Session: P-59. New Drug Development

Background. Tebipenem, an orally bioavailable carbapenem administered as a pro-drug, completed a phase 3 clinical trial for evaluating its safety and efficacy for the treatment of complicated urinary tract infection and acute pyelonephritis. The purpose of this study was to investigate the in vitro activity of tebipenem and comparators against a recent collection of Gram-positive isolates associated with clinical infections.

Methods. The susceptibility of 580 Gram-positive organisms were tested, including: methicillin-susceptible Staphylococcus aureus (MSSA, 489 isolates), methicillin-susceptible Staphylococcus epidermidis (MSSe, 31), other methicillin-susceptible coagulase-negative staphylococci (MCNSN, 29), and vancomycin-susceptible Enterococcus faecalis (31). The isolates were collected primarily from pneumonia in hospitalized patients (498 isolates; 85.9%), urinary tract infections (42 isolates; 7.2%), and bloodstream infections (38 isolates; 6.6%). Organisms were tested using reference broth microdilution methods in a central laboratory.

Results. Tebipenem had an MIC50 value of 0.03 µg/mL against MSSA and 0.015 µg/mL against MSSE isolates. Ertapenem MIC50 values were 8-fold higher against MSSA (MIC50, 0.25 µg/mL) and 32-fold higher against MSSE (MIC50, 0.5 µg/mL). Tebipenem displayed an MIC50 value of 0.03 µg/mL against MCNSN species other than S. epidermidis. This result was 8- and 32-fold lower than those of meropenem (MIC50, 0.25 µg/mL) and ertapenem (MIC50, 1 µg/mL), respectively. Tebipenem inhibited all E. faecalis isolates at ≤1 µg/mL (MIC50, 1 µg/mL), with an MIC50 value at least 2-fold lower than meropenem (MIC50 >1 µg/mL) and 16-fold lower than ertapenem (MIC50 > 8 µg/mL).

Conclusion. Tebipenem displayed potent activity against methicillin susceptible staphylococci, including MSSA, MSSE, and other MCNSN. Tebipenem in vitro activity was greater than meropenem and ertapenem when tested against E. faecalis. These data indicate that tebipenem may be an option for treating urinary tract infections caused by these organisms or as an empiric option to provide broader coverage against Gram-positive and -negative organisms.