A placebo-controlled trial of didanosine plus stavudine, with and without hydroxyurea, for HIV infection. The Swiss HIV Cohort Study

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OBJECTIVE: To explore the short-term effects on surrogate markers for HIV progression of didanosine (d4T) plus stavudine (d4T), with or without hydroxyurea. DESIGN: Randomized, double-blinded, prospective study. SETTING: Swiss HIV Cohort Study. PATIENTS: A total of 144 patients (75% antiretroviral-naive) were studied (mean baseline HIV-1 RNA, 4.53 log10 copies/ml; mean CD4 cell count, 370 x 10(6)/l). INTERVENTION: Patients received d4T (200 mg twice daily) plus d4T (40 mg twice daily), with additional hydroxyurea (500 mg twice daily) or placebo. MAIN OUTCOME MEASURES: The primary endpoint was a reduction of viraemia below 200 copies/ml after 12 weeks. At that time, patients who did not reach the primary endpoint were withdrawn in the hydroxyurea arm, whereas patients in the placebo group had the option of adding hydroxyurea to d4T and d4T. All patients were followed until week 24. RESULTS: After 12 weeks, 54% of the patients randomized to hydroxyurea had viraemia below 200 copies/ml, compared with 28% on placebo (P < 0.001). Using an ultrasensitive assay with a limit of detection of 20 copies/ml, 19% of patients receiving hydroxyurea had viraemia levels below 20 copies/ml, compared with 8% on placebo (P = 0.05). Mean decrease in HIV-1 RNA was 2.3 and 1.7 log10 copies/ml for hydroxyurea and placebo groups, respectively (P = 0.001). Hydroxyurea was found to induce lymphopenia (-124 x 10(6)/l). Increase in CD4 cell counts was +28 x 10(6)/l during hydroxyurea treatment compared with +107 x 10(6)/l on placebo (P = 0.001). CONCLUSIONS: Hydroxyurea improved the antiviral activity of d4T and d4T over a 12-week period, but was associated with a smaller increase in CD4 cell counts due to hydroxyurea-induced lymphopenia.

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