The objectives of this study were as follows:

**Background**
Evaluate the safety and tolerability of solithromycin when co-administered with digoxin
Assess the effect of a loading dose of solithromycin on the PK of digoxin
Evaluate the effect of oral solithromycin on oral digoxin PK at near steady-state levels of both drugs in healthy adult subjects
The effect of a loading dose of solithromycin on the PK of digoxin at steady state was also studied,
A total of 14 subjects were enrolled in the study. Subjects were confined at the Clinical Research Unit (CRU) from Day 1 through the duration of the drug administration (10 days) and for 24 hr after the last dose.

**Methods**

**Study Design**
This was an open-label, single-center, parallel, 2-exposure, crossover, drug-drug interaction (DDI) study with healthy male and female subjects (18-45 years of age) with a body mass index (BMI) of 18-30 kg/m² and a total body weight of >50 kg.
A total of 10 subjects were enrolled in the study. Subjects were confined at the Clinical Research Unit (CRU) from Day 1 through the duration of the drug administration (10 days) and for 24 hr after the last dose.
During the first period (Days 1-5), subjects received digoxin, and during the second period (Day 6), subjects received solithromycin (Day 6: Oral solithromycin 800 mg (4×200 mg capsule) as a single dose). During the first period (Days 1-5), subjects received digoxin, and during the second period (Day 6), subjects received solithromycin (Day 6: Oral solithromycin 800 mg (4×200 mg capsule) as a single dose). During the first period (Days 1-5), subjects received digoxin, and during the second period (Day 6), subjects received solithromycin (Day 6: Oral solithromycin 800 mg (4×200 mg capsule) as a single dose).

**Safety**
Mild contact dermatitis and 1 event of contact urticaria were reported during the study. Of the 28 AEs reported during the study, 26 were mild in severity and 2 were moderate. Mild contact dermatitis and 1 event of contact urticaria were reported during the study. Of the 28 AEs reported during the study, 26 were mild in severity and 2 were moderate. Mild contact dermatitis and 1 event of contact urticaria were reported during the study. Of the 28 AEs reported during the study, 26 were mild in severity and 2 were moderate. Mild contact dermatitis and 1 event of contact urticaria were reported during the study. Of the 28 AEs reported during the study, 26 were mild in severity and 2 were moderate. Mild contact dermatitis and 1 event of contact urticaria were reported during the study. Of the 28 AEs reported during the study, 26 were mild in severity and 2 were moderate. Mild contact dermatitis and 1 event of contact urticaria were reported during the study. Of the 28 AEs reported during the study, 26 were mild in severity and 2 were moderate. Mild contact dermatitis and 1 event of contact urticaria were reported during the study. Of the 28 AEs reported during the study, 26 were mild in severity and 2 were moderate. Mild contact dermatitis and 1 event of contact urticaria were reported during the study. Of the 28 AEs reported during the study, 26 were mild in severity and 2 were moderate. Mild contact dermatitis and 1 event of contact urticaria were reported during the study. Of the 28 AEs reported during the study, 26 were mild in severity and 2 were moderate. Mild contact dermatitis and 1 event of contact urticaria were reported during the study. Of the 28 AEs reported during the study, 26 were mild in severity and 2 were moderate. Mild contact dermatitis and 1 event of contact urticaria were reported during the study. Of the 28 AEs reported during the study, 26 were mild in severity and 2 were moderate. Mild contact dermatitis and 1 event of contact urticaria were reported during the study. Of the 28 AEs reported during the study, 26 were mild in severity and 2 were moderate. Mild contact dermatitis and 1 event of contact urticaria were reported during the study. Of the 28 AEs reported during the study, 26 were mild in severity and 2 were moderate. Mild contact dermatitis and 1 event of contact urticaria were reported during the study. Of the 28 AEs reported during the study, 26 were mild in severity and 2 were moderate. Mild contact dermatitis and 1 event of contact urticaria were reported during the study. Of the 28 AEs reported during the study, 26 were mild in severity and 2 were moderate. Mild contact dermatitis and 1 event of contact urticaria were reported during the study. Of the 28 AEs reported during the study, 26 were mild in severity and 2 were moderate.

**Pharmacokinetic Analysis**
Parameters of digoxin in plasma (AUC0-tau and Cmax increased by ~38% and ~46%, respectively), However, digoxin Ctrough levels were similar for digoxin alone and digoxin co-administered with solithromycin.
No differential P-gp inhibition effect on digoxin exposures attributable to solithromycin was observed when comparing a single 800 mg loading dose and subsequent 800 mg multiple doses solithromycin (Digoxin QD+Solithromycin QD vs Digoxin QD).

**Conclusion**
Administration of multiple once-daily doses of solithromycin resulted in an increase in exposure parameters of digoxin in plasma (AUC0-tau and Cmax increased by ~38% and ~46%, respectively). No differential P-gp inhibition effect on digoxin exposures attributable to solithromycin was observed when comparing a single 800 mg loading dose and subsequent 800 mg multiple doses solithromycin (Digoxin QD+Solithromycin QD vs Digoxin QD).

**Pharmacokinetics**
- Day 10 Versus Day 6: AUC0-tau (pg*hr/mL) 109.60 104.54-114.91 7.35
- Day 10 Versus Day 5: AUC0-tau (pg*hr/mL) 138.39 132.00-145.10 7.35
- Day 6: Multiple oral administration of Digoxin (Digoxin 0.125 mg QD co-administered with a loading dose of 800 mg Solithromycin)
- Day 5: Multiple oral administration of Digoxin (Digoxin 0.125 mg QD administered alone)

**Results**

**Pharmacokinetic**
- A total of 13 (93%) subjects completed the study and were included in the PK and statistical analysis comparisons.
- Mean plasma concentrations are presented in Figure 1.

**Conclusion**
Administration of multiple once-daily doses of solithromycin resulted in an increase in exposure parameters of digoxin in plasma (AUC0-tau and Cmax increased by ~38% and ~46%, respectively). No differential P-gp inhibition effect on digoxin exposures attributable to solithromycin was observed when comparing a single 800 mg loading dose and subsequent 800 mg multiple doses solithromycin (Digoxin QD+Solithromycin QD vs Digoxin QD).

**References**
1. Oldach D, Clark K, Schranz J, Das A, Craft J, Scott D, Jamieson B, Fernandes P. A randomized, double-blind, placebo-controlled, examination, or ECG assessments in this study.