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In Vitro Efficacy of Tigecycline Tested Against Community-Acquired Respiratory Tract Infection (CARTI) and Nosocomial Pneumonia (NP) Pathogens

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AMENDED ABSTRACT

Background:
To compare and contrast the pathogens involved in CARTI and NP cases when tested against tigecycline, a novel glycylcycline (formerly GAR936). All MIC tests were performed by reference broth microdilution methods to determine susceptibility (S) and resistance (R).

Methods:
The organisms numbered 9,347, a total of 2,004 from NP and 7,343 from CARTI. The most frequent CARTI pathogens were: *S. pneumoniae* (SPN; 2,865), *H. influenzae* (HI; 4,011) and *M. catarrhalis* (MCAT; 607). The rank order of NP isolates was: *S. aureus* (SA; 56.9%), *P. aeruginosa* (PSA; 13.9%), SPN (5.8%), *Klebsiella* spp. (KSP; 3.4%), *Enterobacter* spp. (ENT; 3.1%), *Acinetobacter* spp. (AC; 2.6%), *E. coli* (EC; 2.4%), *S. maltophilia* (SM; 1.6%), ß-streptococci (ßST; 1.5%) and *Serratia* spp. (SER; 1.2%). All tests were NCCLS (M7-A7) interpreted using M100-S14.

Results:
The characteristics of the organism collection were (CARTI/NP isolates): SPN PEN-R (34/41%); HI AMP-R (22/19%) and clarithromycin-R (13%/ND); and MCAT ß-lactamase-positive (96%/ND). Tigecycline MIC results are found in the table:

Organism (CARTI/NP)	$MIC_{50/90}$ (mg/L) CARTI	NP	% ≤2/≤4 mg/L
SPN (2,748/117)	≤0.12/≤0.12	≤0.12/≤0.12	100/100
HI (3,995/16)	0.5/1	0.5/1	100/100
MCAT (600/7)	≤0.12/0.25	0.25/-	100/100
SA (-/1,140)	-	0.25/0.5	100/100
KSP (-/69)	-	0.5/1	96/100
AC (-/53)	-	1/4	85/100
EC (-/49)	-	0.25/0.5	100/100
ENT (-/43)	-	0.5/2	98/100
SM (-/32)	-	1/2	88/100
ßSt (-/30)	-	≤0.12/≤0.12	100/100
SER (-/24)	-	1/4	75/92

PSA was less tigecycline-S (MIC_{90}, 16 mg/L), but all ESBL-producing KSP and EC had tigecycline MICs at ≤ 2 mg/L and tetracycline-R strains were also tigecycline-S.

Conclusions: Tigecycline in vitro activity against CARTI and NP pathogens was high, showing potency against R phenotypes of SP, HI, Enterobacteriaceae and some difficult to treat non-fermentative Gram-negative bacilli. Empiric parenteral application of tigecycline for serious pneumonia cases appears prudent for patients less likely to have PSA as the causative pathogen or as directed therapy of S organisms.

INTRODUCTION

Community-acquired and nosocomial respiratory tract infections are significant causes of morbidity and mortality, and have become much more difficult to manage with the escalating resistances being seen among all pathogen groups, including *S. pneumoniae* and *H. influenzae* among community-acquired pathogens and *S. aureus*, Enterobacteriaceae, and non-fermentative Gram-negative bacilli among nosocomial pathogens. The decrease in utility of many penicillins, cephalosporins, ß-lactamase inhibitor combinations and even carbapenems, among many other classes of antimicrobics, has created a critical need for new agents. The search for compounds with greater potency, stability to common resistance mechanisms, favorable pharmacokinetic/pharmacodynamic features and lower potential to select for resistance is essential in addressing this situation.

Tigecycline is a derivative of minocycline that has become the sentinel representative of a new class of agent known as the glycylcyclines. This agent is currently undergoing Phase III evaluations as a parenteral agent for such indications as skin and soft tissue infections, and intra-abdominal infections, and is under priority review by the FDA for fast-track approval. Tigecycline demonstrates potent activity against a broad range of commonly occurring species, including many resistant organisms such as penicillin-resistant *S. pneumoniae*, oxacillin-resistant *S. aureus*, vancomycin–resistant enterococci, and extended-spectrum ß-lactamase producing strains of Enterobacteriaceae. The agent is also active against *H. influenzae, M. catarrhalis*, pathogenic *Neisserias* and many other Gram-negative species, including some nonfermentative Gram-negative bacilli.

In this study we evaluated the in vitro activity of tigecycline against a total of over 9,000 bacterial isolates originating from either nosocomial pneumonias or community-acquired respiratory tract infections to evaluate the potential role this agent may have against such species, and compared its activity to those agents commonly used in the directed or empiric therapy of respiratory tract infections.

MATERIALS AND METHODS

To assess the spectrum of activity and potency of tigecycline against recent clinical isolates from community-acquired and nosocomial respiratory tract infections, a total of 9,347 Gram-positive and -negative bacterial isolates were submitted to a reference laboratory (JMI Laboratories, North Liberty, IA) for testing. Consecutively acquired, non-duplicate, patient isolates were submitted from > 70 participating medical centers representing 29 countries in the five continents of Asia, Australia, Europe, South America and North America.

Isolates were identified by the submitting laboratory and confirmed by the monitoring facility (JMI Laboratories, IA) using colonial characteristics on standard media, rapid tests (catalase, oxidase, coagulase, bile solubility, latex agglutination kits), and use of an automated identification system (Vitek bioMerieux, Hazelwood, MO), among others methods, as necessary. The collection consisted of those species and groups comprising the most commonly encountered respiratory tract pathogens (Table 1).

MIC values for up to 38 antimicrobials including tetracycline and tigecycline were determined using validated, dry-form broth microdilution panels with cation-adjusted Mueller-Hinton medium (TREK Diagnostics Inc., Cleveland, OH). Antimicrobials tested included those classes and examples of drugs most commonly used for the empiric or directed treatment of the indicated infection. When testing *Streptococcus spp.*, supplemental lysed horse blood (2-5%) was added. Haemophilus Test Medium (HTM) was used when testing *Haemophilus* spp. Testing, incubation and MIC interpretation were performed using the manufacturers recommendations and/or recommendations from the Clinical Laboratory Standards Institute (CLSI; formerly NCCLS) [NCCLS, 2003; CLSI, 2005]. Quality control was performed using American Type Culture Collection (ATCC) strains including *Escherichia coli* ATCC 25922 and 35218, *S. aureus* ATCC 29213, *Enterococcus faecalis* ATCC 29212, *S. pneumoniae* ATCC 49619, *H. influenzae* ATCC 49247 and *Pseudomonas aeruginosa* ATCC 27853.

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RESULTS

- Among community-acquired respiratory tract infections, the rank order of identified pathogens was *H. influenzae* (54% of isolates), *S. pneumoniae* (37%) and *M. catarrhalis* (8%; Table 1).
- Tigecycline inhibited 100% of *H. influenzae, S. pneumoniae* and *M. catarrhalis* at 2 mg/L, 1 mg/L and 0.5 mg/L, respectively (Table 1). With the exception of clarithromycin and trimethoprim/sulfamethoxazole for *H. influenzae*, remaining comparators were >98% susceptible for both *H. influenzae* and *M. catarrhalis* (Table 2). *S. pneumoniae* was the most worrisome species with 17.4%, 27.6%, and 21.7% of isolates being resistant to penicillin, erythromycin and tetracycline, respectively. Also of growing concern is the slow but stepwise emergence of fluoroquinolone resistant *S. pneumoniae* (1.1% for levofloxacin).
- The rank order of the ten most prevalent pathogens producing nosocomial pneumonia was *S. aureus* (56.9% of strains), *P. aeruginosa* (13.9%), *S. pneumoniae* (5.8%), *Klebsiella* spp. (3.4%), *Acinetobacter* spp. (2.6%), *E. coli* (2.4%), *Enterobacter* spp. (2.1%), *S. maltophilia* (1.6%), ß-haemolytic streptococci (1.5%) and *S. marcescens* (1.2%).
- At a concentration of 4 mg/L (breakpoint for tetracycline) tigecycline inhibited 100% of the ten listed nosocomial pathogens with the exceptions of *S. marcescens* (92%) and *P. aeruginosa* (22%; Table 1).
- The population of *S. aureus* (47.8% oxacillin resistant) was readily inhibited by tigecycline (MIC_{50} and MIC_{90}, 0.25 mg/L and 0.5 mg/L) with all strains being inhibited by ≤ 1 mg/L (Table 3). While 100% of strains were susceptible to vancomycin and linezolid, tigecycline was four- and eight-fold more potent, respectively.

Table 1. Cumulative frequency distributions for the top ranked Gram-positive and -negative pathogens producing either community-acquired respiratory tract infection (7,343 strains) or nosocomial pneumonia (2,004) when tested against tigecycline (2002 - 2004).

Organisms (no. strains/% of total)	% inhibited at MIC (mg/L) ≤0.12	0.25	0.5	1	2	4	8	16	32
Community-acquired infections[a]									
H. influenzae (3,995/54.4)	1	22	79	98	100	-	-	-	-
S. pneumoniae (2,748/37.4)	95	98	99	100	-	-	-	-	-
M. catarrhalis (600/8.2)	66	94	100	-	-	-	-	-	-
Nosocomial pneumonia									
S. aureus (1,140/56.9)	41	79	98	100	-	-	-	-	-
P. aeruginosa (279/13.9)	<1	1	2	3	6	22	63	94	99
S. pneumoniae (117/5.8)	100	-	-	-	-	-	-	-	-
Klebsiella spp. (69/3.4)	0	17	81	93	96	100	-	-	-
Acinetobacter spp. (53/2.6)	7	21	30	55	85	100	-	-	-
E. coli (49/2.4)	24	78	98	100	-	-	-	-	-
Enterobacter spp. (43/2.1)	0	9	67	88	98	100	-	-	-
S. maltophilia (32/1.6)	3	6	19	56	87	100	-	-	-
ß-haemolytic streptococci (30/1.5)	100	-	-	-	-	-	-	-	-
Serratia spp. (24/1.2)	0	0	8	50	75	92	100	-	-

a. Primarily sinusitis, acute exacerbations of chronic bronchitis and pneumonia.

Table 2. Antimicrobial activity of tigecycline and selected comparators tested against pathogens producing community-acquired respiratory tract infections (7,343 strains; 2000 - 2004).

Organism (no. tested/antimicrobial agent	MIC (mg/L) 50%	90%	Range	% susceptible[a]	% resistant[a]
H. influenzae (3,995)					
Tigecycline	0.5	1	≤0.016-2	-	-[b]
Tetracycline	≤2	≤2	≤2->16	98.1	1.5
Amoxicillin/Clavulanic acid	0.5	1	≤0.06->8	99.9	0.1
Piperacillin/Tazobactam	≤1	≤1	≤1->16	99.7	0.3
Ceftriaxone	≤0.008	≤0.008	≤0.008->16	99.9	-
Azithromycin	1	2	≤0.06->16	99.7	-
Clarithromycin	8	16	≤0.25->32	87.5	1.2
Ciprofloxacin	≤0.12	≤0.12	≤0.12->4	>99.9	-
Chloramphenicol	≤2	≤2	≤2-16	98.5	1.0
Trimethoprim/Sulfamethoxazole	≤0.5	>4	≤0.5->4	80.8	16.8
S. pneumoniae (2,748)					
Tigecycline	≤0.12	≤0.12	≤0.12-1	-	-
Tetracycline	≤2	>16	≤2->16	77.1	21.7
Penicillin	≤0.03	2	≤0.03->32	66.3	17.4
Amoxicillin/Clavulanic acid	≤0.06	2	≤0.06->16	94.2	3.2
Ceftriaxone	0.03	1	≤0.008->32	97.8	1.1
Erythromycin	≤0.25	>32	≤0.25->32	71.0	27.6
Clindamycin	≤0.25	>2	≤0.25->2	85.0	14.3
Quinupristin/Dalfopristin	≤0.5	≤0.5	≤0.5-2	99.8	0.0
Levofloxacin	1	1	≤0.03->4	98.9	1.1
Linezolid	1	1	≤0.06-2	100.0	-
Vancomycin	0.25	0.5	≤0.06-1	100.0	-
M. catarrhalis (600)					
Tigecycline	≤0.12	0.25	≤0.12-0.5	-	-
Tetracycline	≤2	≤2	≤2-16	99.3	0.7
Amoxicillin/Clavulanic acid	0.12	0.25	≤0.06-0.5	100.0	0.0
Piperacillin/Tazobactam	≤1	≤1	≤1-2	99.8	0.2
Ceftriaxone	0.12	0.5	≤0.008-2	100.0	-
Azithromycin	≤0.5	≤0.5	≤0.5-1	100.0	-
Clarithromycin	≤0.25	≤0.25	≤0.25-0.5	100.0	0.0
Ciprofloxacin	≤0.12	≤0.12	≤0.12	100.0	-
Chloramphenicol	≤2	≤2	≤2-4	99.8	0.0
Trimethoprim/Sulfamethoxazole	≤0.5	≤0.5	≤0.5-2	98.3	0.0

a. Criteria as published by the CLSI/NCCLS [2005]; breakpoints used for *M. catarrhalis* are those specified for *Haemophilus* for comparative purposes.
b. Breakpoint criteria have not been defined by CLSI/NCCLS.

- ß-haemolytic streptococci were also very susceptible to tigecycline with the highest MIC being ≤ 0.12 mg/L; among comparators decreased activity was noted for tetracycline, erythromycin, and clindamycin. While resistance to levofloxacin was not observed, 3.3% of strains were intermediate.

Table 3. Antimicrobial activity of tigecycline and selected comparators tested against the most prevalent Gram-positive cocci producing nosocomial pneumonia (1,287 strains; 2000 - 2004).

Organism (no. tested/antimicrobial agent	MIC (mg/L) 50%	90%	Range	% susceptible[a]	% resistant[a]
S. aureus (1,140)					
Tigecycline	0.25	0.5	0.03-1	-	-[b]
Tetracycline	≤4	>8	≤4->8	82.5	16.9
Oxacillin	1	>8	0.12->8	52.2	47.8
Clindamycin	0.12	>8	≤0.06->8	59.7	40.0
Levofloxacin	2	>4	≤0.03->4	49.8	48.3
Trimethoprim/Sulfamethoxazole	≤0.5	>1	≤0.5->1	93.9	6.1
Quinupristin/Dalfopristin	0.25	0.5	≤0.06->8	99.6	0.2
Teicoplanin	0.5	2	≤0.12-16	99.9	0.0
Vancomycin	1	1	0.25-2	100.0	0.0
Linezolid	2	2	≤0.25-4	100.0	-
S. pneumoniae (117 strains)					
Tigecycline	≤0.12	≤0.12	≤0.12	-	-
Tetracycline	≤4	>8	≤4->8	4.3	34.2
Penicillin	0.03	4	≤0.016-8	59.0	25.6
Amoxicillin/Clavulanate acid	≤2	≤2	≤2-16	97.4	0.9
Ceftriaxone	≤0.25	1	≤0.25-2	96.6	0.0
Erythromcyin	≤0.06	>8	≤0.06->8	67.5	31.6
Clindamycin	≤0.06	>8	≤0.06->8	86.3	13.7
Quinupristin/Dalfopristin	0.5	0.5	0.12-1	100.0	0.0
Levofloxacin	1	1	0.5-2	100.0	0.0
Linezolid	1	1	≤0.25-2	100.0	-
Vancomycin	0.25	0.5	≤0.12-0.5	100.0	-
ß-haemolytic streptococci (30)[c]					
Tigecycline	≤0.12	≤0.12	≤0.12	-	-
Tetracycline	≤4	>8	≤4->8	80.0	20.0
Penicillin	≤0.016	0.06	≤0.016-0.12	80.0	-
Ceftriaxone	≤0.25	≤0.25	≤0.25	100.0	-
Erythromcyin	≤0.06	>8	≤0.06->8	86.7	13.3
Clindamycin	≤0.06	0.25	≤0.06->8	93.1	6.9
Levofloxacin	0.5	1	0.25-4	96.7	0.0
Vancomycin	0.25	0.5	≤0.12-1	100.0	-
Linezolid	1	1	0.5-1	100.0	-

a. Criteria as published by the CLSI/NCCLS [2005].
b. Breakpoint criteria have not been defined by CLSI/NCCLS [2005].
c. Includes: *Streptococcus* group A (23 strains), group B (four strains), group C (one strain) and group F (two strains).

Table 4. Antimicrobial activity of tigecycline and selected comparators tested against the most prevalent Enterobacteriaceae producing nosocomial pneumonia (185 strains; 2000 - 2004).

Organism (no. tested/antimicrobial agent	MIC (mg/L) 50%	90%	Range	% susceptible[a]	% resistant[a]
E. coli (49)					
Tigecycline	0.25	0.5	0.06-1	-	-[b]
Tetracycline	4	>8	1->8	53.1	46.9
Ceftriaxone	≤0.25	>32	≤0.25->32	85.7	12.2
Ceftazidime	≤1	>16	≤1->16	87.8	10.2
Cefepime	≤0.12	4	≤0.12->16	91.8	8.2
Piperacillin/Tazobactam	2	>64	1->64	83.7	10.2
Imipenem	≤0.12	0.25	≤0.12-0.5	100.0	0.0
Ciprofloxacin	≤0.03	>4	≤0.03->4	67.3	32.7
Gentamicin	≤2	>8	≤2->8	83.7	16.3
Amikacin	2	8	1-16	100.0	0.0
Klebsiella spp. (69)[c]					
Tigecycline	0.5	1	0.25-4	-	-
Tetracycline	2	>8	0.5->8	76.8	21.7
Ceftriaxone	≤0.25	>32	≤0.25->32	68.1	18.8
Ceftazidime	≤1	>16	≤1->16	73.5	22.1
Cefepime	≤0.12	>16	≤0.12->16	82.6	14.5
Piperacillin/Tazobactam	4	>64	1->64	76.8	20.3
Imipenem	≤0.12	0.25	≤0.12-1	100.0	0.0
Ciprofloxacin	≤0.03	>4	≤0.03->4	76.8	14.5
Gentamicin	≤2	>8	≤2->8	73.9	23.2
Amikacin	2	32	0.5->32	84.1	7.2
Enterobacter spp. (43)[d]					
Tigecycline	0.5	2	0.25-4	-	-
Tetracycline	2	>8	1->8	79.1	16.3
Ceftriaxone	1	>32	≤0.25->32	58.1	18.6
Ceftazidime	≤1	>16	≤1->16	60.5	30.2
Cefepime	≤0.12	4	≤0.12->16	90.5	7.1
Piperacillin/Tazobactam	8	64	1->64	67.4	9.3
Imipenem	0.25	1	≤0.12-1	100.0	0.0
Ciprofloxacin	≤0.03	>4	≤0.03->4	83.7	14.0
Gentamicin	≤2	>8	≤2->8	79.1	16.3
Amikacin	2	32	1->32	88.4	9.3
Serratia spp. (24)[e]					
Tigecycline	1	4	0.5-8	-	-
Tetracycline	>8	>8	4->8	4.2	66.7
Ceftriaxone	≤0.25	>32	≤0.25->32	78.3	13.0
Ceftazidime	≤1	2	≤1->16	95.8	4.2
Cefepime	≤0.12	16	≤0.12->16	87.5	8.3
Piperacillin/Tazobactam	4	>64	2->64	75.0	16.7
Imipenem	0.5	1	0.25-2	100.0	0.0
Ciprofloxacin	0.12	>4	≤0.03->4	75.0	20.8
Gentamicin	≤2	>8	≤2->8	75.0	20.8
Amikacin	2	16	0.5-32	95.8	0.0

a. Criteria as published by the CLSI/NCCLS [2005].
b. Breakpoint criteria have not been defined by CLSI/NCCLS [2005].
c. Includes: *Klebsiella oxytoca* (seven strains), *K. pneumoniae* (60 strains) and *Klebsiella* spp. (two strains).
d. Includes: *Enterobacter aerogenes* (five strains), *E. cloacae* (33 strains) and *Enterobacter* spp. (five strains).
e. Includes: *Serratia marcescens* (22 strains) and *Serratia* spp. (two strains).

- All Enterobacteriaceae (including ESBL-producing *E. coli* and *Klebsiella* spp) among the ranked pathogens were inhibited by ≤ 4 mg/L of tigecycline; only *S. marcescens* was higher (92% at 4 mg/L and 100% at 8 mg/L; Tables 1 and 4). Imipenem was the most potent of all agents tested (MIC_{90}, 0.25 to 1 mg/L; 100% susceptible for the four species presented in Table 4). Increasing resistance to ciprofloxacin was, however, apparent (14% for *Klebsiella* spp. and *Enterobacter* spp. up to 32% for *E. coli*).
- *P. aeruginosa* displayed high resistance rates to most agents tested with polymyxin B being the most active agent (MIC_{50} and MIC_{90}, 0.5 and 1 mg/L, respectively; 99.3% susceptible). Among other comparators only piperacillin/tazobactam and amikacin achieved >80% susceptibility. Tigecycline MIC values were also elevated (Tables 1 and 5).
- Tigecycline was highly active against *Acinetobacter* spp. and *S. maltophilia* strains (MIC_{50}, 1 mg/L and MIC_{90}, 4 mg/L for both); only polymyxin B was more active against *Acinetobacter* (MIC_{50} and MIC_{90}, 0.5 mg/L), and trimethoprim/sulfamethoxazole against *S. maltophilia* (≤ 0.5 mg/L and 1 mg/L).

Table 5. Antimicrobial activity of tigecycline and selected comparators tested against the most prevalent non-fermentative Gram-negative bacilli producing nosocomial pneumonia (364 strains; 2000 - 2004).

Organism (no. tested/antimicrobial agent	MIC (mg/L) 50%	90%	Range	% susceptible[a]	% resistant[a]
P. aeruginosa (279)					
Tigecycline	8	16	≤0.12->32	-	-[b]
Tetracycline	>8	>8	0.5->8	2.5	85.7
Ceftazidime	4	>16	≤1->16	74.2	19.4
Cefepime	4	>16	0.25->16	73.8	12.2
Piperacillin/Tazobactam	8	>64	≤0.5->64	80.6	19.4
Imipenem	1	>8	≤0.12->8	71.7	12.5
Meropenem	1	>8	≤0.06->8	76.7	15.1
Ciprofloxacin	0.5	>4	≤0.03->4	64.2	27.2
Gentamicin	≤2	>8	≤2->8	76.7	20.1
Amikacin	4	32	≤0.25->32	88.9	8.6
Polymyxin B	0.5	1	≤0.12->8	99.3	0.7
Acinetobacter spp. (53)[c]					
Tigecycline	1	4	0.12-4	-	-
Tetracycline	8	>8	1->8	34.0	37.7
Ceftazidime	>16	>16	2->16	22.6	75.5
Cefepime	>16	>16	1->16	24.5	54.7
Piperacillin/Tazobactam	>64	>64	≤0.5->64	20.8	73.6
Imipenem	1	>8	≤0.12->8	81.1	18.9
Meropenem	2	>8	0.25->8	71.7	20.8
Ciprofloxacin	>4	>4	0.12->4	18.9	81.1
Amikacin	>32	>32	1->32	43.4	56.6
Polymyxin B	0.5	0.5	≤0.12-2	100.0	0.0
S. maltophilia (32)					
Tigecycline	1	4	0.12-4	-	-
Tetracycline	>8	>8	≤0.25->8	3.1	75.0
Ceftazidime	16	>16	≤1->16	46.9	43.8
Cefepime	16	>16	1->16	15.6	46.9
Piperacillin/Tazobactam	>64	>64	16->64	3.1	68.8
Ticarcillin/Clavulanic acid	32	128	≤16->128	37.5	34.4
Ciprofloxacin	4	>4	0.25->4	25.0	53.1
Levofloxacin	1	4	0.12->4	81.3	6.3
Trimethoprim/Sulfamethoxazole	≤0.5	1	≤0.5->2	93.8	6.3
Amikacin	>32	>32	4->32	6.3	90.6

a. Criteria as published by the CLSI/NCCLS [2005].
b. Breakpoint criteria have not been defined by CLSI/NCCLS [2005].
c. Includes: *Acinetobacter baumannii* (39 strains), *A. calcoaceticus* (five strains), *A. lwoffii* (one strain) and *Acinetobacter* spp. (eight strains).

CONCLUSIONS

- These in vitro studies demonstrate the potent activity that tigecycline has against the common pathogens producing community-acquired respiratory tract infections and nosocomial pneumonia, including those with resistant phenotypes (*S. pneumoniae, H. influenzae, S. aureus*, Enterobacteriaceae, and some of the difficult to treat non-fermentative Gram-negative bacillary infections).
- While the proposed initial indications for tigecycline include infections of skin and soft tissues, and intra-abdominal infections, further clinical studies should consider the role that this agent may play in therapy of severe respiratory tract infections, both of nosocomial and community origin.
- Specifically, use of parenterally administered tigecycline may prove beneficial for severe pneumoniae cases for those patients less likely to have *P. aeruginosa* as the causative pathogen or for those with documented susceptible organisms, warranting further investigation for these indications.