Analysis of solithromycin bactericidal activity against vancomycin-susceptible and vancomycin-resistant enterococci

Abstract 1593

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Objectives: Solithromycin (SOL) is a novel fluoroketolide in late clinical development that has an in vitro activity spectrum that is different and frequently more potent than currently available macrolides. Against Enterococcus faecalis (EFA) and E. faecium (EFM), including vancomycin resistant strains, SOLI has an MIC_{90} of 2 mg/L. Currently, linezolid is the only antibiotic that also has an MIC_{90} of 2 mg/L against these strains. This study was performed to evaluate the activity SOL against enterococci, both VS and VR, based on time-kill kinetic analysis, in comparison to linezolid.

Methods: Two strains of EFA (vancomycin-susceptible [VS] and vancomycin-resistant [VR]) and EFM (VS and VR) were selected for analysis. Broth microdilution testing according to CLSI M7 guidelines was used to determine SOL MICs for each strain, and linezolid was used as the comparator. Time-kill kinetic studies were done using drug concentrations of 2X, 4X, and 8X the MIC and CFU/mL determinations for cidality were done at 0, 2, 4 and 24 hr. Bactericidal activity was defined as a 3 log_{10} decrease in CFU/ml after 24 h incubation relative to the concentration of the starting inoculum.

Results: The following table provides the log10 CFU/mL reductions of initial inocula after 24 hours at 2X, 4X, and 8X the SOL and LZD MICs.

			Log10 CFU/mL Reduction After 24 Hours					
	MIC (mg/L)		2X MIC		4X MIC		8X MIC	
Organism	SOL	LZD	SOL	LZD	SOL	LZD	SOL	LZD
EFA VR	0.25	1	0.81	0.68	1.13	1.30	1.06	1.25
EFA VS	0.06	2	-0.45	-0.76	0.05	0.02	0.14	0.18
EFM VR	0.06	2	0.81	0.23	1.83	0.58	1.83	1.13
EFM VS	0.06	2	2.92	1.71	2.76	1.21	2.92	1.71

Conclusions: Although SOL MICs for each enterococcal strain tested were relatively low (0.06 - 0.25 mg/L), bactericidal activity was not achieved against any of the strains. As a comparator, linezolid also failed to demonstrate bactericidal activity against any of the four strains tested. However, against the EFM VS strain, SOL activity that approached cidality was noted. This finding may warrant further analysis of a greater variety of enterococcal strains and indicates that SOL's spectrum can be quite different from those of older macrolides and ketolides.

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