**Evaluation of Sulfamethoxazole (CEM-101), a Novel Fluoroketolide, in Murine Infection Models**

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**Abstract**

Background: Sulfamethoxazole (CEM-101) has demonstrated significantactivity against gram-positive pathogens including L. monocytogenes, E. faecalis and macrolide 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 controls were administered as a single oral dose 1 hr post infection. PD50 were determined at 48 hr post infection. MICs were determined at 72 hr post infection. CEM-101 was evaluated in a cryopreserved mouse model of pneumonia infection. At 6, 24, and 36 hrs post lung infection with a mef(E), erm(Bl) 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: CEM-101 has continued to demonstrate significant activity over telithromycin and clarithromycin against resistant isolates in systemic infections.

Conclusions: CEM-101 is a novel fluoroketolide currently in clinical development.

This compound demonstrates:

- Significant in vivo MICs against susceptible and macrolide resistant isolates.
- Increased in vivo activity over telithromycin and clarithromycin against resistant S. pneumoniae isolates in systemic infections.
- Equal or better activity against E. faecalis and L. monocytogenes in systemic infection models.
- Potent activity against a resistant S. pneumoniae isolate in a lung bio-burden efficacy model.

**Introduction**

CEM-101, a novel fluoroketolide antimicrobial agent, has demonstrated substantial activity against both susceptible and macrolide resistant bacterial strains in vitro susceptibility testing (1, 2, 7). We have previously reported on the in vivo efficacy of CEM-101 against both susceptible and macrolide resistant gram positive isolates, including respiratory pathogens such as S. pneumoniae (5, 6). In these series of studies we continue to challenge CEM-101 with additional macrolide resistant isolates in both systemic and tissue burden models. In order to further challenge the activity of CEM-101 we have evaluated clinically relevant strains such as S. pneumoniae serotype 19 as well as a macrolide resistant isolate with a mef and erm resistant genotype (2). CEM-101 has also demonstrated significant in vitro activity against intracellular L. monocytogenes and selected strains of E. faecalis (3).