Mutations Associated with Ketolide Resistance in Streptococcus pneumoniae
Collected in the 2009 SENTRY Antimicrobial Surveillance Program

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Background
Ketolide resistance (R) is very rare in S. pneumoniae (SPN) and is usually associated with a variety of ribosomal mutations and/or mutations in the erm(B) gene that control expression. We investigated the mechanisms of resistance to ketolides, telithromycin (TLR), or roxithromycin in the SENTRY program (2009) and assessed the activity of solithromycin (CEM-101), a new fluoroketolide in clinical development.

Methods
1,283 SPN isolates obtained from patients with community-acquired bacterial pneumonia in 23 countries were tested for susceptibility to TLR by CLSI methods (M77-07 and M80-A3). Only 5/283 (1.8%) isolates were identified to be TLR-resistant. Strains were screened for erm(B) and mef(E) resistance genes by PCR, and in the 23S rRNA, L22 and L4 proteins, and the erm(B) promoter region by PCR and DNA sequencing.

Results
The 5 TLR-resistant strains were from the Peoples Republic of China and had TELI MIC values of 8 µg/ml, however the CEM-101 MICs were only 0.06-0.25 µg/ml. Significant 23S rRNA, L4/L22 riboprotein genes for any of the five strains contained mutations.

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