

Efficacy of Solithromycin for Treatment of Experimental Syphilis Infection

Abstract B-1301

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Background:

Since 2004, macrolide resistance mutations have been identified in the 23SrDNA of *Treponema pallidum* strains from many geographical regions. Solithromycin (SOLI) is a fluoroketolide antibiotic that binds multiple sites on the bacterial 23s ribosome, which could overcome macrolide resistance. We tested SOLI for efficacy against strains of *T. pallidum* with and without macrolide resistance mutations.

Methods:

Groups of 3 rabbits were infected intradermally with *T. pallidum* Nichols (wild type) or a macrolide-resistant mutant: either Street 14 (mutation A2058G) or UW330 (mutation A2059G). After lesions developed, rabbits were treated with benzathine penicillin G (BPG; 200,000 MU IM single dose), Azithromycin (AZ; 15 mg/kg PO daily for 10 days), or SOLI (10 mg/kg/d or 15mg/kg/d IV for 10 days); controls were untreated. On days 0 (pre-treatment) and 3, 5, 7, 9, 11 after treatment initiation, lesion aspirates were examined by darkfield microscopy. Blood was collected weekly for quantitative Venereal Disease Research Laboratory (VDRL) testing. Popliteal lymph nodes of selected rabbits were transferred into naïve rabbits to detect latent infection.

Results:

Following treatment, *T. pallidum* could not be detected in Nichols-infected rabbits treated with BPG, AZ or SOLI; tissue transfers were negative; and VDRL titers were significantly lower than in untreated controls. Similar results were seen in Street 14- and UW330-infected rabbits treated with BPG. *T. pallidum* persisted in Street 14- and UW330B-infected rabbits treated with AZ, and VDRL titers were not significantly different from untreated controls. With SOLI at either dose, treponemes persisted in lesions after treatment, and VDRL titers were not significantly different from untreated controls.

Conclusions:

SOLI was as effective as BPG and AZ in treating wild type *T. pallidum* infections in the rabbit model. BPG was effective for Street 14 and UW330 infections, while AZ and SOLI at the doses tested failed to cure *T. pallidum* infection by these strains.