CLINICAL CAPSULES

Risks of Episodic HIV Therapy

A large, international HIV-1 trial was stopped prematurely because patients who received episodic antiretroviral therapy had more than twice the risk of disease progression and a higher rate of major complications as those who received continuous antiretroviral therapy, according to the National Institute of Allergy and Infectious Diseases.

The NIAID originally started the trial because the results of smaller studies had suggested that episodic use of antiretroviral therapy (ART) would yield a rate of progression to clinical AIDS or death that was lower than or similar to that of patients who received continuous ART. It was thought that patients who received episodic ART would have fewer drug side effects, lower costs, and more treatment options in the future because of less viral resistance.

When the Data and Safety Monitoring Board of the NIAID halted the trial on January 11, a total of 5,472 patients had been randomized to one of two groups. One group received continuous ART to suppress HIV viral load. A drug-conservation strategy was used in the other group: These patients received ART only when their level of CD4-positive cells dropped below 250 cells/mm^3, and they stopped ART when their CD4-positive level rose above 350 cells/mm^3.

The trial involved a collaboration of 318 clinical centers in 33 countries. Most patients were from the United States (55%) and European countries (26%). Overseers of the trial told local study investigators that patients in the drug-conservation arm who had received ART in the past should restart ART if they were not already taking it. Investigators will continue to collect data on all patients at follow-up visits.

Sustiva-Viread-Emtriva Combo for HIV

Combination therapy with Sustiva, Viread, and Emtriva was superior to combined Sustiva and Combivir for treating HIV in treatment-naive patients enrolled in a phase III trial.

The prospective, 67-site, noninferiority trial included 517 patients randomized to receive once-daily Sustiva (600 mg efavirenz), Viread (300 mg tenofovir DF), and Emtriva (200 mg emtricitabine) or Sustiva (600 mg) once daily and a fixed dose of Combivir (300 mg zidovudine and 150 mg lamivudine). At 48 weeks, significantly more patients in the Sustiva-Viread-Emtriva group, compared with the Sustiva-Combivir group, reached and maintained HIV RNA levels of fewer than 400 copies/mL (84% vs. 73%), and fewer than 50 copies/mL (80% vs. 70%), reported Dr. Joel E. Gallant of Johns Hopkins University, Baltimore, and his colleagues.

CD4 counts also increased significantly more from baseline in the Sustiva-Viread-Emtriva group (mean increases of 190 cells/μL vs. 158 cells/μL), and fewer patients in that group had adverse events leading to treatment discontinuation (4% vs. 9%), the investigators noted (N. Engl. J. Med. 2006;354:251-60).

Both regimens used in this study are listed in treatment guidelines from the Department of Health and Human Services as "preferred" for managing HIV infection.

Gilead Sciences, which makes Viread and Emtriva, and Bristol-Myers Squibb Co., which makes Sustiva, are working together to develop a once-daily pill combining all three drugs, and in January announced plans to file a new drug application in the second quarter of this year.

Fluoroquinolones Common in Hospitals

About 60% of hospitalized adult patients receive at least one antimicrobial agent during their hospital stays, reported Dr. Conan MacDougall and his colleagues in a poster presented at the annual meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy.

Fluoroquinolones were the most commonly administered agents, followed by cephalosporins, in an analysis of 1,798,084 patients at 130 hospitals, said Dr. MacDougall of Virginia Commonwealth University, Richmond, and his colleagues.

The study was conducted between August 2002 and July 2003. Most of the study hospitals were in the southern and northern central United States, with an average bed size of 288; 115 of the hospitals were nonteaching facilities.

Greater use of antibacterial agents was associated with a higher case-mix index, more ICU patient-days per 1,000 patient-days, more cases of pneumonia and septicemia per 1,000 patient-days, and being located in the southern United States. Neither bed size nor hospital teaching status was a significant predictor of antibacterial use.

Overall, the average use rate for any antibacterial agent (total antibacterials) was 790 days of therapy per 1,000 patient-days. The average use rate for the most commonly used individual agent, levofloxacin, was 122 days of therapy per 1,000 patient-days. Cefazolin was the next most popular agent, averaging 94 therapy days per 1,000 patient-days.

—From staff reports