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P1662 Antimicrobial activity of murepavadin tested against clinical isolates of Pseudomonas aeruginosa collected in Europe, the United States and China

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Background: Murepavadin (formerly POL7080) is a 14-amino-acid cyclic peptide for intravenous administration that targets the lipopolysaccharide transport protein D (LptD) and is being developed for treating hospital-acquired and ventilator-associated pneumonia caused by *Pseudomonas aeruginosa*.

Materials/methods: A total of 1,219 isolates were collected through the SENTRY Antimicrobial Surveillance Program from 40 medical centres in 22 European nations in 2014 (n=491), 62 medical centres located in the US in 2014 (n=417), and 10 medical centres in China in 2012–2013 (n=311) from patients with pneumonia (48%), skin and soft tissue (29%), bloodstream (10%), urinary tract (6%), and other infections (7%). Susceptibility testing was performed by reference broth microdilution method.

Results: Murepavadin ($MIC_{50/90}$, 0.12/0.12 mg/L) was 4- to 8-fold more active than colistin ($MIC_{50/90}$, 1/1 mg/L) and polymyxin B ($MIC_{50/90}$, 0.5/1 mg/L) and inhibited 99.1% of isolates at ≤0.5 mg/L. Only 4 isolates (0.3%) exhibited murepavadin MIC values >2 mg/L; 3 isolates from the US and 1 from Italy. Importantly, murepavadin retained potent *in vitro* activity against multidrug-resistant (MDR; $MIC_{50/90}$, 0.12/0.25 mg/L) and extensively drug-resistant (XDR; $MIC_{50/90}$, 0.12/0.0.25 mg/L) isolates. Among the antipseudomonal agents tested, the polymyxins were the most active with polymyxin B ($MIC_{50/90}$, 0.5/1 mg/L; 100.0% susceptible) being slightly more active than colistin ($MIC_{50/90}$, 1/1 mg/L; 98.9% susceptible), whereas tobramycin ($MIC_{50/90}$, 0.5/>16 mg/L; 87.9% susceptible), amikacin ($MIC_{50/90}$, 4/16 mg/L; 87.4/90.6% susceptible [EUCAST/CLSI]), and cefepime ($MIC_{50/90}$, 2/16 mg/L; 79.8% susceptible) were moderately less active. Murepavadin was equally active against isolates from Europe, the US, and China ($MIC_{50/90}$, 0.12/0.12 mg/L for all 3 regions); isolates from China exhibited slightly higher MIC values for colistin and polymyxin B compared to Europe and US isolates. Further, susceptibility rates for the aminoglycosides, β-lactams, and ciprofloxacin were slightly higher among isolates from the US compared to Europe and China.

Conclusions: Murepavadin demonstrated potent activity against a large collection of clinical *P. aeruginosa* isolates from Europe, the US, and China, including MDR and XDR isolates. Results from ongoing clinical studies will define the role of murepavadin for treating *P. aeruginosa* infections.