In vitro activity of plazomicin, a next-generation aminoglycoside, against carbapenemase-producing Klebsiella pneumoniae

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0.9
Sul1
and other
Sulfonamide
C. pneumoniae
Pneumonia
Fig. 1. Structure of plazomicin

ABSTRACT

Background: Plazomicin is a next-generation aminoglycoside with in vitro activity against multidrug resistant Gram-negative species, including carbapenem-resistant isolates. The Consortium on Resistance Against Carbapenems in Klebsiella and other Enterobacteriaceae (CRACKLE) is a federally funded, prospective multi-center consortium established from 9 US healthcare systems that tracks carbapenem-resistant Enterobacteriaceae. In this study, the in vitro activity of plazomicin (Zemdril, Achaogen, Inc. South San Francisco, CA) (Fig. 1), a next-generation aminoglycoside with activity against multidrug resistant Gram-negative species, including carbapenem resistant isolates, was evaluated against a CRACKLE collection of recent carbapenemase-producing Klebsiella pneumoniae.

Methods: Minimum inhibitory concentrations (MICs) of plazomicin were determined by broth microdilution according to current CLSI guidelines against a collection of 697 carbapenem resistant Klebsiella pneumoniae with defined carbapenemase mechanisms, including KPC and OXA carbapenemases. Isolates were submitted by participating CRACKLE centers.

Results: Carbapenemases present in study isolates included KPC-2 (n=323), KPC-3 (n=364), KPC-4 (n=1), OXA-48-like (n=7) and NDM (n=1). Plazomicin MICs ranged from ≤0.12 to >32 mg/L, with MIC50 and MIC90 values of 0.25 and 3 mg/L, respectively. MICs of 689 (98.8%) isolates were ≤4 mg/L, while MICs of the remaining 8 isolates were >32 mg/L. Plazomicin MICs were associated with specific carbapenemase present in isolates: of 8 isolates with MICs >32 mg/L, 7 contained OXA-48-like and one contained KPC, suggesting that these isolates possess an aminoglycoside resistance mechanism on the same plasmid as their carbapenemase gene, such as a 105s ribosomal RNA methyltransferase, against which plazomicin is not active.

Conclusion: Plazomicin demonstrates potent in vitro activity against a collection of carbapenemase-producing K. pneumoniae, with MIC50 value of 1 mg/L and MIC90 of 4 mg/L for 98.9% of isolates.

RESULTS

Carbapenemases present in study isolates included KPC-2 (n=323), KPC-3 (n=364), KPC-4 (n=1), OXA-48-like (n=7) and NDM (n=1). Plazomicin MICs ranged from ≤0.12 to >32 mg/L, with MIC50 and MIC90 values of 0.25 and 1 mg/L, respectively (Figs. 2-4; Table 1). Overall, 689 (97.6%) isolates were susceptible (MICs ≤2 mg/L), 9 were intermediate (MICs 4 mg/L) while MICs of the remaining 8 isolates were resistant (MICs >32 mg/L).

CONCLUSIONS

Plazomicin demonstrates potent in vitro activity against a collection of carbapenemase-producing K. pneumoniae, with MIC50 value of 1 mg/L and 97.6% of isolates susceptible (MICs ≤2 mg/L).

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