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Activity of the Fluoroketolide, Solithromycin Tested against Bacterial Species Associated with Significant Community-Acquired Bacterial Pneumonia and Other Gram-positive Organisms

DJ BIEDENBACH, M CASTANHEIRA, RN JONES
JMI Laboratories, North Liberty, Iowa, USA

IDWeek 2012
JMI Laboratories
North Liberty, IA, USA
www.jmilabs.com
319.665.3370, 319.665.3371
mariana-castanheira@jmilabs.com

Abstract

Background: Antimicrobial resistance (R) continues to challenge available antimicrobial therapy choices for infection types acquired in the community. We evaluated the activity of solithromycin (SOL) and comparators against bacterial species associated with community-acquired bacterial pneumonia (CABP) and Gram-positive (GP) organisms collected during 2011.

Methods: 12,818 isolates consecutively collected from 49 hospitals (26 in the USA [7,542 isolates] and 23 in Europe [5,276]) in 2011 were susceptibility (S) tested against SOL and comparators by CLSI reference methods.

Results: Against *S. aureus* (SA), SOL ($MIC_{50/90}$, 0.06/>4 µg/mL) displayed similar activity to telithromycin (TEL; $MIC_{50/90}$, ≤0.06/>8 µg/mL) and four-fold greater than erythromycin (ERY; MIC_{50}, 0.5 µg/mL). SOL ($MIC_{50/90}$, ≤0.03/>4 µg/mL) showed comparable activity to TEL against CoNS (78.2% S). Methicillin (M) R SA (40.2%) and CoNS (68.4%) displayed higher SOL MICs compared to MS strains. SOL was moderately active against enterococci (ENT; $MIC_{50/90}$, 0.5/2 µg/mL), but was two-fold more potent than TEL ($MIC_{50/90}$, 1/4 µg/mL). SOL exhibited greater potency against *E. faecalis* (MIC_{50}, 0.06 µg/mL) compared to *E. faecium* (MIC_{50}, 1 µg/mL). SOL was very active against *S. pneumoniae* (SPN; MIC_{90}, 0.12 µg/mL), Viridans group streptococci (MIC_{90}, 0.06 µg/mL) and β-haemolytic streptococci (VGS and BHS; MIC_{90}, 0.06 and ≤0.03 µg/mL). SPN isolates were only 88.9, 59.2 and 77.2% S to penicillin (PEN), ERY and clindamycin (CLI), respectively. SOL was very active against *M. catarrhalis* (MCAT; MIC_{90}, ≤0.12 µg/mL) with lower activity against *H. influenzae* (HI; $MIC_{50/90}$, 2/2 µg/mL); however, SOL displayed four-fold greater activity than ERY against HI.

Conclusions: SOL exhibited greater potency than ERY, CLI and TEL against contemporary (2011) GP and fastidious Gram-negative organisms. This data supports further development of SOL for the treatment of this infection type.

Organism (no.)	Cumulative % at SOL MIC (µg/mL):[a]							
	≤0.03	0.06	0.12	0.25	0.5	1	2	≥4
SA (5,478)	42.6	83.6[b]	85.0	85.4	85.5	85.7	85.9	**100.0**
SPN (2,418)	78.2[b]	84.3	**90.6**	99.3	99.9	100.0		
HI (1,314)	-	-	0.8	1.8	5.1	46.6	**93.4**[b]	100.0
ENT (1,238)	38.7	42.2	44.7	47.6	57.2[b]	83.4	**99.5**	100.0
BHS (909)	**92.2**[b]	97.2	98.9	99.7	100.0			
CoNS (601)	56.7[b]	74.4	78.0	78.5	78.7	78.9	78.9	**100.0**
VGS (435)	85.7[b]	**94.9**	98.6	100.0				
MCAT (425)	-	-	**98.4**[b]	99.8	100.0			

a. - = not tested; bolded / underline = MIC_{90}.
b. MIC_{50}.

Introduction

Ketolides are semisynthetic antimicrobial agents derived from erythromycin A, and were designed to primarily overcome macrolide-resistance in pathogens, including *Streptococcus pneumoniae*. Antimicrobial agents within this class possess a keto group at the C-3 position of the lactone ring, rather than L-cladinose, as found in erythromycin. Telithromycin is the only ketolide approved for clinical use, and while this antimicrobial agent performed well in vitro against Gram-positive and some fastidious Gram-negative species (*Haemophilus influenzae, Moraxella catarrhalis*), issues with hepatotoxicity and other adverse events have limited clinical utility. Telithromycin often lacks activity against constitutive macrolide resistances ($cMLS_B$) and is capable of inducing *erm* methylase genes within a narrow concentration range.

Solithromycin (CEM-101, and formerly OP-1068) is a 2-fluoroketolide with an extended chain composed of 11,12-carbamate-butyl-[1,2,3]-triazol-aminophenyl that inhibits protein synthesis in an *Escherichia coli*-coupled transcription-translation assay with an IC_{50} of only 1.1 µM. This agent was selected as a candidate for oral and/or parenteral therapy of community-acquired respiratory tract (CA-RTI) and other infections. In vitro screening studies indicated potency comparable or superior to telithromycin, erythromycin, azithromycin and clarithromycin, as well as activity against Gram-positive isolates having documented resistances to macrolides or lincosamides. Solithromycin activity is generally focused against Gram-positive pathogens, but also possesses measurable potencies versus *Haemophilus* and *Moraxella* species, atypical bacteria such as *Legionella pneumophila*, *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae*, some Enterobacteriaceae (*Salmonella and Shigella* species), and pathogens causing various sexually transmitted diseases, including azithromycin-resistant *Neisseria gonorrhoeae.*

In this study, we evaluated the activity of solithromycin and comparator agents when tested against 12,818 contemporary clinical isolates of organisms associated with CA-RTI (pneumonias) or other Gram-positive organisms collected in United States (USA) and European medical centers during 2011.

Materials and Methods

Bacterial isolates: A total of 12,818 non-duplicated isolates were collected prospectively during 2011 from 49 medical centers located in the USA (26 centers; 7,542 isolates) and Europe (23 centers; 5,276 isolates). These isolates were recovered consecutively from patients with respiratory tract infections (RTI), bloodstream infections (BSI), or skin and skin structure infections (SSSI) and only one strain per patient episode defined as being clinically significant was included. Identifications were confirmed as needed by the Vitek system (bioMerieux, Hazelwood, Missouri, USA) or conventional tests.

Susceptibility methods: Broth microdilution tests conducted according to the Clinical and Laboratory Standards Institute (CLSI) documents were performed to determine antimicrobial susceptibility of solithromycin and comparator antimicrobial agents. Validated MIC panels were manufactured by ThermoFisher Scientific® (formerly TREK Diagnostics®; Cleveland, Ohio, USA). *Haemophilus* spp. strains were tested in Haemophilus test medium (HTM) and β-haemolytic streptococci were tested in cation adjusted (CA)-MHB supplemented with 2.5-5% lysed horse blood, and all other organisms were tested using CA-MHB, according to CLSI document M7-A09 (2012).

Quality control (QC) included testing of *S. aureus* ATCC 29213, *S. pneumoniae* ATCC 49619 and *H. influenzae* 49247 concomitantly with clinical isolates. Susceptibility percentages and validation of QC results were based on the CLSI guidelines (M100-S22) and two sets of susceptibility breakpoints were used to determine susceptibility/resistance rates (CLSI and EUCAST, 2012).

Results

- Solithromycin displayed good coverage for *S. pneumoniae* isolates. All strains were inhibited at a MIC of ≤1 µg/mL (current CLSI susceptibility breakpoint for telithromycin; Table 1) and only one (0.1%) strain exhibited a MIC value >0.5 µg/mL. All USA *S. pneumoniae* isolates had solithromycin MIC results of ≤0.5 µg/mL (data not shown).
- Solithromycin inhibited 99.2% of the *H. influenzae* strains at ≤4 µg/mL (Table 1), displaying potency comparable to that of azithromycin (MIC_{90}, 2 µg/mL for both agents; Table 2) and was two- to eight-fold more potent than telithromycin and clarithromycin (MIC_{90}, 4 and 16 µg/mL, respectively).
- Against *S. aureus*, solithromycin activity ($MIC_{50/90}$, 0.06/>4 µg/mL; Table 2) was similar to that of telithromycin ($MIC_{50/90}$, ≤0.06/>8 µg/mL) and greater than erythromycin ($MIC_{50/90}$, 0.5/>16 µg/mL). Solithromycin activity against methicillin-resistant *S. aureus* (MRSA; MIC_{50}, 0.06 µg/mL and MIC_{90}, >4 µg/mL) was lower when compared to the activity of this compound when tested against methicillin-susceptible *S. aureus* (MSSA; MIC_{50}, ≤0.03 µg/mL and MIC_{90}, 0.06 µg/mL; Table 1).
- Among coagulase-negative staphylococci, solithromycin inhibited 474 (78.9%) strains at ≤1 µg/mL (telithromycin CLSI breakpoint; Table 1) and the activity of this compound (MIC_{50}, ≤0.03 µg/mL and MIC_{90}, >4 µg/mL) was similar to the activity of telithromycin (MIC_{50}, ≤0.06 µg/mL and MIC_{90}, >8 µg/mL; Table 2).
- Solithromycin (MIC_{50}, 0.5 µg/mL and MIC_{90}, 2 µg/mL; Table 2) demonstrated activity two-fold greater than telithromycin (MIC_{50}, 1 µg/mL and MIC_{90}, 4 µg/mL; Table 2) against *Enterococcus* spp. strains. The activity of solithromycin was better against *E. faecium* (91.4% inhibited at ≤1 µg/mL) than *E. faecalis* (68.3% inhibited at same MIC concentration).
- Solithromycin was very active against *M. catarrhalis* (MIC_{90}, ≤0.12 µg/mL; Tables 1 and 2), β-haemolytic (MIC_{90}, ≤0.03 µg/mL) and Viridans group streptococci (MIC_{90}, 0.06 µg/mL), showing two- to four-fold lower $MIC_{50/90}$ values when compared to telithromycin (Table 2). All comparators were also very active against these organisms (Table 2).

Table 1. Frequency distributions of solithromycin when tested against bacterial pathogens recovered during 2011.

Organism/organism group (no. tested)[a]	No. of isolates at MIC (% of cumulative frequency; µg/mL):								
	≤0.03	0.06	0.12	0.25	0.5	1	2	4	≥8
S. pneumoniae (2418)	1890 (78.2)	149 (84.3)	151 (90.6)	211 (99.3)	16 (100.0)	1 (100.0)			
penicillin-resistant (534)	230 (43.1)	57 (53.7)	70 (66.9)	164 (97.6)	12 (99.8)	1 (100.0)			
penicillin-non-susceptible RTI (268)	46 (17.2)	19 (24.3)	49 (42.5)	147 (97.4)	7 (100.0)				
H. influenzae (1314)	-	-	11 (0.8)	13 (1.8)	43 (5.1)	545 (46.6)	615 (93.4)	76 (99.2)	7 (100.0)
β-lactamase-positive (299)			4 (1.3)	2 (2.0)	10 (5.4)	106 (40.8)	157 (93.3)	17 (99.0)	3 (100.0)
M. catarrhalis (425)	-	-	418 (98.4)	6 (99.8)	1 (100.0)				
S. aureus (5478)	2336 (42.6)	2241 (83.6)	79 (85.0)	22 (85.4)	8 (85.5)	11 (85.7)	10 (85.9)	8 (86.1)	763 (100.0)
MSSA (3278)	1846 (56.3)	1261 (94.8)	49 (96.3)	8 (96.5)	5 (96.7)	5 (96.8)	1 (96.9)	1 (96.9)	102 (100.0)
MRSA (2200)	490 (22.3)	980 (66.8)	30 (68.2)	14 (68.8)	3 (69.0)	6 (69.2)	9 (69.6)	7 (70.0)	661 (100.0)
Coagulase-negative staphylococci (601)	341 (56.7)	106 (74.4)	22 (78.0)	3 (78.5)	1 (78.7)	1 (78.9)	0 (78.9)	1 (79.0)	126 (100.0)
MSCoNS (190)	133 (70.0)	39 (90.5)	4 (92.6)	1 (93.2)	1 (93.7)	0 (93.7)	0 (93.7)	0 (93.7)	12 (100.0)
MRCoNS (411)	208 (50.6)	67 (66.9)	18 (71.3)	2 (71.8)	0 (71.8)	1 (72.0)	0 (72.0)	1 (72.3)	114 (100.0)
Enterococcus spp. (1238)	479 (38.7)	44 (42.2)	30 (44.7)	36 (47.6)	119 (57.2)	324 (83.4)	200 (99.5)	4 (99.8)	2 (100.0)
E. faecalis (757)	364 (48.1)	41 (53.5)	24 (56.7)	23 (59.7)	83 (70.7)	157 (91.4)	64 (99.9)	1 (100.0)	
E. faecium (435)	82 (18.9)	2 (19.3)	6 (20.7)	11 (23.2)	34 (31.0)	162 (68.3)	134 (99.1)	3 (99.8)	1 (100.0)
Beta-haemolytic streptococci (909)	838 (92.2)	46 (97.2)	15 (98.9)	7 (99.7)	3 (100.0)				
Viridans group streptococci (435)	373 (85.7)	40 (94.9)	16 (98.6)	6 (100.0)					

a. MSSA=methicillin-susceptible *Staphylococcus aureus*; MRSA=methicillin-resistant *Staphylococcus aureus*; MSCoNS= methicillin-susceptible Coagulase-negative staphylococci; MRCoNS= methicillin-resistant Coagulase-negative staphylococci.

Table 2. Activity of solithromycin and comparator agents tested against 12,818 Gram-positive and fastidious Gram-negative organisms collected in 2011.

Organism (no. tested)/ antimicrobial agent	MIC_{50}	MIC_{90}	Range	CLSI[a] %S / %R	EUCAST[a] %S / %R
S. pneumoniae (2418)					
Solithromycin	≤0.03	0.12	≤0.03 – 1	- / -	- / -
Telithromycin	≤0.06	0.5	≤0.06 – 2	99.9 / 0.0	89.5 / 1.0
Erythromycin	≤0.12	>16	≤0.12 – >16	59.2 / 40.5	59.2 / 40.5
Clindamycin	≤0.25	>2	≤0.25 – >2	77.2 / 22.4	77.6 / 22.4
Penicillin[b]	≤0.06	4	≤0.06 – 8	88.9 / 1.4	- / -
Penicillin[c]	≤0.06	4	≤0.06 – 8	59.7 / 22.1	59.7 / 11.1
Amoxicillin/clavulanate	≤1	4	≤1 – >8	85.2 / 9.8	- / -
Ceftriaxone	≤0.06	1	≤0.06 – >8	90.4 / 1.0	76.8 / 1.0
Tetracycline	0.5	>8	≤0.25 – >8	73.2 / 26.4	72.7 / 26.8
Trimethoprim/sulfamethoxazole	≤0.5	>4	≤0.5 – >4	66.6 / 23.1	72.8 / 23.1
Levofloxacin	1	1	≤0.12 – >4	98.7 / 1.2	98.7 / 1.3
H. influenzae (1314)					
Solithromycin	2	2	≤0.12 – >16	- / -	- / -
Telithromycin	2	4	≤0.06 – >8	98.5 / 0.5	0.8 / 0.5
Azithromycin	1	2	≤0.03 – >4	99.4 / -	0.8 / 0.6
Clarithromycin	8	16	≤0.12 – >16	87.4 / 1.3	1.6 / 0.0
Ampicillin	0.25	>8	≤0.12 – >8	76.2 / 22.3	76.2 / 23.8
Amoxicillin/clavulanate	≤1	≤1	≤1 – 8	99.8 / 0.2	90.5 / 9.5
Ceftriaxone	≤0.06	≤0.06	≤0.06 – 0.12	100.0 / -	100.0 / 0.0
Levofloxacin	≤0.12	≤0.12	≤0.12 – >4	99.9 / -	99.9 / 0.1
Tetracycline	0.5	0.5	≤0.12 – >16	98.2 / 1.7	97.7 / 1.8
M. catarrhalis (425)					
Solithromycin	≤0.12	≤0.12	≤0.12 – 0.5	- / -	- / -
Telithromycin	0.12	0.25	≤0.06 – 2	- / -	98.6 / 0.2
Penicillin	>2	>2	≤0.03 – >2	- / -	- / -
Amoxicillin/clavulanate	≤1	≤1	≤1	100.0 / 0.0	100.0 / 0.0
Ceftriaxone	0.25	0.5	≤0.06 – 2	100.0 / -	99.3 / 0.0
Tetracycline	0.25	0.25	≤0.12 – 2	100.0 / 0.0	99.8 / 0.0
Trimethoprim/sulfamethoxazole	≤0.5	≤0.5	≤0.5 – 4	97.2 / 0.2	97.2 / 0.9
Levofloxacin	≤0.12	≤0.12	≤0.12	100.0 / -	100.0 / 0.0
S. aureus (5,478)					
Solithromycin	0.06	>4	≤0.03 - >4	- / -	- / -
Telithromycin	≤0.06	>8	≤0.06 – >8	85.3 / 14.5	- / -
Erythromycin	0.5	>16	≤0.12 – >16	50.8 / 47.0	51.0 / 48.4
Clindamycin	≤0.25	>2	≤0.25 – >2	84.8 / 15.1	84.5 / 15.2
Oxacillin	0.5	>2	≤0.25 – >2	59.8 / 40.2	59.8 / 40.2
Levofloxacin	0.25	>4	≤0.12 – >4	65.3 / 32.9	65.3 / 32.9
Vancomycin	1	1	≤0.12 – 2	100.0 / 0.0	100.0 / 0.0
Linezolid	2	2	0.25 – 8	>99.9 / <0.1	>99.9 / <0.1
Tetracycline	≤0.25	0.5	≤0.25 – >8	94.6 / 4.9	93.4 / 5.8
Trimethoprim/sulfamethoxazole	≤0.5	≤0.5	≤0.5 – >4	98.9 / 1.1	98.9 / 0.9
MRSA (2,200)					
Solithromycin	0.06	>4	≤0.03 – >4	- / -	- / -
Telithromycin	0.12	>8	≤0.06 – >8	68.7 / 31.0	- / -
Erythromycin	>16	>16	≤0.12 – >16	14.8 / 83.0	15.1 / 84.3
Clindamycin	≤0.25	>2	≤0.25 – >2	67.9 / 32.0	67.5 / 32.1
Levofloxacin	4	>4	≤0.12 – >4	26.4 / 70.3	26.4 / 70.3
Vancomycin	1	1	0.25 – 2	100.0 / 0.0	100.0 / 0.0
Linezolid	1	1	0.25 – 8	99.9 / 0.1	99.9 / 0.1
Tetracycline	≤0.25	1	≤0.25 – >8	93.4 / 6.2	91.3 / 6.8
Trimethoprim/sulfamethoxazole	≤0.5	≤0.5	≤0.5 – >4	98.1 / 1.9	98.1 / 1.7
Coagulase-negative staphylococci (601)					
Solithromycin	≤0.03	>4	≤0.03 – >4	- / -	- / -
Telithromycin	≤0.06	>8	≤0.06 – >8	78.2 / 21.6	- / -
Erythromycin	>16	>16	≤0.12 – >16	41.1 / 57.6	41.3 / 58.4
Clindamycin	≤0.25	>2	≤0.25 – >2	76.9 / 22.6	74.7 / 23.1
Oxacillin	2	>2	≤0.25 – >2	31.6 / 68.4	31.6 / 68.4
Levofloxacin	0.5	>4	≤0.12 – >4	51.9 / 43.6	51.9 / 43.6
Vancomycin	1	2	0.25 – 4	100.0 / 0.0	99.3 / 0.7
Linezolid	0.5	1	≤0.12 – >8	99.5 / 0.5	99.5 / 0.5
Tetracycline	0.5	>8	≤0.25 – >8	84.2 / 14.5	72.0 / 18.1
Trimethoprim/sulfamethoxazole	≤0.5	>4	≤0.5 – >4	65.7 / 34.3	65.7 / 21.1
MRCoNS (411)					
Solithromycin	≤0.03	>4	≤0.03 – >4	- / -	- / -
Telithromycin	≤0.06	>8	≤0.06 – >8	71.5 / 28.5	- / -
Erythromycin	>16	>16	≤0.12 – >16	31.6 / 66.7	31.9 / 67.6
Clindamycin	≤0.25	>2	≤0.25 – >2	70.1 / 29.4	67.2 / 29.9
Levofloxacin	4	>4	≤0.12 – >4	35.5 / 58.6	35.5 / 58.6
Vancomycin	2	2	0.25 – 4	100.0 / 0.0	99.3 / 0.7
Linezolid	0.5	1	≤0.12 – >8	99.3 / 0.7	99.3 / 0.7
Tetracycline	1	>8	≤0.25 – >8	80.8 / 17.5	67.6 / 22.4
Trimethoprim/sulfamethoxazole	1	>4	≤0.5 – >4	56.7 / 43.3	56.7 / 25.8
Enterococcus spp. (1,238)					
Solithromycin	0.5	2	≤0.03 – >4	- / -	- / -
Telithromycin	1	4	≤0.06 – >8	- / -	- / -
Erythromycin	>16	>16	≤0.12 – >16	7.1 / 63.5	- / -
Ampicillin	1	>8	≤0.25 – >8	66.2 / 33.8	66.0 / 33.8
Levofloxacin	>4	>4	≤0.12 – >4	47.9 / 50.6	- / -
Linezolid	1	2	0.25 – 8	99.7 / 0.2	99.8 / 0.2
Teicoplanin	≤2	>16	≤2 – >16	81.2 / 18.3	80.9 / 19.1
Vancomycin	1	>16	0.25 – >16	79.5 / 19.5	79.5 / 20.5
E. faecalis (757)					
Solithromycin	0.06	1	≤0.03 – 4	- / -	- / -
Telithromycin	0.12	4	≤0.06 – >8	- / -	- / -
Erythromycin	>16	>16	≤0.12 – >16	7.8 / 53.9	- / -
Ampicillin	1	2	≤0.25 – >8	99.7 / 0.3	99.5 / 0.3
Levofloxacin	1	>4	≤0.12 – >4	69.7 / 29.9	- / -
Linezolid	1	2	0.25 – 8	99.9 / 0.1	99.9 / 0.1
Teicoplanin	≤2	≤2	≤2 – >16	96.8 / 3.2	96.6 / 3.4
Vancomycin	1	2	0.5 – >16	96.7 / 3.3	96.7 / 3.3
E. faecium (435)					
Solithromycin	1	2	≤0.03 – >4	- / -	- / -
Telithromycin	2	4	≤0.06 – >8	- / -	- / -
Erythromycin	>16	>16	≤0.12 – >16	2.5 / 83.2	- / -
Ampicillin	>8	>8	≤0.25 – >8	7.4 / 92.6	7.1 / 92.6
Levofloxacin	>4	>4	1 – >4	6.9 / 90.1	- / -
Linezolid	1	1	0.25 – 8	99.3 / 0.5	99.5 / 0.5
Teicoplanin	≤2	>16	≤2 – >16	52.9 / 45.7	52.6 / 47.4
Vancomycin	8	>16	0.5 – >16	49.9 / 49.2	49.9 / 50.1
β-haemolytic streptococci (909)					
Solithromycin	≤0.03	≤0.03	≤0.03 – 0.5	- / -	- / -
Telithromycin	≤0.06	0.12	≤0.06 – >8	- / -	97.4 / 1.4
Erythromycin	≤0.12	>16	≤0.12 – >16	73.9 / 26.1	73.9 / 26.1
Clindamycin	≤0.25	>2	≤0.25 – >2	85.7 / 14.2	85.8 / 14.2
Penicillin	≤0.06	≤0.06	≤0.06 – 0.12	100.0 / -	100.0 / 0.0
Levofloxacin	0.5	1	≤0.12 – >4	99.2 / 0.6	94.4 / 0.8
Linezolid	1	1	0.25 – 2	100.0 / -	100.0 / 0.0
Trimethoprim/sulfamethoxazole	≤0.5	≤0.5	≤0.5 – >4	- / -	97.9 / 1.8
Vancomycin	0.5	0.5	≤0.12 – 1	100.0 / -	100.0 / 0.0
Viridans group streptococci (435)					
Solithromycin	≤0.03	0.06	≤0.03 – 0.25	- / -	- / -
Telithromycin	≤0.06	0.12	≤0.06 – 8	- / -	- / -
Erythromycin	1	>16	≤0.12 – >16	48.7 / 50.6	- / -
Clindamycin	≤0.25	>2	≤0.25 – >2	82.1 / 17.2	82.8 / 17.2
Penicillin	≤0.06	1	≤0.06 – >8	70.1 / 5.5	78.6 / 5.5
Levofloxacin	1	2	≤0.12 – >4	92.6 / 6.4	- / -
Linezolid	1	1	≤0.12 – 2	100.0 / -	- / -
Vancomycin	0.5	1	≤0.12 – 1	100.0 / -	100.0 / 0.0

a. Criteria as published by the CLSI [2012] and EUCAST [2012].
b. Criteria as published by the CLSI [2012] for "Penicillin parenteral (non-meningitis)".
c. Criteria as published by the CLSI [2012] for "Penicillin (oral penicillin V)".

Conclusions

- Solithromycin displayed good coverage (% inhibited at probably breakpoints [≤1 µg/mL or ≤4 µg/mL]) and potency when tested against organisms associated with CA-RTI and other clinically relevant Gram-positive pathogens, regardless of most common resistance patterns noted within each presented organism group.
- The activity of solithromycin against respiratory tract associated pathogens, such as *S. pneumoniae*, *H. influenzae* and *M. catarrhalis* was stable during four consecutive surveillance years (2008-2011). This confirms that solithromycin remains a highly promising agent for treatment of bacterial pathogens causing RTI and other infections. Its further development appears warranted.

Acknowledgment

This study was sponsored by a research grant from Cempra Pharmaceuticals Inc.

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