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Activity of plazomicin and comparator agents tested against recent clinical isolates collected in the Asia-Pacific region, Europe and Latin America

Mariana Castanheira*[1], Jennifer Streit[1], Lalitagauri M. Deshpande[1], Rodrigo E. Mendes[1], Robert Flamm[1]

[1]*Jmi Laboratories*

Background: Plazomicin is a next-generation aminoglycoside that was developed to overcome common aminoglycoside-resistance mechanisms and under development for the treatment of patients with serious bacterial infections due to MDR Enterobacteriaceae, including ESBL-producing and carbapenem-resistant Enterobacteriaceae (CRE). We evaluated the activity of plazomicin and comparators tested against 3,830 clinical isolates collected in hospitals from the Asia-Pacific (APAC) region, Europe and Latin America (LATAM) during 2015.

Material/methods: A total of 3,375 Enterobacteriaceae, 252 Gram-positive cocci, 101 *Pseudomonas aeruginosa* (PSA) and 102 *Acinetobacter* spp. were collected in hospitals in APAC (n=851), Europe (n=2,365) and LATAM (n=614). Isolates were susceptibility (S) tested using reference broth microdilution method. CLSI and EUCAST interpretative criteria were applied. CRE isolates were screened for carbapenemase encoding genes by PCR/sequencing.

Results: Overall, plazomicin ($MIC_{50/90}$, 0.5/1 mg/L) inhibited 90.9 and 95.8% of Enterobacteriaceae at ≤1 and ≤2 mg/L, respectively. Plazomicin displayed good activity against the main Enterobacteriaceae species, including *E. coli* ($MIC_{50/90}$, 0.5/1 mg/L), *K. pneumoniae* ($MIC_{50/90}$, 0.25/0.5 mg/L) and *E. cloacae* ($MIC_{50/90}$, 0.25/0.5 mg/L). Against ESBL-phenotype isolates that were not CRE ($MIC_{50/90}$, 0.25/1 mg/L), plazomicin inhibited 94.1 and 95.8% at ≤1 and ≤2 mg/L, respectively. Among 187 CRE isolates, 52 carried bla_{KPC-2}, 43 bla_{KPC-3}, 41 bla_{NDM-1}, 37 bla_{OXA-48}-like and 1 bla_{VIM-1}. Plazomicin ($MIC_{50/90}$, 0.25/>128 mg/L for CRE) inhibited 84/95 isolates carrying bla_{KPC}, 27/37 isolates carrying bla_{OXA-48}-like and 11/42 isolates carrying metallo-beta-lactamase genes. The activity of plazomicin ($MIC_{50/90}$, 4/8 mg/L) against PSA was similar to the activity of amikacin ($MIC_{50/90}$, 4/4 mg/L) and lower than the activity of gentamicin ($MIC_{50/90}$, 1/4 mg/L) against these isolates. Plazomicin demonstrated good activity against coagulase-negative staphylococci (CoNS; $MIC_{50/90}$, 0.25/0.5 mg/L) and *S. aureus* ($MIC_{50/90}$, 0.5/1 mg/L). Plazomicin activity was limited against *Acinetobacter* spp. ($MIC_{50/90}$, 8/>128 mg/L), *Enterococcus* spp. ($MIC_{50/90}$, 32/64 mg/L) and *S. pneumoniae* ($MIC_{50/90}$, 32/64 mg/L). The

activity of plazomicin and other aminoglycosides displayed slight variability according to geographic region (Table).

Conclusions: Plazomicin was active against Enterobacteriaceae isolates, including isolates displaying an ESBL phenotype and carrying genes encoding serine-carbapenemases. This data supports the current development plan for plazomicin for the treatment of serious infections caused by resistant Enterobacteriaceae where treatment options are limited.

Organism/Group (no. tested)	MIC_{50}/MIC_{90} in mg/L[a]:								
	Asia-Pacific			Europe			Latin America		
	PLZ	AMK	GEN	PLZ	AMK	GEN	PLZ	AMK	GEN
Enterobacteriaceae (3,375)	0.5/1	2/4	0.5/8	0.5/1	2/8	0.5/>8	0.5/2	2/8	0.5/>8
ESBL-phenotype non CRE (663)	0.5/1	2/8	1/>8	0.25/1	2/8	1/>8	0.5/1	2/8	>8/>8
CRE (187)	0.25/1	4/16	0.5/>8	0.25/>128	16/>32	>8/>8	0.25/>128	16/>32	>8/>8
P. aeruginosa (101)	4/8	4/4	1/4	4/8	2/16	1/>8	4/16	4/16	1/>8
S. aureus (65)	0.5/1	-	≤1/>8	0.5/1	-	≤1/≤1	0.5/0.5	-	≤1/>8
CoNS (64)	0.25/0.5	-	≤1/>8	0.25/0.5	-	≤1/>8	0.25/0.5	-	8/>8

[a] PLZ= plazomicin, AMK= amikacin, GEN= gentamicin.