Activity of Plazomicin and Comparator Agents Tested against Gram-Negative and -Positive Clinical Isolates Collected in USA Hospitals During 2015

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Abstract

Background: Plazomicin (PLZ) is a novel antibiotic that acts as an aminoglycoside that is stable in the presence of most aminoglycoside-modifying enzymes. We evaluated the activity of PLZ and comparator against 2,306 isolates collected in USA hospitals during 2015 from 194 Enterobacteriaceae (CRE) and 15 Enterococcus spp. (64) and compared against 35218, an MDR isolate.

Methods: A total of 2,306 clinical isolates collected in 30 USA hospitals during 2015 were susceptibility (S) tested against PLZ and comparators using broth microdilution methods. ESBL, carbapenem-resistant (imipenem and/or doripenem), and vancomycin-resistant (vancomycin MIC ≥ 2 µg/mL) Enterobacteriaceae (CRE) were defined according to CLSI criteria.

Results: PLZ inhibited 97.7% and 96.9% of the Enterobacteriaceae isolates at 0.5 and 4 µg/mL, respectively, and PLZ (MICMIC 0.25 µg/mL): S. aureus Wayne, PA: CLSI.

Among Enterobacteriaceae species, Plazomicin showed activity against enterococci (99.9% and 99.5% at ≤2 and ≤8 µg/mL, respectively), including 100.0% of these isolates were inhibited by PLZ at ≤2 µg/mL. All CRE isolates were inhibited by PLZ at ≤2 µg/mL.

Conclusions: Since CRE is a major challenge in treating infections in hospitalized patients, new antimicrobials are essential. Plazomicin is a next-generation aminoglycoside with good activity against Enterobacteriaceae species, including multidrug-resistant (MDR) isolates from USA hospitals during 2015.

Introduction

Aminoglycosides are a class of broad-spectrum antibiotics. These agents display a broad spectrum of activity and bind to the 30S ribosomal RNA leading to inhibition of prokaryotic ribosome synthesis and subsequent cell death. Resistance to aminoglycosides may occur due to changes in bacteria, modification of the antibiotic, or synthesis of modified aminoglycoses (1). These agents can be grouped as aminoglycosides, nucleoside analogs, or phosphonates of aminoglycosides.

Plazomicin is a next-generation aminoglycoside synthetically derived from avilamycin 3,000 and is stable in the presence of most aminoglycoside-modifying enzymes (1). It is a unique aminoglycoside, unlike other aminoglycosides that are susceptible to the enzymatic modification of aminoglycosides. Plazomicin is active against Enterobacteriaceae species complex, including multidrug-resistant (MDR) isolates.

Results

- **Plazomicin (MCJ29; MICMIC 0.25 µg/mL) inhibited 93.3% and 97.7% of 2,069 Enterobacteriaceae isolates at ≤1 and ≤2 µg/mL, respectively.** Applying the CLSI susceptibility breakpoints for Enterobacteriaceae (including 15 methicillin-resistant Staphylococcus aureus (MRSA) isolates and their vancomycin MICs (Table).**

- **Among Enterobacteriaceae species, plazomicin inhibited all 657 Enterobacteriaceae isolates at ≤1 µg/mL, 0.25 and 0.25 µg/mL; S. pneumoniae and Staphylococcus aureus, respectively:** (Table).**

<table>
<thead>
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<th>Isolates</th>
<th>MIC ≤1 µg/mL</th>
<th>0.25 µg/mL</th>
<th>0.5 µg/mL</th>
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<tr>
<td>Enterobacteriaceae isolates</td>
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<td>S. pneumoniae</td>
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<td>S. aureus</td>
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In this study, we evaluated the activity of plazomicin and comparator agents against 2,306 clinical isolates collected in USA hospitals during 2015.

Methods

**Bacterial isolates:** A total of 2,306 clinical isolates, 1,809 Enterobacteriaceae, 193 P. aeruginosa, and 94 Acinetobacter spp., were consecutively collected in 30 USA hospitals during 2015. These non-duplicate isolates, collected from clinical and research sites, were identified using Genotype-ID (IDT) with a 100% identity cut-off. Enterobacteriaceae were defined as ESBL, carbapenem-resistant (imipenem and/or doripenem), and vancomycin-resistant (vancomycin MIC ≥ 2 µg/mL) Enterobacteriaceae (CRE) and 15 Enterococcus spp. (64) and compared against 35218, an MDR isolate.

Susceptibility testing: Plazomicin and comparator antimicrobial agents were tested by broth microdilution testing methods according to the Clinical and Laboratory Standards Institute guidelines (CLSI M07-A10). Quality control (QC) testing was performed to assure positive (S. aureus 50, 90, 100.0% and 99). For the isolates non-susceptible to other aminoglycosides, the isolates non-susceptible to amikacin (AMK; MICMIC 0.5/1 µg/mL; CRE isolates were inhibited by PLZ at ≤2 µg/mL.

Additional therapeutic options to treat multidrug-resistant (MDR) organisms, mainly from Gram-negative species are needed and plazomicin displayed potent in vitro activity against Enterobacteriaceae isolates, including those that might display an MDR phenotype such as CRE.

Acknowledgements

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Conclusions

- Plazomicin demonstrated potent in vitro activity against Enterobacteriaceae, including CRE, and is stable in the presence of an ESBL phenotype and those isolates non-susceptible to other aminoglycosides.

- The new aminoglycoside was active against carbapenem-resistant staphylococci and S. auriae, including MRSA, but limited activity was observed against Enterococcus spp., P. aeruginosa, and Acinetobacter spp.

- Additional therapeutic options to treat multidrug-resistant (MDR) organisms, mainly from Gram-negative species are needed and plazomicin displayed potent in vitro activity against Enterobacteriaceae isolates, including those that might display an MDR phenotype such as CRE.

References