Evaluation of Safety, PK, and PD of a New Quinolone Antibiotic, CFC-222, in Healthy Volunteers

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To evaluate the safety, PK, and PD of a new quinolone antibiotic CFC-222, single-blind, randomized, placebo-controlled, parallel group studies were conducted in 56 healthy volunteers. The volunteers were randomly allocated to single dose groups of 100mg, 200mg, 400mg, 600mg, or multiple dose groups of 100mg, 200mg, 300mg. The 200mg single dose group was further studied for food interaction in a crossover fashion. Drug concentrations in plasma, saliva, and urine were measured by HPLC.

Pharmacodynamic efficacy was evaluated by serum bactericidal titers (SBT).

CFC-222 showed linear PK for AUC, Cmax, and half-life, but CL/F showed a tendency to decrease with increasing dose. The plasma half-life was 20 hrs and Tmax 1.6 hrs. In urine, 15~28% of the administered dose was recovered unchanged. Drug administration after food intake decreased the extent and rate of absorption, and the relative bioavailability was 82.6%. SBT results showed significant *ex vivo* bactericidal activity up to 24 hours for standard strains of *S. aureus*, *E. coli*, and clinical strains of *S. aureus*.

Transient slight increases in serum creatinine levels were noted in most of the subjects, but all levels were within normal range and returned to baseline values after the end of dosing. Urinary *N*-acetyl glucosaminidase levels did not show any change, and it is possible that that the increased creatinine levels reflect transient inhibition of tubular creatinine secretion by CFC-222.

CFC-222 was generally safe and well tolerated for up to 600mg single doses or 300mg multiple doses. The results suggest that CFC-222 is suitable for once daily dosing.