Evaluation of Solithromycin (CEM-101), a Novel Fluroketolide, in Murine Infection Models

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Background:

Solithromycin (CEM-101) has demonstrated significant activity against gram positive pathogens including *L. monocytogenes*, *E. faecalis* and marcolide resistant strains of *S. pneumoniae*.

Methods:

Efficacy was evaluated in an acute systemic infection model. CD-1 female mice were infected IP; CEM-101 or comparators were administered as a single oral dose 1 hr post infection. PD_{50}s were determined at 48 hr post infection. *L. monocytogenes* was delivered IV with treatment at 1 hr post infection. PD_{50} determined at 72 hr post infection. CEM-101 was evaluated in a cyclophosphamide induced neutropenic mouse model of pneumonia infection. At 5, 24, and 36 hrs post lung infection with a *mef*(E), *erm*(B) resistant *S. pneumoniae* isolate, mice were orally dosed with CEM-101 or control drugs. Twenty-four hr after the end of treatment, the lungs were processed and CFU/gram of lung determined.

Results:

Mouse Systemic Infection Model PD_{50} (mg/kg)			
	CEM -101	Telithromycin	Clarithromycin
S. pneumoniae Serotype 19A (erythromycin R)	**20.6 (15.7–25.4)**	>30	>30
S. pneumoniae *mef*(E) & *erm*(B)	**21.2 (12.9–29.4)**	> 30	> 30
E. faecalis (macrolide susceptible)	**11.5 (8.5-14.5)**	10.9 (5.0-16.7)	21.8 (16.7-26.8)

In the systemic infection model, *L. monocytogenes* demonstrated PD_{50} values for CEM-101, ampicillin, and azithromycin of 7.6, 55.1, and 11.6 mg/kg, respectively. Reduction in bio-load was evaluated against a resistant *S. pneumoniae* isolate in a neutropenic mouse pneumonia model. CEM-101 achieved 1, 2, and 3 $\log_{10}$ reductions from controls at 30, 46.5 and 85 mg/kg, respectively. Telithromycin achieved a 1 and 2 $\log_{10}$ reductions at 46 and > 100 mg/kg, respectively. Clarithromycin and Azithromycin were unable to effect a significant reduction in bio-load.

Conclusions:

CEM-101 has continued to demonstrate significant *in vivo* activity against susceptible and resistant bacteria strains.