Guidelines Endorse Earlier Treatment of HIV

BY JEFF EVANS
Senior Writer

Initial antiretroviral treatment of HIV infection in asymptomatic adults should begin before CD4 cell counts drop below 350/mcL, according to new treatment guidelines announced at the 2008 International AIDS Conference in Mexico City.

The guidelines, issued by the International AIDS Society–USA Panel, update 2006 recommendations. The change reflects improvements in drug pharmacokinetics and treatment response, as well as the need to stem increases in the relative burden of diseases that are not traditionally associated with HIV infection, such as non-AIDS cancers and end-organ damage (JAMA 2008;300:555-70).

Updates to the 2006 guidelines were necessary because of the Food and Drug Administration's approval of several new antiretroviral drugs as well as the availability of new data to use in choosing drugs for initial therapy and managing treatment failure, according to the panel.

More than 30 individual antiretroviral agents and fixed-dose combinations have been approved by the Food and Drug Administration since the first antiretroviral drug was approved 21 years ago, Dr. Scott M. Hammer, chair of the IAS-USA panel, said at a media briefing on HIV/AIDS sponsored by JAMA.

The 14-member panel emphasized that the guidelines are most applicable to "developed and selected mid-level economies," but that their core principle—"pathogenesis-directed therapy with regimens designed to achieve full virologic suppression with minimal toxicity and maximal simplicity"—also is relevant to the developing world.

The specific time at which antiretroviral treatment should begin in asymptomatic adults should be based on comorbidities, risk of disease progression, and patient willingness and ability to adhere to long-term treatment. Early treatment of asymptomatic individuals is favorable when there is a rapid decline in CD4 cell count; plasma HIV-1 RNA level is greater than 100,000 copies/mL; and in the presence of active hepatitis B or C, HIV-associated nephropathy, or cardiovascular disease risk factors.

The core principle is 'pathogenesis-directed therapy with regimens designed to achieve full virologic suppression with minimal toxicity.'

"There is no upper CD4 cell limit for starting therapy when 1 or more of these considerations are present," the panelists wrote, although "no definitive evidence has emerged that supports routine initiation of antiretroviral therapy in primary HIV infection."

Dr. Hammer, chief of the division of infectious diseases at Columbia University, New York, commented that "we've had cutoffs because it's convenient for guidelines. It has been convenient to look at cohort studies and very convenient for randomized, controlled trials. But there is no difference in a patient with a CD4 count of 360 and 340 or 210 and 190."

The guidelines advocate initial treatment regimens that consist of two nucleoside reverse transcriptase inhibitors (NRTIs) plus either the non-nucleoside reverse transcriptase inhibitor (NNRTI) efavirenz or a ritonavir-boosted protease inhibitor (PI/r).

The guidelines advise a treatment goal of less than 50 copies/mL of HIV-1 RNA. Until the viral load is suppressed, its levels should be monitored—along with CD4 cell count—at 2, 4, and 8 weeks and every 4 weeks thereafter until the concentration drops below the assay detection limits. Afterward, the viral load and CD4 cell count can be assessed every 3-4 months. Cell count monitoring can be reduced to every 6 months when measurements are consistently at levels of at least 350/mcL. Comorbidity and toxicity assessment should occur before and throughout treatment.

Genotypic testing for resistance is necessary in all treatment-naive patients. In addition, it should be considered whenever a new treatment regimen is introduced if the trajectory of viral load reduction is not optimal, the panel recommended.

Many of the panel members disclosed financial ties to multiple manufacturers of antiretroviral drugs, including the manufacturers of maraviroc (Pfizer Inc.), raltegravir (Merck & Co.), and etravirine (Tibotec). ■