The adolescent PK trial was completed and the results are summarized herein.

Materials and Methods

- We performed a phase 1, open-label, multi-center study to determine the PK of oral solithromycin, and its two metabolites, N-acetyl solithromycin and 3-hydroxy solithromycin, in adolescents with suspected or confirmed infections.
- In order to identify optimal dosing for this study, we modeled phase 1 adult data and simulated adolescent exposure by scaling the model parameters using an allometric relationship with body weight.
- Based on the simulation results, adolescents received oral capsules solithromycin 12 mg/kg up to 800 mg adult maximum on Day 1 and 6 mg/kg up to 400 mg adult maximum on Days 2-5 as add-on therapy. Doses were rounded up to the next highest 50 mg.
- We collected PK samples at 0.5–1.5, 2–4, 8–10, and 23–<24 hours on Days 2-5 for up to 5 days. We measured solithromycin concentrations in plasma using a validated HPLC-MS/MS assay. We collected PK samples at 0.5–1.5, 2–4, 8–10, and 23–24 hours after the first and multi-dose administration of solithromycin. We performed noncompartmental PK analysis using the software Phoenix WinNonLin (version 6.3).

RESULTS: Thirteen adolescents (median [range] age 16 years [12-17]; weight 64 kg [30-84]) completed the study, of whom 10 (77%) were male. Most adolescents received an 800 mg loading dose followed by 400 mg daily dosing, the same as the adults received.

- Twelve adverse events were reported, of which 9, including 1 serious adverse event (limb abscess), were unrelated to solithromycin.
- Two separate episodes of mild headache and 1 episode of increased transaminases (<3x upper limit of normal) were deemed related to study drug. These adolescents were also on other concomitant medications.

- In order to identify optimal dosing for this study, we modeled phase 1 adult data and simulated adolescent exposure by scaling the model parameters using an allometric relationship with body weight.

- We collected PK samples at 0.5–1.5, 2–4, 8–10, and 23–<24 hours on Days 2-5 for up to 5 days. We measured solithromycin concentrations in plasma using a validated HPLC-MS/MS assay. We collected PK samples at 0.5–1.5, 2–4, 8–10, and 23–24 hours after the first and multi-dose administration of solithromycin. We performed noncompartmental PK analysis using the software Phoenix WinNonLin (version 6.3). PK parameter estimates for solithromycin were compared to adult estimates from Phase 1 studies.

- We performed a phase 1, open-label, multi-center study to determine the PK of oral solithromycin, and its two metabolites, N-acetyl solithromycin and 3-hydroxy solithromycin, in adolescents with suspected or confirmed infections.

- Most adolescents received an 800 mg loading dose followed by 400 mg daily dosing, the same as the adults received.
- The exposure, safety, and PK of solithromycin in a small cohort of adolescents were comparable to that reported in adults.

Conclusions

- Most adolescents received an 800 mg loading dose followed by 400 mg daily dosing, the same as the adults received.
- The exposure, safety, and PK of solithromycin in a small cohort of adolescents were comparable to that reported in adults.

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