

In Vitro Activity of CEM-101 Compared to Clarithromycin Against *Nocardia* Species

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Sulfonamides are usually the treatment of choice for *Nocardia* infections. Central nervous system and disseminated nocardiosis, however, continues to be difficult to manage. Drug resistant species of *Nocardia* such as *N. farcinica* or *N. otitidiscaviarum*, and sulfonamide intolerance require the use of alternative drugs. Promising reports of the effectiveness of clarithromycin (CLA) have been published, although clinical experience is still limited. In this study, the activity of CEM-101, a new ketolide, was evaluated *in vitro* compared to CLA, a structurally related macrolide, against *Nocardia* spp.

CLA, obtained from Abbott Laboratories (Abbott Park, IL), was dissolved in DMSO at a concentration of 1 mg/mL. CEM-101, provided by Cempra Pharmaceuticals Inc. (Chapel Hill, NC), was dissolved in double distilled water with 3% glacial acetic acid at a concentration of 1 mg/mL. Thirty one isolates of *Nocardia*, belonging to seven species, were obtained from the American Type Culture Collection (Manassas, VA), Barbara Body, and Betty Ann Forbes. Isolates were grown in cation supplemented Mueller-Hinton (MH) broth and diluted in MH broth to yield a standard turbidity of 100 Klett units per mL (1.2×10^6 - 6.0×10^7 CFU/mL). An *in vitro* broth microdilution method similar to that recommended by the Clinical and Laboratory Standards Institute (CLSI) was utilized for susceptibility testing.

The MIC₅₀ and MIC₉₀ for CEM-101 were 0.062 mcg/mL and 32 mcg/mL, respectively, compared to 0.125 mcg/mL and 128 mcg/mL for CLA. Two groups of isolates could be clearly distinguished in terms of susceptibility. A resistant group, with MICs ≥ 8 mcg/mL (14 isolates) and a susceptible group, with MICs ≤ 0.25 mcg/mL (17 isolates). There was good concordance with the activity of CEM-101 and CLA in each of these groups.

CEM-101 was demonstrated to be active *in vitro* against *Nocardia* spp, showing equal or better activity than CLA against most of the isolates tested. CEM-101 should be further evaluated against Mycobacteria to define its spectrum of activity.