

# Evaluation of CEM-101, a Novel Fluoroketolide, in a Rat *H. influenzae* Pulmonary Infection Model.

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## Background:

CEM-101, a clinical candidate for the treatment of community-acquired bacterial pneumonia, previously demonstrated significant gram-positive activity in several animal efficacy models. We evaluated the activity of CEM-101 against *H. influenzae*, a gram-negative pathogen, utilizing a difficult-to-treat pulmonary infection model.

## Methods:

Male Sprague Dawley rats were infected with a macrolide-susceptible strain of *H. influenzae*. *H. influenzae* was prepared from a plate culture, adjusted to an OD of 0.1 in saline, and diluted 1:2 in 1% molten agarose for infection. Anesthetized rats were infected intratracheally with 0.5 mL of the bacterial suspension. Rats were treated with CEM-101 or clarithromycin via oral gavage at 5, 24, 48, and 72 hours post-infection. Animals were euthanized 24 or 48 hours after the completion of treatment. The lungs were processed for CFU determination.

## Results:

CEM-101 demonstrated significant efficacy, achieving 1 and 2 log<sub>10</sub> reductions in CFUs at 32 and 44 mg/kg when assessed at 24 hours post-treatment. This reduction in bio-load persisted when the time of lung harvest was extended to 48 hours post-treatment. At 48 hours post-treatment, 1 and 2 log<sub>10</sub> CFU reductions were achieved with 31 and 42 mg/kg of CEM-101. Clarithromycin was unable to elicit a significant reduction in the lung bioburden levels of *H. influenzae* in this model.

## Conclusions:

CEM-101 demonstrated significant efficacy in this difficult-to-treat infection model of *H. influenzae* by its ability to effect a bactericidal response. Not only did CEM-101 demonstrate reductions in bio-loads at the classic 24-hour post-treatment harvest assessment, but it also demonstrated significant efficacy when the harvest time was extended to 48 hours post-treatment.