

Activity of Telavancin against 8,686 Gram-Positive Cocci Associated with Infections in Canadian Hospitals from 2007-2012

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ABSTRACT

Background: Telavancin is a bactericidal lipoglycopeptide with activity against methicillin-resistant *Staphylococcus aureus* and other Gram-positive pathogens. As part of the ongoing national CANWARD surveillance study, we assessed the activity of telavancin and comparators against Gram-positive cocci from Canadian hospitals.

Methods: Between 2007 and 2012, tertiary-care medical centres across Canada submitted isolates from patients attending hospital clinics, emergency rooms, medical and surgical wards, and intensive care units. Annually, each centre was asked to submit pathogens (consecutive, one per patient per infection site) from blood, respiratory specimens, urine, and wound/intravenous infections. 29,932 isolates were collected in total, including 8,686 Gram-positive cocci. Susceptibility testing was performed by broth microdilution using CLSI methodology for comparator agents and FDA-approved dry-form panels for telavancin.

Results: Telavancin MIC ranges as well as MIC₅₀ and MIC₉₀ values for telavancin, vancomycin, daptomycin and linezolid versus 8,686 Gram-positive cocci are shown below:

Organism (n)	Telavancin MIC Range	Telavancin MIC ₅₀ /MIC ₉₀	Vancomycin MIC ₅₀ /MIC ₉₀	Daptomycin MIC ₅₀ /MIC ₉₀	Linezolid MIC ₅₀ /MIC ₉₀
MSSA (4734)	≤0.06 - 1	0.25 / 0.5	1 / 1	0.25 / 0.25	2 / 2
MRSA (1391)	≤0.06 - 1	0.25 / 0.5	1 / 1	0.25 / 0.25	2 / 2
- HA-MRSA (936)	0.12 - 1	0.25 / 0.5	1 / 1	0.12 / 0.25	2 / 4
- CA-MRSA (415)	≤0.06 - 1	0.25 / 0.5	1 / 1	0.25 / 0.25	2 / 2
MSSE (533)	≤0.06 - 1	0.25 / 0.5	1 / 2	0.12 / 0.25	0.5 / 1
MRSE (97)	≤0.06 - 1	0.25 / 0.25	1 / 2	0.12 / 0.25	1 / 1
<i>S. pneumoniae</i> - All (1931)	≤0.06 - 0.12	≤0.06 / ≤0.06	≤0.25 / 0.25	0.06 / 0.12	0.5 / 1
- PenS (1543)	≤0.06 - 0.12	≤0.06 / ≤0.06	≤0.25 / 0.25	0.06 / 0.12	0.5 / 1
- PenI (254)	≤0.06 - 0.06	≤0.06 / ≤0.06	≤0.25 / 0.5	0.06 / 0.12	1 / 1
- PenR (84)	≤0.06 - 0.06	≤0.06 / ≤0.06	≤0.25 / 0.5	0.06 / 0.12	0.5 / 1

MSSA, methicillin-susceptible *S. aureus*; MRSA, methicillin-resistant *S. aureus*; HA-MRSA, healthcare-associated MRSA; CA-MRSA, community-associated MRSA; MSSE, methicillin-susceptible *S. epidermidis*; MRSE, methicillin-resistant *S. epidermidis*.

Conclusions: Telavancin is more active in vitro than vancomycin and linezolid and has comparable activity to daptomycin against MSSA, MRSA (including CA-MRSA and HA-MRSA), MSSE, MRSE and *S. pneumoniae*.

BACKGROUND

Antibiotic resistance among Gram-positive pathogens such as *Streptococcus pneumoniae*, *Staphylococcus aureus* and *Staphylococcus epidermidis* is a growing concern. The global escalation in both community- and healthcare-acquired antibiotic-resistant organisms is threatening our ability to effectively treat patients by significantly limiting the therapeutic options available to clinicians and increasing the risk of treatment failures. Management of infections caused by these difficult-to-treat pathogens is often complicated further by the fact that many of these strains are multidrug-resistant. These observations underscore the need for continued surveillance, more judicious antibiotic prescribing practices and new treatment alternatives.

Telavancin is a semisynthetic lipoglycopeptide with a dual mechanism of action against a broad spectrum of clinically relevant Gram-positive bacteria, including both susceptible and multidrug-resistant staphylococci and streptococci (1-4). The rapid bactericidal activity of telavancin is derived from its ability to inhibit synthesis of the bacterial cell wall as well as to disrupt bacterial membrane integrity and increase cell membrane permeability (1-4).

PURPOSE

The purpose of this study was to assess the activity of telavancin and comparators against Gram-positive cocci obtained from Canadian hospitals between 2007 and 2012 as part of the ongoing national CANWARD surveillance study.

MATERIALS & METHODS

CANWARD Study Design

Between January 2007 and December 2012, 29,932 clinical isolates, including 8,686 Gram-positive cocci, were collected as part of the ongoing CANWARD study assessing pathogen prevalence and antibiotic resistance in Canadian hospitals. Isolates were received from tertiary-care medical centres (12 in 2007, 10 in 2008, 15 in 2009, 14 in 2010, 15 in 2011, 12 in 2012) that were geographically distributed in a population-based fashion in eight of the ten Canadian provinces. Annually, each study site was asked to submit clinical isolates (consecutive, one per patient per infection site) from inpatients and outpatients with respiratory, urine, wound and bloodstream infections. Isolates were collected from patients attending hospital clinics, emergency rooms, medical/surgical wards and intensive care units. All organisms were identified by the submitting centre and were deemed clinically significant using local site criteria. Isolates were shipped on Amies semi-solid transport media to the coordinating laboratory (Health Sciences Centre, Winnipeg, Canada) where they were subcultured onto appropriate media and stocked in skim milk at -80°C.

Antimicrobial Susceptibility Testing

Following two subcultures from frozen stock, the *in vitro* activities of telavancin and comparator agents, including ceftazolin, ceftiraxone, clarithromycin, clindamycin, ciprofloxacin, daptomycin, doxycycline, eropenem, levofloxacin, linezolid, meropenem, moxifloxacin, penicillin, piperacillin-tazobactam, tigecycline, trimethoprim-sulfamethoxazole and vancomycin, were determined by broth microdilution in accordance with Clinical and Laboratory Standards Institute (CLSI) guidelines (5). Antimicrobial minimum inhibitory concentrations (MICs) were determined using 96-well custom designed microtitre panels for comparator agents and Trek Sensititre dry-form panels for telavancin. Quality control was performed using the following ATCC organisms: *S. pneumoniae* ATCC 49619 and *S. aureus* ATCC 29213. MIC interpretive standards were defined according to CLSI breakpoints (6). The following interpretive breakpoints (FDA) were used with *S. aureus*: telavancin susceptible, ≤1 µg/ml; tigecycline susceptible, ≤0.5 µg/ml. With *S. pneumoniae*, an interpretive breakpoint (FDA) of ≤0.06 µg/ml was used for tigecycline susceptible. Tetracycline breakpoints were used to interpret *S. pneumoniae* doxycycline MIC values.

ACKNOWLEDGMENTS

Financial support for the CANWARD study was provided in part by Astellas Pharma Canada, Inc. and Theravance, Inc.

The authors would like to thank the participating centres, investigators and laboratory site staff for their continued support:

Dr. D. Roscoe – Vancouver Hospital, Vancouver

Dr. J. Fuller – University of Alberta Hospital, Edmonton

Dr. J. Blondeau – Royal University Hospital, Saskatoon

Drs. D. Hoban/G. Zhanel – Health Sciences Centre, Winnipeg

Dr. M. John – London Health Sciences Centre, London

Dr. S. Poutanen – UHN and Mount Sinai Hospital, Toronto

Dr. L. Matukas – St. Michael's Hospital, Toronto

Dr. C. Lee – St. Joseph's Hospital, Hamilton

Dr. F. Chan – Children's Hospital of Eastern Ontario, Ottawa

Dr. M. Desjardins – The Ottawa Hospital, Ottawa

Dr. M. Laverdière – Hôpital Maisonneuve-Rosemont, Montreal

Dr. V. Loo – Montreal General Hospital, Montreal

Dr. V. Loo – Royal Victoria Hospital, Montreal

Dr. M. Goyette – CHRTR Pavillon Ste. Marie, Trois-Rivières

Dr. M. Kuhn – South East Regional Health Authority, Moncton

Dr. R. Davidson – Queen Elizabeth II HSC, Halifax

RESULTS

Table 1. Activity of telavancin and comparators against Gram-positive cocci from CANWARD 2007-2012

Organism (n), Antibiotic	% of Isolates per Category			MIC ₅₀	MIC ₉₀	Range Min	Range Max
	S	I	R				
S. aureus							
MSSA (4734)							
Telavancin*	100			0.25	0.5	≤ 0.06	1
Vancomycin	100			1	1	≤ 0.25	2
Ceftazolin	100			≤ 0.5	1	≤ 0.5	32
Clarithromycin	74.9	0.2	24.9	0.25	> 16	≤ 0.25	> 16
Clindamycin	92.8	0.3	6.9	≤ 0.25	≤ 0.25	≤ 0.25	> 8
Daptomycin	100			0.25	0.25	≤ 0.06	1
Levofloxacin	90.1	0.3	9.6	0.25	1	≤ 0.06	> 32
Linezolid	100			2	2	≤ 0.12	4
Meropenem	100			0.12	0.25	≤ 0.12	4
Moxifloxacin	90.1	0.6	9.3	≤ 0.06	0.5	≤ 0.06	> 16
Pip-Tazo	99.9			0.1	≤ 1	≤ 1	32
Tigecycline*	99.9			0.1	0.12	0.25	≤ 0.03
TMP/SMX	99.4			0.6	≤ 0.12	≤ 0.12	> 8
MRSA (1391)							
Telavancin*	100			0.25	0.5	≤ 0.06	1
Vancomycin	99.9	0.1		1	1	≤ 0.25	4
Ceftazolin	100			100 ^b	64	> 128	1
Clarithromycin	13.0	0.1	86.9	> 16	> 16	≤ 0.25	> 128
Clindamycin	50.0	0.1	49.9	0.5	> 8	≤ 0.25	> 8
Daptomycin	100			0.25	0.25	0.06	1
Levofloxacin	14.1			85.9	> 32	0.12	> 32
Linezolid	100			2	2	≤ 0.12	4
Meropenem	100			100 ^b	8	32	0.12
Moxifloxacin	15.5	2.2	82.3	8	> 16	≤ 0.06	> 16
Pip-Tazo	100			100 ^b	32	128	≤ 1
Tigecycline*	99.6			0.4	0.25	0.5	0.06
TMP/SMX	92.5			7.5	≤ 0.12	≤ 0.12	> 8
CA-MRSA (415)							
Telavancin*	100			0.25	0.5	0.12	1
Vancomycin	100			1	1	0.5	2
Ceftazolin	100			100 ^b	16	64	1
Clarithromycin	26.0	0.2	73.8	> 16	> 16	≤ 0.25	> 128
Clindamycin	86.9			13.1	≤ 0.25	> 8	≤ 0.25
Daptomycin	100			0.25	0.25	0.12	1
Levofloxacin	40.0			60.0	4	8	0.12
Linezolid	100			2	2	1	4
Meropenem	100			100 ^b	2	4	0.12
Moxifloxacin	35.8	6.7	57.5	2	2	≤ 0.06	16
Pip-Tazo	100			100 ^b	16	32	2
Tigecycline*	100			0.25	0.25	0.06	0.5
TMP/SMX	100			≤ 0.12	≤ 0.12	≤ 0.12	2
HA-MRSA (936)							
Telavancin*	100			0.25	0.5	≤ 0.06	1
Vancomycin	99.9	0.1		1	1	≤ 0.25	4
Ceftazolin	100			100 ^b	128	> 128	1
Clarithromycin	4.9			95.1	> 16	> 16	≤ 0.25
Clindamycin	32.1	0.1	67.8	> 8	> 8	≤ 0.25	> 8
Daptomycin	100			0.25	0.25	0.06	1
Levofloxacin	2.9			97.1	> 32	> 32	0.12
Linezolid	100			2	4	≤ 0.12	4
Meropenem	100			100 ^b	8	> 32	0.25
Moxifloxacin	3.5	0.2	96.3	8	> 16	≤ 0.06	> 16
Pip-Tazo	100			100 ^b	64	128	≤ 1
Tigecycline*	99.4			0.6	0.25	0.5	0.06
TMP/SMX	88.9			11.1	≤ 0.12	8	≤ 0.12
S. pneumoniae							
All (1931)							
Telavancin	No BP			≤ 0.06	≤ 0.06	≤ 0.06	0.12
Vancomycin	100			≤ 0.25	0.25	≤ 0.25	1
Ceftiraxone	99.3	0.5	0.2	≤ 0.12	≤ 0.12	≤ 0.12	4
Clarithromycin	80.0	3.5	16.5	≤ 0.03	4	≤ 0.03	> 32
Clindamycin	93.0	0.5	6.5	≤ 0.12	≤ 0.12	≤ 0.12	> 8
Doxycycline ^c	93.2	3.0	3.8	≤ 0.25	1	≤ 0.25	> 16
Levofloxacin	99.0	0.2	0.8	1	1	≤ 0.06	32
Linezolid	100			0.5	1	≤ 0.12	2
Meropenem	95.5	2.8	1.7	≤ 0.06	≤ 0.06	≤ 0.06	2
Penicillin	82.0	13.5	4.5	≤ 0.03	0.25	≤ 0.03	> 8
Tigecycline*	99.7			0.3	0.03	0.06	≤ 0.03
TMP/SMX	85.1	6.4	8.5	≤ 0.12	2	≤ 0.12	> 8
PSPP (1543)							
Telavancin	No BP			≤ 0.06	≤ 0.06	≤ 0.06	0.12
Vancomycin	100			≤ 0.25	0.25	≤ 0.25	1
Ceftiraxone	100			≤ 0.12	≤ 0.12	≤ 0.12	0.25
Clarithromycin	87.8	2.7	9.5	≤ 0.03	0.5	≤ 0.03	> 32
Clindamycin	97.6	0.4	2.0	≤ 0.12	≤ 0.12	≤ 0.12	> 8
Doxycycline ^c	96.9	1.5	1.6	≤ 0.25	≤ 0.25	≤ 0.25	> 16
Levofloxacin	99.3	0.2	0.5	0.5	1	≤ 0.06	32
Linezolid	100			0.5	1	≤ 0.12	2
Meropenem	99.9	0.1		≤ 0.06	≤ 0.06	≤ 0.06	0.5
Penicillin	100.0			≤ 0.03	0.06	≤ 0.03	0.06
Tigecycline*	99.9			0.1	0.03	0.06	≤ 0.03
TMP/SMX	91.9	5.4	2.7	≤ 0.12	0.5	≤ 0.12	> 8
PISP (254)							
Telavancin	No BP			≤ 0.06	≤ 0.06	≤ 0.06	0.06
Vancomycin	100			≤ 0.25	0.5	≤ 0.25	1
Ceftiraxone	98.8	0.8	0.4	≤ 0.12	0.5	≤ 0.12	4
Clarithromycin	49.0	9.5	41.5	0.5	> 32	≤ 0.03	> 32
Clindamycin	79.5	1.1	19.4	≤ 0.12	> 8	≤ 0.12	> 8
Doxycycline ^c	75.9	6.3	17.8	≤ 0.25	16	≤ 0.25	> 16
Levofloxacin	98.0			2.0	1	0.25	16
Linezolid	100			1	1	≤ 0.12	2
Meropenem	91.7	7.5	0.8	≤ 0.06	0.25	≤ 0.06	1
Penicillin	100			0.25	1	0.12	1
Tigecycline*	99.2			0.8	0.03	0.06	≤ 0.03
TMP/SMX	66.1	12.6	21.3	0.25	8	≤ 0.12	> 8
PRSP (84)							
Telavancin	No BP			≤ 0.06	≤ 0.06	≤ 0.06	0.06
Vancomycin	100			≤ 0.25	0.5	≤ 0.25	1
Ceftiraxone	88.1	8.3	3.6	0.5	2	≤ 0.12	