Dynamics of viral load rebound and immunological changes after stopping effective antiretroviral therapy

García, Felipe; Plana, Montserrat; Vidal, Carmen; Cruceta, Anna; O'Brien, William A.; Pantaleo, Giuseppe; Pumarola, Tomás; Gallart, Teresa; Miró, José M.; Gatell, José M.

ABSTRACT

Background: This study addresses the dynamic of viral load rebound and immune system changes in a cohort of eight consecutive HIV-1-infected patients in very early stages [all the patients were taking highly active antiretroviral therapy (HAART) and were recruited in the coordinating center from a larger study] who decided to discontinue HAART after 1 year of treatment and effective virologic response. The safety of this procedure and the outcome with reintroduction of the same treatment was also investigated.

Methods: Plasma, cerebrospinal fluid (CSF), and lymphatic tissue viral loads were measured at baseline; lymphocyte immunophenotyping and CD4 lymphocyte proliferative responses to mitogens and specific antigens were assessed. The same antiretroviral therapy was reintroduced as soon as plasma viral load became detectable (above 200 copies/ml).

Results: At day 0, plasma viral load was below 20 copies/ml in all eight patients (and below 5 copies/ml in five of eight patients). A rebound in plasma viral load was detected in all patients from day 3 to day 31 with a mean doubling time of 2.01 (SE 0.29) days. Three out of eight patients achieved a peak plasma viral load at least 0.5 log10 above baseline, pretreatment values. Mutations associated with resistance to reverse transcriptase or protease inhibitors were not detected. After 31 days off therapy, CD4 lymphocytes decreased [mean 45% (SE 4) to 37% (SE 3); P=0.04], CD8+CD28+ lymphocytes decreased [mean 59% (SE 5) to 43% (SE 4); P=0.03], and CD8+CD38+ lymphocytes increased [mean 55% (SE 3) to 66% (SE 4); P=0.009]. Mean stimulation indices of lymphocytes treated with phytohemagglutinin (PHA) and CD3 decreased from day 0 to day 31 from 34% (SE 8) to 17% (SE 9) (P=0.06) and from 24% (SE 8) to 5% (SE 2) (P=0.02), respectively. These changes were mainly contributed by the group of five patients with plasma viral load below 5 copies/ml at day 0. Viral load dropped below 20 copies/ml in all patients after 1 month of restarting the same antiretroviral regimen.

Conclusions: Discontinuation of HAART after 1 year of successful treatment is followed by a rapid rebound of viral load; this rapidly returns to undetectable levels following reintroduction of the same treatment. In patients with more effective control of virus replication (viremia below 5 copies/ml), discontinuation of treatment was associated with more severe impairment of immunologic parameters.

A randomized study comparing triple versus double antiretroviral therapy or no treatment in HIV-1 infected patients in very early stage disease: the Spanish Earth-1 Study

García, Felipe; Romeu, Joan; Grau, Inmaculada; Sambeat, María Antonia; Dalmau, David; Knobel, Hernando; Gomez-Sirvent, Juan Luis; Arrizabalaga, Julio; Cruceta, Anna; Clotet, Bonaventura; Podzamczer, Daniel; Pumarola, Tomás; Gallart, Teresa; O'Brien, William A.; Miró, José M.; Gatell, José M.

ABSTRACT

Background: Most current guidelines state that antiretroviral therapy should be considered for HIV-infected patients with plasma HIV RNA > 5000-10 000 copies/ml and CD4 cells > 500 3 106 cells/l. However, there is increasing concern about whether this is the optimal point to begin treatment or whether it is better to delay the initiation to more advanced stages.

Objective: To study the immunological and virological benefits of starting antiretroviral therapy at these early stages.