Antimicrobial activity of the fluoroketolide, solithromycin (CEM-101), against *Neisseria gonorrhoeae*

**Abstract E-781**

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**Background:**
To evaluate the *in vitro* activity of solithromycin against clinical gonococcal isolates as well as its intra-cellular activity against isolates highly resistant to azithromycin.

**Methods:**
A total of 196 clinical *N. gonorrhoeae* isolates collected from 2008 to 2011 at the Ontario Public Health Laboratory, Toronto, Canada, were studied, including isolates previously characterized1 and a collection of strains with different levels of azithromycin resistance. *In vitro* activity of solithromycin was compared to azithromycin using the agar dilution method according to Clinical and Laboratory Standards Institute guidelines. The role of pH in MIC determinations was determined using pH-adjusted agar plates (pH range, 5.6 to 7.6). To investigate the intracellular activity of solithromycin, *in vitro* invasion assays were performed using monolayers of HeLa epithelial cells and 5 clinical gonococci expressing different azithromycin susceptibility profiles. Infected cultures were treated with solithromycin and its intracellular activity was determined by bacterial counting after 3 and 20 hours of exposure.

**Results:**
Solithromycin displayed an MIC\(_{50}\) and MIC\(_{90}\) of 0.0625 and 0.125 µg/ml, respectively, making its activity at least 4-fold higher than azithromycin. Clinical isolates with elevated MICs for azithromycin (MICs >2,048 µg/ml, and 4-8µg/ml) showed solithromycin MIC values of 8 µg/ml and 0.5µg/ml, respectively. In contrast to azithromycin, solithromycin MICs were not significantly affected by acidic pHs, suggesting more stability at lower pH. Moreover, exposure of infected HeLa cell cultures to 1x or 4x the solithromycin MICs resulted in the progressive loss of viability of all tested strains, suggesting very high intracellular antimicrobial activity.

**Conclusions:**
Solithromycin was demonstrated to be stable and potent against *N. gonorrhoeae*, even on strains with high azithromycin MICs. These *in vitro* results suggest that solithromycin might be an effective treatment option for gonorrhea.