



Oral Communication

Session/Topic: Antiretroviral Therapy

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OC 6 **Factors related to over-time viral failure in HIV-infected patients with previous C-ART failures**

Authors:

S. Rusconi¹, M.M. Santoro², A. Cozzi-Lepri³, A. Antinori⁴, S. Bonora⁵, A. Cingolani⁶, N. Gianotti⁷, F. Ceccherini Silberstein², A. Tavelli⁸, A. d'Arminio Monforte⁹, for the Icona Foundation Study Group

Affiliation:

¹University of Milan, DIBIC Luigi Sacco, Milan, Italy, ²University of Rome Tor Vergata, Rome, Italy, ³University College London, UK, ⁴National Institute for Infectious Diseases L. Spallanzani, IRCCS, Rome, Italy, ⁵University of Turin, Turin, Italy, ⁶Catholic University, Rome, Italy, ⁷San Raffaele Hospital, IRCCS, Milan, Italy, ⁸Icona Foundation, Milan, Italy, ⁹University of Milan, ASST Santi Paolo e Carlo, Milan, Italy

Abstract:

Background: HIV-infected patients (pts) with prior virological failures (VFs) to cART are at an increased risk of subsequent failure, emergence of resistance, and death. There is little data on the population dynamics of VF covering recent years. Thus, we aimed at looking at previous history of VF and current calendar year as potential predictors after controlling for other factors known to be associated with the risk of subsequent VF.

Material and Methods: We analysed all HIV-infected pts in Icona Cohort who achieved virological suppression (two consecutive HIV-RNA ≤ 50 cps/mL: baseline) on cART after Jan 01, 2006. Main exposure factors investigated were current calendar period (stratified as: 2006-2009; 2010-2012; 2013-2016) and number of VFs (0; 1-3; >3) prior to baseline. Current VF was defined as the first of two consecutive HIV-RNA >200 cps/mL while the pt was receiving cART. Rates of VF were calculated as number of previous VFs divided by PYFU and unadjusted and adjusted relative rates (RR) were estimated from fitting a Poisson regression model.

Results: 6,660 HIV-infected patients, who achieved confirmed viral suppression after 2006 were included. At baseline they have been virologically suppressed for a median (IQR) of 20 (10, 36) months and have been subsequently followed for 25,296 PYFU. 347 patients experienced VF for an overall rate of 1.37 per 100 PYFU (95% CI: 1.23-1.52). The risk of VF was higher with larger number of previously experienced VFs. In particular, patients with >3 previous VFs had a rate of 2.80 per 100 PYFU (95% CI: 2.19, 3.58), 2.6-fold higher than that observed in patients without any previous VF. This result was confirmed after controlling for potential confounding factors, adjusted RR=2.61 (95% CI: 1.97-3.45, $p < 0.001$). In contrast the rate of VF was lower with more recent calendar periods, ranging from 2.75 (2.38, 3.18) in 2006-2009 to 0.70 (0.55, 0.87) in 2013-2016. This association remained significant after adjustment for the same set of confounders: adjusted RR=0.38 (95% CI: 0.26-0.54, $p < .001$: comparing 2013-2016 vs. 2006-2009). The risk of VF associated with previous VF did not vary by current period of viral suppression (interaction $p = 0.37$). The median (IQR) value of HIV-RNA (log₁₀) recorded at VF did not differ among the 3 time periods: 4.09 (2.98, 4.87) in 2006-2009, 3.64 (2.92, 4.46) in 2010-2012, and 3.63 (2.59, 4.36) in 2013-2016 ($p = 0.10$). Other factors independently associated with the risk of VF are shown in Table.

Conclusion: In HIV-infected patients who achieved viral suppression in recent years, after controlling for a number of demographic, health-related, viro-immunologic and therapeutic factors, the rate of VF continued to decline when comparing 2013-2016 with the incidence recorded in earlier calendar periods. Nevertheless, the risk of VF in 2013-2016 associated with multiple VF (>3 regimens) prior to achieving viral suppression remains similar to that estimated for previous periods.

Factors independently associated with the risk of VF >200 copies/mL from fitting a Poisson regression model

	Relative Rates of virological failure						
	No. current VF	PYFU	Rates (95% CI)	Unadjusted RR (95% CI)	p-value	Adjusted ^a RR (95% CI)	p-value
No. of virological failures before baseline^b							
None	207	19232	1.08 (0.94, 1.23)	1.00		1.00	
1-3 failures	76	3782	2.01 (1.60, 2.52)	1.87 (1.44, 2.43)	<.001	1.79 (1.22, 2.62)	0.003
>3 failures	64	2282	2.80 (2.19, 3.58)	2.61 (1.97, 3.45)	<.001	2.61 (1.68, 4.06)	<.001
Calendar year of baseline^c							
2006-2009	180	6542	2.75 (2.38, 3.18)	1.00		1.00	
2010-2012	93	8120	1.15 (0.93, 1.40)	0.42 (0.32, 0.53)	<.001	0.62 (0.44, 0.87)	0.006
2013-2016	74	10635	0.70 (0.55, 0.87)	0.25 (0.19, 0.33)	<.001	0.38 (0.26, 0.54)	<.001
Nationality							
Foreign	51	2615	1.95 (1.48, 2.57)	1.00		1.00	
Italian	296	22681	1.31 (1.16, 1.46)	0.67 (0.50, 0.90)	0.008	0.52 (0.35, 0.75)	<.001
Current duration of viral suppression, years							
0-1	288	19475	1.48 (1.32, 1.66)	1.00		1.00	
2-3	43	3882	1.11 (0.82, 1.49)	0.75 (0.54, 1.03)	0.077	0.52 (0.33, 0.82)	0.005
>3	16	1940	0.82 (0.51, 1.35)	0.56 (0.34, 0.92)	0.023	0.40 (0.19, 0.86)	0.019
Education							
None	330	23045	1.43 (1.29, 1.60)	1.00		1.00	
University	17	2251	0.76 (0.47, 1.21)	0.53 (0.32, 0.86)	0.010	0.23 (0.08, 0.61)	0.003
Current third drug							
Efavirenz	195	22841	0.85 (0.74, 0.98)	1.00		1.00	
Etravirine	3	109	2.74 (0.88, 8.50)	3.21 (1.03, 10.04)	0.045	3.82 (1.21, 12.07)	0.023

^aAdjusted for gender, nationality, time from HIV diagnosis, diagnosis of neurological disorders, duration of suppression, whether receiving a single tablet regimen at baseline, HCV coinfection status, mode of HIV infection, level of education, employment status, 3rd drug currently in use, previous failure with a NNRTI. ^bAdjusted also for calendar years. ^cAdjusted also for the number of previous virological failures.