range of 68% (*Acinetobacter spp.*) to 100% (*Haemophilus influenzae*). When CXA-201 potency was analyzed by site of infection, approximately 95% of all isolates had an MIC ≤8 µg/mL, with a range of 94% (blood) to 96.9% (urine).

Whether sorted by site or source, approximately 95% of isolates had an MIC value <8 µg/mL. All pathogens had an MIC_{90} ≤8 µg/mL except *Enterobacter cloacae* (88% inhibited at ≤8 µg/mL) and *Acinetobacter spp.* (68.5% inhibited at ≤8 µg/mL). Thus, CXA-201 is predicted to achieve excellent target attainment of 40% T>MIC against common ICU pathogens and multidrug-resistant gram-negative pathogens, including *P. aeruginosa* (99.3% inhibited at ≤8 µg/mL).

Tigecycline Plus Standard Therapy Is More Effective Than Standard Therapy Alone For Treating Infections in Febrile Neutropenic Cancer Patients

Written by Eric Butterman

Tigecycline, first in a new class of glycylcyclines, in combination with piperacillin/tazobactam, is effective, safe, and well tolerated in high-risk febrile neutropenic oncohematologic patients. Giampaolo Bucaneve, MD, University of Perugia, Perugia, Italy, believes that tigecycline in combination should be considered one of the "first-line" empiric antibiotic therapies (particularly in a specific epidemiological setting (eg, high rate of extended-spectrum β-lactamase-producing gram-negatives and/or methicillin-resistant *Staphylococci*). This combination therapy may aid in reducing the increase and extensive use of carbapenems, which have been associated with an increase in multidrug-resistant bacteria.

This prospective, randomized, multicenter study included 364 cancer patients from 28 Italian oncohematological departments with profound (<500 neutrophils/mmc) chemotherapy-induced neutropenia and fever (>38.5°C once or >38°C on at least two occasions during a period of 12 hours) due to presumed infection. Patients were randomized centrally and stratified according to center and underlying disease (acute leukemia vs lymphoma and solid tumors). Patients received either IV (n=174) piperacillin/tazobactam (4.5 g 3x daily) plus tigecycline (50 mg twice daily) or IV (n=190) piperacillin/tazobactam (4.5 g 3x daily) as monotherapy. All other antibiotic therapy was stopped at randomization.

Successful treatment was defined as resolution of fever (maintained for at least 4 days) or any clinical sign of infection whenever present and eradication of the infecting microorganism whenever isolated, without change in the initial allocated treatment. Failure was defined as one of the following: death from primary infection, persistence of bacteremia beyond the first 24 hours of therapy, breakthrough bacteremia, documented pathogen resistant to assigned antibiotic(s), lack of response that required antibacterial therapy modification, development of shock or acute respiratory distress syndrome or disseminated intravascular coagulation or multiple organ failure, relapse of infection within 7 days of treatment discontinuation, or toxicity requiring treatment discontinuation.

Overall response to therapy was significantly ($p<0.01$) more effective following piperacillin/tazobactam plus tigecycline (72%) compared with monotherapy (47%; Table 1). Piperacillin/tazobactam plus tigecycline treatment success rates were significantly ($p\leq0.01$) greater for microbiologically (with bacteremia) and clinically documented infections compared with monotherapy. Single gram-positive and -negative (*E. coli*) bacteremias and coagulase-negative *Staphylococcus* species were more successfully treated with combination therapy than monotherapy (Table 2).

Table 1. Classification of Febrile Episodes and Response To Therapy.

Type of infection	Piperacillin/ tazobactam + tigecycline*	Piperacillin/ tazobactam*	p value
Total febrile episodes	174	190	
Microbiologically documented infections	54/88 (61%)	27/96 (28%)	<0.01
with bacteremia	52/86 (60%)	26/94 (27%)	<0.01
without bacteremia	2/2 (62%)	1/2 (25%)	0.5
Clinically documented infections	16/19 (84%)	9/19 (47%)	0.01
Unexplained fever	56/67 (83%)	54/75 (72%)	0.07
Total	126/174 (72%)	90/190 (47%)	<0.01

*success/total

Table 2. Agents of Bacteremias and Antibiotic Susceptibility.

Organism	Tigecycline*	Piperacillin/ tazobactam*
Total Gram-positives	80/89 (90%)	23/94 (24%)
Total Gram-negatives	53/66 (80%)	45/71 (63%)
Coagulase-negative *Staphylococcus*	54/58 (93%)	4/62 (6.5%)

Treatment success rates were significantly ($p \leq 0.01$) higher with combination therapy for infections that were associated with skin and soft tissues and for bacteremias of unknown origin. Overall treatment failures were greater for monotherapy. Overall mortality rates, deaths due to bacteremia, and treatment-related adverse events were similar between the two arms.

Tigecycline in combination with piperacillin/tazobactam, compared with the standard regimen of piperacillin/tazobactam, is more effective overall in bacteremias and clinically documented infections as well.

Interventions Aimed at Reducing MRSA BSIs Led to Decreased Rates of Nosocomial MSSA BSIs: Ten-Year Data from a UK Center

Written by Eric Butterman

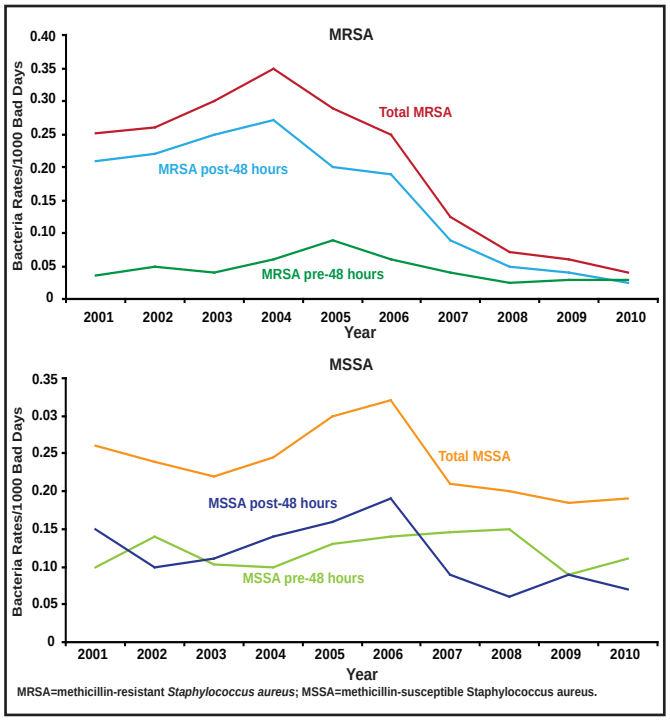
Addenbrooke's Hospital in Cambridge, United Kingdom, once known for having high rates of *Staphylococcus aureus* bloodstream infections (BSIs), has been able to significantly reduce rates of methicillin-susceptible *S. aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA) BSIs using a number of infection control interventions under the lead of Infection Control Doctor Nick Brown, MD. Staff physician Theodore Gouliouris, MD, presented data from a study that showed a decline in MRSA and MSSA BSI rates that was driven by reductions in nosocomial infections.

The purpose of the study was to analyze trends of MSSA and MRSA BSIs according to onset (community vs hospital) and assess the impact of infection control interventions. The interventions were initiated over several years and included: starting a hand hygiene campaign (November 2004), establishing a vascular access team (January 2006), improving line care bundles (June 2006), screening all emergency (April 2007) and elective (January 2009) admissions for MRSA carriage, and routinely decolonizing all MRSA-positive patients (entire study period). This was a retrospective study in a tertiary referral university hospital setting with 1200 beds and 70,000 in-patient admissions per year. All *S. aureus* bacteremia (SAB) episodes from January 2001 to December 2010 at Addenbrooke's Hospital were included. The number of episodes was converted to rates per 1000 bed days, which allowed comparison with other hospitals. Only the first episode of SAB per patient during the study period was analyzed. Patients were categorized according to onset: community onset (<48 hours from hospital admission) and nosocomial onset (≥48 hours from hospital admission).

There were 1607 SAB episodes following deduplication; 861 (53.6%) MSSA, of which 437 (50.8%) were community onset and 424 (49.2%) were nosocomial onset, and 746 (46.4%) MRSA, of which 163 (21.8%) were community onset and 583 (78.2%) were nosocomial onset.

MRSA rates started to decline in 2004, driven more by a reduction in nosocomial infections, with the largest decrease (53%) occurring during the 2006 to 2007 period. MSSA rates started to decline in 2006, driven again by reductions in nosocomial infections, with the largest decrease (59%) occurring during 2006–2007. Community-acquired infections remained stable over the same period (Figure 1). Hand washing affected MRSA transiently but not MSSA rates, while having a vascular access team and performing line care bundle had a large impact on decreases for both MRSA and MSSA. Extended MRSA screening may have contributed to the larger decline in MRSA infections. Potential confounders (hospital 1000 bed-day activity and number of blood cultures processed) did not influence results.

Figure 1. Community Acquired Infection Rates.



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