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Paper Poster Session
Susceptibility trends for old and new antibiotics

In Vitro activity of plazomicin tested against contemporary clinical isolates collected in Asia-Pacific, Europe and Latin America

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Background: Plazomicin is a next generation aminoglycoside that is stable against common aminoglycoside modifying enzymes and displays activity against Enterobacteriaceae, *S. aureus* (SA), including methicillin-resistant isolates and some *P. aeruginosa* (PSA). Like other aminoglycosides, this agent is not active against isolates producing 16S rRNA methylases (RNAmet). We evaluated the activity of plazomicin and comparators tested against 3,660 clinical isolates collected in hospitals from the Asia-Pacific (APAC), Europe and Latin America (LATAM) during 2014.

Material/methods: 3,224 Enterobacteriaceae, 236 Gram-positive cocci, 100 PSA and 100 *Acinetobacter* spp. were collected in hospitals in APAC (n=789), Europe (n=2315) and LATAM (n=556). Isolates were susceptibility (S) tested using reference broth microdilution method. CLSI and EUCAST interpretative criteria were applied. Enterobacteriaceae displaying plazomicin MICs ≥128 mg/L were screened for the presence of RNAmet-encoding genes using PCR and sequencing.

Results: Overall, plazomicin ($MIC_{50/90}$, 0.5/2 mg/L) inhibited 89.4 and 96.2% of Enterobacteriaceae at ≤1 and ≤2 mg/L, respectively; and the number of isolates inhibited at these values were 91.8 and 96.8% in APAC, 88.7 and 96.1% in Europe and 88.8 and 95.6% in LATAM. Plazomicin displayed good activity against *E. coli* ($MIC_{50/90}$, 0.5/1 mg/L), *K. pneumoniae* (KPN; $MIC_{50/90}$, 0.25/0.5 mg/L) and *E. cloacae* ($MIC_{50/90}$, 0.5/0.5 mg/L). Among ESBL-phenotype isolates, 98.8% of the *E. coli* (one isolate displayed MIC at 16 and two at >128 mg/L) and 92.9% of KPN were inhibited at ≤2 mg/L of plazomicin. Additionally, 86.7% of the carbapenems-resistant Enterobacteriaceae (CRE) were inhibited by plazomicin at ≤2 mg/L. Among 55 (1.7%) Enterobacteriaceae with plazomicin MIC results ≥8 mg/L, 33 were KPN (3.0% for this species) and 30 had plazomicin MICs ≥128 mg/L (17 [2.4%] from Europe, nine [3.9%] from APAC, and four [2.6%] from LATAM). Plazomicin MICs for Indole-positive *Proteus* spp. and *P. mirabilis* were slightly higher ($MIC_{50/90}$ ranges, 1-4/4-8 mg/L) when compared to other Enterobacteriaceae species. All 36 (1.1%) Enterobacteriaceae isolates displaying plazomicin MICs at ≥128 mg/L carried 16S RNAmet -encoding genes: 19 *rmtB*, eight *rmtF*, seven *armA*, one of each *rmtA*, *rmtC* and *rmtD1*. Plazomicin ($MIC_{50/90}$, 4/8 mg/L) inhibited 67.0% of PSA at ≤4 mg/L (68.0% in APAC, 70.0% in Europe and 60.0% in LATAM). All coagulase-negative staphylococci ($MIC_{50/90}$, 0.12/0.25 mg/L) were inhibited by plazomicin at ≤0.25 mg/L, and 98.4 and 100.0% of *S. aureus* ($MIC_{50/90}$, 0.5/1 mg/L) were inhibited at ≤1 and ≤2 mg/L, respectively. Plazomicin activity was limited against *Acinetobacter* spp. ($MIC_{50/90}$, 32/>128 mg/L), *Enterococcus* spp. and *S. pneumoniae* ($MIC_{50/90}$, 64/64 mg/L for both).

Conclusions: Plazomicin displayed good activity against contemporary Enterobacteriaceae isolates, including CRE isolates. In all cases where plazomicin MICs were ≥128 mg/L, the isolates produced RNAmet. This compound was also potent against staphylococci, but its activity was compromised for PSA, *Acinetobacter* spp. and streptococci.