Mycobacterium leprae is Susceptible to Solithromycin (CEM-101)

Abstract 1137

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Solithromycin (CEM-101), a new macrolide-ketolide in clinical development, has been found to be a minimum of 4-fold more active than other macrolides, mainly clarithromycin and azithromycin and 2-4 fold more active than Telithromycin. It is active against a variety of macrolide-resistant pathogenic strains of *S. aureus*, *S. pyogenes*, and *S. pneumoniae*. The efficacy of Solithromycin (CEM-101) against *Mycobacterium leprae*, the causative agent for leprosy, was investigated in the present study.

Thai-53 isolate of *M. leprae*, maintained by serial passages in athymic *nu*/*nu* mice footpads, was used for all experiments. For axenic testing freshly harvested viable *M. leprae* were incubated in medium along with different concentrations of the drugs (CEM-101, clarithromycin and rifampin) for 7 days at 33^{o}C. At the end of this incubation drug-treated *M. leprae* were subjected to radiorespirometry to assess viability based on oxidation of ^{14}C palmitate. For intracellular testing peritoneal macrophages from Swiss mice were infected with freshly harvested viable *M. leprae* at a MOI of 20:1 for 12 hours. At the end of the infection macrophage cultures were washed free of extracellular bacteria and drugs added at different concentrations and incubated for 3 days at 33^{o}C. At the end of 3 days cells were lysed to obtain the intracellular *M. leprae* for viability testing by radiorespirometry and staining with viability dyes to assess the extent of membrane damage.

Solithromycin (CEM-101) at 0.15 mg/ml was able to significantly (P<0.001) reduce the viability of *M. leprae* in both axenic and intracellular cultures when compared to controls. Inhibition by CEM-101 was not statistically different from inhibition obtained with clarithromycin under identical conditions and at the same concentration against the claithromycin-susceptible *M. leprae*.

Solithromycin (CEM-101) is effective against *M. leprae* potentially expanding the drugs available to treat leprosy.