

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.

Table: Description of the 10 individuals

Pt	sART stopped	HIV DNA copies/10 ⁶ PBMC			Plasma HIV RNA copies/mL			CD4/mm ³			CD4/CDB ratio		
		Baseline	Viral rebound	RxR+W12	Baseline	Viral rebound	Last visit	Baseline	Viral rebound	Last visit	Baseline	Viral rebound	Last visit
1	TDF+FTC+RPV	33	292	77	<20	3883 W4	<20 RxR+W24	870	746	823 RxR+W24	2.08	1.94	1.39 RxR+W24
2	ETR+RAL	85	282	119	<20	496 W12	<20 RxR+W24	582	709	705 RxR+W24	2.11	0.55	1.28 RxR+W24
3	TDF+FTC	106	416	94	<20	176548 W4	<20 RxR+W24	1190	578	745 RxR+W24	1.79	1.57	1.39 RxR+W24
4	DRVr	53	1370	87	<20	1443 W2	<20 RxR+W24	1335	1388	1273 RxR+W24	2.09	2.41	2.09 RxR+W24
5	TDF+FTC+RAL	33	193	33	<20	41490 W4	<20 RxR+W24	859	690	761 RxR+W24	1.78	1.33	1.67 RxR+W24
6	TDF+FTC+MVC				<20		88 W40	915		781 W40	2.82		2.18 W40
7	TDF+FTC+DRVr				<20	544 W4	<20 RxR+W12	792	722	835 RxR+W12	1.15	1.08	1.16 RxR+W12
8	TDF+FTC				<20	1756 W4	<20 RxR+W4	1429	1438	1326 RxR+W4	1.80	1.48	1.10 RxR+W4
9	DTG				<20	59790 W4	<20 RxR+W4	1177	744	1062 RxR+W4	1.90	0.62	1.19 RxR+W4
10	ABC+3TC+ATV				<20	2125 W2	49 RxR+W4	1739	1049	1212 RxR+W4	2.00	1.81	1.20 RxR+W4

RxR: treatment resumption

[Description of the 10 individuals]

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.