

CEM-101, a novel fluoroketolide: Activity against recent(2008) isolates of multidrug-resistant (MDR) *S. pneumoniae* (SPN)

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Background:

CEM-101 is a new fluoroketolide with potent activity against Gram-positive pathogens and key respiratory tract Gram-negative species (*H. influenzae* and *M. catarrhalis*). We report CEM-101 potencies tested against SPN isolates focusing on various MDR subsets.

Methods: 1737 SPN strains were collected in 2008 from medical centers in the USA, Europe, and Latin America. A central monitoring laboratory susceptibility (S) tested each isolate against > 25 antimicrobials by CLSI (M07-A8, M100-S19) methods. MDR patterns were defined by resistance (R) to penicillin (PEN), erythromycin (ERY), clindamycin (CLI), tetracycline (TET), and TMP/SMX (T/S). A ketolide, telithromycin (TEL), and levofloxacin (LEV) were also tested.

Results: The CEM-101 inhibition at $\leq 1 \mu\text{g/ml}$ was compared in a SPN population with the following R-rates (%): PEN (21.4), ERY (36.3), CLI (20.0), TET (25.8), T/S (21.7) and LEV (1.1). CEM-101 ($\text{MIC}_{50/90}$, 0.016/0.25 $\mu\text{g/ml}$) showed increased MIC_{50} and MIC_{90} results for MDR patterns that included ERY and CLI (0.25/0.5 $\mu\text{g/ml}$, respectively). TEL (S rate, 99.9%) MIC results were slightly higher than CEM-101 (100.0%S). Amoxicillin/clavulanate non-S rate was 12.8%, but 86.9% among isolates R to all 5 listed drugs (Table). Ceftriaxone non-S rate was an alarming 8.6% (8.2% for cefepime). CEM-101 was effective ($\text{MIC}, \leq 1 \mu\text{g/ml}$) versus all LEV-R isolates and those strains with ciprofloxacin MIC values at $\geq 4 \mu\text{g/ml}$ (QRDR mutants).

Conclusions: CEM-101 was the most active agent against all SPN at $\leq 1 \mu\text{g/ml}$, like glycopeptides and linezolid. MDR isolates with ERY-CLI R showed elevated, yet S-level CEM-101 MIC values. CEM-101 potency against current SPN indicates potential use against community-acquired bacterial pneumonia. Count: 363(1,950 allowed)1719 + 200 table= 1919

Category:

Key words: *S. pneumoniae*, CEM-101, ketolide, global surveillance

R patterns						MIC ($\mu\text{g/ml}$)			
PEN	ERY	CLI	TET	T/S	LEV	No. tested	50%	90%	% $\leq 1 \mu\text{g/ml}$
X						371	0.06	0.25	100.0
X	X					307	0.06	0.5	100.0
X	X	X				184	0.25	0.5	100.0
X	X	X	X			165	0.25	0.5	100.0
X	X	X	X	X		145	0.06	0.25	100.0
					X	21	0.016	0.12	100.0
All strains						1737	0.016	0.25	100.0