

A Phase 1 Trial to Evaluate the Safety and Pharmacokinetics of Single Doses of Intravenous (IV) Solithromycin (CEM-101) in Healthy Adult Subjects

Abstract O95

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Background

To determine the safety, pharmacokinetics (PK), dose limiting toxicity and maximum tolerated dose of single escalating doses of IV solithromycin. Solithromycin is the first and only fluoroketolide with an oral (phase 2) and IV formulation (phase 1) in development for the treatment of community acquired bacterial pneumonia (CABP) and other infections.

Method

This was a Phase 1 single-center, randomized, double-blind, placebo-controlled, single IV dose-escalation study in healthy adults. Each cohort consisted of 7 subjects, randomized 5:2 (CEM-101:placebo). Subjects were given IV CEM-101 or vehicle placebo over 1.5 h and remained in the Clinical Research Unit for 48 hours post-dose for safety monitoring and PK assessments, returning on Day 6 for safety assessment. Physical examinations, vital signs, ECGs, clinical laboratory tests, and adverse events (AEs) were monitored. Dose escalation was based on stringent safety criteria. PK was assessed pre-dose, during the infusion and up to 48 hours post-dose.

Results

A total of 42 subjects (six cohorts of 7 subjects) were enrolled in the single ascending dose portion of this ongoing study. 30 subjects received CEM-101 doses of 25, 50, 100, 200, 400, and 800 mg and 10 received vehicle placebo. There were no serious AEs, clinically significant systemic adverse events, QT prolongation or clinically significant laboratory abnormalities. PK (C_{max} and AUC_{inf}) appeared linear up to 200 mg and slightly more than dose proportional at higher doses. Clearance decreased with dose. Volume of distribution was large and relatively constant over the dose range.

Conclusion

Solithromycin, the first broad spectrum fluoroketolide, was systemically well tolerated and showed favorable PK in single doses up to 800 mg when given IV, achieving clinically relevant plasma concentrations (~4 mcg/mL). IV exposure was 1.3-3 fold higher than what was observed with equivalent oral doses. Multiple ascending doses (7 days) are under investigation as well as determination of absolute bioavailability. Due to favorable findings in this single dose escalation study, further development is warranted.