

Pharmacokinetics and Safety of Solithromycin in Adolescents with Suspected or Confirmed Bacterial Infection

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BACKGROUND: Solithromycin is a new fourth generation macrolide fluoroketolide antibiotic which is undergoing Phase 3 investigations in adults. The drug is available in oral capsule and intravenous formulations and has activity against pathogens implicated in community-acquired pneumonia and other infections, with expanded coverage including activity against methicillin-resistant *S. aureus*.

OBJECTIVE: We performed a phase 1, open-label study involving six centers to assess the pharmacokinetics (PK) and safety of solithromycin capsules in adolescents.

METHODS: We enrolled adolescents (12 to 17 years of age) with suspected or confirmed bacterial infections and administered solithromycin (capsules) as add-on therapy (12 mg/kg on Day 1 [800 mg adult maximum], 6 mg/kg daily on Days 2-5 [400 mg adult maximum]) 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 a 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 which 10 (77%) were male. The median (range) Day 1 dose was 800 mg (400-800), and Days 2-5 dose was 400 mg (200-400). Observed drug exposure on Day 1 and Days 3-5 are shown in Table 1. Twelve adverse events were reported of which nine, including one serious adverse event (limb abscess), were unrelated to solithromycin administration. Two separate episodes of mild headache and one episode of increased transaminases (<3 x upper limit of normal) were deemed related to study drug.

Table 1. Mean (SD) solithromycin PK parameters in adolescents and historical adults.

Day	Parameter	Adolescents (n=13)*	Adult Value
1	C _{MAX} (µg/mL)	0.97 (0.73)	1.32 (0.92)
	AUC ₀₋₂₄ (µg*h/mL)	11.62 (8.55)	12.45 (8.53)
3/4/5	C _{MAX} (µg/mL)	0.74 (0.61)	0.90 (0.46)
	AUC ₀₋₂₄ (µg*h/mL)	9.28 (6.30)	7.92 (4.39)
	T _{1/2} (h)	5.65 (1.29)	5.60 (1.20)

*Not all parameters have a total of thirteen adolescents contributing data because of samples observed below the quantification limit.

CONCLUSION: The exposure, safety, and PK of solithromycin in a small cohort of adolescents were comparable to that reported in adults.