PRELIMINARY MICROBIOLOGY RESULTS FROM A PHASE III OMIGANAN PENTAHYDROCHLORIDE CLINICAL TRIAL: IN VITRO ACTIVITY AGAINST BACTERIAL AND FUNGAL PATHOGENS

Poster #422

THOMAS R FRITSCHE, JAMES E ROSS, PAUL R RHOMBERG, RONALD N JONES

JMI Laboratories, North Liberty, IA, USA

JMI Laboratories
345 Beaver Kreek Centre, Suite A
North Liberty, IA, 52317
Phone: 319-665-3370
Fax: 319-665-3371
Email: thomas-fritsche@jmilabs.com

AMENDED ABSTRACT

Background: Omiganan (OMI) is a rapidly cidal cationic antimicrobial peptide with broad-spectrum activity against bacteria and yeast. A multicenter, randomized, blinded Phase III clinical trial to study the safety and efficacy of topical OMI 1% gel (10,000 µg/ml) compared to "standard of care" in preventing catheter-associated infections (CAI) is currently ongoing.

Objective: To present a preliminary microbiology assessment of pathogens recovered from the Phase III clinical trial to date and their associated antibiogram profiles.

Methods: Forty-one active clinical trial sites in the United States and Europe submitted 2,709 isolates from 1,494 patients to a central laboratory for organism identification confirmation and susceptibility (S) testing by CLSI broth microdilution methods. Isolates originated from bloodstream (peripheral [471] and catheter line [826]), catheter insertion sites (190), and catheter tip and subcutaneous segments using roll plate (488 and 360, respectively) and sonication (203 and 171, respectively) methods. All patient isolates were included in the analysis. Treatment assignments have not been unblinded for this preliminary assessment.

	OMI MIC in µg/ml		
Organism (no.)	**MIC_{50}**	**MIC_{90}**	**Range**
Coagulase-negative staphylococci (CoNS; 1,604)	4	8	0.5-64
Oxacillin (OXA)-S (456)	4	8	0.5-16
OXA-resistant (-R) (1148)	4	8	0.5-64
Staphylococcus aureus (SA; 231)	16	32	8-32
OXA-S (149)	16	16	8-32
OXA-R (82)	16	32	8-32
Enterococcus spp. (211)	128	128	4-128
Candida spp. (95)	64	128	8-512
Enterobacter spp. (92)	128	256	32-512
Corynebacterium spp. (70)	2	4	0.5-8
Pseudomonas aeruginosa (65)	128	256	64-512
Acinetobacter spp. (52)	64	64	≤4-128
Escherichia coli (47)	32	64	16-64
Serratia marcescens (45)*	256	>512	64->512

Results: Ranking pathogens by frequency (see Table) and key R profiles: CoNS (71.6% OXA-R); SA (35.5% OXA-R); *Enterococcus* spp. (0.9% vancomycin-R); *Candida* spp. (14.7% fluconazole non-S); *Enterobacter* spp. (42.4% ceftazidime-R); *Corynebacterium* spp.; *P. aeruginosa* (10.8 % meropenem-R); and *Acinetobacter* spp. (69.2% meropenem-resistant). ESBL-phenotypes for *E. coli* and *Klebsiella* spp. were 19.1 and 29.4%, respectively. OMI potency was unaffected by OXA-R in CoNS and increased only 2-fold in OXA-R SA. Mupirocin $MIC_{90/50}$ (% high-level R) results for CoNS and SA were ≤4/>256 (18.4%) and ≤4/≤4 µg/ml (2.6%), respectively. OMI MIC_{50} results among yeast were: *C. glabrata* (256 µg/ml), *C. parapsilosis* (128), *C. albicans* (64) and *C. tropicalis* (8).

Conclusions: OMI inhibited 99.4% of the top 10 suspect pathogens implicated in CAI at MIC values ≤512 µg/ml, a concentration approximately 20-fold below the 1% gel formulation under study. As a novel topical antimicrobial agent, OMI displays critical attributes required for prevention of CAI, especially a broad-spectrum cidal action, including activity against fungal pathogens. Correlation of microbiological results with clinical outcomes is warranted.

*Updated to correct *S. marcescens* MIC_{50} value.

INTRODUCTION

Omiganan pentahydrochloride is a rapidly bactericidal and fungicidal cationic peptide being developed as a topical antimicrobial agent for prevention of catheter-related infections. The compound has a broad spectrum of cidal activity including Gram-positive and -negative bacterial species and, importantly, yeast, and is known to significantly reduce normal skin flora counts following topical applications.

The compound is currently in a Phase III clinical trial for prevention of catheter-associated infections, including local catheter-site infections (primary endpoint) and catheter-related bloodstream infections, and is in preclinical development for other indications. The majority of catheter-related blood stream infections are thought to arise from colonization of the catheter and infection of skin and subcutaneous tissues around the site of catheter placement. Data from the National Nosocomial Infections Surveillance (NNIS) system has shown that the most commonly occurring organisms include coagulase-negative staphylococci (CoNS), *Staphylococcus aureus* (including oxacillin- [methicillin]-resistant strains; MRSA), *Pseudomonas* spp., *Enterococcus* spp., Enterobacteriaceae and *Candida* spp., among others.

Given the importance of these pathogens in producing local and systemic infections secondary to the presence of indwelling venous access devices, prevention of their occurrence can be expected to have significant impact on overall patient morbidity and mortality, and related health care costs (primarily extended hospital stays and additional treatment). The continued emergence of resistance among these pathogens further confounds this problem and poses special challenges in patient management.

The purpose of this study was to provide an updated microbiology assessment of the breadth of spectrum and potency of omiganan and comparator agents, including other topicals, against organisms recovered as part of a large, multicenter Phase III clinical trial being conducted in Europe and the United States (USA). All organisms were recovered per protocol from peripheral or catheter blood draws, catheter insertion sites, or from cultured catheter segments using the roll plate and sonication techniques (upon meeting threshold criteria for significance).

MATERIALS AND METHODS

Organism collection studied: A total of 2,709 isolates from 1,494 enrolled patients were submitted from 41 trial sites in North America and Europe to a central laboratory (JMI Laboratories, North Liberty, Iowa) for organism identification confirmation and susceptibility (S) testing by CLSI broth microdilution methods. Isolates originated from bloodstream (catheter line [826] and peripheral blood samples [471]), catheter insertion sites (190), catheter tips (roll plate [488] and sonication [203]) and subcutaneous segments (roll plate [360] and sonication [171]) using methods as published. All isolates (including duplicates) submitted from each patient were included in this analysis (see Table 1 for a listing of the top ranked species/ organism groups recovered). Treatment assignments have not been unblinded for this preliminary assessment.

Susceptibility test methods: Broth microdilution MIC testing was performed according to Clinical and Laboratory Standards Institute (CLSI) methods (documents M7-A7 [2006]; M100-S18 [2008]; and M27-A2 [2002]). Panels were produced by JMI Laboratories using cation-adjusted Mueller-Hinton broth (with addition of 2 - 5 % lysed horse blood supplements for testing of fastidious species) and buffered RPMI 1640 for testing of yeasts. Interpretive criteria for comparator agents, where available, were those as published by CLSI (M100-S18 [2008] and M27-S3 [2008]). Other breakpoints utilized included mupirocin high-level resistance at >256 µg/mL and neomycin susceptibility at ≤10 mg/L (based upon available literature for a systemic only breakpoint).

RESULTS

- The top 11 ranked pathogens from this clinical trial (92.7% of the total; see Table 1) and key resistant markers included: coagulase-negative staphylococci (59.2%; 71.6% oxacillin-resistant) > *S. aureus* (8.5%; 35.5% oxacillin-resistant) > enterococci (7.8%; 0.9% vancomycin-resistant) > *Candida* spp. (3.5%; 14.7% fluconazole non-susceptible) > *Enterobacter* spp. (3.4%; 42.4% ceftazidime-resistant) > *Corynebacterium* spp. (2.6%) > *P. aeruginosa* (2.4%; 10.8% meropenem-resistant) > *Acinetobacter* spp. (1.9%; 69.2% meropenem-resistant) > *E. coli* (1.7%; 19.1% ESBL phenotype) > *Serratia marcescens* (1.7%) > *Klebsiella* spp. (1.3%; 29.4% ESBL-phenotype).
- Among ranking pathogens, all (100%) Gram-positive isolates were inhibited by ≤128 µg/ml of omiganan, and >99% of Gram-negative species and 100% of yeasts by ≤512 µg/ml. Only *S. marcescens* displayed elevated MIC values (Tables 1 and 2).

Table 1. Cumulative percent inhibited at omiganan MIC values tested against species/groups of bacterial and fungal pathogens recovered as part of the Phase III omiganan clinical trial (2,709 total isolates).

	Cumulative % inhibited at MIC values (µg/ml):									
Organism group (no. tested)	**≤0.5**	**1**	**2**	**4**	**8**	**16**	**32**	**64**	**128**	**256**	**512**
Coagulase-neg. staphylococci (1,604)	0.1	0.5	2.8	65.3	98.2	99.8	99.9	100			
Oxacillin-susceptible (456)	0.2	0.9	5.5	73.2	99.8	100					
Oxacillin-resistant (1,148)	0.1	0.3	1.7	62.1	97.6	99.7	99.9	100			
S. aureus (231)					16.0	79.7	100				
Oxacillin-susceptible (149)					20.8	91.9	100				
Oxacillin-resistant (82)					7.3	57.3	100				
Enterococcus spp. (211)				3.3	10.9	11.8	12.8	44.5	100		
Candida spp. (95)					5.3	6.3	21.1	65.3	91.6	98.9	100
Enterobacter spp. (92)							16.3	43.5	71.7	94.6	100
Corynebacterium spp.(70)	1.4	21.4	58.6	95.7	100						
P. aeruginosa (65)								3.1	61.5	93.8	100
Acinetobacter spp. (52)					1.9	13.5	17.3	36.5	92.3	100	
E. coli (47)						6.4	61.7	100			
Serratia marcescens (45)								2.2	2.2	62.2	68.9

Table 2. Activity of omiganan and comparator antimicrobial agents tested against ranking Gram-positive bacterial species recovered from catheter-associated infections.

Organism (no. tested)/ Antimicrobial agent	**MIC (µg/mL) 50%**	**90%**	**Range**	**% susceptible/ resistant[a]**
S. aureus (231)				
Omiganan	16	32	8-32	- / -
Oxacillin	0.5	>2	≤0.25->2	64.5/35.5
Erythromycin	0.5	>8	0.12->8	55.0/41.1
Clindamycin	≤0.25	>4	≤0.25->4	72.7/27.3
Ciprofloxacin	0.5	>4	0.06->4	65.4/34.6
Tetracycline	≤2	≤2	≤2->16	90.9/9.1
Trimethoprim/sulfamethoxazole	≤0.5	≤0.5	≤0.5-1	100.0/0.0
Neomycin	0.5	>16	≤0.12->16	69.3/-
Mupirocin	≤4	≤4	≤4->256	>2,6
Vancomycin	1	1	≤0.12-2	100.0/0.0
Coagulase-neg. staphylococci (1,604)				
Omiganan	4	8	0.5-64	- / -
Oxacillin	>2	>2	≤0.25->2	28.4/71.6
Erythromycin	>8	>8	≤0.06->8	37.1/72.3
Clindamycin	≤0.25	>4	≤0.25->4	67.6/31.2
Ciprofloxacin	4	>4	≤0.03->4	39.9/55.7
Tetracycline	≤2	8	≤2->16	89.2/9.7
Trimethoprim/sulfamethoxazole	≤0.5	>2	≤0.5->2	65.8/34.2
Neomycin	≤0.12	8	≤0.12->16	90.2/-
Mupirocin	≤4	>256	≤4->256	>18.4
Vancomycin	1	2	0.25-4	99.3/0.0
Enterococcus spp. (211)				
Omiganan	128	128	4-128	- / -
Ampicillin	0.5	2	0.25->8	91.0/9.0
Ciprofloxacin	>4	>4	0.12->4	47.9/51.2
Erythromycin	>8	>8	0.12->8	8.5/69.2
Quinupristin/dalfopristin	>2	>2	0.5->2	4.7/89.1
Gentamicin (HL)	≤500	>500	≤500->500	55.9/44.1
Neomycin	>16	>16	2->16	3.8/-
Mupirocin	256	256	≤4->256	-/-
Vancomycin	1	2	0.5->16	99.1/0.9
Corynebacterium spp. (70)				
Omiganan	2	4	0.5-8	- / -
Oxacillin	>2	>2	≤0.25->2	- / -
Erythromycin	>8	>8	≤0.06->8	- / -
Clindamycin	>4	>4	≤0.25->4	- / -
Ciprofloxacin	>4	>4	≤0.03->4	- / -
Tetracycline	≤2	>16	≤2->16	- / -
Trimethoprim/sulfamethoxazole	>2	>2	≤0.5->2	- / -
Neomycin	4	>16	≤0.12->16	- / -
Mupirocin	>256	>256	>256	- / -
Vancomycin	0.5	1	≤0.12-1	- / -

a. Susceptibility defined by the CLSI [2008]. β-lactam susceptibility should be directed by the oxacillin test results. Also the following criteria: mupirocin high level resistance at >256 µg/ml; neomycin at ≤10 µg/ml (susceptible), - = no interpretive criteria.

- Omiganan potency (MIC_{50} values) was unaffected by oxacillin resistance in the coagulase-negative staphylococci compared with susceptible strains (both 8 µg/ml), and increased only two-fold (16 to 32 µg/ml) among oxacillin-resistant *S. aureus*.
- High level resistance to mupirocin was detected among both coagulase-negative staphylococci (18.4%) and *S. aureus* (2.6%).
- While >99% of oxacillin-susceptible coagulase negative staphylococci and *S. aureus* were susceptible to neomycin (systemic breakpoint only, ≤10 µg/ml; one of the active components of triple antibiotic ointment), fewer oxacillin-resistant strains were susceptible (86.5 and 14.6% susceptible, respectively).
- Neomycin was inactive against enterococci and variably active against Gram-negative species (*E. coli*, 91.5% susceptible; *Klebsiella* spp., 100.0%; *Enterobacter* spp., 98.9%, *P. aeruginosa*, 72.3% and *Acinetobacter* spp., 82.7%).
- *Candida* spp. isolates from this trial were all susceptible to the marketed antifungal agents for which breakpoints exist with the following exceptions: *C. parapsilosis* (50.0% non-susceptible to fluconazole), *C. glabrata* (25.0% non-susceptible to fluconazole and 75.0% non-susceptible to itraconazole) and *C. tropicalis* (88.9% non-susceptible to itraconazole). All strains were inhibited by ≤512 µg/ml of omiganan (Tables 3 and 4).

Table 3. Activity of omiganan and comparator antimicrobial agents tested against ranking Gram-negative bacterial species recovered from catheter-associated infections.

Organism (no. tested)/ Antimicrobial agent	**MIC (µg/mL) 50%**	**90%**	**Range**	**% susceptible/ resistant[a]**
E. coli (47)				
Omiganan	32	64	16-64	- / -
Ampicillin	>16	>16	≤1->16	40.4/59.6
Ceftazidime	≤1	>16	≤1->16	83.0/17.0
Piperacillin-tazobactam	2	16	≤1->64	93.6/6.4
Meropenem	≤0.12	≤0.12	≤0.12	100.0/0.0
Ciprofloxacin	≤0.03	>4	≤0.03->4	70.2/29.8
Gentamicin	≤2	>8	≤2->8	83.0/17.0
Neomycin	2	4	0.5->16	91.5/-
Tetracycline	≤2	>8	≤2->8	66.0/44.0
Klebsiella spp. (34)				
Omiganan	64	256	16-512	- / -
Ampicillin	>16	>16	8->16	11.8/61.8
Ceftazidime	≤1	>16	≤1->16	79.4/20.6
Piperacillin-tazobactam	4	32	≤1-64	88.2/0.0
Meropenem	≤0.12	≤0.12	≤0.12-0.25	100.0/0.0
Ciprofloxacin	≤0.03	>4	≤0.03->4	79.4/20.6
Gentamicin	≤2	≤2	≤2	100.0/0.0
Neomycin	0.5	4	0.25-8	100.0/-
Tetracycline	≤2	4	≤2->8	91.2/8.8
Enterobacter spp. (92)				
Omiganan	128	256	32-512	- / -
Ampicillin	>16	>16	>16	0.0/100.0
Ceftazidime	4	>16	≤1->16	54.3/42.4
Piperacillin-tazobactam	8	>64	≤1->64	62.0/23.9
Meropenem	≤0.12	0.5	≤0.12-1	100.0/0.0
Ciprofloxacin	0.06	>4	≤0.03->4	70.7/29.3
Gentamicin	≤2	>8	≤2->8	67.4/29.3
Neomycin	1	8	0.5-16	98.9/-
Tetracycline	≤2	>8	≤2->8	64.1/34.8
Serratia marcescens (45)				
Omiganan	256	>512	64->512	-/-
Ampicillin	>16	>16	8->16	4.4/91.1
Ceftazidime	≤1	≤1	≤1-4	100.0/0.0
Piperacillin-tazobactam	2	8	≤1-16	100.0/0.0
Meropenem	≤0.12	≤0.12	≤0.12-0.25	100.0/0.0
Ciprofloxacin	0.06	0.12	≤0.03-1	100.0/0.0
Gentamicin	≤2	≤2	≤2	100.0/0.0
Neomycin	1	2	0.5-2	100.0/-
Tetracycline	8	>8	4->8	11.1/24.4
P. aeruginosa (65)				
Omiganan	128	256	64-512	-/-
Ceftazidime	8	>16	≤1->16	62.5/23.4
Cefepime	4	>16	1->16	81.5/10.8
Piperacillin-tazobactam	8	>64	4->64	83.1/16.9
Meropenem	2	16	≤0.12->16	55.4/10.8
Ciprofloxacin	0.25	>4	≤0.03->4	84.6/12.3
Gentamicin	≤2	8	≤2->8	84.6/9.2
Neomycin	8	>16	2->16	72.3/-
Acinetobacter spp. (52)				
Omiganan	64	64	≤4-128	-/-
Ceftazidime	>16	>16	≤1->16	21.2/75.0
Cefepime	>16	>16	≤0.12->16	21.2/76.9
Piperacillin-tazobactam	>64	>64	≤1->64	21.2/78.8
Meropenem	>16	>16	≤0.12->16	23.1/76.9
Ciprofloxacin	>4	>4	≤0.03->4	19.2/80.8
Gentamicin	>8	>8	≤2->8	26.9/73.1
Neomycin	4	>16	0.25->16	82.7/-

a. Susceptibility defined by the CLSI [2008] and the following criteria: neomycin at ≤10 µg/ml (susceptible only); - = no interpretive criteria.

Table 4. Activity of omiganan and comparator antimicrobial agents tested against ranking yeast species recovered from catheter-associated infections.

Organism (no. tested)/ Antimicrobial agent	**MIC (µg/mL) 50%**	**90%**	**Range**	**% susceptible/ resistant[a]**
Candida spp. (95)				
Omiganan	64	128	8-512	-/-
Amphotericin B	0.5	1	0.06-1	-/-
Fluconazole	0.5	16	≤0.12-128	85.3/1.1
5-Flucytosine	0.06	0.12	≤0.03-1	100.0/0.0
Itraconazole	0.03	0.25	≤0.008-2	81.1/2.1
Voriconazole	≤0.008	0.25	≤0.008-0.5	100.0/0.0
Candida albicans (52)				
Omiganan	64	128	32-128	-/-
Amphotericin B	0.5	1	0.06-1	-/-
Fluconazole	0.25	0.5	≤0.12-1	100.0/0.0
5-Flucytosine	0.06	0.12	≤0.03-1	100.0/0.0
Itraconazole	0.016	0.06	≤0.008-0.06	100.0/0.0
Voriconazole	≤0.008	≤0.008	≤0.008-0.016	100.0/0.0
Candida parapsilosis (20)				
Omiganan	128	128	32-512	-/-
Amphotericin B	0.25	0.5	0.12-0.5	-/-
Fluconazole	2	32	0.25-32	50.0/00
5-Flucytosine	≤0.03	0.12	≤0.03-0.25	100.0/0.0
Itraconazole	0.06	0.12	0.03-0.12	100.0/0.0
Voriconazole	0.03	0.5	≤0.008-0.5	100.0/0.0
Candida glabrata (12)				
Omiganan	256	256	64-256	-/-
Amphotericin B	0.5	1	0.12-1	-/-
Fluconazole	4	16	1-16	75.0/0.0
5-Flucytosine	≤0.03	≤0.03	≤0.03	100.0/0.0
Itraconazole	0.25	1	0.06-2	25.0/16.7
Voriconazole	0.06	0.25	≤0.008-0.25	100.0/0.0
Candida tropicalis (9)				
Omiganan	8	-	8-32	- / -
Amphotericin B	1	-	0.5-1	- / -
Fluconazole	1	-	≤0.12-2	100.0 / 0.0
5-Flucytosine	0.12	-	0.06-0.25	100.0 / 0.0
Itraconazole	0.25	-	0.03-0.5	11.1 / 0.0
Voriconazole	0.03	-	≤0.008-0.12	100.0 / 0.0

a. Criteria as published by the CLSI [2008]. - = no interpretive criteria.

CONCLUSIONS

- Omiganan represents a 'first-in-class' agent that displays antimicrobial activity against all major bacterial and fungal pathogens recovered during a clinical trial targeting prevention of local catheter site and catheter-related bloodstream infections.
- At the clinical formulation concentration of 1% (topical gel; 10,000 µg/ml), omiganan was active against >99% of common skin bacteria and yeast known to produce catheter-associated infections at ≤512 µg/ml, including strains with the most worrisome emerging resistance profiles.
- Ongoing surveillance of antimicrobial susceptibility of bacterial and fungal pathogens implicated in intravascular catheter-associated infections is warranted to detect emerging resistance trends, and susceptibility testing for omiganan should be considered following introduction into clinical practice.

SELECTED REFERENCES

Anderegg TR, Fritsche TR, Jones RN (2004). Quality control guidelines for MIC susceptibility testing of omiganan pentahydrochloride (MBI 226), a novel antimicrobial peptide. *J Clin Microbiol* 42: 1386-1387.

Clinical and Laboratory Standards Institute. (2006). *M7-A7, Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically; approved standard - seventh edition*. Wayne, PA: CLSI.

Clinical and Laboratory Standards Institute. (2007). *M100-S17, Performance standards for antimicrobial susceptibility testing, 17th informational supplement*. Wayne, PA: CLSI.

Clinical and Laboratory Standards Institute. (2008). *M27-S3. Quality control minimal inhibitory concentration (MIC) limits for broth microdilution and MIC interpretive breakpoints*. Wayne, PA: CLSI.

Deshpande LM, Fix AM, Pfaller MA, Jones RN (2002). Emerging elevated mupirocin resistance rates among staphylococcal isolates in the SENTRY Antimicrobial Surveillance Program (2000): correlations of results from disk diffusion, Etest and reference dilution methods. *Diagn Microbiol Infect Dis* 42: 283-290.

Fritsche TR, Rhomberg PR, Sader HS, Jones RN (2008). Antimicrobial activity of omiganan pentahydrochloride against contemporary fungal pathogens responsible for catheter-associated infections. *Antimicrob Agents Chemother* 52: 1187-1189.

Fritsche TR, Rhomberg PR, Sader HS, Jones RN (2008). In vitro activity of omiganan pentahydrochloride tested against vancomycin-tolerant, -intermediate and -resistant *Staphylococcus aureus*. *Diagn Microbiol Infect Dis* 60: 399-403.

Jones RN, Li Q, Kohut B, Biedenbach DJ, Bell J, Turnidge JD (2006). Contemporary antimicrobial activity of triple antibiotic ointment: A multiphased study of recent clinical isolates in the United States and Australia. *Diagn Microbiol Infect Dis* 54: 63-71.

Melo MN, Dugourd D, Castanho MA (2006). Omiganan pentahydrochloride in the front line of clinical applications of antimicrobial peptides. *Recent Patents Anti-Infect Drug Disc* 1: 201-207.

National Committee for Clinical Laboratory Standards. (2002) M27-A2. *Reference method for broth dilution antifungal susceptibility testing of yeasts*. Wayne, PA: NCCLS.

NNIS (1999). National Nosocomial Infections Surveillance (NNIS) System Report, Data Summary from January 1990-May 1999, Issued June 1999. *Am J Infect Control* 27: 520-532.

Sader HS, Fedler KA, Rennie RP, Stevens S, Jones RN (2004). Omiganan pentahydrochloride (MBI 226), a topical 12-amino-acid cationic peptide: Spectrum of antimicrobial activity and measurements of bactericidal activity. *Antimicrob Agents Chemother* 48: 3112-3118.

Viale P, Stefani S (2006). Vascular catheter-associated infections: A microbiological and therapeutic update. *J Chemother* 18: 235-249.

DISCLOSURES

This study was supported by a grant from Cadence Pharmaceuticals.

Omiganan is under investigation by Cadence Pharmaceuticals as a topical antimicrobial agent for the prevention of catheter-related infections.

The authors are all employees of JMI Laboratories.