P0093 Plazomicin activity against Enterobacteriaceae collected from Europe, Latin America, and Asia-Pacific during 2016, including those with aminoglycoside and beta-lactam resistance mechanisms

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Background: Plazomicin, a next-generation aminoglycoside, was developed to overcome common aminoglycoside-resistance mechanisms. We evaluated plazomicin activity against Enterobacteriaceae clinical isolates collected in Europe (n=2,045), Latin America (n=511), and Asia-Pacific (n=682) during 2016 and evaluated aminoglycoside and beta-lactam resistance mechanisms among these isolates.

Materials/methods: A total of 3,238 Enterobacteriaceae were susceptibility tested using the reference broth microdilution method. ESBL-phenotype, carbapenem-resistant Enterobacteriaceae (CRE), and isolates resistant to ≥1 aminoglycoside were screened for resistance genes using whole genome sequencing analysis.

Results: Plazomicin (MIC\textsubscript{50/90}, 0.5/1 mg/L) inhibited 96.3% and 98.2% of the Enterobacteriaceae at ≤2 mg/L and ≤4 mg/L, respectively. Amikacin, gentamicin, and tobramycin inhibited 94.3%, 82.1%, and 75.9% of these isolates, respectively (EUCAST breakpoints). Plazomicin displayed activity against E. coli (n=1,182; MIC\textsubscript{50/90}, 0.5/1 mg/L), K. pneumoniae (n=1,115; MIC\textsubscript{50/90}, 0.25/0.5 mg/L), and E. cloacae (n=56; MIC\textsubscript{50/90}, 0.25/0.5 mg/L). Plazomicin (MIC\textsubscript{50/90}, 0.25/1 mg/L) inhibited 94.6% and 94.8% of the 688 isolates carrying ESBL genes at ≤2 mg/L and ≤4 mg/L, respectively. The most common ESBL genes were \textit{bla}\textsubscript{CTX-M-15} (n=486) and \textit{bla}\textsubscript{CTX-M-14} (n=51). Plazomicin inhibited 78.8% of the 170 CRE at ≤2 mg/L or ≤4 mg/L. Other aminoglycosides inhibited 14.1% to 48.8% of these isolates (EUCAST breakpoints). Carbapenemase genes were found in 138 CRE isolates and included 74 \textit{bla}\textsubscript{KPC}, 39 \textit{bla}_{OXA-48}-like, and 26 \textit{bla}_{NDM-1}. Aminoglycoside-modifying enzymes (AME) were observed among 630/644 isolates tested and the most common genes were \textit{aac(6')-Ib-cr} (n=352) and \textit{aac(3)-IIa} (n=312). Plazomicin (MIC\textsubscript{50/90}, 0.5/2 mg/L) inhibited 92.7% and 93.5% of the AME-carrying isolates at ≤2 mg/L and ≤4 mg/L, respectively. Amikacin, gentamicin, and tobramycin inhibited 75.1%, 17.5%, and 1.7%, respectively, of these isolates using the EUCAST breakpoints. 16S rRNA methylases were detected in 48/644 isolates, and these isolates were resistant to all AMGs; plazomicin MIC values were ≥128 mg/L. One Providencia stuartii isolate was highly resistant to all aminoglycosides, including plazomicin, and carried \textit{aac(2')-Ia}.

Conclusions: Plazomicin was active against the Enterobacteriaceae tested, including ESBL- and AME-carrying isolates and approximately 80% of the CRE. Our results support the development plan
for plazomicin to treat serious infections caused by resistant *Enterobacteriaceae* when treatment options are limited.

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