Long-term non-progressors and elite controllers

PE54

Ultrastop: Is remission achievable in HIV-1 patients with low HIV DNA reservoir?

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Background: Viral remission is observed in elite controllers and post early-treatment controllers (PTCs). All share a good immune status and extremely low blood total cell-associated HIV-DNA levels. ULTRASTOP investigates whether HIV remission after ART discontinuation can be achieved in long-term HIV chronically-infected patients with good immunological status and low-level DNA.

Methods: This proof-of-concept study was designed to involve 3 cohorts of 5 patients (pts) with pVL < 50 copies (cp)/mL for >2 years on ART, CD4 > 500/mm3, CD4/CD8 > 0.9, CD4 nadir > 300/mm3 and HIV-DNA < 100 cp/106 PBMCs, selected for treatment interruption. Ultrasensitive pVL, CD4, triplicate HIV-DNA were measured at D0, W2, W4, and every 4 weeks off-ART until W48 and at W4, W12 and W24 after ART resumption (RxR). Treatment was resumed in case of pVL rebound > 400 cp/mL or CD4 < 400 cells or HIV-related clinical event. The primary endpoint was the percentage of patients who did not reach RxR criteria at W24. Enrolment in cohort 2 started, when 1/5 pts remained in success at W8. Cohort 3 did not start.

Results: Ten patients were enrolled in cohort 1, then 2, with median (min-max) duration of ART of 5.3 years (3.0-15.5), viral suppression 4.9 years (2.9-8.3), CD4 nadir 495/mm3 (330-739), baseline CD4 1118/mm3 (608-1494), CD4/CD8 2.1 (1.4-2.6), HIV-DNA 66 cp/106 PBMC (< 66-80). One patient remained off-ART at W40. Viral rebound occurred in 9/10 pts: W2 (2pts), W4 (6pts) and W12 (1pt) with CD4 counts of 745/mm3 (578-1438), pVL was resuppressed on cART (< 50 cp/ml) at W4 (8pts) and W12 (1pt) with a median of 835 CD4/mm3 (705-1326), CD4/CD8 ratio of 1.3 (1.1-2.1). In all patients from cohort 1 (cohort 2 on-going), HIV-DNA after increasing at time of rebound, returned to baseline values within 12 weeks following RxR.
Conclusions: Despite excellent immuno-virological characteristics apparently close to those of PTCs treated at primary infection, chronically-infected patients had viral rebound in a short delay. Extensive analyses of the viral and cellular dynamics are on-going. Importantly, rapid kinetics of HIV-DNA levels after ART discontinuation and RxR with return of each patient to their baseline status, suggests that the intervention with this study design has not been deleterious.