

Solithromycin (CEM-101) Displays High Antimicrobial Activity Against Extracellular and Intracellular *Neisseria gonorrhoeae*

Abstract 1614

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The goals of this study are to evaluate the *in vitro* activity of solithromycin, a fluoroketolide, against clinical gonococcal isolates, and test its intra-cellular activity against isolates highly resistant to macrolides.

Clinical isolates (N=196) collected from 2008 to 2011 at the Public Health Ontario Laboratories, Toronto, Canada, were studied, including isolates previously characterized¹ and a collection of strains with different levels of azithromycin (AZI) resistance. MICs of solithromycin and AZI were compared by agar dilution method, and the role of pH into these determinations was defined (pH range, 5.6 to 7.6). Monolayers of HeLa epithelial cells infected with gonococci expressing different AZI susceptibility profiles were treated with solithromycin to test its intracellular activity by bacterial counting after 3 and 20 hours of exposure.

Solithromycin displayed MIC₅₀ and MIC₉₀ of 0.0625 and 0.125 µg/ml, respectively, making its activity at least 4-fold higher than AZI. Clinical isolates with elevated AZI MICs (>2,048 µg/ml, and 4-8µg/ml) showed solithromycin MICs of 8 µg/ml and 0.5µg/ml, respectively. Solithromycin displayed more stability at lower pH since MICs were not significantly affected by acidic pHs, compared to AZI MICs in the same pH conditions. Moreover, the exposure of infected HeLa cells cultures to 1x or 4x the bacterial solithromycin MICs resulted in marked loss of viability of all tested strains, suggesting a very high intracellular antimicrobial activity.

In conclusion, solithromycin demonstrated to be stable and potent against *N. gonorrhoeae*, even on strains with high azithromycin MICs. These extracellular and intracellular results suggest that solithromycin might be an effective treatment option for gonorrhoea.

¹ Allen et al, 2012. Antimicrob. Agents Chemother. **55**:703-12.