

# Evaluation of CEM-101, a Novel Macrolide, in Murine Infection Models

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## Background:

CEM-101 has demonstrated significant activity against gram + pathogens including macrolide resistant streptococci and MRSA.

## Methods:

Efficacy was evaluated in several infection models. CD-1 female mice were infected IP; CEM-101 or comparators were administered as a single oral dose 1 hr post infection. PD<sub>50</sub>s were determined 24 hr post infection. CEM-101 was further evaluated in a subcutaneous abscess mouse model against *S. pneumoniae*. CD-1 female mice were infected via SC injection of bacteria mixed with cyclodextran beads. Two hr post infection, mice received a single oral dose of CEM-101 or control agents. At 48 hr post dose, mice were euthanized, abscesses aseptically removed and bacteria enumerated. CFU per abscess was determined and compared to the untreated control. Further evaluation of CEM-101 was performed in cyclophosphamide induced neutropenic mice. At 1.5 hr post thigh infection with *S. pneumoniae*, mice were orally dosed with CEM-101 or control drugs. 24 hr post treatment, the thighs were processed and CFU/gram of thigh determined.

## Results:

Mouse Systemic Infection Model (mg/Kg)			
	CEM-101	Telithromycin	Clarithromycin
<i>S. aureus</i>	<b>16.3</b> (11.2-21.3)	>30	22.7 (11.3-34.1)
MRSA	<b>7.5</b> (6.0-8.9)	ND	5.0
<i>S. pneumoniae</i> (macrolide susceptible)	<b>6.0</b> (2.0-10.0)	19.9 (9.6-30.2)	32.1 (12.3-52.0)
<i>S. pneumoniae</i> ( <i>mef</i> R)	<b>23.2</b> (15.6-30.7)	10.6 (2.6-18.6)	>30
<i>S. pyogenes</i> (macrolide susceptible)	<b>9.4</b> (7.3-11.5)	7.8 (5.7-9.8)	24.8 (18.1-30.4)
<i>S. pyogenes</i> (erythromycin R)	<b>5.1</b> (4.2-6.1)	4.4 (3.8-4.9)	22.8 (14.6-30.9)

ND= not determined

In the abscess, a 10 mg/Kg QD dose of CEM-101 demonstrated a 4.2 log<sub>10</sub> decrease while clarithromycin (CL) only achieved a 1.5 log<sub>10</sub> reduction from untreated mice. CEM-101 in the thigh required 8.0 mg/Kg to achieve a 3 log<sub>10</sub> reduction from the untreated mice. Telithromycin and CL required 15.5 and 13.5 mg/Kg respectively to achieve the same log<sub>10</sub> CFU reductions.

## Conclusions:

CEM-101 demonstrates significant *in vivo* activity in a wide range of infection models.