

Potent In Vitro Activity of Solithromycin (CEM-101) Against Vancomycin-Resistant and -Susceptible Enterococci

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Introduction: Enterococci are important nosocomial pathogens. Enterococci are intrinsically less susceptible to antibiotics and the combination of high-level resistance to ampicillin, vancomycin, and aminoglycosides is common among hospital-acquired strains. Although linezolid is approved for use in enterococcal infections, enterococci resistant to linezolid have emerged. Thus, new therapeutic options for treating enterococcal infections are urgently needed. Recognizing this need, *Enterococcus* species have recently been recognized as a qualified infectious disease pathogen (QIDP) by the FDA. Due to high intrinsic resistance and bacteriostatic activity, macrolides are not used for treating enterococcal infections, either alone or in combination with other drugs. However, linezolid, also a bacteriostatic agent, has proven efficacious and has been approved for use in enterococcal infections. We have investigated the activity of Solithromycin (CEM-101, SOLI) a potent 4th generation macrolide, the first fluoroketolide in clinical development, against vancomycin-susceptible (Van-S) and vancomycin-resistant (Van-R) enterococci. Linezolid, vancomycin, daptomycin and other antibiotics were tested as comparators.

Methods: Eighty-eight strains of *E. faecalis* and *E. faecium* collected from blood cultures at the Univ. of Rochester Med. Ctr. in 2011 thru 2013 were tested. The strains were characterized as Van-S or Van-R. Minimal inhibitory concentrations (MIC) were determined by the broth microdilution method according to CLSI guidelines.

Results and Discussion: The in vitro activity of SOLI against Van-S and Van-R strains and comparator antibiotics is shown below.

	MICs (µg/ml) for Van-R strains ^a		MICs (µg/ml) for Van-S strains ^b	
	MIC Range	MIC 90%	MIC Range	MIC 90%
SOLI	0.004-1	1	0.002-1	0.5
Penicillin	4->64	32	0.25->64	64
Vancomycin	256->1024	1024	0.25-2	2
Ceftaroline	4->16	>16	0.12->16	>16
Azithromycin	1->32	>32	0.5->32	>32
Gentamicin	16->1024	256	8->1024	1024
Linezolid	0.5-4	2	0.06-8	4
Daptomycin	0.25-8	4	0.12-8	4

^a 37 strains of Van-R *E. faecium*

^b 41 strains of Van-S *E. faecalis* and 10 strains of Van-S *E. faecium* strains

Conclusion: New antibiotics are needed for the treatment of enterococcal infections. SOLI is being studied in Phase 3 studies in CABP and should be studied in other indications including enterococcal infections.