Efavirenz-Based Tx Better at Reducing Viral Load

The best regimen was efavirenz plus two nucleosides for initial treatment, even in advanced HIV disease.

ARTICLES BY FRAN LOWRY
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TORONTO — A large, randomized comparison of three standard regimens for the initial treatment of HIV has demonstrated that all three are safe and effective, but a regimen of efavirenz plus two nucleosides was significantly better at reducing HIV viral load, investigators reported at the 16th International AIDS Conference.

The regimens for first-line therapy of HIV that are currently recommended by the Department of Health and Human Services are the protease inhibitor lopinavir and the nonnucleoside reverse transcriptase inhibitor efavirenz, each given with two nucleoside reverse transcriptase inhibitors.

However, these regimens have not been compared in adequately powered, randomized clinical trials. Nor has the nucleoside-sparing regimen of efavirenz plus lopinavir, said Dr. Sharon A. Riddler, of the University of Pittsburgh, in a late-breaking clinical trial session.

Dr. Riddler and her coinvestigators of the open-label, prospective AIDS Clinical Trials Group (ACTG) 5142 study compared these three regimens in 753 naive subjects with HIV RNA greater than 2,000 copies/mL and any CD4 cell count. Participants were randomized equally to one of three arms: lopinavir soft gel capsules plus two nucleosides, efavirenz plus two nucleosides, and lopinavir soft gel capsules plus efavirenz.

With a median follow-up of 112 weeks, the time to virologic failure was significantly shorter in the lopinavir plus two nucleosides arm, compared with the efavirenz plus two nucleosides arm. At week 96, the proportion of subjects without virologic failure was 76% for those in the efavirenz plus two nucleosides arm, 74% for lopinavir plus efavirenz, and 67% for lopinavir plus two nucleosides, Dr. Riddler reported.

"Our findings suggest that the efavirenz plus two nucleosides was the best of the three approaches as initial therapy, even in patients with relatively advanced HIV disease," she said.

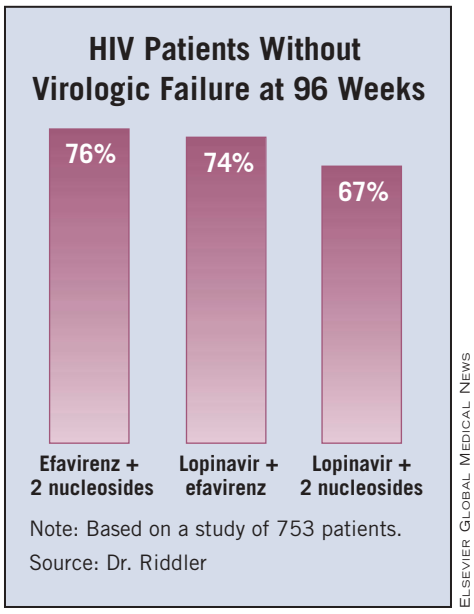
However, she cautioned that the study is undergoing further analysis and that the results are still preliminary.

"The main message from this study is that it is an incremental step toward understanding the most useful regimens to be used for initial therapy in HIV-infected individuals," Dr. Riddler said in an interview.

"All of the three regimens were effective, with significant increases in CD4 cell counts and the vast majority of individuals having undetectable viral loads, regardless of which regimen was initiated," he continued.

"ACTG 5142 is a very important study," said Dr. Scott M. Hammer, professor of medicine at Columbia University, New York, and an ACTG investigator. "It's the first study to look at these three standard-of-care regimens in naive individuals randomized upfront, and the data are important for how we actually tease out a lopinavir-based regimen compared to an efavirenz-based regimen.

"The results may change or reinforce our standards of care, but they are definitely going to influence them," Dr. Hammer concluded. ■



ELSEVIER GLOBAL MEDICAL NEWS

New Agents Raise the Treatment Standard for Drug-Resistant HIV

TORONTO — The new goal of therapy for HIV-infected adults who have repeatedly failed several drug regimens should be to decrease their viral load to undetectable levels with new drug regimens, according to updated guidelines announced at the 16th International AIDS Conference.

"The management of highly treatment-experienced individuals who are experiencing their third, fourth, or even fifth failure with multidrug-resistant virus and three-class drug experience now includes the use of appropriate new drug regimens which can reduce their viral load to under 50 copies of HIV RNA per milliliter of blood," Dr. Scott M. Hammer, Harold C. Neu Professor of Medicine, professor of epidemiology, and chief of the division of infectious diseases at Columbia University Medical Center, New York, said in an interview.

'Our first attempt is to really drive their virus down to undetectable levels, and that's a new era.'

DR. HAMMER

In the past, clinicians used to settle for CD4+ cell counts in a higher range. "While we still have to settle for that in some individuals, our first attempt is to really drive their virus down to undetectable levels, and that's a new era," said Dr. Hammer, lead author of the new guidelines issued by the International AIDS Society–USA Panel.

He estimated that as many as two-thirds of HIV-infected individuals who are refractory to current regimens can benefit from the newer drugs that have emerged since the panel published its last guidelines 2 years ago.

"The approval of the protease inhibitor darunavir and the fusion inhibitor enfuviritide … can give us a good chance of reducing our patients' viral load to under 50 copies, especially when combined with other agents," he said.

The International AIDS Society–USA Panel, which is not related to the International AIDS Society, is made up of 16 members who represent countries in the developed world. The panel's recommendations are geared for areas where there is no restriction of resources to treat AIDS, and were derived after a review of data published or presented at scientific conferences from mid 2004 through May 2006.

Other key AIDS-USA recommendations include:

► Treatment in symptomatic and asymptomatic patients when CD4 cell count falls below 350/μL but before it declines to 200/μL.

► Initial regimen remains a combination of two nucleoside (or nucleotide) reverse transcriptase inhibitors (nRTIs) with either a nonnucleoside reverse transcriptase inhibitor (NNRTI) or a protease inhibitor (PI) with low-dose ritonavir.

► Choice of therapy should be based on the individual patient profile.

► Therapy should be changed when toxicity, intolerance, or documented treatment failure occurs.

► Adherence to therapy in both the short and long term is crucial for treatment success and must be continually reinforced.

The 2006 Recommendations of the International AIDS Society–USA Panel were published in the Journal of the American Medical Association (JAMA 2006;296:827-43). ■

Older Patients Beat Younger Ones on HAART Compliance

TORONTO — With age comes enhanced adherence to HIV therapy, according to results of a study presented at the 16th International AIDS Conference.

Michael J. Silverberg, Ph.D., of Kaiser Permanente's Division of Research, Oakland, Calif., and his associates took a prospective look at approximately 5,000 patients in their registry from 1995 to 2004. Of those, 1,000 were aged 50 years or older. All patients were in the Kaiser Permanente Northern California health plan for the 6 months prior to antiretroviral therapy.

Older patients were also 15% more likely to reach undetectable levels of HIV infection and had higher CD4 counts.

DR. SILVERBERG

The investigators found that subjects over the age of 50 were more adherent to highly active antiretroviral therapy (HAART)—a cocktail of a protease inhibitor plus two reverse transcriptase inhibitors—than were younger individuals.

As a result, they were 15% more likely to reach undetectable levels of HIV infection and had higher CD4 counts after 3 years of HAART therapy than did their younger counterparts, Dr. Silverberg said. These good results were entirely due to their excellent adherence, he added.

Patients older than 50 years were more likely to achieve HIV RNA levels of less than 500 copies/mL; and, like patients aged 40-49 years, they had a blunted immune response in the first year of therapy. That response was compensated for, however, by faster subsequent increases in CD4 cell counts compared with those of patients aged 18-39, Dr. Silverberg reported.

Older patients were more likely to have more comorbidities such as metabolic syndrome, abnormal blood lipids, and heart disease, which was linked to a higher first-year incidence of laboratory abnormalities, he said. In addition, antiretroviral therapy was associated with reduced tolerability of the drugs.

Laboratory abnormalities frequently seen after initiation of HAART in older individuals included hyperglycemia, abnormal bilirubin, neutrophil, ALT and AST levels, and raised creatinine.

"Because of these abnormalities, we feel that older patients need particularly close monitoring, especially at the beginning of their therapy," Dr. Silverberg said. "However, they do quite well. Some of the patients were quite a bit older than 50, and the oldest was in his 70s. I guess with age, people become more disciplined with their treatment," he added. ■