Expanded studies of CEM-101, a novel fluoroketolide, tested against invasive isolates of N. meningitidis, including fluoroquinolone-non-susceptible resistant strains

R. Jones[1], D. Biedenbach[1], L. Woosley[1], G.Gerken[1], M. Castaheira[1]
[1] JMI Laboratories, North Liberty, IA, USA

Objectives: To evaluate the potential role/potency of CEM-101 tested against N. meningitidis (NM) as a decolonizing regimen. More than 100 invasive clinical isolates were screened, including three cases of ciprofloxacin-non-susceptible NM (C-NSNM) provided by the CDC (Drs. H. Wu and M. Warton) occurring in North Dakota and California (2007-2008).

Methods: 62 isolates were previously studied and that collection was expanded to 103, including the CNSNM (ciprofloxacin MICs, 0.06-0.25 mg/L). The strains (>90% blood cultures) were collected in 1997-2009 from 43 medical centers in North (58 strains) and South (13) America, Europe (31) and Asia-Pacific (1). Strains were tested by CLSI broth microdilution methods for susceptibility (S) to CEM-101 and 11 comparators, including beta-lactams, fluoroquinolones (FQs), macrolides and three other classes.
Serological identification was performed for serogroups (SGs) B, C, Y and W135. NM displaying elevated ciprofloxacin MIC values (>=0.06 mg/L) were evaluated for mutations on gyrA or B and parC or E, and in the efflux pump gene mtrR.

Results: Penicillin-S was 84.5% with no resistant (R) strains detected. All isolates were S to ceftriaxone, azithromycin, minocycline and rifampin. 97.1% of NM were S to ciprofloxacin and levofloxacin (<=0.015mg/L); however, about one-quarter of the strains had reduced S to nalidixic acid (MIC, >= 8 mg/L), which can correlate with diminished S to FQs, and 3 isolates (CDC strains) were frankly non-S. R to trimethoprim/sulfamethoxazole (T/S) was 47.6%. Of MLSB agents, CEM-101 was the most active (MIC90, <=0.015 mg/L) compared to telithromycin (0.03 mg/L), azithromycin and clarithromycin (0.12 mg/L) and erythromycin (0.25 mg/L). The prevalence rates (%) of SGs were: B (41.7), C (37.9), Y (12.6) and W135 (2.9); only 5 were not typeable. Three strains with ciprofloxacin MIC values at >=0.06 mg/L harbored gyrA mutations that generated the amino acid substitution T91I. These strains carried no alterations on the remaining tested genes (gyrB, parC, parE and mtrR).

Conclusions: CEM-101 was the most active MLSB agent tested against NM strains (all MICs <= 0.06 mg/L), with a potency two-to >=16 fold greater than any other in class drug. CEM-101 was active against NM isolates non-S to beta-lactams, T/S and especially FQs. Further studies should determine if CEM-101 can eradicate NM from the nasopharynx of at-risk patients in cases where R to other potential decolonizing agents has emerged.