C-622

Activity of Solithromycin Tested Against Pathogens Associated with Community-acquired Bacterial Pneumonia: Global Surveillance Results for 2014

DJ FARRELL, RK FLAMM, HS SADER, RN JONES
JMI Laboratories, North Liberty, Iowa, USA

ICAAC 2015
JMI Laboratories
North Liberty, IA, USA
www.jmilabs.com
ph. 319.665.3370, fax 319.665.3371
david-farrell@jmilabs.com

AMENDED ABSTRACT

Background: Solithromycin (SOL) is a fluoroketolide with wide spectrum of activity against pathogens associated with community-acquired bacterial pneumonia (CABP). SOL has a potency generally equal to or two-fold greater than telithromycin (TEL), and azithromycin (AZI), as well as demonstrated activity against Gram-positive isolates having documented resistances to macrolides or lincosamides, and measurable potencies versus fastidious Gram-negative species causing CABP. We report results from a global study of SOL potency and resistance (R) rates for 2014.

Methods: A total of 4,622 isolates, including *Streptococcus pneumoniae* (SPN; 1,713), *Haemophilus influenzae* (HI; 1,308), *Moraxella catarrhalis* (MC; 577), and *Staphylococcus aureus* (SA; 1,024), were susceptibility (S) tested by CLSI broth microdilution methods with categorical interpretations (M07-A10, M100-S25) against SOL, TEL, AZI, and other comparator agents. The geographic samples included 2,012 strains from the USA, 1,990 from Europe, 297 from Latin America, and 323 from Asia Pacific.

Results: SOL was very active (Table) against SPN, demonstrating two-fold greater activity than TEL ($MIC_{50/90}$, 0.015/0.25 µg/mL) and 16- to >256-fold greater activity than AZI ($MIC_{50/90}$, 0.12/>32 µg/mL) and 100.0% were inhibited at a SOL MIC of 1 µg/mL. Against HI, SOL showed identical potency to that of TEL ($MIC_{50/90}$, 1/2 µg/mL) and both were two-fold less potent than azithromycin ($MIC_{50/90}$, 0.5/1 µg/mL). All but one MC isolate were inhibited by solithromycin at ≤0.25 µg/mL. SOL inhibited 85.3% of SA isolates at ≤1 µg/mL, TEL inhibited 84.5% of these isolates and AZI only 57.8%. SOL activity was lower against MRSA ($MIC_{50/90}$, 0.06/>32 µg/mL) compared to MSSA ($MIC_{50/90}$, 0.06/0.06 µg/mL). Little variation in SOL activity was observed by geographic region for the species tested.

Conclusions: SOL showed wide coverage of CABP pathogens in a four continent sample. High potency and spectrum of activity make SOL a promising parenteral/oral candidate for further study as a therapeutic agent for CABP.

Pathogen (no. tested)	MIC (µg/ml)		Cum. % inhibited at SOL MIC:						
	50%	90%	≤0.03	0.06	0.12	0.25	0.5	1	2
SPN (1713)	0.008	0.12	80.6	86.0	93.5	98.9	99.8	100.0	-
HI (1308)	1	2	0.0	0.1	0.5	3.4	21.6	73.5	97.6
MC (577)	0.06	0.12	9.0	67.9	99.0	99.8	99.8	99.8	100.0
SA (1024)	0.06	>32	15.3	83.0	84.6	84.8	85.0	85.3	85.5

INTRODUCTION

Solithromycin (formerly CEM-101), is a 4th generation oral and intravenous macrolide in Phase III clinical development for the treatment of moderate to moderately-severe community-acquired bacterial pneumonia (CABP).

Streptococcus pneumoniae is the predominant causative agent of CABP and solithromycin has demonstrated potent activity against this pathogen, including multidrug-resistant (MDR) and macrolide-resistant strains and genotypes.

Solithromycin has also demonstrated activity comparable to azithromycin against *Haemophilus influenzae*, very potent activity against *Moraxella catarrhalis*, beta-hemolytic streptococci, *Legionella pneumophila*, *Mycoplasma pneumoniae* (including macrolide-resistant strains), and *Chlamydophila pneumoniae*, and variable activity against *S. aureus* (activity dependent upon the type of macrolide resistance mechanisms present).

In this study, we report solithromycin and comparator antimicrobial agent activities, measured by reference Clinical and Laboratory Standards Institute (CLSI) methods, tested against a total of 4,622 CABP pathogens collected in medical centers globally during 2014.

MATERIALS AND METHODS

A total of 4,622 non-duplicated isolates were collected prospectively during 2014 from 91 medical centers located in the USA (38 centers, 2,012 isolates), Europe (35 centers, 1,990 isolates), Latin America (8 centers, 297 isolates) and Asia Pacific (10 centers, 323 isolates). These isolates were recovered consecutively from patients with respiratory tract infections (RTI), bloodstream infections (BSI), skin and skin structure infections (SSSI), and other infection types with only one strain per patient infection episode defined as being clinically significant being included.

Isolates were identified by the submitting laboratories and confirmed by JMI Laboratories (North Liberty, Iowa, USA) using standard bacteriologic algorithms and methodologies, including the use of Vitek Identification Systems (bioMerieux, Hazelwood, Missouri, USA), matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS; Bruker Daltonics, Bremen, Germany), and DNA sequencing based methods, when required.

Isolates were tested for susceptibility by broth microdilution methods, according to the recommendations of CLSI. For solithromycin, telithromycin and azithromycin, MIC results were obtained using validated broth microdilution trays produced by JMI Laboratories (North Liberty, Iowa). For other antimicrobial agents, panels were used that were manufactured by Thermo Scientific (formerly TREK Diagnostics Systems/Sensititre; Cleveland, Ohio, USA). Validation of the MIC values was performed by concurrent testing of the following quality control (QC) strains: *S. pneumoniae* American Type Culture Collection (ATCC) 49619, *Enterococcus faecalis* ATCC 29212, *S. aureus* ATCC 29213, and *H. influenzae* ATCC 49247. In addition, the inoculum density was monitored by colony counts to ensure an adequate number of cells for each testing event. MIC interpretations were based on CLSI and EUCAST breakpoint criteria.

RESULTS

- Solithromycin was very active ($MIC_{50/90}$, 0.008/0.12 µg/mL) against 1,713 *S. pneumoniae* isolates, demonstrating two-fold greater activity than telithromycin ($MIC_{50/90}$, 0.015/0.25 µg/mL) and 16- to >256-fold greater activity than azithromycin ($MIC_{50/90}$, 0.12/>32 µg/mL, (**Table 2**). All pneumococci were inhibited at solithromycin MIC values of ≤1 µg/mL (current CLSI susceptibility breakpoint for telithromycin, **Tables 1** and **2**). Applying EUCAST breakpoint criteria (susceptible at ≤0.25 µg/mL), telithromycin was active against 90.4% of the isolates tested and, using the same breakpoint, 98.9% of the *S. pneumoniae* isolates would be categorized as susceptible to solithromycin varying from 98.7% in the USA and Europe to 100.0% in Latin America and Asia Pacific.
- Penicillin (using CLSI oral breakpoints)/azithromycin susceptibility rates were 61.5/62.2% overall (**Table 2**, **Figure 1**), 57.2/51.3% in the USA, 66.0/70.3% in Europe, 53.6/63.9% in Latin America, and 63.5/73.1% in Asia Pacific (note: 8/10 centers were in Australia and New Zealand hence these values may not reflect the true prevalence in the region). Overall, ceftriaxone susceptibility (using CLSI non-meningitis breakpoints) was 92.1%, tetracycline 73.0%, trimethoprim-sulfamethoxazole 66.0%, clindamycin 79.8%, moxifloxacin 98.7%, and vancomycin 100.0% (**Table 2**).
- Among 1,308 *H. influenzae* isolates collected in 2014, nearly all (99.2%) were inhibited by solithromycin at ≤4 µg/mL (**Table 1**). At the same breakpoint MIC value, telithromycin inhibited 98.7% of these isolates (**Tables 1** and **2**). Solithromycin showed identical potency to that of telithromycin ($MIC_{50/90}$, 1/2 µg/mL) and both were two-fold less active than azithromycin ($MIC_{50/90}$, 0.5/1 µg/mL) against these isolates (**Table 2**). Telithromycin and azithromycin were active against 98.7 and 99.4%, respectively, of *H. influenzae* isolates at current CLSI breakpoints. Susceptibility rates were very low against telithromycin and azithromycin when applying EUCAST breakpoint criteria (0.5 to 2.5%). Additional comparators showing >99% susceptibility rates included: moxifloxacin, amoxicillin/clavulanate, and ceftriaxone (**Table 2**).
- All but one of the *M. catarrhalis* isolates were inhibited by solithromycin at ≤0.25 µg/mL (**Table 1**). The single isolate displaying solithromycin and telithromycin MIC results of 2 µg/mL was recovered from the tracheal aspirate of a 3 year old ambulatory male patient in New York, USA. Solithromycin ($MIC_{50/90}$, 0.06/0.12 µg/mL) was approximately two-fold more potent than telithromycin ($MIC_{50/90}$, 0.12/0.12 µg/mL; **Table 2**). *M. catarrhalis* isolates were generally very susceptible to tested antimicrobial agents (**Table 2**).
- Solithromycin inhibited 85.3% (873/1,024) of the *S. aureus* isolates at ≤1 µg/mL (**Table 1**). Macrolide resistance was high in *S. aureus*; using CLSI breakpoints, 40.9% of *S. aureus* were resistant to azithromycin (**Table 2**). As observed in previous surveillance years, the activity of solithromycin was lower against methicillin-resistant *S. aureus* (MRSA; $MIC_{50/90}$, 0.06/>32 µg/mL) when compared to methicillin-susceptible (MSSA; $MIC_{50/90}$, 0.06/0.06 µg/mL; **Tables 1** and **2**) strains. Additionally, the activity of solithromycin against European *S. aureus* isolates was greater ($MIC_{50/90}$, 0.06/2 µg/mL) than the activity of this compound when tested against strains recovered in the USA ($MIC_{50/90}$, 0.06/>32 µg/mL), which is most likely associated with the higher MRSA rates among the USA isolates (44.1% versus 28.1% in Europe).

Figure 1. Penicillin and azithromycin activity against 1,713 *S. pneumoniae* isolates by geographical region.

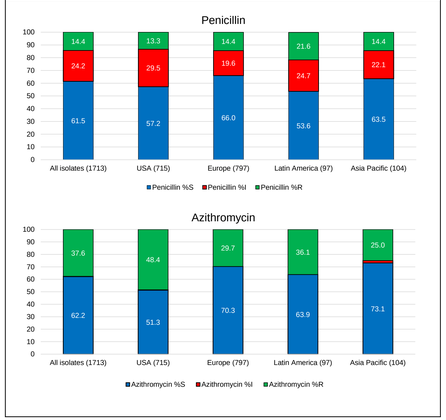

Table 1. Frequency distributions of solithromycin when tested against bacterial pathogens recovered as part of the global surveillance program (2014).

Organism group (no. tested)	0.002	0.004	0.008	0.015	0.03	0.06[a]	0.12	0.25	0.5	1	2	4	8	>8	$MIC_{50/90}$
S. pneumoniae (1,713)	1 (0.1)	7 (0.5)	1035 (60.9)	227 (74.1)	111 (80.6)	92 (86.0)	128 (93.5)	93 (98.9)	16 (99.8)	3 (100.0)					0.008/0.12
USA (715)	1 (0.1)	1 (0.3)	371 (52.2)	73 (62.4)	62 (71.0)	49 (77.9)	86 (89.9)	63 (98.7)	8 (99.9)	1 (100.0)					0.008/0.25
Europe (797)	0 (0.0)	5 (0.6)	532 (67.4)	128 (83.4)	37 (88.1)	32 (92.1)	29 (95.7)	24 (98.7)	8 (99.7)	2 (100.0)					0.008/0.06
Latin America (97)	0 (0.0)	0 (0.0)	57 (58.8)	12 (71.1)	9 (80.4)	10 (90.7)	5 (95.9)	4 (100.0)							0.008/0.06
Asia Pacific (104)	0 (0.0)	1 (1.0)	75 (73.1)	14 (86.5)	3 (89.4)	1 (90.4)	8 (98.1)	2 (100.0)							0.008/0.06
H. influenzae (1,308)	-[b]	-	-	-	-	1 (0.1)	6 (0.5)	37 (3.4)	238 (21.6)	680 (73.5)	314 (97.6)	22 (99.2)	4 (99.5)	6 (100.0)	1/2
USA (615)	-	-	-	-	-	1 (0.2)	4 (0.8)	24 (4.7)	97 (20.5)	305 (70.1)	164 (96.7)	14 (99.0)	2 (99.4)	4 (100.0)	1/2
Europe (572)	-	-	-	-	-	0 (0.0)	2 (0.3)	10 (2.1)	117 (22.6)	308 (76.4)	126 (98.4)	6 (99.5)	1 (99.7)	2 (100.0)	1/2
Latin America (60)	-	-	-	-	-	0 (0.0)	0 (0.0)	2 (3.3)	19 (35.0)	30 (85.0)	8 (98.3)	0 (98.3)	1 (100.0)		1/2
Asia Pacific (61)	-	-	-	-	-	0 (0.0)	0 (0.0)	1 (1.6)	5 (9.8)	37 (70.5)	16 (96.7)	2 (100.0)			1/2
M. catarrhalis (577)	1 (0.2)	2 (0.5)	10 (2.3)	10 (4.0)	29 (9.0)	340 (67.9)	179 (99.0)	5 (99.8)	0 (99.8)	0 (99.8)	1 (100.0)				0.06/0.12
USA (281)	1 (0.4)	1 (0.7)	4 (2.1)	5 (3.9)	16 (9.6)	180 (73.7)	70 (98.6)	3 (99.6)	0 (99.6)	0 (99.6)	1 (100.0)				0.06/0.12
Europe (216)	0 (0.0)	1 (0.5)	3 (1.9)	2 (2.8)	9 (6.9)	122 (63.4)	77 (99.1)	2 (100.0)							0.06/0.12
Latin America (30)	0 (0.0)	0 (0.0)	2 (6.7)	1 (10.0)	1 (13.3)	16 (66.7)	10 (100.0)								0.06/0.12
Asia Pacific (50)	0 (0.0)	0 (0.0)	1 (2.0)	2 (6.0)	3 (12.0)	22 (56.0)	22 (100.0)								0.06/0.12
S. aureus (1,024)	0 (0.0)	0 (0.0)	2 (0.2)	3 (0.5)	152 (15.3)	693 (83.0)	16 (84.6)	2 (84.8)	2 (85.0)	3 (85.3)	3 (85.5)	3 (85.8)	1 (85.9)	144 (100.0)	0.06/>32
USA (401)	0 (0.0)	0 (0.0)	2 (0.5)	1 (0.7)	33 (9.0)	284 (79.8)	8 (81.8)	1 (82.0)	2 (82.5)	1 (82.8)	0 (82.8)	2 (83.3)	1 (83.5)	66 (100.0)	0.06/>32
Europe (405)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	58 (14.6)	295 (87.4)	7 (89.1)	1 (89.4)	0 (89.4)	1 (89.6)	3 (90.4)	0 (90.4)	0 (90.4)	39 (100.0)	0.06/2
Latin America (110)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	29 (26.4)	50 (71.8)	0 (71.8)	0 (71.8)	0 (71.8)	1 (72.7)	0 (72.7)	1 (73.6)	0 (73.6)	29 (100.0)	0.06/>32
Asia Pacific (108)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.9)	32 (30.6)	64 (89.8)	1 (90.7)	0 (90.7)	0 (90.7)	0 (90.7)	0 (90.7)	0 (90.7)	0 (90.7)	10 (100.0)	0.06/0.12

a. ≤0.06 µg/mL for *H. influenzae*; b. "-" = not tested at this concentration

Table 2. Activity of solithromycin and comparators when tested against bacterial pathogens recovered as part of the global surveillance program for 2014.

	MIC (µg/mL)			CLSI[a]			EUCAST[a]		
	MIC_{50}	MIC_{90}	Range	%S	%I	%R	%S	%I	%R
***S. pneumoniae* (1,713 isolates)**									
Solithromycin	0.008	0.12	0.002 — 1	-	-	-	-	-	-
Telithromycin	0.015	0.25	0.004 — >32	99.7	0.1	0.2	90.4	7.6	2.0
Azithromycin	0.12	>32	0.015 — >32	62.2	0.2	37.6	61.8	0.4	37.8
Clindamycin	≤0.25	>2	≤0.25 — >2	79.8	1.1	19.2	80.8	-	19.2
Amox/Clav	≤1	4	≤1 — >8	89.4	3.4	7.2[c]	76.7	9.7	13.6
Ampicillin	≤0.25	4	≤0.25 — >8	-	-	-	76.7	9.7	13.6
				61.5	24.2	14.4[d]	61.5	-	38.5[e]
Penicillin	≤0.06	2	≤0.06 — >8	61.5	-	38.5[e]	61.5	31.9	6.6[g]
				93.4	5.9	0.7[f]	-	-	-
				80.7	11.4	7.9[e]	80.7	18.2	1.1
Ceftriaxone	≤0.06	1	≤0.06 — >8	92.1	6.8	1.1[f]	-	-	-
Linezolid	1	1	≤0.12 — 2	100.0	-	-	100.0	0.0	0.0
Moxifloxacin	≤0.12	0.25	≤0.12 — >4	98.7	0.9	0.4	98.3	-	1.7
Tetracycline	≤0.5	>8	≤0.5 — >8	73.0	0.6	26.4	73.0	0.6	26.4
TMP/SMX	≤0.5	>4	≤0.5 — >4	66.0	11.2	22.9	72.9	4.2	22.9
Vancomycin	0.25	0.5	≤0.12 — 1	100.0	-	-	100.0	-	0.0
***H. influenzae* (1,308 isolates)**									
Solithromycin	1	2	≤0.06 — >8	-	-	-	-	-	-
Telithromycin	1	2	≤0.06 — >8	98.7	0.7	0.6	0.5	98.9	0.6
Azithromycin	0.5	1	≤0.03 — >4	99.4	-	-	2.5	96.9	0.6
Clarithromycin	4	8	≤0.12 — >16	94.5	4.2	1.3	2.2	97.8	0.0
Amox/Clav	≤1	2	≤1 — 8	99.9	-	0.1	98.9	-	1.1
Ampicillin	≤0.25	>8	≤0.25 — >8	76.9	1.3	21.8	76.9	-	23.1[b]
Ceftriaxone	≤0.06	≤0.06	≤0.06 — 0.25	100.0	-	-	99.9	-	0.1
Moxifloxacin	≤0.12	≤0.12	≤0.12 — 4	99.8	-	-	99.5	-	0.5
Tetracycline	0.5	0.5	≤0.12 — >16	98.5	0.1	1.4	98.5	0.1	1.5
TMP/SMX	≤0.5	>4	≤0.5 — >4	65.2	7.0	27.8	65.2	2.1	32.7
***M. catarrhalis* (577 isolates)**									
Solithromycin	0.06	0.12	0.002 — 2	-	-	-	-	-	-
Telithromycin	0.12	0.12	0.002 — 2	-	-	-	99.7	0.2	0.2
Azithromycin	0.03	0.06	0.002 — 0.5	99.8	-	-	99.8	0.2	0.0
Clarithromycin	≤0.12	≤0.12	≤0.12 — 16	99.8	-	-	99.7	0.2	0.2
Amox/Clav	≤1	≤1	≤1 — ≤1	100.0	-	0.0	100.0	-	0.0
Ampicillin	1	2	≤0.25 — >8	-	-	-	-	-	-
Penicillin	>0.12	>0.12	≤0.03 — >0.12	-	-	-	-	-	-
Ceftriaxone	0.25	0.5	≤0.06 — 2	100.0	-	-	99.8	0.2	0.0
Moxifloxacin	≤0.12	≤0.12	≤0.12 — 0.5	-	-	-	100.0	-	0.0
Tetracycline	≤0.12	0.25	≤0.12 — >16	99.7	0.0	0.3	99.7	0.0	0.3
TMP/SMX	≤0.5	≤0.5	≤0.5 — 2	94.5	5.5	0.0	94.5	3.8	1.7
***S. aureus* (1,024 isolates)**									
Solithromycin	0.06	>32	0.008 — >32	-	-	-	-	-	-
Telithromycin	0.06	>32	0.008 — >32	84.5	0.1	15.4	-	-	-
Azithromycin	1	>32	0.008 — >32	57.8	0.4	40.9	57.8	0.9	41.3
Oxacillin	0.5	>2	≤0.25 — >2	65.1	-	34.9	65.1	-	34.9
Amox/Clav	≤1	>8	≤1 — >8	65.1	-	34.9	65.1	-	34.9
Penicillin	8	>8	≤0.06 — >8	16.5	-	83.5	16.6	-	83.4
Ceftriaxone	4	>8	1 — >8	65.1	-	34.9	-	-	-
Clindamycin	≤0.25	>2	≤0.25 — >2	84.7	0.1	15.2	84.2	0.5	15.3
Linezolid	1	1	≤0.12 — 2	100.0	-	0.0	100.0	-	0.0
Moxifloxacin	≤0.12	4	≤0.12 — >4	68.0	7.6	24.5	68.0	7.6	24.5
Tetracycline	≤0.5	≤0.5	≤0.5 — >8	93.7	0.4	5.9	92.2	0.6	7.2
TMP/SMX	≤0.5	≤0.5	≤0.5 — >4	97.8	-	2.2	97.8	0.2	2.1
Vancomycin	1	1	0.25 — 2	100.0	0.0	0.0	100.0	-	0.0
MSSA (667 isolates)									
Solithromycin	0.06	0.06	0.03 — >32	-	-	-	-	-	-
Telithromycin	0.06	0.12	0.015 — >32	96.6	0.0	3.4	-	-	-
Azithromycin	1	>32	0.008 — >32	77.5	0.6	21.9	76.5	1.0	22.5
Clindamycin	≤0.25	≤0.25	≤0.25 — >2	96.3	0.0	3.7	95.7	0.6	3.7
Amox/Clav	≤1	≤1	≤1 — >8	100.0	-	0.0	100.0	-	0.0
Penicillin	2	>8	≤0.06 — >8	25.3	-	74.7	25.3	-	74.7
Ceftriaxone	4	4	1 — >8	100.0	-	0.0	-	-	-
Linezolid	1	1	0.25 — 2	100.0	-	0.0	100.0	-	0.0
Moxifloxacin	≤0.12	≤0.12	≤0.12 — >4	93.8	1.6	4.7	93.8	1.6	4.7
Tetracycline	≤0.5	≤0.5	≤0.5 — >8	96.1	0.3	3.6	94.9	0.0	5.1
TMP/SMX	≤0.5	≤0.5	≤0.5 — >4	99.1	-	0.9	99.1	0.1	0.7
Vancomycin	1	1	0.25 — 2	100.0	0.0	0.0	100.0	-	0.0
MRSA (357 isolates)									
Solithromycin	0.06	>32	0.008 — >32	-	-	-	-	-	-
Telithromycin	0.12	>32	0.008 — >32	61.9	0.3	37.8	-	-	-
Azithromycin	>32	>32	0.25 — >32	23.5	0.0	76.5	23.0	0.6	76.5
Clindamycin	≤0.25	>2	≤0.25 — >2	63.0	0.3	36.7	62.7	0.3	37.0
Amox/Clav	>8	>8	≤1 — >8	0.0	-	100.0	0.0	-	100.0
Penicillin	>8	>8	0.12 — >8	0.0	-	100.0	0.3	-	99.7
Ceftriaxone	>8	>8	8 — >8	0.0	-	100.0	-	-	-
Linezolid	1	1	≤0.12 — 2	100.0	-	0.0	100.0	-	0.0
Moxifloxacin	2	>4	≤0.12 — >4	22.3	18.2	59.5	22.3	18.2	59.5
Tetracycline	≤0.5	>8	≤0.5 — >8	89.2	0.6	10.2	87.3	1.7	11.0
TMP/SMX	≤0.5	≤0.5	≤0.5 — >4	95.2	-	4.8	95.2	0.3	4.5
Vancomycin	1	1	0.25 — 2	100.0	0.0	0.0	100.0	-	0.0

a. Criteria as published by CLSI [2015] and EUCAST [2015]
b. "-" = breakpoints not available to interpret
c. Using Non-Meningitis breakpoints
d. Using Oral breakpoints
e. Using Parenteral, Meningitis breakpoints
f. Using Parenteral, Non-Meningitis breakpoints
g. Using EUCAST "infections other than meningitis" breakpoints

CONCLUSIONS

- Solithromycin demonstrated potent activity against global and contemporary (2014) pathogens that are the major causative agents of CABP, including against most macrolide-resistant strains.
- Similar to surveillance studies from previous years, solithromycin was the most potent antimicrobial agent tested against *S. pneumoniae*.
- These data support and encourage the continued clinical development of solithromycin for the treatment of community-acquired bacterial pneumonia.

ACKNOWLEDGEMENT

This work was funded through a grant provided by CEMPRA Pharmaceuticals (Chapel Hill, North Carolina).

REFERENCES

1. Clinical and Laboratory Standards Institute (2015). *M07-A10. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically; approved standard- tenth edition*. Wayne, PA: CLSI.
2. Clinical and Laboratory Standards Institute (2015). *M100-S25. Performance standards for antimicrobial susceptibility testing: 25th informational supplement.* Wayne, PA: CLSI.
3. EUCAST (2015). Breakpoint tables for interpretation of MICs and zone diameters. Version 5.0, January 2015. Available at: http://www.eucast.org/clinical_breakpoints/. Accessed January 2015.
4. Farrell DJ, Castanheira M, Sader HS, Jones RN (2010). The in vitro evaluation of solithromycin (CEM-101) against pathogens isolated in the United States and Europe (2009). *J Infect* 61: 476-483.
5. Farrell DJ, Mendes RE, Jones RN (2015). Antimicrobial activity of solithromycin against serotyped macrolide-resistant *Streptococcus pneumoniae* isolates collected from U.S. medical centers in 2012. *Antimicro Agents Chemother* 59: 2432-2434.
6. Mallegol J, Fernandes P, Melano RG, Guyard C (2014). Antimicrobial activity of solithromycin against clinical isolates of *Legionella pneumophila* serogroup 1. *Antimicrob Agents Chemother* 58: 909-915.
7. Roblin PM, Kohloff SA, Hammerschlag MR (2008). In vitro activity of CEM101, a new ketolide antibiotic against *Chlamydia trachomatis* and *Chlamydia pneumoniae*. Abstr. F1-3978. *48th ICAAC, October 25-28, 2008,* Washington DC, USA.
8. Waites KB, Crabb DM, Duffy LB (2009). Comparative in vitro susceptibilities of human mycoplasmas and ureaplasmas to a new investigational ketolide, CEM-101. *Antimicrob Agents Chemother* 53: 2139-2141.