

# CEM-101, a Novel Macrolide/Ketolide, Shows Improved Intracellular Activity Against Phagocytised *S. aureus* in Comparison with Azithromycin (AZM), Clarithromycin (CLR), or Telithromycin (TEL)

*S Lemaire, F Van Bambeke, PM Tulkens*

## Background:

Intracellular activity of antibiotics is an important determinant for fast and complete eradication. We have determined the intracellular activity of CEM-101, a novel macrolide/ketolide antibiotic, against *S. aureus* in comparison with azithromycin and clarithromycin (macrolides) and telithromycin (ketolide).

## Methods:

MICs and extracellular activities of antibiotics were determined in MHB at both neutral and acidic pH. Intracellular activity was determined against *S. aureus* (ATCC 25923) phagocytosed by THP-1 macrophages as previously described (AAC, 2006;50:841-851). Results were expressed as change in bacterial counts compared to time 0.

## Results:

	CEM-101	AZM	CLR	TEL
<b>1. MICs (mg/L)</b>				
pH 7.4	0.125	0.5	0.5	0.5
pH 5.5	1-2	256	16	8
<b>2. Extracellular activity (24h): D log cfu from time 0h</b>				
<b>pH 7.4</b>				
E <sub>max</sub> <sup>1</sup>	-1.4 ± 0.1	-1.2 ± 0.6	-1.4 ± 0.2	-1.0 ± 0.4
Static conc. <sup>2</sup>	~0.06	~3.63	~1.41	~0.28
<b>pH 5.5</b>				
E <sub>max</sub> <sup>1</sup>	-1.6 ± 0.4	+2.1 ± 0.1	-1.5 ± 0.8	-1.4 ± 0.9
Static conc. <sup>2</sup>	~1.48	>25	~10.47	~9.33
<b>3. Intracellular activity (24h): D log cfu from time 0h</b>				
E <sub>max</sub> <sup>1</sup>	-0.8 ± 0.2	0.10 ± 0.0	-0.1 ± 0.1	-0.4 ± 0.2
Static conc. <sup>2</sup>	~0.02	~7.8	~0.98	~0.23
<sup>1</sup> Maximal decrease of intracellular cfu compared to initial, post-phagocytosis inoculum (calculated from non-linear regression [sigmoidal] of dose-effect response) run in broth (extracell.) or with infected macrophages (intracell).				
<sup>2</sup> Extracellular concentration (in mg/L) yielding an apparent static effect				

## Conclusions:

Compared to AZM, CLR, and TEL, CEM-101 activity was less affected by acidic pH in broth and showed greater potency (lower static dose) and larger maximal efficacy (E<sub>max</sub>) against intracellular *S. aureus*.