

BACKGROUND (I)

Lower plasma HIV-1 viral loads (VLs) in women than in men (ALIVE cohort of IDUs seroconverters, Baltimore, US)

Authors	Study	VL				
		Timing	Method	Men	women	p
Farzadegan et al, 1998	Cross-sectional (n=527)	Baseline	bDNA	8,907	3,365	0.001
Sterling et al, 1999	Longitudinal nested case-control study (n=24)	Baseline (< 12 months after seroconversion)	RT-PCR	148,354	14,918	0.001
		Follow-up within 5 yrs of seroconversion		+0.003 Log ₁₀ /yr	+0.24 Log ₁₀ /yr	0.002
Sterling et al, 2001	Longitudinal (n=202)	Baseline (< 12 months after seroconversion)	RT-PCR	50,766	15,103	<0.001 ^a

^a: but no significant difference in the risk of progression to AIDS according to gender

BACKGROUND (II)

Considerations for antiretroviral therapy in women (US Guidelines)

- ✓ Current guidelines for the initiation of antiretroviral treatment:

Current threshold : $\geq 20,000$ cp/mL

% eligible according to the first VL obtained after seroconversion:

74% among men vs. 37% among women ($p < 0.001$)

- ✓ Towards gender-specific guidelines (especially in women with $CD4^+$ T cell counts > 350 cells/mm³)?
 - lower plasma HIV RNA thresholds for initiating therapy in women?
 - insufficient data to determine an appropriate threshold

BACKGROUND (III)

Less convincing results from European Cohorts

- ✓ Swiss HIV cohort study (Junghans et al., 1999)
Slightly lower VL among female IDUs (0.13 Log₁₀) but not among heterosexually infected women
- ✓ Italian Seroconverter Study (ISS) (Lyles et al., 1999)
11,165 cp/mL (men) vs. 4,851 cp/mL (women) (p=0.065)
- ✓ Currently, the European guidelines for initiating antiretroviral therapy are applied uniformly to women and men.

OBJECTIVES

What about association between VL and gender in sub-Saharan Africa?

The question is important because :

Of 28 millions infected African subjects, ~ half of them are women

Access to antiretrovirals are currently implemented in sub-Saharan Africa

PATIENTS AND METHODS (I)

- ✓ **Prospective cohort (PRIMO-CI) of 127 HIV-1 and HIV-1+2 seroconverters** constituted of regular blood donors recruited since June 1997 by the National blood bank in Abidjan, Côte d'Ivoire.
- ✓ These subjects were followed as early as possible after their diagnosis of seroconversion.
- ✓ **Estimated date of seroconversion:** mid-point between the last between the last negative and the first positive HIV serological (test EIA, Murex ICE 1-O-2, Abbott, North Chicago, IL, USA; Pepti-Lav 1-2, Pasteur Diagnostics, Marnes-la-Coquette, France)

PATIENTS AND METHODS (II)

Laboratory assays

- ✓ **HIV-1 RNA copy number measurements**
Roche Amplicor HIV-1 Monitor, 1.5 version
Threshold : 200 HIV-1 RNA copies/mL
- ✓ **CD4⁺ cell count**
Flow cytometry technique (FACScan, Becton Dickinson, Aalst-Erembodegem, Belgium)

RESULTS (I)

Baseline characteristics according to gender (n=127)

	Male n=98		Female n=29		<i>p</i>
	Median	IR*	Median	IR*	
Viral load (log10 copies/mL)	4.6	4.1-5.1	4.3	3.6-4.9	0.09
CD4⁺ (/mm ³)	539	381-698	488	304-597	0.05
Interval seroconversion /inclusion	7.6	4.3-20.9	12.3	9.7-15.8	0.09

*interquartile range

RESULTS (II)

Association between viral load and other baseline characteristics

Viral load associated to:	<i>p</i> *
Gender	0.01
CD4⁺ (/mm³)	0.001
Interval seroconversion /inclusion (months)	0.02

* Multiple linear regression

RESULTS (III)

Predictors of HIV disease progression (CDC category B or C, or death)

	Univariate analysis	Multivariate analysis*	
	<i>p</i>	HR [†]	95%CI
Gender	0.80	-	-
Viral load (log ₁₀ copies/mL)	0.03	1.57	1.01-2.43
CD4⁺ (/mm ³)	0.89	-	-
Interval seroconversion /inclusion (months)	0.004	0.95	0.91-0.99

*Cox model; † Hazard ratios adjusted for other variables in table

DISCUSSION (I)

✓ In our study performed in an adult population mainly heterosexually infected with the HIV-1 recombinant form CRF02_AG, the **median initial viral load at entry in the cohort tended to be lower in women** than in men , but this difference is not statistically different

✓ Limitation

Small sample size, particularly in women (n=29)

DISCUSSION (II)

- ✓ **Median viral load adjusted** for both time since seroconversion and CD4 cell count **was lower in women** (0.3 Log 10 difference)
- ✓ This difference is not explicated by CD4 cell count as CD4 in women are lower than in men

DISCUSSION (III)

- ✓ A **high viral load** was an **independant predictor** of time to **symptomatic HIV disease**
(HR=1.57 for a one log increase of HIV RNA)
- ✓ Gender was not predictor of time to symptomatic disease
- ✓ Limitations:
 - small sample size
 - short follow up (median:28 months),
 - few number of progressors (n=25)

PRIMO-CI cohort

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