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Activity of Dalbavancin Against *S. aureus, S. epidermidis, Enterococcus* spp. and *S. pneumoniae* Isolated from Canadian Hospitals: Results of CANWARD 2007-2008

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ABSTRACT

Background: Dalbavancin (DAL) is a new teicoplanin-related lipoglycopeptide with activity against Gram-positive organisms. The purpose of this study was to assess the activity of DAL, linezolid (LIN) and vancomycin (VAN) against Gram-positive pathogens isolated from Canadian hospitals.

Methods: From January 2007 through December 2008,12 sentinel hospitals (10 centres - 2008) across Canada submitted pathogens from patients attending all hospital wards. A total of 5238 Gram-positive pathogens were collected and susceptibility testing was performed using CLSI broth microdilution methods.

Organism (n)	DAL	LIN	VAN
SPN- PenS (931)	≤0.03/≤0.03	1/1	≤0.25/≤0.25
SPN- PenI (181)	≤0.03/≤0.03	1/1	≤0.25/0.5
SPN- PenR (56)	≤0.03/≤0.03	1/1	≤0.25/0.5
MSSA (1832)	0.06/0.06	2/2	1/1
CA-MRSA (149)	0.06/0.06	2/2	1/1
HA-MRSA (477)	0.06/0.06	2/4	1/1
MSSE (191)	≤0.03/0.06	0.5/1	1/2
MRSE (28)	≤0.03/0.06	1/1	2/2
E. faecalis (254)	0.06/0.06	2/2	1/2
E. faecium (107)	0.06/2	2/2	0.5/>32
Enterococcus spp.(409)	0.06/0.06	2/4	1/2
VRE (18)	2/>16	2/4	>32/>32

SPN=*S.pneumoniae*, PenS=penicillin-susceptible, PenI=penicillin-intermediate, PenR=penicillin-resistant, MSSA=methicillin-susceptible *S. aureus*, MR=methicillin-resistant, CA=community-associated, HA=healthcare-associated, SE=*S. epidermidis*, VRE=vancomycin-resistant enterococci.

Conclusions: Dalbavancin is more active than linezolid and vancomycin versus *S. pneumoniae*, MRSA, MRSE and *Enterococcus* spp.

MATERIALS AND METHODS

Bacterial Isolates

In 2007 and 2008, each participating Canadian hospital submitted consecutive bacterial isolates collected from four specimen sources: urines (100/100, respectively), lower respiratory tract (200/150), wound/iv infections (50/50) and blood cultures (30/20 per month for 12 months). Total isolates submitted from each hospital site were 730 and 540, respectively.

Antimicrobial Susceptibilities

A custom microtitre panel was prepared in accordance with Clinical and Laboratory Standards Institute guidelines(CLSI, M100-S18, 2008). Polysorbate 80 (0.002% final concentration) was added to both the stock solution of dalbavancin and cation-adjusted broth used for panels. The following interpretive breakpoints (FDA) were used for tigecycline (µg/ml): *Staphylococcus aureus* (MSSA and MRSA) ≤ 0.5 (S); *Enterococcus* spp., ≤ 0.25 (S). MIC interpretive standards for the remaining antimicrobials agents were defined according to CLSI breakpoints (M100-S18, 2008).

Table 1. Methicillin-susceptible *S. aureus* (MSSA, n=1826)

	% of Isolates per Category					Range	Range
Antibiotic	S[a]	I	R	MIC_{50}	MIC_{90}	Min	Max
Cefazolin	99.9		0.1	0.5	1	≤0.5	32
Clarithromycin	74.5	0.4	25.1	0.25	>16	≤0.25	>16
Clindamycin	91.6	0.6	7.8	≤0.25	≤0.25	≤0.25	>8
Dalbavancin	no BP[b]			0.06	0.06	≤0.03	0.25
Daptomycin	100			0.12	0.25	≤0.06	1
Levofloxacin	90.5	0.3	9.2	0.25	1	≤0.06	>32
Linezolid	100			2	2	≤0.12	4
Meropenem	100				0.12	≤0.12	1
Pip-Tazo	100			≤1	≤1	≤1	8
Tigecycline	100[d]			0.25	0.25	≤0.03	0.5
TMP/SMX	99.1		0.9	≤0.12	≤0.12	≤0.12	>8
Vancomycin	100			1	1	≤0.25	2

Table 2. Methicillin-resistant *S. aureus* (MRSA, n=657)

	% of Isolates per Category					Range	Range
Antibiotic	S	I	R	MIC_{50}	MIC_{90}	Min	Max
Cefazolin			100[c]	128	>128	1	>128
Clarithromycin	10.8	0.2	89.0	>16	>16	≤0.25	>16
Clindamycin	40.6	0.2	59.2	>8	>8	≤0.25	>8
Dalbavancin	no BP[b]			0.06	0.06	≤0.03	0.12
Daptomycin	100			0.12	0.25	0.06	1
Levofloxacin	12.0		88.0	>32	>32	0.12	>32
Linezolid	100			2	2	≤0.12	4
Meropenem			100[c]	8	>32	0.12	>32
Pip-Tazo			100[c]	64	128	≤1	512
Tigecycline	100[d]			0.25	0.5	0.06	0.5
TMP/SMX	88.6		11.4	≤0.12	8	≤0.12	>8
Vancomycin	99.8	0.2		1	1	≤0.25	4

Table 3. Community-associated MRSA (CA-MRSA, n=149)

	% of Isolates per Category					Range	Range
Antibiotic	S	I	R	MIC_{50}	MIC_{90}	Min	Max
Cefazolin			100[c]	16	64	1	>128
Clarithromycin	26.2	0.6	73.2	>32	>32	≤0.03	>32
Clindamycin	84.6		15.4	≤0.12	>8	≤0.12	>8
Dalbavancin	no BP[b]			0.06	0.06	≤0.03	0.12
Daptomycin	100			0.12	0.5	0.12	1
Levofloxacin	36.2		63.8	4	8	0.12	32
Linezolid	100			2	2	1	4
Meropenem			100[c]	1	4	0.12	16
Pip-Tazo			100[c]	16	32	2	64
Tigecycline	100[d]			0.25	0.25	0.06	0.5
TMP/SMX	100			≤0.12	≤0.12	≤0.12	2
Vancomycin	100			1	1	0.5	1

Table 4. Hospital-associated MRSA (HA-MRSA, n=477)

	% of Isolates per Category					Range	Range
Antibiotic	S	I	R	MIC_{50}	MIC_{90}	Min	Max
Cefazolin			100[c]	128	>128	1	>128
Clarithromycin	4.2		95.8	>32	>32	≤0.03	>32
Clindamycin	25.8	0.2	74.0	>8	>8	≤0.12	>8
Dalbavancin	no BP[b]			0.06	0.06	≤0.03	0.12
Daptomycin	100			0.12	0.25	0.06	1
Levofloxacin	2.7		97.3	>32	>32	0.12	>32
Linezolid	100			2	4	≤0.12	4
Meropenem			100[c]	8	>32	0.25	>32
Pip-Tazo			100[c]	64	256	≤1	512
Tigecycline	100[d]			0.25	0.5	0.12	0.5
TMP/SMX	84.5		15.5	≤0.12	>8	≤0.12	>8
Vancomycin	99.8		0.2	1	1	≤0.25	4

Table 5. Methicillin-susceptible *S. epidermidis* (MSSE, n=185)

	% of Isolates per Category					Range	Range
Antibiotic	S	I	R	MIC_{50}	MIC_{90}	Min	Max
Cefazolin	100			1	4	≤0.5	8
Clarithromycin	32.4	1.6	66	>16	>16	≤0.25	>16
Clindamycin	63.2		36.8	≤0.25	>8	≤0.25	>8
Dalbavancin	no BP[b]			≤0.03	0.06	≤0.03	1
Daptomycin	100			0.12	0.25	≤0.06	1
Levofloxacin	49.7	1.6	48.7	2	32	0.12	>32
Linezolid	100			0.5	1	≤0.12	2
Meropenem	86.0	7.0	7.0	1	8	≤0.12	32
Pip-Tazo	98.9		1.1	≤1	2	≤1	16
Tigecycline	no BP[b]			0.25	0.5	≤0.03	1
TMP/SMX	62.2		37.8	0.25	8	≤0.12	>8
Vancomycin	100			1	2	≤0.25	4

Table 6. Methicillin-resistant *S.epidermidis* (MRSE, n=28)

	% of Isolates per Category					Range	Range
Antibiotic	S	I	R	MIC_{50}	MIC_{90}	Min	Max
Cefazolin			100	64	128	32	128
Clarithromycin	7.1		92.9	>16	>16	0.25	>16
Clindamycin	10.7		89.3	>8	>8	≤0.25	>8
Dalbavancin	no BP[b]			≤0.03	0.06	≤0.03	0.06
Daptomycin	100			0.12	0.25	≤0.06	0.5
Levofloxacin			100	>32	>32	4	>32
Linezolid	100			1	1	0.25	1
Meropenem			100[c]	32	32	16	64
Pip-Tazo			100[c]	32	64	8	128
Tigecycline	no BP[b]			0.25	0.25	0.06	0.5
TMP/SMX	28.6		71.4	4	8	≤0.12	>8
Vancomycin	100			2	2	1	2

Table 7. *S. pneumoniae* (n=1182)

	% of Isolates per Category					Range	Range
Antibiotic	S	I	R	MIC_{50}	MIC_{90}	Min	Max
Ceftriaxone	99.5	0.3	0.2	≤0.06	0.12	≤0.06	4
Clarithromycin	80.7	4.4	14.9	≤0.03	2	≤0.03	>32
Clindamycin	93.0	0.3	6.7	≤0.12	≤0.12	≤0.12	>8
Dalbavancin	no BP[b]			≤0.03	≤0.03	≤0.03	0.12
Doxycycline	no BP[b]			≤0.25	1	≤0.25	>16
Levofloxacin	99.0	0.2	0.8	1	1	≤0.06	32
Linezolid	100			1	1	≤0.12	2
Meropenem	96.2	2.9	0.9	≤0.06	≤ 0.06	≤0.06	2
Penicillin	79.8	15.4	4.8	≤0.03	0.25	≤0.03	>8
Tigecycline	no BP[b]			≤0.03	0.06	≤0.03	0.5
TMP/SMX	84.7	7	8.3	≤0.12	2	≤0.12	>8
Vancomycin	100			≤0.25	≤0.25	≤0.25	1

Table 8. Penicillin-resistant *S. pneumoniae* (n=56)

	% of Isolates per Category					Range	Range
Antibiotic	S	I	R	MIC_{50}	MIC_{90}	Min	Max
Ceftriaxone	91.1	5.3	3.6	0.5	1	≤0.06	4
Clarithromycin	44.6	3.6	51.8	1	>32	≤0.03	>32
Clindamycin	64.3		35.7	≤0.12	>8	≤0.12	>8
Dalbavancin	no BP[b]			≤0.03	≤0.03	≤0.03	≤0.03
Doxycycline	no BP[b]			1	4	≤0.25	>16
Levofloxacin	100			1	1	0.25	2
Linezolid	100			0.5	1	0.25	2
Meropenem	37.5	44.6	17.9	0.5	1	≤0.06	2
Penicillin			100	2	4	2	>8
Tigecycline	no BP[b]			≤0.03	0.06	≤0.03	0.12
TMP/SMX	21.4	8.9	69.7	4	>8	≤0.12	>8
Vancomycin	100			≤0.25	0.5	≤0.25	1

Table 9. *E. faecalis* (n=254)

	% of Isolates per Category					Range	Range
Antibiotic	S	I	R	MIC_{50}	MIC_{90}	Min	Max
Ciprofloxacin	41.7	22.8	35.5	2	>16	0.25	>16
Clarithromycin	no BP[b]			2	>16	≤0.25	>16
Clindamycin	no BP[b]			>8	>8	≤0.12	>8
Dalbavancin	no BP[b]			0.06	0.06	≤0.03	0.25
Daptomycin	100			0.5	1	≤0.06	4
Ertapenem	no BP[b]			8	16	0.25	>32
Levofloxacin	66.5	1.2	32.3	2	>32	0.25	>32
Linezolid	99.2	0.8		2	2	0.5	4
Meropenem	no BP[b]			4	8	≤0.06	>32
Pip-Tazo	no BP[b]			4	8	≤1	512
Tigecycline	98.4[d]			0.12	0.25	0.06	0.5
Vancomycin	100			1	2	0.5	4

Table10. *E. faecium* (n=107)

	% of Isolates per Category					Range	Range
Antibiotic	S	I	R	MIC_{50}	MIC_{90}	Min	Max
Ciprofloxacin	8.4	4.7	86.9	>16	>16	0.5	>16
Clarithromycin	no BP[b]			>16	>16	0.12	>16
Clindamycin	no BP[b]			>8	>8	≤0.25	>8
Dalbavancin	no BP[b]			0.06	2	≤0.03	>16
Daptomycin	100			1	2	≤0.03	4
Ertapenem	no BP[b]			>4	>4	4	>4
Levofloxacin	13.1	1.8	85.1	>32	>32	1	>32
Linezolid	95.3	4.7		2	2	0.5	4
Meropenem	no BP[b]			>32	>32	2	>32
Pip-Tazo	no BP[b]			>512	>512	2	>512
Tigecycline	no BP[b]			0.12	0.12	≤0.03	2
Vancomycin	84.1		15.9	0.5	>32	≤0.25	>32

Table 11. Non-speciated *Enterococcus* (n=407)

	% of Isolates per Category					Range	Range
Antibiotic	S	I	R	MIC_{50}	MIC_{90}	Min	Max
Ciprofloxacin	37.4	21.6	41.0	2	>16	≤0.06	>16
Clarithromycin	no BP[b]			>16	>16	≤0.25	>16
Clindamycin	no BP[b]			>8	>8	≤0.25	>8
Dalbavancin	no BP[b]			0.06	0.06	≤0.03	0.5
Daptomycin	100			0.5	1	≤0.06	4
Ertapenem	no BP[b]			16	32	≤0.06	>32
Levofloxacin	60.7	0.5	38.8	2	>32	≤0.06	>32
Linezolid	97.5	2.5		2	2	≤0.12	>4
Meropenem	no BP[b]			4	16	≤0.06	>32
Pip-Tazo	no BP[b]			4	8	≤1	>512
Tigecycline	no BP[b]			0.12	0.25	≤0.03	1
Vancomycin	99.8		0.2	1	2	≤0.25	>32

Table 12. Vancomycin-resistant *Enterococcus* spp. (VRE, n=18)

	% of Isolates per Category					Range	Range
Antibiotic	S	I	R	MIC_{50}	MIC_{90}	Min	Max
Ciprofloxacin			100	>16	>16	>16	>16
Clarithromycin	no BP[b]			>16	>16	2	>16
Clindamycin	no BP[b]			>8	>8	≤0.25	>8
Dalbavancin	no BP[b]			2	>16	≤0.03	>16
Daptomycin	100			1	2	≤0.06	2
Ertapenem	no BP[b]			>4	>4	>4	>4
Levofloxacin			100	>32	>32	32	>32
Linezolid	88.9	11.1		2	4	0.5	4
Meropenem	no BP[b]			>32	>32	>32	>32
Pip-Tazo	no BP[b]			>512	>512	>512	>512
Tigecycline	no BP[b]			0.12	0.12	0.06	0.25
Vancomycin			100	>32	>32	32	>32

[a] S, susceptible; I, intermediate; R, resistant; [b] No BP, no breakpoint defined, [c] based on oxacillin susceptibilty, [d] FDA breakpoints
MIC, minimum inhibitory concentration (µg/mL); Pip-Tazo, piperacillin-tazobactam; TMP-SMX, trimethoprim-sulfamethoxazole

Table 13. MIC distribution of dalbavancin against gram-positive cocci

		MIC (Minimal Inhibitory Concentration µg/mL)											
Organism	No. tested	<=0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	>16
Methicillin-susceptible *S. aureus*	1826	448	1343	32	3	-	-	-	-	-	-	-
Methicillin-resistant *S. aureus*	657	126	513	18	-	-	-	-	-	-	-	-
Community-associated MRSA	149	20	127	2	-	-	-	-	-	-	-	-
Hospital-associated MRSA	477	98	363	16	-	-	-	-	-	-	-	-
Methicillin-susceptible *S. epidermidis*	185	125	52	7	-	-	1	-	-	-	-	-
Methicillin-resistant *S. epidermidis*	28	23	5	-	-	-	-	-	-	-	-	-
S. pneumoniae	1182	1164	15	3	-	-	-	-	-	-	-	-
Penicillin-resistant *S. pneumoniae*	56	56	-	-	-	-	-	-	-	-	-	-
E. faecalis	254	69	172	12	1	-	-	-	-	-	-	-
E. faecium	107	16	40	31	6	3	-	2	1	2	6	-
Enterococcus spp.	407	143	230	32	1	1	-	-	-	-	-	-
VRE	18	1	1	2	-	3	-	2	1	2	6	-

REFERENCES

1. Weshnowski et al. ICAAC 2008.
2. DeCorby et al. ICAAC 2007.
3. Biedenbach et al. 2007. J.Clin Microbiol. 45:998-1004.

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CONCLUSIONS

1. Dalbavancin is more active than comparators against methicillin-susceptible and methicillin-resistant *S.aureus*, community-associated and healthcare-associated.

2. Dalbavancin is more active than comparators against methicillin-susceptible and methicillin-resistant *S. epidermidis*.

3. Dalbavancin is more active than comparators against *S. pneumoniae*, including penicillin-resistant isolates.

4. Dalbavancin is more active than comparators against *E.faecalis*, *E. faecium* and non-speciated *Enterococcus*.

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