

ABSTRACT

Objectives: Assess the effect of IL-2 therapy on the stock of latently HIV-infected cells, by quantifying proviral DNA in PBMC.

Methods: ANRS 079 is a randomized study of HAART +/- SC IL-2 therapy in naive (n=60) or pretreated patients (n=50). All patients who had frozen aliquots of PBMC were included in this study. PBMC were stored at -80°C until analysis. HIV RNA was quantified at baseline and at week 0, 81, 161, 241, 321, 401, 481, 561, 641, 721, 801, 881, 961, 1041, 1121. Results were expressed as log₁₀ copies/mL PBMC.

Results: At week 72, CD4+ T cell counts were +30% in IL-2 group and +20% in HAART group. Mean HIV RNA in PBMC was +45% in IL-2 group and +20% in HAART group. After adjustment for pre-treatment, HIV DNA was 3.04 log₁₀/10⁶ PBMC and 2.99 in IL-2 and HAART groups respectively, their 2.69 and 2.46 at week 28, 2.58 and 2.46 at week 0 and 2.45 at week 121 (all comparisons were NS). Mean HIV DNA decrease between weeks 0 and 2.45 in IL-2 group (3.03) and HAART group (2.45) were not significantly different (p=0.29). Similar results were observed between weeks 0 and week 28 (p=0.74) and between weeks 28 and week 72 (p=0.76).

Conclusions: Our results show similar levels of decrease of HIV DNA in both groups, indicating that IL-2 therapy does not reduce significantly the stock of latently HIV-infected cells. However, a significantly higher decrease of HIV RNA was observed in the IL-2 group.

OBJECTIVES

To assess the long term impact of IL-2 therapy on the stock of latently HIV-infected blood cells, by quantifying proviral DNA in PBMC in patients with CD4 counts 200-550 cells/mm³.

Does IL-2 increase the antiretroviral effect of HAART on the stock of infected cells or may induce an expansion of HIV infected cells despite HAART ?

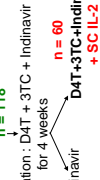
PATIENTS AND METHODS

All patients with sequential aliquots of frozen PBMC were included in this sub-study of the trial ANRS 079 (randomized study of HAART +/- SC IL2 therapy in naive (n=60) or pretreated patients (n=50)) - see poster 514-M).

HIV DNA in PBMC was quantified using a prototype assay based on the Monitor test (Roche). HIV RNA was quantified by real time PCR. Total DNA amounts were quantified by fluorometry. HIV DNA PCR was performed in the gag gene and quantification was done using a HIV DNA internal standard as a reference. Results were expressed as log₁₀ copies per 10⁶ PBMC.

ANRS 079 Study design

Patients with CD4(200-550), naive to ART or pretreated with bithérapie



Duration: 18 months (10 cycles) + Extended follow-up .24 months

HIV DNA : PBMC samples available for each group

Entry	HAART		SC IL-2 + HAART	
	W0	W21	W19	W40
End of randomized phase	41	40	40	81
Extended follow-up 1st year	W72	44	47	91
	W122	30	34	64

Statistical analysis

- Randomization was stratified by prior antiretroviral status (naive to antiretrovirals or naive to PI).
- Inten-to-treat approach was used.
- Proviral DNA means (log₁₀ copies/10⁶ PBMC) were compared by analysis of variance stratified by prior antiretroviral status.
- HAART group vs IL-2 group unadjusted p-values were presented.

LONG TERM EFFICACY OF SUBCUTANEOUS IL-2 THERAPY IN HIV-INFECTION PROVIRAL DNA IN PATIENTS OF THE ANRS 079 TRIAL

M. Burgard^{1,*}, C. Durier², C. Capitant², A.S. Lascaux³, C. Michon⁴, E. Netzer², C. Goujard⁵, V. Foubert², J.-P. Abouliker², J.-F. Delfrayssy⁵, Y. Levy³, C. Rouzioux¹ and the ANRS 079 study group

¹Hosp. Necker, Paris; ²INSERM, Villejuif; ³Hosp. H.Mondor, Créteil; ⁴Hosp. L.Mourier, Colombes; ⁵Hosp. Bicêtre, Kremlin-Bicêtre; and ⁶ANRS, Paris, France

RESULTS

HIV DNA in PBMC (log ₁₀ copies /10 ⁶ PBMC)				
Adjusted mean* [95% Confidence Limits]	HAART	SC IL-2 + HAART	p-value*	
Entry	W0	2.99 [2.72, 3.27]	3.05 [2.80, 3.30]	0.76
	W28	2.65 [2.47, 2.83]	2.69 [2.52, 2.87]	0.74
End of randomized phase	W72	2.46 [2.30, 2.62]	2.58 [2.42, 2.75]	0.29
Extended follow-up	W122	2.45 [2.26, 2.64]	2.59 [2.39, 2.79]	0.32

* Adjusted for differences due to prior antiretroviral status

HIV DNA decrease

HIV DNA change (log ₁₀ copies/10 ⁶ PBMC)			
Adjusted mean* [95% Confidence Limits]	HAART	SC IL-2 + HAART	p-value*
HIV DNA at W0	2.99	3.05	0.76
Change between W0 and W28	-0.30 [-0.41, -0.18]	-0.19 [-0.30, -0.08]	0.16
W0 and W72	-0.45 [-0.62, -0.29]	-0.33 [-0.47, -0.19]	0.24
W72 and W122	-0.16 [-0.24, -0.09]	-0.14 [-0.21, -0.06]	0.64

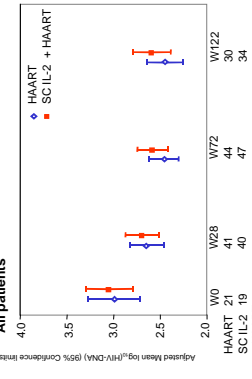
All decreases are significantly different from 0

ANRS 079 trial

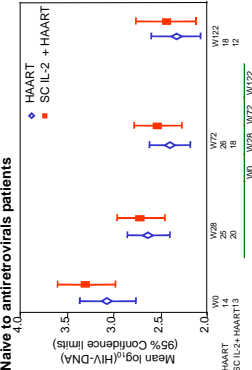
Immunological and virological results

CD4 cell count (median [min, max])	HAART		SC IL-2 + HAART		p-value
	W0	W74	W74	W122	
	334 [204, 492]	+262 [-237, 658]	343 [200, 549]	+865 [-42, 3031]	<0.0001
Number of patients (%) with HIV RNA < 50 copies/ml	W0	1/58 (2%)	3/65 (5%)	37/46 (80%)	0.27

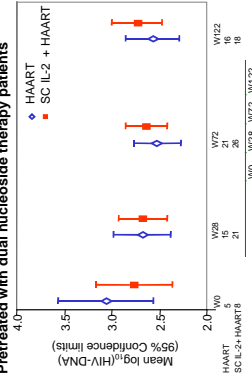
MEAN HIV-DNA OVER TIME (95% CI)



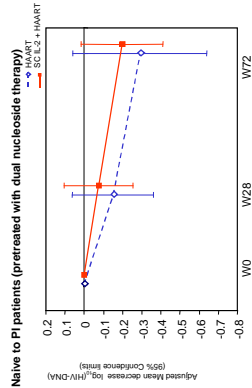
MEAN HIV-DNA OVER TIME (95% CI) Naive to antiretrovirals patients



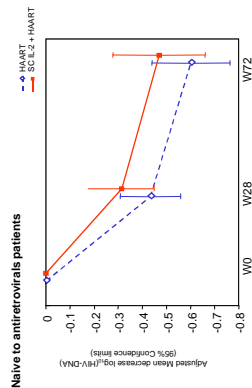
MEAN HIV-DNA OVER TIME (95% CI) Pretreated with dual nucleoside therapy patients



MEAN HIV-DNA DECREASE (95% CI) Naive to PI patients (pretreated with dual nucleoside therapy)



MEAN HIV-DNA DECREASE (95% CI) Naive to antiretrovirals patients



CONCLUSION

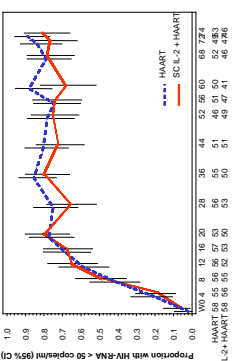
Our results showed a similar decrease of HIV DNA in both groups : HAART and HAART + SC IL-2. Moreover, the decrease of HIV DNA was significantly lower in pretreated patients compared to naive patients (p=0.02 at week 72) whatever the group of treatment.

Our results indicated that patients with CD4 [200-550] treated with IL-2 and HAART experienced a significant increase of CD4 counts without expansion of the pool of latently HIV infected cells.

ANRS 079 STUDY GROUP

Principal Investigator		Scientific Board	
Y. Levy (H. Mondor, Créteil)	J.-P. Abouliker	Y. Levy	J. Maral
C. Michon (Colombes)	C. Capitant	C. Goujard	
E. Netzer (St Louis, Paris)	K. Bouchenata	C. Michon	
M. Kazatchkine, L. Weiss (Broussais, Paris)	V. Foubert	C. Rouzioux	
J.-F. Delfrayssy, C. Goujard (Bicêtre)	E. Netzer	J.-P. Abouliker	
J.-P. Viard (Necker, Paris)	C. Durier	D. Epalle	
E. Bouvet (Bicêtre, Paris)	Management	M.-L. Goujon	
F. Boue (Clamart)	S. Izard	C. Rabian	
J.-L. Pasqualini (Strasbourg)	Investigators	CHIRON B.V.	
		M. Burgard	
		C. Rouzioux	
		(Necker, Paris)	

PROPORTION OF PATIENTS WITH PLASMA HIV-RNA BELOW 50 COPIES/ML



MEDIAN CD4 COUNTS CHANGES FROM BASELINE

