Amended Abstract

Objectives: To assess the potency of CEM-101, a fluoroketolide in clinical development, against strains observed to be resistant (R) to other agents in the same class. Reports have described telithromycin-resistant S. pyogenes strain TR1 (TEL) species worldwide, most recently S. pyogenes (Group A) from Europe. CEM-101 was tested against a collection of 43 TEL-R β-haemolytic streptococci (BHS). Methods: A total of 53 (1.3%) BHS were identified among 3,958 in the SENTRY Antimicrobial Surveillance Program (2003-2006) that were TEL-R (MIC > 0.12 mg/L). 43 strains (36 Group A, 1 Group C, 6 Group G) were available for testing in 20 hospitals in Europe (31 strains), North America (11) and Latin America (1). Susceptibility (S) testing methods when testing other streptococci such as S. pneumoniae (CLSI M07-A8, 2009 and M100-S19). Forty-three of these strains were available for further study, from 20 hospitals in Europe (31 strains), USA (11 strains), and Latin America (one strain). The most common species were S. pyogenes (Group A; 36 strains), Group C (one strain) and Group G (six strains).

Results: CEM-101 remained active against all TEL-R (MIC ≤ 0.12 mg/L) BHS with all MICs at ≤0.03 mg/L, that breakpoint used for telithromycin when testing other streptococci such as S. pneumoniae, consistent with “non-susceptibility” by USA-FDA and CLSI breakpoints.

Conclusions: CEM-101 demonstrated potent activity against TEL-R β-haemolytic streptococci with the degree of rRNA dimethylation by Erm. MIC 0.03 mg/L. Further development is warranted, especially in endemic areas (Europe) of ketolide resistance (erm [B] and 23S RNA mutations).

Selected References