Phase 1 Pharmacokinetic and Safety of Multiple Doses and Effects of Food on the Bioavailability of Oral Solithromycin (CEM-101) in Healthy Adult Subjects

Abstract A1-689

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Background:

Solithromycin (CEM-101) is a potent new fluoroketolide for treatment of bacterial respiratory tract and other infections.

Methods:

In a randomized, double-blind, placebo-controlled study, escalating oral doses (200 [n=7], 400 [n=14], and 600 [n=14] mg) were administered once daily for 7 days (5:2, active: placebo). Physical examinations, vital signs, ECGs, clinical laboratory tests, and adverse events were monitored throughout the study. Plasma PK samples were collected pre-dose and up to 24 h (Day 1) and 72 h (Day 7) post-dose. A separate randomized, 400 mg single-dose, two-period, fed/fasted crossover bioequivalence study assessed the effects of food [12 fasted, 12 high fat diet].

Results:

PK: Mean C_{max} values on Days 1 and 7 were 0.113 and 0.248 mg/L (200 mg), 0.579 and 1.09 mg/L (400 mg) and 0.862 and 1.50 mg/L (600 mg). Corresponding $AUC_{(0\text{-}24)}$ values were 0.888 and 2.31 mg•h/L, 4.85 and 13.30 mg•h/L, and 7.64 and 18.40 mg•h/L on Days 1 and 7. Mean T_{max} ranged from 3.0 to 3.75 hours on Day 1 and from 3.5 to 4.0 hours on Day 7, and mean $T_{1/2}$ increased from 3.64 to 5.06 hours on Day 1 and from 5.39 to 7.64 hours on Day 7. After single oral doses of CEM-101 400 mg, differences in plasma C_{max}, $AUC_{(0\text{-}T)}$ and $AUC_{(0\text{-}inf)}$ between fasted and fed subjects were insignificant ($p \geq 0.05$). **SAFETY**: Gastrointestinal (GI) AEs, mostly mild, occurred in each dose group. Mild, reversible, clinically insignificant ALT or AST increases occurred in 4 of 10 subjects (600 mg group); The incidence of GI AEs was slightly reduced following fed treatment.

Conclusions:

Multiple daily doses (200 to 600 mg) of CEM-101 were safe and well tolerated. C_{max} and $AUC_{0\text{-}inf}$ increases were more than dose proportional, and moderate accumulation of CEM-101 was noted after 7 days. Oral bioavailability of CEM-101 following a single oral dose of 400 mg was not affected by food.