

Pharmacokinetics-Pharmacodynamics (PK-PD) of CEM-102 (Sodium Fusidate) Against *Streptococcus pyogenes* Using *In Vitro* Pharmacodynamic Models (IVPM)

Abstract A1-021

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Background:

The PK-PD of CEM-102, an oral antibiotic in development for the treatment of complicated skin & skin structure infections, was evaluated for *S. pyogenes* using IVPM.

Methods:

Using a 1 compartment IVPM (1CIVPM), CEM-102 PK-PD against *S. pyogenes* 991 (MIC=4 mg/L) with an initial 10⁶ CFU/mL inoculum was evaluated over 48h. Broth in the 1CIVPM was supplemented with human albumin (4g/dL). CEM-102 regimens (AUC₄₈:MIC ratio) evaluated included: 600 mg q12h (468), 1200 mg q24h (639), front loaded (FL)1200-600 mg q12h (922), FL1500-600 mg q12h (1096), 1200 mg q12h (1148) and 2400 mg q24h (1328). The relationship between the log ratio (AUCCFU_{drug} / AUCCFU_{Control}) and AUC₄₈:MIC was evaluated using a Hill-type model. Select regimens were evaluated over 240 h using a hollow fiber infection model (HFIM).

Results:

CEM-102 regimens demonstrated the following net changes in log₁₀ CFU in the 1CIVPM at 24h/48h: 600 mg q12h, -2.2/-2.5; 1200 mg q24h, -2.4/-3.5; FL1200-600 mg q12h, -1.9/-3.4; FL1500-600 mg q12h, -2.0/-3.4; 1200 mg q12h, -2.2/-3.2; and 2400 mg q24h, -2.3/-3.4. Log ratios were -2.7, -2.6, -2.7, -2.6, -2.6 and -3.1, respectively. The relationship between log ratio and AUC₄₈:MIC was well described by a Hill-type model (r²=0.97). AUC₄₈:MICs (%SE) associated with a 1, 2 and 2.5 decline in the log ratio were 26 (160), 110 (143) and 335 (103), respectively. In the HFIM, net changes in log₁₀ CFU at 48h/240h of -2.4/-5.8, -2.5/-5.8 and -2.4/-5.8 and log ratio reductions of -3.5, -3.5 and -3.6 for the 600 mg q12h, FL1200-600 mg q12h and FL1500-600 mg q12h regimens, respectively, were observed. All regimens suppressed resistance development over 240 h.

Conclusions:

CEM-102 regimens evaluated were effective against *S. pyogenes* as demonstrated by > 2 log₁₀ CFU reduction at 48 h and suppression of resistance over 10 days.