**Antimicrobial Activity of Ceftazidime and Piperacillin-Tazobactam Tested in Combination with a Potentiator Molecule (SPR741) against Enterobacteriaceae Causing Urinary Tract Infections**

**Introduction**
- Computed urological tract infections (cUTIs) are commonly caused by gram-negative pathogens.
- The prevalence of cUTIs in the United States has been estimated at approximately 24 per 1,000 hospital discharges, with similar prevalence reported worldwide.
- Treatment of cUTIs, particularly in immunocompromised patients, is challenging.
- Antimicrobial resistance is associated with significant adverse impact on clinical outcomes, including increased healthcare resource utilization, length of hospital stay, and overall mortality.
- Current cephalosporins are widely prescribed for the treatment of cUTIs, especially for susceptible strains of *Escherichia coli* and *Klebsiella pneumoniae*.
- For susceptible strains, intravenous cephalosporins are recommended for the treatment of cUTIs.

**Materials and Methods**

**Organism collection**
- A total of 400 bacteriologic clinical isolates selected from the KLEO Antibiotic Surveillance Program database collection were included in the fixed concentration of 8.
- All isolates were collected from geographically diverse medical centers in the United States (222; 55.5%) or Europe (178; 44.5%).
- During the 2016 surveillance year and were recognized for documented UTIs.
- Species included Enterobacteriaceae (61 isolates), Felapathogenae (113), and Enterobacter cloacae species (72 isolates).

**Susceptibility testing**
- The methodology for susceptibility testing was performed in accordance with the Clinical and Laboratory Standards Institute (CLSI) M02-A12 (2017) document.
- Bacterial strains were tested against in combination with SPR741 at a fixed concentration of 8.
- Complete susceptibility testing was performed in accordance with the Clinical and Laboratory Standards Institute (CLSI) M02-A9 (2018).

**Results**
- MIC results obtained against clinical isolates were interpreted using the CLSI M02-A12 (2017) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) 2016 documents, as available.
- The definition of susceptibility to SPR741 in combination with SPR741 by CLSI was based on the susceptibility breakpoints for the respective in vitro, for comparison purposes.

**Conclusions**
- Overall, adding SPR741 to a fixed concentration of 8 improved the activity of ceftazidime and piperacillin-tazobactam when tested against cUTIs.
- The in vivo activity of ceftriaxone increased from 63.1% to 91.0% in susceptible isolates when combined with SPR741 against *E. coli* and *K. pneumoniae*, respectively.
- Waksa tested against all seven isolates showed piperaceillin-tazobactam activity increased from 64.5% to 84.8% when combined with SPR741.
- These findings provide evidence for the activity of SPR741 and warrant further clinical and microbiological development of this combination.

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**References**