Comparison of Plazomicin MIC Test Strip and Broth Microdilution MIC Results for 125 Enterobacteriaceae

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Abstract (updated)

Background: Plazomicin (PLZ), is a next-generation aminoglycoside with in vitro activity against multidrug-resistant Enterobacteriaceae, including CRE. PLZ has been approved by the FDA for the treatment of complicated urinary tract infections (cUTI), including pyelonephritis caused by the following uropathogenic microorganisms: Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, and Enterobacter cloacae. This study was performed to evaluate the performance of a newly developed gradient strip, the plazomicin MIC Test Strip (MTS) from Labfischer, Walden, VA compared to the broth microdilution method against relevant Enterobacteriaceae pathogens.

Methods: The study isolates included 125 Enterobacteriaceae (12 species as shown in the table), which were chosen to include a range of plazomicin MICs and isolates with known resistance mechanisms. Each isolate was tested for PLZ MIC by both broth microdilution (BMD) and BMD prepared from strips and by PLZ MTS on 100 mm Mueller Hinton agar (MDA) plates. (Becton, Dickinson, Sparks, MD) and a subset of 20 strains was also tested on MHA plates from two additional manufacturers (Hardy, Santa Colsa, CA and Remel, Lenexa, KS). Quality control (QC) strains (E. coli ATCC 29522 and P. aeruginosa ATCC 27853) were tested on each day of testing and results compared to CLSI expected ranges.

Results: As shown in the Table 1, 2 PLZ MTS and BMD results were within +/- one doubling dilution (sensitivity agreement) for 99.2% of all isolates. The category agreement rate was 91.5% (based on proposed susceptible/intermediate/resistant breakpoints of 4/8/16-µg/mL). The QC results were within CLSI published ranges. PLZ results for MTS tested on Remel and Hardy MHA were similar to BMD MIC results (99.2% of isolates were within 2 doubling dilution, 78% within a single doubling dilution).

Conclusions:

As demonstrated, further evaluation of the plazomicin MTS showed good correlation to BMD MIC. Further testing with additional isolates and media at multiple test sites was warranted.

Introduction

Plazomicin is an aminoglycoside that acts by binding to bacterial 30S ribosomal subunit, thereby inhibiting protein synthesis. The in vitro activity of plazomicin has been demonstrated against Enterobacteriaceae in the presence of certain beta-lactamases, including extended-spectrum-β-lactamases (ESBL) and metallo-β-lactamases (MER, KPC, NDM). Plazomicin is not active against isolates that express 16S rRNA methyltransferases, or strains that produce extended-spectrum-β-lactamases, or express carbapenemases.

L. Koeth et al. (2017) evaluated the plazomicin MIC Test Strip (MTS) in vitro and compared to broth microdilution (BMD) against 125 Enterobacteriaceae isolates. The study was performed to evaluate the performance of the MTS against CRE isolates. The clinical drug development of plazomicin has been discussed in previous studies. The MTS was compared to the BMD method for the determination of MICs for plazomicin against Enterobacteriaceae isolates.

Methods

Study isolates: 125 Enterobacteriaceae species were selected to include a range of plazomicin MICs and isolates with known resistance mechanisms. Each isolate was tested for PLZ MIC by both broth microdilution (BMD) and BMD prepared from strips and by PLZ MTS on 100 mm Mueller Hinton agar (MDA) plates. (Becton, Dickinson, Sparks, MD) and a subset of 20 strains was also tested on MHA plates from two additional manufacturers (Hardy, Santa Colsa, CA and Remel, Lenexa, KS). Quality control (QC) strains (E. coli ATCC 29522 and P. aeruginosa ATCC 27853) were tested on each day of testing and results compared to CLSI expected ranges.

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As demonstrated, further evaluation of the plazomicin MTS showed good correlation to BMD MIC. Further testing with additional isolates and media at multiple test sites was warranted.

Figure 1. Plazomicin MTS MIC compared to BMD MIC for 125 Enterobacteriaceae (P value for each MIC result).

Figure 2. Plazomicin MTS MIC compared to BMD MIC for a subset of 25 genetically characterized carbapenemase-producing Enterobacteriaceae (number of results at each MIC).

Figure 3. Comparison of plazomicin MTS MIC results on Hardy and Remel MHA compared to BD MHA for 20 strains.

Conclusion:

Overall there was good correlation of plazomicin MTS MIC results to BMD MIC results. No statistically significant differences were found between the MTS and BMD results.

References:

