/tazobactam has also demonstrated good activity against Enterobacteriaceae, but the structure and efficacy of ceftolozane/tazobactam compared with other available agents are unclear.

- We evaluated the in vitro activity of ceftolozane/tazobactam, ceftriaxone, piperacillin/tazobactam, and other comparators against a range of Gram-negative pathogens isolated from patients hospitalized with pneumonia in the United States (US) and Europe (EU).

**MATERIALS AND METHODS**

- The study used a total of 672 isolates (274 from the US and 408 from EU) that were collected from medical centers in the US and EU from patients with pneumonia. The study group comprised 509 clinical isolates (382 from the US and 127 from EU) and 217 reference isolates (224 from the US and 13 from EU) from patients with pneumonia.

- Antimicrobial susceptibility testing was performed with the broth microdilution method as described in CLSI [2013] and EUCAST [2013].

- Exploratory analysis was performed using the CLSI guidelines for determining susceptibility breakpoints for Enterobacteriaceae, and the EUCAST clinical breakpoints were applied for other species. Sensitivity rates were calculated according to the CLSI methodology for the US and EU clinical isolates.

- Statistical analysis was performed using the two-tailed Fisher exact test, and differences were considered statistically significant at p ≤ 0.05.

**RESULTS**

- Ceftolozane/tazobactam was the most active β-lactam tested against P. aeruginosa (95.3% susceptible at ≤8 µg/mL), followed by meropenem (90.6% susceptible at ≤8 µg/mL), ceftriaxone (82.7% susceptible at ≤8 µg/mL), and piperacillin/tazobactam (83.2% susceptible at ≤8 µg/mL). Ceftriaxone was the least active β-lactam against P. aeruginosa (62.9% susceptible at ≤8 µg/mL)

- Ceftolozane/tazobactam was active against 14 of 20 (70.0%) P. aeruginosa strains (MIC50/90, 8/8 µg/mL), 100% inhibited at <8 µg/mL, and 89.9% inhibited at ≤4 µg/mL.

- In vitro susceptibility breakpoints were applied to classify strains from the US and EU, and the following susceptibility rates were observed: 92.1% inhibited at ≤8 µg/mL, 70.8% inhibited at ≤2 µg/mL, and 39.5% inhibited at ≤1 µg/mL.

- Ceftolozane/tazobactam was active against 4 of 6 (66.7%) P. aeruginosa strains (MIC50/90, 0.5/4 µg/mL), and 100% inhibited at ≤4 µg/mL, withMIC90 ≤0.25 µg/mL.

- **CONCLUSIONS**

- Ceftolozane/tazobactam generally demonstrated greater in vitro activity than the currently available agents: moxifloxacin, ciprofloxacin, and piperacillin/tazobactam, when tested against P. aeruginosa.

- Ceftolozane/tazobactam exhibited remarkable activity against XDR and MDR P. aeruginosa.

- Against Enterobacteriaceae, ceftolozane/tazobactam activity was greater than that of currently available cephalosporins, carbapenems, and P/T when tested against A. baumannii and other common Gram-negative pathogens. The i

**REFERENCES**
