INTRODUCTION

Gepotidacin (GSK2140944) is a novel triazaacenaphthylene bacterial type II topoisomerase inhibitor in Phase 3 clinical development for the treatment of uncomplicated urinary tract infections (uUTI) and gonorrhea.

Gepotidacin inhibits bacterial DNA gyrase and topoisomerase IV by a unique mechanism.

This study evaluated the correlation of gepotidacin in vitro activity by various antimicrobial susceptibility testing methods using a large collection of recent clinical isolates.

GOOD CORRELATION WAS OBSERVED BETWEEN VARIOUS ANTIMICROBIAL SUSCEPTIBILITY METHODS FOR GEPOTIDACIN.

- >95% of all BMD and gradient diffusion MICs for all isolates combined were in essential agreement (±1 dilution)
- >99% of inhibition zone diameters were in essential agreement (±3 mm) between disk manufactures

Figure 1. Gepotidacin broth microdilution vs gradient diffusion MICs for all isolates - ***E. coli*** (n = 3,379) and ***S. saprophyticus*** (n = 264)

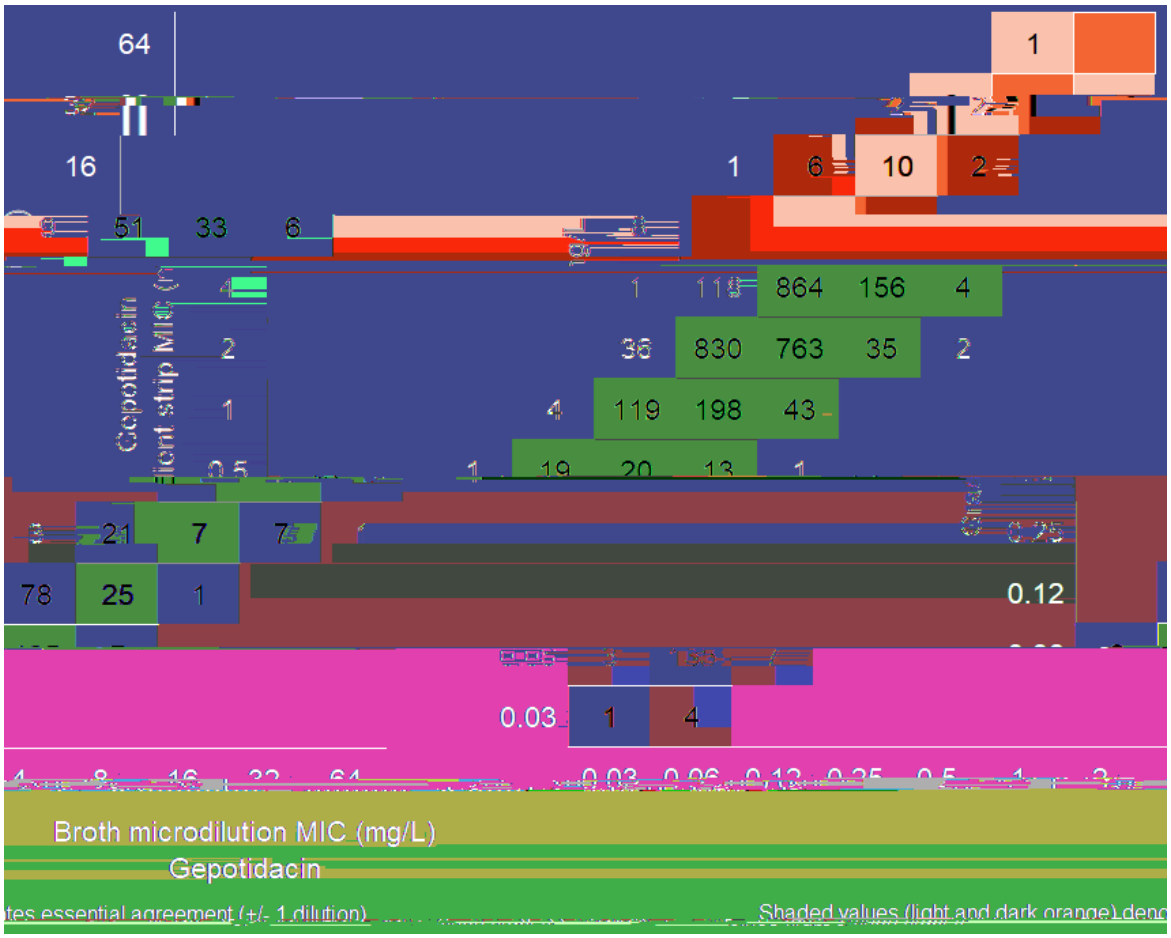
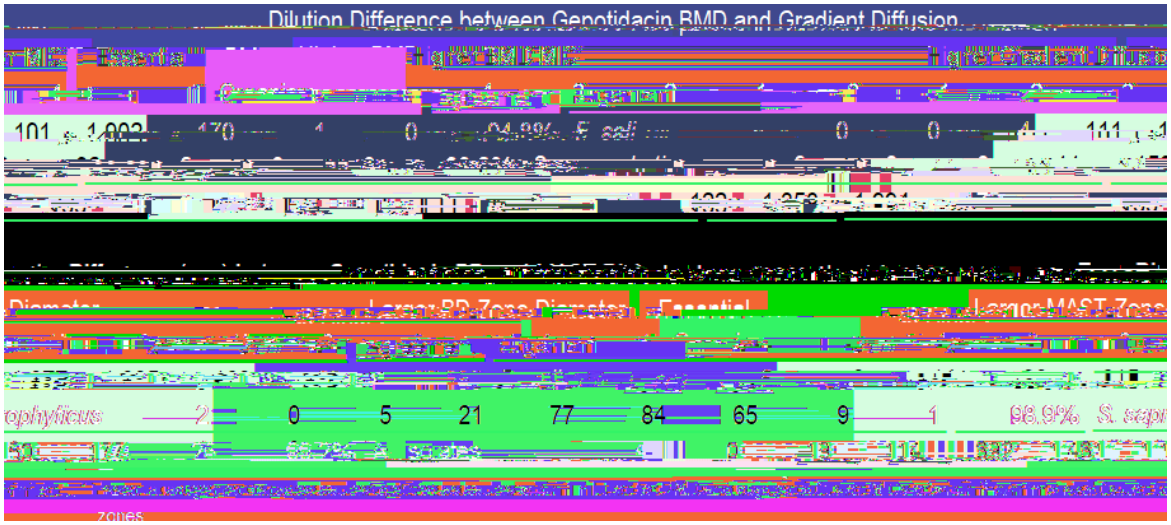


Table 1. Summary of agreement between various Gepotidacin AST methods


Dilution Difference between Genotidacin BMD and Gradient Diffusion
Essential
Essential
0
0
Larger BD Zone Diameter
Essential
Larger MAST Zone
0
5
21
77
84
65
9
1
98.9%
zones

RESULTS

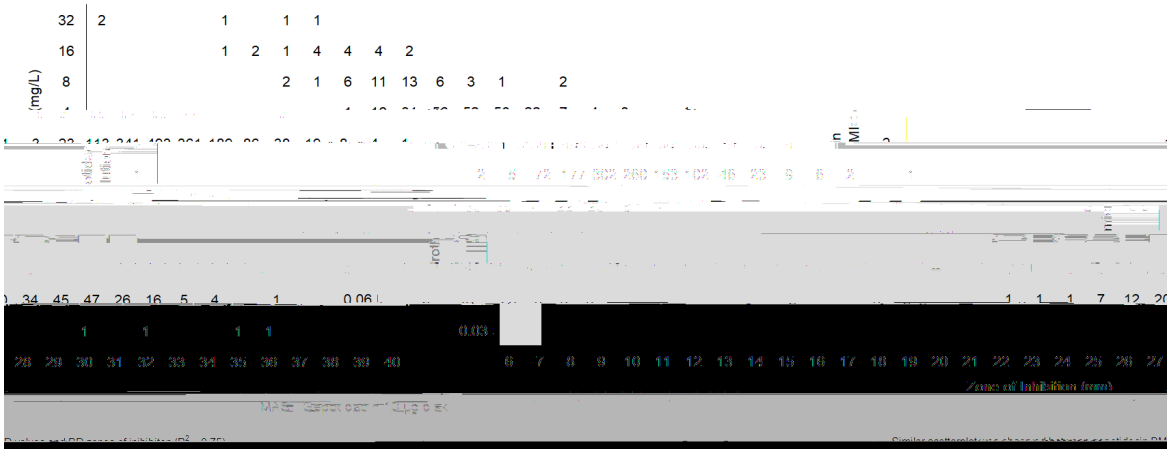
A strong correlation (R^2 = 0.82) was observed between gepotidacin BMD and gradient diffusion MIC values for all isolates tested.

Essential agreement was observed for these two methods, with 94.8% of gepotidacin values for ***E. coli*** and 99.2% of values for ***S. saprophyticus*** falling within 1 $\log_2$ dilution.

56.3% of the gepotidacin gradient diffusion MIC values against ***E. coli*** were 1 doubling dilution higher than their corresponding BMD MIC value.

When gepotidacin BMD MIC results were compared by scattergram analysis to zone diameters, acceptable correlations (R^2 = 0.75 to 0.77) were observed for the two commercial disks.

Figure 2. Gepotidacin broth microdilution MICs vs MAST disk diffusion zones of inhibition for all isolates - ***E. coli*** (n = 3,379) and ***S. saprophyticus*** (n = 264)



The two gepotidacin commercial disks performed similarly, with 99.2% agreement (±3 mm) between zone diameter values and an R^2 = 0.94.

On average, the gepotidacin BD disk zones diameters measured 1.2 mm larger than the observed gepotidacin Mast disk zones.

CONCLUSIONS

Correlations with R coefficients >0.75 were observed between various antimicrobial susceptibility methods for gepotidacin, including BMD versus gradient diffusion and BMD versus disk diffusion.

Similar performance for gepotidacin susceptibility results was observed for all methods regardless of whether ***E. coli*** or ***S. saprophyticus*** isolates were tested.

This data should prove useful for developing alternative and reliable susceptibility methods for clinical microbiology laboratories testing gepotidacin.

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N Scangarella-Oman and D Butler are employees and share holders of GlaxoSmithKline

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