10° CONGRESSO NAZIONALE
ICAR Italian Conference on AIDS and Antiviral Research
10 ANNIVERSARY
22-24 MAGGIO 2018 ERGIFE PALACE HOTEL ROMA
Presidenza del Congresso Massimo Andreoni, Roma Andrea Antinori, Roma Carlo Federico Perno, Milano

**Oral Communication** **Session/Topic:** **Clinical HIV**

**N.** **Title:**

OC 58 **HIV viral load kinetcs during first-line antiretroviral treatment and risk of virological non-response or rebound among patient with high pre-treatment HIV-RNA**

**Authors:**

G. Lapadula[1], A. d'Arminio Monforte[2], A. Castagna[3], S. Rusconi[4], C. Mussini[5], E. Colella[1], A. Gori[1], C. Fabrizio[6], V. Spagnuolo[3], E. Schiaroli[7], A. Antinori[8], A. Cozzi-Lepri[9] for the "ICONA Alte Viremie" collaboration

**Affiliation:**

[1]Ospedale "San Gerardo", ASST Monza, [2]Ospedale "San Paolo", Università di Milano, Italy, [3]Ospedale San Raffaele, Università "Vita e Salute", Milan, Italy, [4]Ospedale "Luigi Sacco", Università di Milano, Italy, [5]Policlinico di Modena, Università di Modena e Reggio Emilia, Italy, [6]Clinic of Infectious Diseases, University of Bari, Bari, Italy, [7]Unit of Infectious Diseases, Department of Medicine, University of Perugia, Perugia, Italy, [8]Istituto Nazionale Malattie Infettive, Rome, Italy, [9]University College of London, UK

**Abstract:**

**Background:** Although overall response to modern first-line antiretroviral (ARV) regimens is >90% in clinical trials, high pre-ARV viral load (VL) can delay or hamper the chance of HIV-RNA suppression. There is debate regarding the optimal management of patients with high VL and whether VL kinetics during treatment is predictive of virological failure remains unestablished.

**Methods:** The ICONA cohort database was merged with the databases of six large Italian outpatient clinics using the HICDEP SOP. All patients, previously ARV-naive, who had initiated a regimen with >/=3 ARV agents after January 1, 2010, whose pre-ARV VL was >100,000 copies/ml and whose Month (M) 12 VL was available, were selected. M1,3,6 and 12 VL were defined using windows of 2 months widths around the defined time-point. Virological failure (VF) at M12 was defined by a VL>50 copies/mL or a stop of ≥1 drug due to failure before M12. ARV switches due to reasons other than VF were ignored (ITT model), censored at the date of stop (OT model) or considered as failures (ITT-switch=F model). Logistic regression was used to evaluate the associations between M1, M3 and M6 VL (absolute values and change from pre-ARV VL) and VF at M12, after controlling for a number of potential confounders (listed in footnote of Table). Among those who achieved a M12 VL≤50 copies, we estimated the time to confirmed viral rebound>50 copies/mL using Kaplan-Meier curves and multivariable Cox regression.

**Results:** Among 1,888 enrolled patients, 15% were female and 45% MSM. The median pre-ARV VL was 5.47 log10 copies/ml (IQR: 5.2-5.82) and in 32% it was >500,000 copies/ml; 32% were treated with an integrase inhibitor (INI) and 11% with a regimen including >3 active ARV drugs. At M12, 1,592 patients (84%) had VL <50 copies/ml. After controlling for confounders, M3 or M6 VL >50 copies/mL, as well as a VL drop <2.5 log10 at M3 or M6, were associated with a significantly higher risk of M12 VF, whereas levels of M1 VL only when >1,000 copies/mL (Table 1). Pre-ARV VL was the only other factor independently associated with the risk of M12 VF. Neither use of INI or of >3 active ARV drugs was associated with this outcome. Results were similar using the OT or the ITT-switch=F analyses.

A M3 and M6 VL >50 copies/ml was also associated with a significantly higher risk of viral rebound after M12 suppression (Log-rank test P=0.011 and P=0.049, respectively). After controlling for the same set of confounders used in the Logistic regression, M3 VL>50 copies/ml remained marginally associated with risk of viral rebound (aHR=1.84, 95%CI: 0.97-3.46).

**Conclusions:** Although a VL ≤50 copies/mL is obtained and maintained by the majority of patients, those with M3 and M6 VL >50 copies/ml are at greater risk of VF or or viral rebound after M12 suppression than those who quicker suppress to ≤50 copies/mL. Such patients merit close monitoring and enhanced strategies to obtain early virological suppression.

**Table 1 Association between HIV-RNA kinetics and risk of HIV-RNA >50 copies/ml at month 12 (ITT Model)**

| | Odds ratios of Virological Failure at month 12[&] | | | | | |
|---|---|---|---|---|---|---|
| **Characteristic** | **VL>50** | **<=50** | **Unadjusted OR (95% CI)** | **p-value** | **Adjusted[*] OR (95% CI)** | **p-value** |
| ***Month 1 VL (copies/mL), n(%)*** | N= 308 | N= 1312 | | | | |
| 0-50 | 7 (2.3%) | 93 (7.1%) | 1.00 | | 1.00 | |
| 51-1000 | 78 (25.3%) | 552 (42.1%) | 1.88 (0.84, 4.19) | 0.125 | 1.76 (0.67, 4.64) | 0.254 |
| 1000+ | 223 (72.4%) | 667 (50.8%) | 4.44 (2.03, 9.71) | <.001 | 3.59 (1.37, 9.39) | 0.009 |
| ***Change from pre-ARV Month 1 VL (log10 copies/mL), n(%)*** | N= 308 | N= 1312 | | | | |
| 2.5+ | 103 (33.4%) | 633 (48.2%) | 1.00 | | 1.00 | |
| 1-2.5 | 93 (30.2%) | 335 (25.5%) | 1.71 (1.25, 2.33) | <.001 | 1.66 (1.11, 2.47) | 0.013 |
| 0-1 | 112 (36.4%) | 344 (26.2%) | 2.00 (1.49, 2.70) | <.001 | 1.55 (1.08, 2.21) | 0.016 |
| ***Month 3 VL (copies/mL), n(%)*** | N= 283 | N= 1233 | | | | |
| 0-50 | 60 (21.2%) | 570 (46.2%) | 1.00 | | 1.00 | |
| 51-1000 | 174 (61.5%) | 599 (48.6%) | 2.76 (2.01, 3.78) | <.001 | 2.50 (1.69, 3.69) | <.001 |
| 1000+ | 49 (17.3%) | 64 (5.2%) | 7.27 (4.60, 11.49) | <.001 | 6.94 (3.91, 12.30) | <.001 |
| ***Change from pre-ARV Month 3 VL (log10 copies/mL), n(%)*** | N= 283 | N= 1233 | | | | |
| 2.5+ | 245 (86.6%) | 1164 (94.4%) | 1.00 | | 1.00 | |
| 1-2.5 | 27 (9.5%) | 58 (4.7%) | 2.21 (1.37, 3.56) | 0.001 | 2.05 (1.16, 3.62) | 0.013 |
| 0-1 | 11 (3.9%) | 11 (0.9%) | 4.75 (2.04, 11.08) | <.001 | 5.05 (1.80, 14.16) | 0.002 |
| ***Month 6 VL (copies/mL), n(%)*** | N= 255 | N= 1212 | | | | |
| 0-50 | 93 (36.5%) | 952 (78.5%) | 1.00 | | 1.00 | |
| 51-1000 | 136 (53.3%) | 244 (20.1%) | 5.71 (4.23, 7.69) | <.001 | 4.94 (3.45, 7.07) | <.001 |
| 1000+ | 26 (10.2%) | 16 (1.3%) | 16.63 (8.61, 32.12) | <.001 | 19.60 (8.73, 44.03) | <.001 |
| ***Change from pre-ARV Month 6 VL (log10 copies/mL), n(%)*** | N= 255 | N= 1212 | | | | |
| 2.5+ | 232 (91.0%) | 1197 (98.8%) | 1.00 | | 1.00 | |
| 1-2.5 | 15 (5.9%) | 7 (0.6%) | 11.05 (4.46, 27.41) | <.001 | 9.65 (3.11, 29.89) | <.001 |
| 0-1 | 8 (3.1%) | 8 (0.7%) | 5.16 (1.92, 13.89) | 0.001 | 14.41 (4.03, 51.53) | <.001 |

[*]Adjusted for pre-ARV HIV-RNA, gender, mode of transmission, region of origin, HCV status, pre-ARV CD4 count, use of INI, use of >3 ARVs, use of abacavir and year of starting ARV

[&]Absolute values and change are separate models; model including the change is not adjusted for pre-ARV HIV-RNA