Intrapulmonary Penetration of CEM-101 in Healthy Adult Subjects

Abstract – A1-690

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Background:

CEM-101 is a novel fluoroketolide with activity against typical and atypical bacterial respiratory organisms including *Streptococcus pneumoniae*. It is currently being evaluated for the treatment of patients with community-acquired bacterial pneumonia. The penetration of CEM-101 into the epithelial lining fluid (ELF) and alveolar macrophages (AM) were assessed in a Phase 1 clinical study.

Methods:

30 subjects received 400 mg of CEM-101 orally daily for 5 days. On Day 5, each subject underwent a single bronchoscopy and bronchoalveolar lavage at 1 of 5 time points (3, 6, 9, 12, or 24 h post-dose) to obtain ELF and AM samples (6 subjects/time point). Plasma samples were collected pre-dose on Days 1 to 5 and serially post-dose on Day 5 and 6. The samples collected were assayed for CEM-101 using LC/MS/MS. Urea in the plasma and ELF was used to correct the ELF CEM-101 concentrations. Non-compartmental pharmacokinetic (PK) analysis using the median concentrations at each time point was used to calculate the Day 5 AUC_{0-24}. In addition, a population PK model (PPM) was used to determine Day 5 AUC_{0-24} for each subject in plasma and ELF. Intrapulmonary penetration of CEM-101 into the ELF and AM was determined by dividing the Day 5 AUC_{0-24} of each matrix by the Day 5 plasma AUC_{0-24}.

Results:

CEM-101 penetrated well into ELF and AM. Plasma, ELF, and AM AUC_{0-24} were 7.12, 63.2, and 1282 mg/L*hr, respectively. ELF and AM penetration ratios for CEM-101 were 8.88 and 180, respectively. ELF penetration ratio determined by the PPM was 8.71. 0.06 mg/L).

Conclusions:

CEM-101 achieved higher exposures in ELF (>8 times) and AM (180 times) compared to plasma concentrations during the 24 hour period after drug administration in healthy adults. CEM-101 provides a good intrapulmonary penetration profile for the treatment of susceptible pathogens associated with lower respiratory tract infections.