

# Tigecycline Promising for Complicated Infections

*First antibiotic in glycylicycline class is specifically designed to fight bacterial resistance mechanisms.*

BY MIRIAM E. TUCKER  
Senior Writer

WASHINGTON — Tigecycline, a novel broad-spectrum antibiotic, appears effective in treating a variety of serious infections, including those caused by resistant organisms, Evan Loh, M.D., said at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

Wyeth's tigecycline, the first of the glycylicycline class, is a modification of the minocycline molecule designed specifically to overcome two major bacterial resistance mechanisms. It has activity against gram-positive, gram-negative, atypical, anaerobic, and antibiotic-resistant bacteria. Phase III data thus far demonstrate efficacy in the treatment both complicated intraabdominal infections and skin/skin structure infections, said Dr. Loh, vice president, cardiovascular/infectious disease, Wyeth Research, Collegeville, Pa.

"This agent offers a broad spectrum of activity that offers an exciting opportunity for physicians to consider as empiric therapy when individuals with serious in-

fections present in the hospital setting," he said in a symposium at the meeting.

In late-breaker poster presentations, Nathalie Dartois, M.D., of Wyeth Research in Paris reported data from two phase III clinical trials. Tigecycline monotherapy was compared with the combination imipenem/cilastatin (IMI/CIS) regimen (Primaxin) in 817 adult patients with a wide variety of complicated intraabdominal infections, including appendicitis with perforation and abscess (41%), cholecystitis with evidence of perforation or empyema (22%), postoperative intraabdominal abscess (11%), and intestinal perforation with abscess or fecal contamination (9%). The patients were predominantly white (88%) and male (59%), with a mean age of 49 years.

Of the total 523 microbiologically evaluable cases, 265 were treated with tigecycline in an initial intravenous dose of 100 mg, followed by 50 mg every 12 hours in 100 mL saline over 30 minutes, followed 6 hours later by 100 mL normal saline placebo infused over 30 minutes for an average duration of 7.7 days. The other 258

patients received IMI/CIS every 6 hours in a volume of 100 mL normal saline for a mean duration of 7.8 days.

Clinical cure, assessed at 12-44 days after the last dose, was achieved in 91% of the tigecycline subjects and 90% of the IMI/CIS group, Dr. Dartois reported.

Safety profiles were also similar between the two regimens, with adverse events reported by a total of 60% of the tigecycline and 59% of IMI/CIS subjects. Nausea was the most common, reported by 18% of the tigecycline group and 13% with IMI/CIS. Vomiting occurred in 13% and 9%, respectively. The findings demonstrate "noninferiority" to the combination regimen, she said.

In the other trial, tigecycline was compared with combination vancomycin/aztreonam (V/A) in 543 adults with skin and skin structure infections, including 324 with deep soft tissue infections, 308 with cellulitis (many had both), 157 with major abscesses, 44 with infected ulcers, and 17 with burns.

Tigecycline was given in an initial in-

travenous dose of 100 mg, followed by 50 mg every 12 hours in 250 mL normal saline over 60 minutes, then 100 mL normal saline placebo over 60 minutes. The V/A group received an initial 1-g intravenous vancomycin dose in 250 mL normal saline over 60 minutes, followed by 2 g aztreonam in 100 mL normal saline over 60 minutes every 12 hours.

Clinical cure at 14-90 days after the last dose was achieved in 90% of 223 tigecycline patients (ranging from 83% for the ulcers to 100% among the burns), compared with 94% of the 213 treated with V/A (92% of soft tissue infections to 100% ulcers and burns). Among the total 312 patients for whom results were microbiologically evaluable, the eradication rate was 85% for tigecycline and 93% for V/A, she said.

Adverse events were reported by 52% with tigecycline and 44% for V/A. Nausea and vomiting were significantly more frequent with tigecycline than V/A (25% and 12% vs. 5% and 2%), while rash was more common with V/A (4% vs. 1%). ■

**The antibiotic tigecycline has activity against gram-positive, gram-negative, atypical, anaerobic, and antibiotic-resistant bacteria.**

## Penicillins Topped Oral Antibiotic Rx in 2001-2003

BY MITCHEL L. ZOLER  
Philadelphia Bureau

WASHINGTON — During 2001-2003, penicillins were the most commonly prescribed oral antibiotics in the United States, followed closely by macrolides, based on data from nine managed care plans.

But the pattern was highly dependent on infection sites, Katie J. Suda, Pharm.D., said in presenting a poster at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

In addition, 5% of all oral antibiotic prescriptions were written for viral infections, including the common cold and influenza. Macrolides were most often prescribed for these infections, followed by penicillins, said Dr. Suda of the pharmacy administration office at Baptist Memorial Health Care Corp. in Memphis, Tenn.

The data collected from the managed care plans included 42,971 prescriptions for oral anti-infective drugs that were written for 23,762 patients. The average age of the patients who received these prescriptions was 34 years old, and two-thirds were women. The average duration of treatment was 10 days.

Penicillins were prescribed 29% of the time, followed by macrolides, 27%; fluoroquinolones, 15%; cephalosporins, 14%; tetracyclines, 8%; and other antibiotics, 7%.

Dr. Suda and her associates broke the infections into four main types: urinary tract, skin and soft tissue, upper respiratory tract, and lower respiratory tract.

Fluoroquinolones were the most com-

monly prescribed antibiotic class for urinary tract infections, used by about 31% of patients, followed by sulfonamides (24%). These rates showed little change over the 3 years of the study.

The most commonly prescribed class for skin and soft-tissue infections was first-generation cephalosporins, used by about 46% of patients. The next most common class was the fluoroquinolones (19%). Use of first-generation cephalosporins surged during the 3 years of the study, jumping from 39% of all antibiotic prescriptions for these infections in 2001 to 47% in 2002 and 51% in 2003, Dr. Suda said.

For patients with upper respiratory tract infections, the most commonly prescribed drug class was the macrolides, used by 33%, followed by the penicillins, used by about 27% of patients. The study period featured a rise in prescriptions of both macrolides, which increased from 28% in 2001 to 37% in 2003, and in fluoroquinolones, which rose from 7% of all prescriptions for this indication in 2001 to 13% in 2003. Penicillin use declined modestly, from 30% in 2001 to 27% in 2003.

Among patients with lower respiratory tract infections, the most commonly used class was the macrolides, in 43%, followed by the fluoroquinolones, in about 29%. During the study period, macrolide use was flat, but fluoroquinolone use jumped from 21% in 2001 to 32% in 2002 and 35% in 2003. During the same time, use of  $\beta$ -lactamase inhibitor agents dropped from 15% of prescriptions for this indication in 2001 to 2% in 2003. ■

## Primary Care Survey Shows Antibiotic Overprescribing Still a Problem

BY DEEANNA FRANKLIN  
Senior Writer

WASHINGTON — Physicians understand that overuse of antibiotics is contributing to rising resistance rates, yet a large minority continue to prescribe antibiotics for viral illnesses, Mohamad G. Fakih, M.D., reported in a poster presentation at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

Dr. Fakih and his colleagues approached primary care physician members of Blue Cross Blue Shield of Michigan in four separate regions of the state, and 277 physicians out of a total of 875 completed surveys. Among the respondents, 73 were pediatricians, 126 were family physicians, and 58 were internists. They were questioned on age; specialty; years and type of practice; geographic region; views regarding their education, medical knowledge, and management of upper respiratory infections (URIs); antibiotic use and resistance; and patient expectations.

Regarding their management of URIs, 75% of family physicians, 81% of internists, and 90% of pediatricians felt very secure in rating their knowledge at above average to excellent.

When queried about their treatment approach for URI with pharyngitis, with or without exudates and/or lymphadenopathy, internists were more likely than were family physicians and pediatricians to prescribe antibiotics when more symptoms were present.

Among doctors practicing for less than 10 years, 43% believed that managed care affected their choice of antibiotics, compared with 24% of physicians practicing more than 10 years who felt this way. Also, physicians practicing 10 years or less were more likely to believe patients were satisfied once they were given an antibiotic prescription (57% vs. 41%).

Antibiotic prescribing appeared to hinge on symptoms. Physicians offered antibiotics to more symptomatic patients, with 89% of them using diagnostic tests, such as a rapid antigen detection test or culture, said Dr. Fakih, an infectious diseases specialist at St. John Hospital and Medical Center, Detroit.

"Physicians agreed that overuse of antibiotics is the major factor in increasing resistance; however, more than half of them would give an antibiotic when the diagnosis is not certain," the researchers said.

A big surprise in the study was that 55% of those surveyed thought that penicillin resistance to group A streptococci was emerging. "There has never been any evidence of resistance to penicillin," Dr. Fakih told this newspaper.

He could not explain the regional prescribing variances, but suggested that differences in education or in patient populations might be involved. There were significant differences in knowledge of URI depending on region, with more antibiotic prescribing for viral symptoms in more populous areas. But demanding patients aren't the only factor; "physicians need to be educated. We can't blame it on the patients," he said. ■