HIV Reservoirs in Semen at the Time of Primary Infection

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Background

Primary-HIV-Infection (PHI) is a high-risk period for viral transmission.

Few data are available on the efficacy of cART initiated at the time of PHI on HIV genital shedding, and none regarding HIV reservoir in the genital tract (C.D.Pilcher, AIDS 2007).

Results from the ANRS-147 OPTIPRIM trial showed that the efficacy on HIV blood reservoirs of a two year-early pentatherapy containing raltegravir plus maraviroc did not differ from standard cART (Cheret, Lancet ID 2015).

The objective of this substudy was to assess HIV shedding in semen. Blood and semen HIV-RNA and HIV-DNA were quantified to assess the impact of early treatment in patients with PHI.

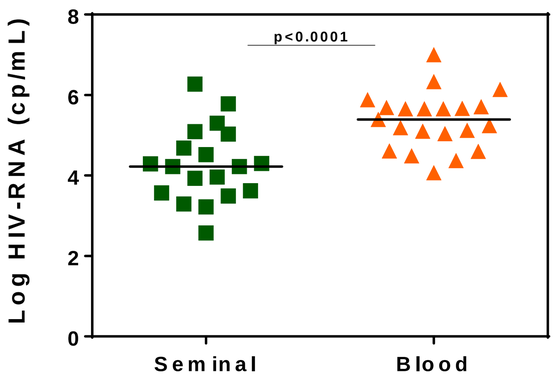
Methods

Patients presenting with PHI (inclusion criteria: HIV-1 western-blot (WB) ≤4 antibodies (Ab) and positive HIV-RNA, and CD4<500/mm^3 in case of asymptomatic PHI) were enrolled in the ANRS-147 OPTIPRIM study and received two years of an early cART. 21 patients also agreed to participate in this HIV reservoir substudy.

Total HIV-DNA and HIV-RNA in blood, semen cells and seminal plasma taken at inclusion and month 24 were quantified using an ultrasensitive real-time-PCR (Biocentric, Bandol, France). Wilcoxon signed rank test was used to estimate differences between HIV-RNA levels in semen and blood and Spearman test to estimate correlations with quantitative baseline characteristics.

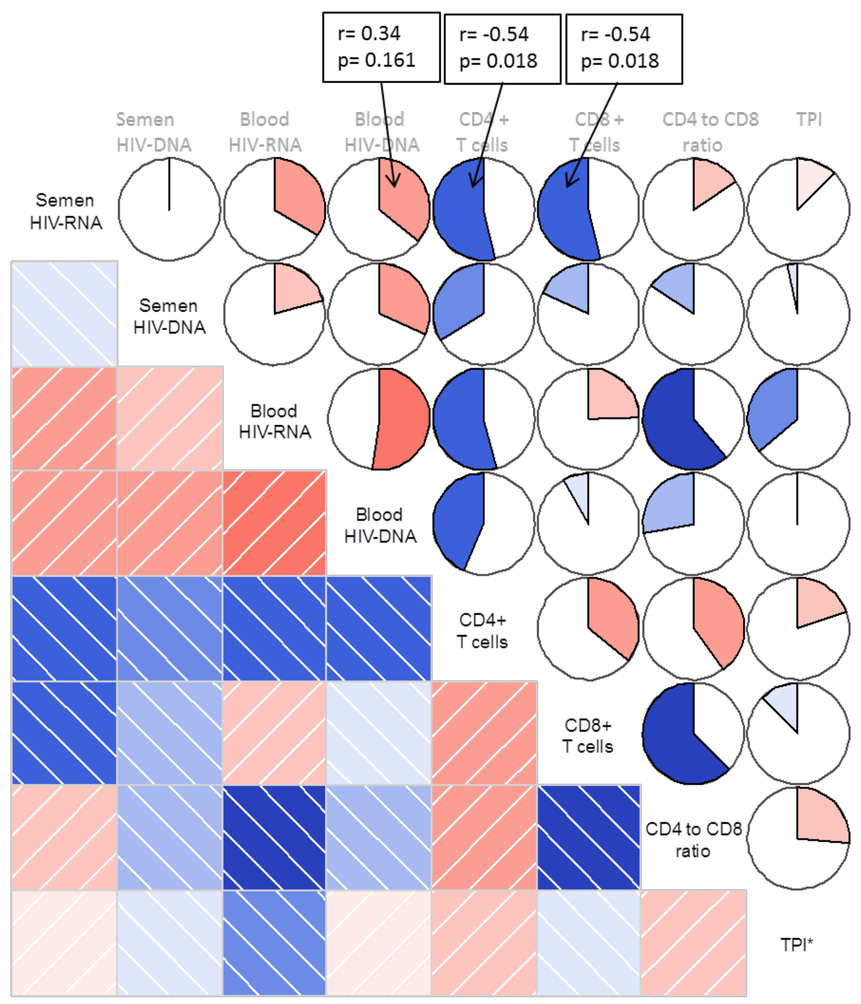
	Total N=90	Substudy N=21
Men	83 (92%)	21 (100%)
MSM	68 (76%)	19 (90%)
Age,years, *median (min-max)*	36 (18 – 64)	36 (20 - 59)
Place of birth:	71 (79%)	18 (86%)
Europe	6 (7%)	1 (5%)
sub-saharan Africa	13 (14%)	2 (10%)
Other		
Symptomatic primary infection	87 (97%)	20 (95%)
Acute primary infection	38 (42%)	8 (38%)
Time between estimated date of infection and enrolment, days	35.5 (19 – 77)	33 (19 - 49)
Seminal plasma HIV-RNA, log cp/mL	-	19, 4.22 (2.57 - 6.27)
Seminal plasma HIV-DNA, log cp/mL	-	19, 0.31 (0.00 – 3.58)
Seminal plasma HIV-DNA, Detectable Indetectable	-	10/19 (53%) 9/19 (47%)
Blood plasma HIV-RNA, log cp/mL	5.40 (3.20 - 7.01)	5.39 (4.07 - 7.00)
Blood HIV-DNA, log cp/ 10^6 PBMC	3.60 (2.58 - 4.77)	3.59 (2.78 - 4.50)
CD4 count, cells per µL	472 (116 - 1116)	465 (163 - 1116)
CD8 count, cells per µL	1136 (229 - 8157)	1088 (438 - 5148)
CD4 to CD8 ratio	0.42 (0.08 - 1.35)	0.42 (0.14 - 1.18)
HIV-1 subtype B (vs. non B)	58 (64%)	13 (62%)
R5 HIV-1 tropism (vs. X4)	81 (90%)	21 (100%)

Table: Baseline characteristics
Acute infection: HIV-1 WB ≤1 Ab

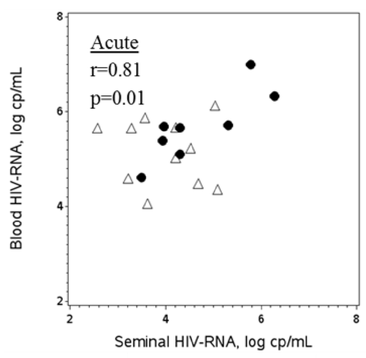


HIV-RNA levels at inclusion were significantly higher in blood plasma than in semen, (Δ=1.12, p-value for paired data).

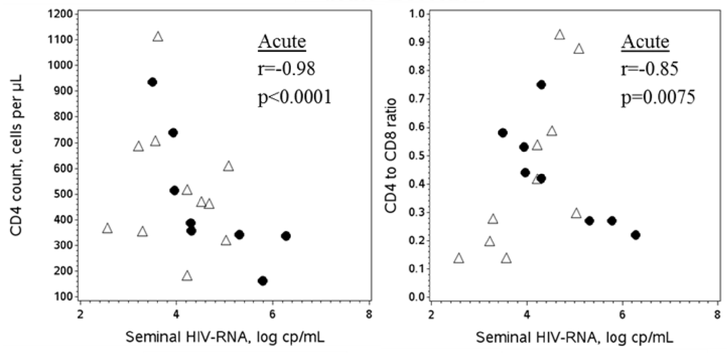
At inclusion



Correlogram of baseline virological and immunological markers.
TPI: Time between estimated date of infection and enrolment
Heatmaps and pie-charts indicate associations between the variables. Red color displays a positive correlation and blue a negative correlation. Their intensity and size of pie, represent the strength of the association.



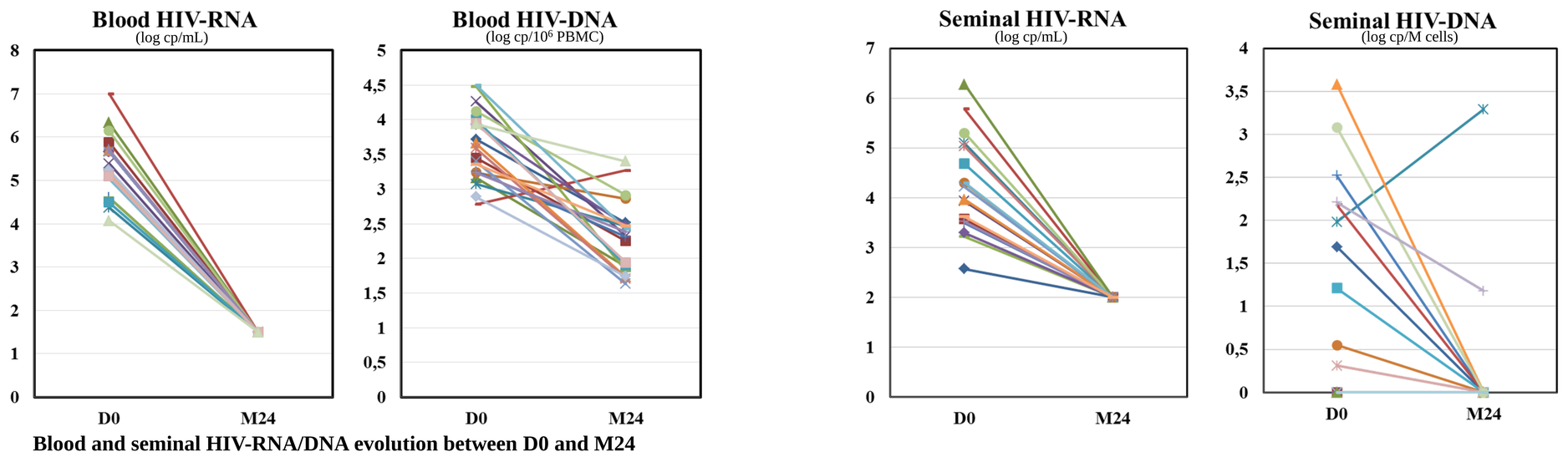
● acute Δ recent



● acute Δ recent ● acute Δ recent

Correlations among 8 patients presenting acute infection.

Impact of two years early-cART



Blood and seminal HIV-RNA/DNA evolution between D0 and M24
All patients had indetectable level of blood and seminal HIV-RNA at M24.
Interestingly, the only one patient with seminal HIV-DNA increase during treatment reported use of recreational drugs (cocaïn) at M23, which might explain this positive HIV-DNA quantification at M24.

Conclusion

This is the **first study quantifying HIV-reservoir cells in semen** of patients with acute infection. We showed that levels of HIV reservoirs in semen are linked with the immunosuppression severity. Infected cells in semen represent a factor associated with an increased risk of HIV transmission via cell to cell transmission.

Two years of early HAART allows purging not only viral particles but also infected cells and reduces drastically the risk of HIV transmission.

ANRS -147- Optiprim study group:

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