In the Literature

Tigecycline Treatment for Patients with Complicated Skin and Skin Structure Infections (SSTIs)


Adults with complicated SSTIs were randomized in this multicenter, international, double-blind, noninferiority trial to receive either vancomycin (1 g intravenously [iv] every 12 h) plus aztreonam (2 g iv every 12 h) or tigecycline (a 100-mg iv loading dose, followed by 50 mg iv every 12 h) plus a placebo. The predetermined acceptable lower limit of the 2-sided 95% CI for the difference was −15%, and the study had a power of ≥90% for the determination of noninferiority. A primary end point was clinical response at the test-of-cure visit, which occurred 12–92 days after the end of therapy in the modified intent-to-treat (m-mITT) population (who received at least 1 dose of the study drug), who met entry clinical criteria for SSTI.

Another primary end point was clinical cure in the clinically evaluable population, which comprised patients in the c-mITT population who did not have a monomicrobial eradication of the adequacy of source control, a critical factor in determining the outcome of intra-abdominal infections. Nonetheless, tigecycline appears to be an effective agent for patients with complicated intra-abdominal infections. The major downside

Tigecycline Treatment for Patients with Complicated Intra-abdominal Infection


Adults with complicated intra-abdominal infections were randomized in this multicenter, international, double-blind, noninferiority trial to receive either imipenem-cilastatin (500 mg iv every 6 h) or tigecycline (a 100-mg loading dose, followed by 50 mg iv every 12 h). The predetermind acceptable lower limit of the 2-sided 95% CI for the difference was −15%, and the study had a power of ≥90% for the determination of noninferiority. The primary end points were clinical response at the test-of-cure visit 4–35 days after the end of therapy in both the microbiologically-modified intent to treat population (m-mITT; defined as patients

with an isolate at baseline who received at least 1 dose of the study drug) and in the microbiologically evaluable population subset of the m-mITT population. The latter comprised patients in the m-mITT population who had a positive culture result at baseline, with at least 1 isolate susceptible to both study drugs, and who received ≥5 days of therapy without use of any additional nonstudy antibiotics through their test of cure visit.

Approximately 60% of patients had complicated appendicitis; only 8.8% had a perforated intestine (whether it involved the small or large bowel is not specified). The clinical cure rate in the 502 microbiologically evaluable patients was 80.6% among tigecycline recipients and 82.4% among imipenem-cilastatin recipients, whereas the rates were 73.5% and 78.2%, respectively, among the 621 m-mITT patients. Neither comparison yielded a statistically significant difference, and noninferiority was inferred. Microbiological eradication was achieved for 80.6% of tigecycline recipients and 82.4% of imipenem-cilastatin recipients. Microbiological response rates were comparable for individual pathogens, although the small numbers of some individual pathogens present make it difficult to come to any conclusions.

Adverse events involving the gastrointestinal tract (i.e., nausea, vomiting, and diarrhea) occurred in 56.9% of tigecycline recipients and 49.8% of imipenem-cilastatin recipients (P = .043). Discontinuation of assigned therapy associated with drug-related adverse events occurred in 6.5% and 3.6% of patients, respectively (P = .80).

A potentially important issue with this study is the lack of a formal assessment of the adequacy of source control, a critical factor in determining the outcome of intra-abdominal infections. Nonetheless, tigecycline appears to be an effective agent for patients with complicated intra-abdominal infections. The major downside
to the drug is the high frequency of associated nausea and vomiting.

Antibody Testing for Herpes Simplex Virus (HSV) Type 2 (HSV-2)


In a proficiency testing exercise, the College of American Pathologists sent a serum sample that had tested positive for HSV type 1 (HSV-1) antibodies but negative for HSV-2 antibodies to 172 participating laboratories. Although nearly all of the laboratories correctly identified the presence of antibody to HSV-1, more than one-half incorrectly reported the presence of antibody to HSV-2. False-positive HSV-2 antibody test results were reported by 47.7% of laboratories that used an EIA and by 88.5% that used other methods. Of the 94 laboratories that indicated the test manufacturer, 44 used a HSV glycoprotein G–based EIA, and these laboratories reported no false-positive results for HSV-2 antibody. Thus, all of the false-positive results occurred with assays using an antigen other than glycoprotein G.

The dismal results with assays that are not based on glycoprotein G are the result of significant antigenic cross-reactivity between the 2 types of HSV. As a consequence, it has previously been recommended that only type-specific antibody tests be used. Often, however, in the current environment of managed care and hospital contracts with outside laboratories, the clinician has little or no control over what type of testing is performed and may even have difficulty learning the details of the testing from the outside laboratory.

Another problem is the widespread use of IgM antibody tests for the diagnosis of recent HSV infection. Morrow and colleagues point out that there are no commercially available IgM antibody tests that are specific for glycoprotein G. Furthermore, even when such tests are used, their sensitivity for a proven first episode of genital HSV-2 infection is only ~50%; in addition, more than one-third of individuals with recent HSV-2 infection have detectable IgM antibody to glycoprotein G. Finally, recurrent orolabial episodes of HSV-2 infection can be associated with IgM antibody that is cross-reactive with HSV-2.

All of this would be less important if not for the social, emotional, and sometimes legal baggage associated with a diagnosis of genital HSV-2 infection. The final lesson for the clinician is to insist on use of IgG antibody tests for HSV-2 that are specific for glycoprotein G and to discount the results of IgM antibody tests.

Is the Administration of >1 Antibiotic Associated with Improved Survival in Patients with Pneumococcal Sepsis?


Several recent retrospective studies have concluded that administration of antibiotics in combination is associated with improved survival rates among patients with bacteremic or nonbacteremic pneumococcal pneumonia, compared with administration of a single agent [1]. Whether these results are a reflection of a true therapeutic effect or of some as-yet unrecognized confounding factor that leads clinicians to choose one or the other form of therapy is unclear.

In this study, the records for patients with microbiologic evidence of invasive Streptococcus pneumoniae infection who were extracted from a database of patients who had been enrolled in 2 placebo-controlled trials of anti-TNF in the treatment of severe sepsis or septic shock. The intervention had no effect on mortality, allowing examination of other interventions across the entire database of 1840 patients.

The choice of antibiotic therapy was not specified in the protocol. Of 107 patients with monomicrobial pneumococcal sepsis (75 of whom had bacteremia), 25 (23%) received monotherapy, usually with a β-lactam, whereas 77 (77%) were given combination therapy. The combinations chosen were highly variable: only 34 received a β-lactam together with a macrolide, whereas another 11 received a β-lactam plus clindamycin, and 6 patients received a regimen that included a fluoroquinolone.

The mortality rate was 20% in each group. Analysis of the 75 bacteremic patients revealed mortality rates of 12.5% and 20.3% in the monotherapy and combination therapy arms, respectively. Among those who received a cephalosporin, either as monotherapy or as part of a combination regimen, the mortality rates were 15.9% and 16.7%, respectively.

Although this analysis was retrospective, the clinical and laboratory data were collected prospectively, and the level of care was uniform. Unfortunately, the antibiotic therapy was not uniform. In addition, the number of patients was insufficient to provide robust power to the study. Nonetheless, although this analysis does not definitively answer the question posed, it does provide sufficient contrary data to make the previous observations suspect.

At least 2 recent systematic reviews have concluded that, with regard to empirical therapy given to patients with community-acquired pneumonia, combination therapy fails to demonstrate a benefit significantly greater than that of monotherapy [2, 3], except for a subset of patients with legionellosis [2]. Of note is that, unlike previous reports, these reviews included studies in which respiratory fluoroquinolones were given as monotherapy.

References