Fewer Side Effects with Videx/Epivir vs. Combivir

March 1, 2007 By Tim Horn

A team of Spanish researchers is finding that, when combined with Sustiva® (efavirenz), Videx® EC (didanosine capsules) matched with Epivir® results in fewer treatment discontinuations due to side effects than Combivir® (zidovudine plus lamivudine). The 24-week data from the 48-week GESIDA 3903 study also suggest that once-daily Sustiva/Videx/Epivir is comparable to Sustiva/Combivir with respect to viral load outcomes, with a possible CD4 cell count advantage.

According to the U.S. Department of Health and Human Services, in its Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents, only Combivir and Truvada (tenofovir plus emtricitabine) are considered "preferred" nucleoside reverse transcriptase inhibitors (NRTIs) to combine with either a non-nucleoside reverse transcriptase inhibitor (NNRTI) or a protease inhibitor (PI) for HIV-positive patients starting therapy for the first time. Videx EC combined with Epivir, prescribed separately but approved for once-daily use, is an "alternative" DHHS recommendation. The reason for the more limited support of Videx EC and Epivir as a possible NRTI "backbone" to combine with suggested NNRTIs and PIs is a lack of data comparing this dual-NRTI combo to current leading NRTI pairings (e.g., Combivir).

GESIDA 3903 randomized 369 HIV-positive patients, none of whom had used antiretroviral therapy in the past, to Videx EC (400 mg) and Epivir (300 mg) once daily or Combivir twice daily, with both NRTI pairings taken with a standard dose of Sustiva (600 mg).

The average viral load at study entry was 100,000 copies and the average CD4 count was approximately 210. Approximately 7% of patients in the Videx/Epivir group and 3% of patients in the Combivir group had chronic hepatitis B virus infection; approximately 20% in both groups had active hepatitis C virus infection.

In the strict intent-to-treat analysis, which included everyone enrolled in the study even if they discontinued their treatment due to limited effectiveness or side effects, 71% of those in the Videx/Epivir group and 66% of those in the Combivir group had viral loads below 50 copies (undetectable) after 24 weeks. In the more liberal on-treatment analysis, which only included the patients who completed 24 weeks of treatment, 82% of those in the Videx/Epivir group and 85% of those in the Combivir group had undetectable viral loads.

The differences between the two groups with respect to undetectable viral loads at week 24, in the intent-to-treat and on-treatment analysis, were not statistically significant, meaning they could

have been due to chance.

CD4 count gains were significantly greater in the Videx/Epivir group compared to the Combivir group. After 24 weeks, CD4 counts increased by an average of 128 cells (compared to study entry numbers) in the Videx/Epivir group, compared to a 110 CD4 cell count increase in the Combivir group. This difference – along with differences in CD4 cell count increases at week 4 and 12 – were statistically significant.

As for side effects, significantly more patients in the Combivir group (21%) discontinued treatment early due to side effects, compared to those in the Videx/Epivir group (13%). Hematologic problems requiring treatment discontinuation, notably anemia and neutropenia, were much more common among those taking Combivir (6%) compared to Videx/EC (0.5%).

There were no statistically significant differences between the two groups with respect to moderate-to-severe side effects like rash and central nervous system problems (caused by Sustiva), liver enzyme increases, or lipid (blood fat) level increases.

While these data are encouraging and support the use of Videx combined with Epivir as a worthy NRTI backbone pairing among patients starting therapy for the first time, the full 48-week data are required to draw any firm conclusions.

Source:

Berenguer J, Ribera E, Domingo P, et al. Didanosine, lamivudine, and efavirenz vs zidovudine, lamivudine, and efavirenz, for initial treatment of HIV infection: planned 24-week analysis of a prospective randomized non-inferiority clinical trial, GESIDA 39/03 [Abstract 504]. 14th Conference on Retroviruses and Opportunistic Infections, Los Angeles, 2007.
