# Efavirenz plus zidovudine and lamivudine was more effective than indinavir plus zidovudine and lamivudine in adults with HIV-1 infection

Staszewski S, Morales-Ramirez J, Tashima KT, et al., for the Study 006 Team. **Efavirenz plus zidovudine and lamivudine, efavirenz plus indinavir, and indinavir plus zidovudine and lamivudine in the treatment of HIV-1 infection in adults.** N Engl J Med. 1999 Dec 16;341:1865-73.

## QUESTION

Are drug regimens containing a combination of efavirenz, zidovudine, and lamivudine or a combination of efavirenz and indinavir as effective and safe as a combination of indinavir, zidovudine, and lamivudine for adults with HIV-1 infection?

## DESIGN

Randomized {allocation concealed*}†, blinded (outcome assessor),* controlled trial with follow-up at 48 weeks.

## SETTING

34 sites in the United States, Europe, and Canada.

## PATIENTS

450 patients > 13 years of age (mean age 36 y, 86% men) who had laboratory evidence of HIV-1 infection, CD4+ cell count > 50 cells/mm$^3$, and plasma HIV-1 RNA level > 10 000 copies/mL. Follow-up was 90%.

## INTERVENTION

148 patients were allocated to open-label efavirenz, 600 mg/d, plus indinavir, 1000 mg every 8 hours (EI); 154 were allocated to efavirenz, 600 mg/d, plus zidovudine, 300 mg twice daily, and lamivudine, 150 mg twice daily (EZL); and 148 were allocated to indinavir, 800 mg every 8 hours, plus zidovudine, 300 mg twice daily, and lamivudine, 150 mg twice daily (IZL).

## MAIN OUTCOME MEASURES

The main outcome was the percentage of patients with suppression of plasma HIV-1 RNA to < 400 copies/mL at 48 weeks (standard assay). Secondary outcomes included the percentage of patients with suppression of plasma HIV-1 RNA to < 50 copies/mL (ultrasensitive assay) and the percentage of patients who discontinued therapy because of adverse effects.

## MAIN RESULTS

Intention-to-treat analysis showed that the EZL group had a higher rate of suppression of plasma HIV-1 RNA to < 400 copies/mL and to < 50 copies/mL than did the IZL group ($P < 0.05$) (Table); the EI and IZL groups did not differ. The EI and EZL groups had lower rates of discontinuation as a result of adverse effects than did the IZL group ($P < 0.001$).

## CONCLUSION

A regimen of efavirenz plus zidovudine and lamivudine had greater antiviral activity and was better tolerated than was a regimen of indinavir plus zidovudine and lamivudine in adults with HIV-1 infection.

*Source of funding: Dupont Pharmaceuticals.*

*For correspondence: Dr. D.J. Manion, Dupont Pharmaceuticals Company, Chestnut Run Plaza, Room HR 2003, 974 Centre Road, Wilmington, DE 19805, USA. FAX 302-892-8545.* ■

*See Glossary.

†Information provided by author.

**Efavirenz plus zidovudine and lamivudine (EZL) vs indinavir plus zidovudine and lamivudine (IZL) for HIV-1 infection in adults at 48 weeks‡**

| Level of suppression of plasma HIV-1 RNA | EZL | IZL | RBI (95% CI) | NNT (CI) |
|---|---|---|---|---|
| < 400 copies/mL | 70% | 48% | 46% (20 to 79) | 5 (4 to 10) |
| < 50 copies/mL | 64% | 43% | 49% (20 to 87) | 5 (4 to 11) |

‡Abbreviations defined in Glossary; RBI, NNT, and CI calculated from data in article.

## COMMENTARY

During the past few years, major changes have occurred in the management of HIV disease owing to an ongoing search for more effective and patient-friendly drug regimens. A desirable regimen should reduce plasma viral load to undetectable levels regardless of baseline, be easy to take, and have minimal side effects. Highly active antiretroviral therapy, which comprises ≥ 3 antiretroviral drugs, should reduce virus levels below the limits of detection in previously untreated patients with HIV infection. Some evidence suggests that these regimens may reduce the incidence of AIDS-related events (1–3).

In this multicenter, randomized study, Staszewski and colleagues compared 2 regimens containing efavirenz with a standard regimen. The intention-to-treat analysis showed that the absolute proportion of patients with viral loads < 400 HIV-1-RNA copies/mL was approximately 20% higher in patients who received the EZL combination than in those who received the IZL combination. Efficacy was confirmed by similar results obtained by using an ultrasensitive assay after stratification for baseline viral loads. The EZL regimen had fewer side effects.

The study supports the use of drug combinations containing efavirenz as a first-line therapy. It appears to be more effective and better tolerated, and fewer doses are required. A double-blind study would have been even more convincing, but as the authors point out, such a design would have required a complex dosing schedule that might have affected patient compliance and safety.

*Evelyn V. Hess, MD*
*University of Cincinnati Medical Center*
*Cincinnati, Ohio, USA*

***References***

1. **Sparano JA, Anand K, Desai J, et al.** Effect of highly active antiretroviral therapy on the incidence of HIV-associated malignancies at an urban medical center. J Acquir Immune Defic Syndr. 1999;21:S18-22.
2. **Miralles P, Berenguer J, Garcia de Viedma D, et al.** Treatment of AIDS-associated progressive multifocal leukoencephalopathy with highly active antiretroviral therapy. AIDS. 1998;12:2467-72.
3. **Shafer RW, Vuitton DA.** Highly active antiretroviral therapy (HAART) for the treatment of infection with human immunodeficiency virus type 1. Biomed Pharmacother. 1999;53:73-86.