Poster Number:
518

VL SUPPRESSION AT ULTRASENSITIVE LEVELS IS ASSOCIATED WITH INSTI-INITIATION ART

Sidonie Lambert-Niclot[1,2,3], Anders Boyd[2], Djeneba Fofana[2,3], Nadia Valin[4], Jean-Luc Meynard[4], Rachid Agher[5], Vincent Calvez[1,2,6], Christine Katlama[1,2,5], Pierre-Marie Girard[1,2,4], Anne-Geneviève Marcelin[1,2,6] Laurence Morand-Joubert[1,2,3]

[1]Sorbonne Université, F75006, Paris, France; [2]INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique (IPLESP), F75013, Paris, France; [3]AP-HP, Laboratoire de Virologie, Hôpital Saint-Antoine, F75012, Paris, France;
[4]Département de Maladies Infectieuses, Hôpital Saint-Antoine, F75012, Paris, France; [5]Département de Maladies Infectieuses, Hôpital Pitié Salpêtrière, F75013, Paris, France; [6]AP-HP, Laboratoire de Virologie, Hôpital Pitié Salpêtrière, F75013, Paris, France;

Dr Sidonie LAMBERT-NICLOT
Sidonie.lambert@aphp.fr

BACKGROUND

Achieving and maintaining viral load VL<50 copies/m in European and French guidelines or <200 copies/mL in USA guidelines is the recommended therapeutic goal of cART.

Some HIV-infected patients on antiretroviral therapy (ART) present ultrasensitive HIV RNA viral loads (US-VL) below detection levels of current commercially-available VL assays.

In France, HAART permitted to have close to 90% of treated patient harboring VL <50 copies/mL), current objectives were now to study residual viremia, between 1 and 20 copies/mL.

→ To determine the effect of US VL on virological failure in a large database

→ To analyse associated factors with virological failure and with residual viremia, more specifically the impact of different ARV classes.

METHODS

- Between 2009 and 2013, 716 patients initiating ART with HIV RNA >200 copies/ml at ART-initiation, achieving <50 copies/mL during ART, and with at least 2 follow-up time points were included from 2 French Hospital Centers.
- Virological failure was defined as having either 2 consecutive viral load measurements >50 copies/mL or 1 viral load measurement >200 copies/mL.
- Viral loads determined by COBAS TaqMan Roche assay: quantitative results for HIV-RNA ≥20 copies/mL, qualitative results for HIV-RNA 1-20 copies/mL, and no detection <1 copy/mL when no signal is detected.
- Determinants for US-VL <1 copy/mL evaluated using random-effect Poisson regression and determinants for virological failure using a conditional risk set, Cox proportional model.

RESULTS

Table:1. Description of the study population at antiretroviral therapy initiation (*n*=716)

	N=716
Male/Female (% males)	525/191 (73.3)
Age* [N=715]	39 (32-46)
Hospital	
La Pitié-Salpétrière	518 (72.4)
Saint-Antoine	198 (27.7)
Time since first positive HIV serology*, years	0.2 (0.1-2.4)
AIDS-defining illness	102 (14.3)
CD4+ T cell count*, /mm³ [N=665]	306 (181-441)
Nadir CD4+ T cell count*, mm³	275 (159-375)
CD8+ T cell count*, /mm³ [N=689]	779 (540-1141)
CD4:CD8 ratio* [N=689]	0.35 (0.21-0.57)
HIV RNA viral load*, $\log_{10}$ copies/mL	4.84 (4.36-5.24)
HIV RNA viral load >10⁵ copies/mL	291 (40.6)
Number of antiretroviral agents*	3 (3-3)
Antiretroviral treatment n (%)	
NRTI+PI	418 (58.4)
NRTI+NNRTI	211 (29.5)
NRTI+Integrase inhibitor	87 (12.2)
Positive HCV RNA [N=291]	18 (6.2)
HCV RNA viral load, $\log_{10}$ IU/mL*†	6.20 (5.70-6.55)
Positive HBsAg serology [N=704]	24 (3.4)

Table 2: Cumulative proportion of patients with VL <50 copies/mL or VL<1 copy/mL after 12 or 24 months of initiation treatment.

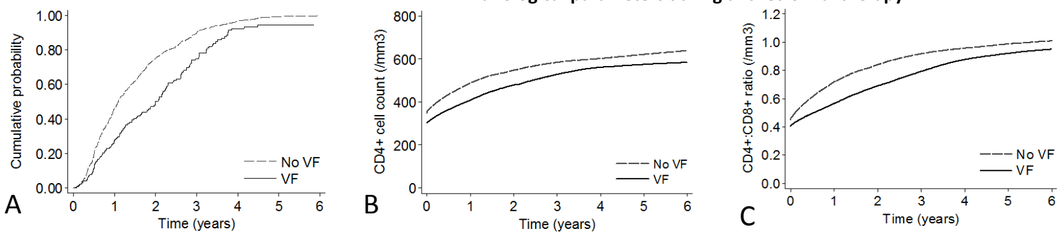
	12 Months	24 Months
Cumulative proportion of patients presenting VL<50 copies/mL	78.2% (n=564)	92.7% (n=664)
Cumulative proportion of patients presenting VL<1 copy/mL	42.5% (n=304)	70.4% (n=501)

Table 3. Determinants of having an HIV RNA at ultrasensitive viral loads (<1 copy/mL) across time-points while undergoing antiretroviral therapy

	Univariable		Multivariable*	
	IRR (95%CI)	p	IRR (95%CI)	p
Age (per 10 years) [N=715]	0.87 (0.83-0.92)	<0.001	0.89 (0.85-0.94)	**<0.001**
Gender				
Male	1.00		1.00	
Female	1.13 (1.00-1.29)	0.049	1.14 (1.01-1.29)	**0.03**
Baseline HIV RNA				
<10⁵ copies/mL	1.00		1.00	
≥10⁵ copies/mL	0.67 (0.60-0.75)	<0.001	0.71 (0.64-0.80)	**<0.001**
Baseline CD4+ T cell count [N=665]				
>500 cells/mm³	1.00		1.00	
350-500 cells/mm³	0.92 (0.77-1.08)	0.3	0.90 (0.76-1.06)	0.2
<350 cells/mm³	0.63 (0.54-0.74)	<0.001	0.66 (0.57-0.77)	**<0.001**
Baseline CD4+ T cell nadir				
≥250 cells/mm³	1.00			
<250 cells/ mm³	0.68 (0.61-0.76)	<0.001		
Baseline CD4:CD8 ratio [N=642]				
≥1	1.00			
<1	0.67 (0.52-0.86)	0.002		
Time -varying CD4:CD8 ratio [N=680]				
≥1	1.00			
<1	0.88 (0.79-0.98)	0.02		
ART backbone during follow-up				
NNRTI	1.00		1.00	
PI	1.00 (0.90-1.12)	0.9	0.99 (0.88-1.10)	0.8
Integrase inhibitor	1.14 (0.99-1.31)	0.08	1.17 (1.01-1.35)	**0.03**
Other combination	0.87 (0.72-1.05)	0.14	0.85 (0.70-1.04)	0.11

The model takes into account all HIV RNA viral load measurements during antiretroviral therapy and not at a specific time-point. Incident rate ratios (IRR) describe factors for which HIV RNA <1 copies/mL occurs more or less frequently during treatment.

Figure 1. Evolution of proportion of patients with US VL<1copy/mL and immunological parameters during antiretroviral therapy



Cumulative proportion of patients reaching an undetectable HIV RNA viral load with detection threshold at ultrasensitive levels (1 copy/mL) is depicted in (**A**). Locally-weighted scatterplot smoothing lines are constructed for CD4+ T-cell count (**B**) and CD4+:CD8+ ratio (**C**) during follow-up. All figures are stratified on patients with or without virological failure (VF).

Table 4. Determinants of virological failure after antiretroviral therapy initiation

	Univariable*		Multivariable***	
	HR (95%CI)	P	HR (95%CI)	p
Age (per 10 years) [N=715]	0.92 (0.78-1.08)	0.3		
Gender				
Male	1.00			
Female	0.78 (0.52-1.16)	0.2		
Baseline HIV RNA				
<10⁵ copies/mL	1.00		1.00	
≥10⁵ copies/mL	1.37 (0.99-1.90)	0.06	1.41 (1.00-2.00)	**0.05**
Baseline CD4+ T cell count [N=665]				
>500 cells/mm³	1.00			
350-500 cells/mm³	1.67 (0.96-2.92)	0.07		
<350 cells/mm³	1.33 (0.79-2.24)	0.3		
Baseline CD4+ T cell nadir				
≥250 cells/mm³	1.00			
<250 cells/mm³	0.82 (0.57-1.19)	0.3		
Baseline CD4:CD8 ratio [N=642]				
≥1	1.00			
<1	1.83 (0.92-3.68)	0.09		
Time -varying CD4:CD8 ratio [N=680]				
≥1	1.00			
<1	0.85 (0.56-1.30)	0.5		
ART backbone during follow-up				
NNRTI	1.00		1.00	
PI	1.43 (0.91-2.26)	0.12	1.53 (0.97-2.43)	0.07
Integrase inhibitor	1.02 (0.42-2.45)	0.9	1.10 (0.48-2.56)	0.8
Other combination	1.82 (0.94-3.53)	0.08	1.98 (1.02-3.82)	**0.04**
Number of HIV RNA tests per year				
≤3	0.35 (0.20-0.62)	<0.001	0.36 (0.20-0.64)	**<0.001**
3-4	0.78 (0.41-1.46)	0.4	0.76 (0.40-1.43)	0.4
4-6	1.35 (0.74-2.45)	0.3	1.21 (0.67-2.18)	0.5
>6	1.00		1.00	

In post-hoc analysis, cumulative duration under <1 copy/mL was significantly and inversely associated with VF in the multivariable model (aHR/year of suppression=0.40, 95%CI=0.26-0.62, p<0.001)

Cumulative proportion of patients reaching an US-VL<1 copy/ml was achieved more rapidly in patients without VF versus with VF (Figure 1A). In parallel, CD4 cell count and CD4/CD8 ratio were higher and increased more rapidly in patients without VF versus with VF (Figure 1B and 1C).

CONCLUSION

- Decreased age, female gender, lower baseline VL, baseline CD4+ >500 versus <350/mm³ were associated with US-VL<1 copy/mL
- No detection of residual viremia is associated with the use of INSTI-class ART along with common determinants of HIV RNA <50 copies/mL .
- Longer periods at VL<1 copy/mL appear to protect against VF.