Viral Set Point after Cessation of Antiretroviral Therapy Initiated in Acute Primary HIV Infection

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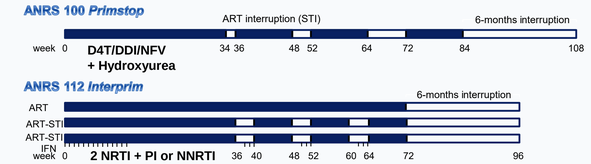
Background

- There are potential long-term benefits of immediate treatment in acute or early HIV infection.
- Several characteristics at the onset of infection or at antiretroviral (ART) therapy completion have been associated with viral control after ART cessation: sex, size of the viral reservoir, pretreatment plasma HIV RNA and CD4 and CD8 T cell counts.
- Most of the results are from observational studies. A pooled analysis of data from 2 prospective clinical trials in acute HIV infection which included an analytical interruption of treatment was performed.

Methods

Pooled Analysis of ANRS 100 (*Primstop*) and ANRS 112 (*Interprim*) trials

	ANRS 100 PRIMSTOP	ANRS 112 INTERPRIM
Patient Population	Symptomatic primary HIV infection	Ongoing primary HIV-1 infection (symptomatic)
	with at least 2 of the criteria within 4 weeks prior to inclusion: • Positive p24 antigenemia • Negative HIV ELISA • ≤ 3 bands on HIV Western blot.	with detectable HIV-RNA or positive p24 antigenemia and ≤ 3 bands on HIV Western blot.
Nb of patients	N = 29 3 lost to follow-up	N = 89 3 lost to follow-up
Nb of clinical sites	11	25
Period	2000-2001	2002-2004
Coordination	Inserm SC10-US19 – Villejuif	Inserm U897 - Bordeaux



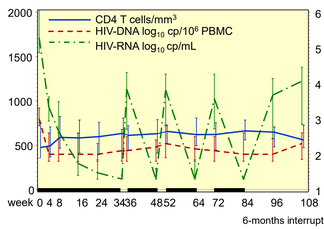
ANRS 100: ART with STI (n=26)
ANRS 112: three randomized groups (continuous ART n=30; ART-STI n=30; ART-STI-Peg Interferon n=29
Peg-IFN administrated subcutaneously at one µg/kg/week)

Virological endpoint : HIV-RNA 24 weeks after ART discontinuation
- PRIMSTOP (N=26) Local laboratories – w108
  Predictive factors of HIV-RNA ≤ 1,000 cp/mL published in [1]
- INTERPRIM (N=86) Central Laboratory - Cobas Roche - mean of w92 and w96
  Predictive factors of HIV-RNA < 5,000 cp/mL published in [2]

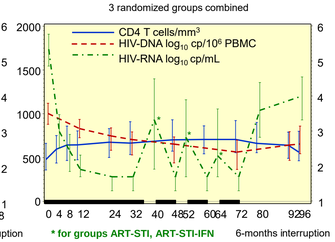
Predictive factors : ANRS 100 vs. ANRS 112, demographic characteristics, numbers of Western-blot bands at screening, baseline CD4 and CD8 T-cell counts, baseline HIV-RNA level, baseline HIV-DNA and HIV-DNA at interruption.

Results

ANRS 100 *Primstop*



ANRS 112 *Interprim*



	ANRS 100 N=26	ANRS 112 N=86	All N=112
Sex Female - n (%)	5 (19%)	8 (9%)	13 (12%)
At baseline			
Age - years	32 (27-41)	34 (30-42)	34 (29-41)
Acute infection symptoms- n (%)	26 (100%)	84 (98%)	110 (98%)
No. of bands - HIV Western Blot	4 (2-5)	2 (0-3)	2 (1-3)
CD4 count - cells/mm³	515 (372-654)	386 (277-561)	425 (299-607)
CD8 count - cells/mm³	1189 (864-1405)	959 (643-1446)	1008 (674-1440)
HIV-RNA log_{10}(cp/mL)	5.3 (4.6-6.1)	5.7 (5.0-5.9)	5.7 (5.0-5.9)
HIV-DNA log_{10}(cp/10^6 PBMC)	3.0 (2.8-3.3)	3.5 (3.2-3.8)	3.5 (3.0-3.7)
At last treatment interruption			
CD4 count - cells/mm³	663 (562-785)	702 (552-923)	682 (556-852)
HIV-RNA < 50 cp/mL – n/N (%)	21/24 (88%)	62/84 (74%)	83/108 (77%)
HIV-DNA log_{10} (cp/10^6 PBMC)	2.0 (1.8-2.6)	2.4 (1.9-2.8)	2.3 (1.8-2.7)
HIV-DNA change from baseline log_{10}(cp/10^6 PBMC)	-1.0 (-1.3 - -0.6)	-1.1 (-1.3 - -0.9)	-1.1 (-1.3 - -0.8)

Data are median (Inter-Quartile Range) or n (%)

HIV-DNA was centrally measured by real time PCR with a detection limit of 70 cp/10^6 PBMC (1.84 log_{10}).

After 6-months of ART interruption

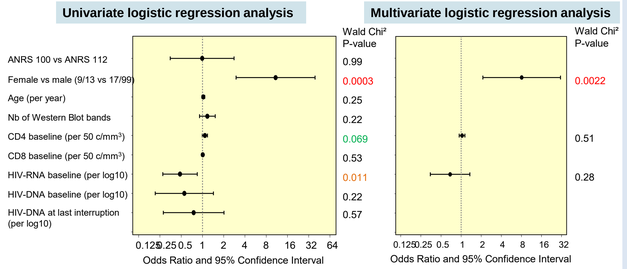
	ANRS 100 N=26	ANRS 112 N=86	All N=112
CD4 count - cells/mm³	561 (473-729)	561 (463-801)	561 (464-774)
HIV-DNA log_{10}(cp/10^6 PBMC)	2.3 (1.8-2.6)	2.6 (2.4-3.2)	2.6 (2.2-3.1)
HIV-RNA log_{10}(cp/mL)	4.05 (2.84-4.45)	3.79 (3.08-4.34)	3.94 (3.04-4.34)
HIV-RNA ≤ 1,000 cp/mL - n (%)	**6 (23)**	**20 (23)**	**26 (23)**
HIV-RNA < 50 cp/mL - n (%)	3 (12)	4 (5)	7 (6)

In ANRS 112, HIV-RNA was the mean of two centralized measures at w92 and w96.

Predictive factors of sustained control of viremia

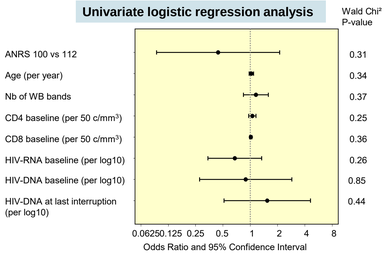
HIV-RNA ≤ 1,000 copies/mL at the end of the 6-months of ART interruption (n = 26 / 112)

All analyzed patients including deviations to final treatment interruption (n= 6) or to treatment resumption (n= 4)



HIV-RNA ≤ 1,000 copies/mL at the end of the 6-months of ART interruption

Men only (n = 17 / 99)

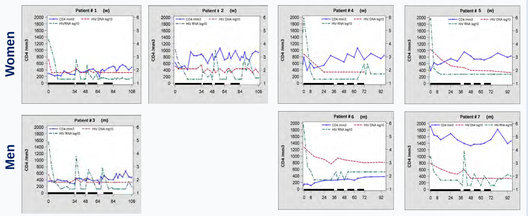


Considering men only (n=99),
- 17% achieved an HIV-RNA ≤1,000 cp/mL 6 months after ART interruption
- no predictive factor of viral set point was identified among CD4 T cell count, HIV-RNA or HIV-DNA level at initiation or at 18 months of treatment.

Patient profiles

HIV-RNA < 50 copies/mL at the end of the 6-months of ART interruption

HIV-RNA was < 50 cp/mL in 7 patients : 4/13 women and 3/99 men, p=0.003 (Fisher's exact test)



Last interruption as planned and no treatment resumption before the end of the interruption period

Conclusions

In this pooled analysis of **ANRS100 (*Primstop*) and ANRS112 (*Interprim*) trials**, with 6-months interruption of a 18 months ART initiated during acute primary HIV Infection

- Women were more likely to control viral replication than men.
- After adjustment on sex, no other pretreatment or end-of-therapy characteristic was identified in this population to predict a low or undetectable HIV viral load 6 months after cessation of ART.
- This difference between men and women deserves further investigation, especially in the era of HAART.

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Acknowledgments

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