

Intravenous Formulation of Solithromycin, a Painless Macrolide Antibiotic for Intravenous Injection

Abstract A2-036

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Background:

Solithromycin is a potent new fluoroketolide in development for treatment of bacterial respiratory tract and other infections. Solithromycin is currently in Phase II trials for the oral dosage form and Phase I trials for the IV dosage form. Historically, macrolide antibiotics, such as clarithromycin and erythromycin, are known to cause pharmacologically-related pain with IV injection. Solithromycin is the first macrolide since azithromycin to have the potential for an IV formulation, allowing for clinical trials in moderately severe to severe community-acquired bacterial pneumonia. In this study, solithromycin IV formulations were evaluated for pain upon injection, using the rabbit ear vein model, and compared to Azithromycin for Injection.

Methods:

(i) Single dose studies: 5 ml of solithromycin IV formulations at 2 and 3 mg/ml were infused into rabbit ear veins at 1, 2, 3, and 4 ml/min. 5 ml of azithromycin (2 mg/ml) was infused at 4 ml/min. **(ii)** Multiple dose study: 5 ml of IV solithromycin was infused at 2 concentrations (2 and 3 mg/ml) at 3 ml/min daily for 5 days, with a control group receiving vehicle only.

Results: In the single dose study, rabbits did not show any pain with solithromycin IV formulations of 2 mg/ml or 3 mg/ml at infusion rates up to 4 ml/min. In contrast, rabbits injected with azithromycin IV solution experienced strong movements of ear, head, and body, with vocalization upon administration, and were removed from the study. In the multiple dose study, rabbits infused with solithromycin did not show any signs of pain for up to 5 days, though some injection site irritation was noted on Days 3-5, probably due to the mechanical irritation of repeated injections. Rabbits infused with the formulation vehicle also experienced similar injection site irritation.

Conclusions:

Solithromycin IV formulations did not cause any pain in the single or multiple dose studies using the rabbit ear vein model. In contrast, Azithromycin for Injection caused a high degree of pain as a single dose at the concentration and infusion rate approved for hospital administration.