

Dettaglio abstract

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Title: Coinfection with Hepatitis B Virus and/or Hepatitis C Virus is a risk factor for HIV virological rebound in course of antiretroviral therapy

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Clinical HIV

Authors: V. Malagnino¹, A. Cozzi-Lepri¹⁰, V. Svicher², E. Girardi³, C.F. Perno⁴, A. Saracino⁵, G. Cuomo⁶, S. Rusconi⁷, M. Puoti⁸, A. d'Arminio Monforte⁹, M. Andreoni¹, L. Sarmati¹ for the ICONA Foundation Study Group

Affiliation: ¹Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy, ²Departmente of Experimental Medicine, University of Tor Vergata, Rome, ³Department of Epidemiology and Pre-Clinical Research, National Institute for Infectious Diseases "L. Spallanzani", Rome, Italy, ⁴IRCCS Bambino Gesù Children's Hospital, Rome, Italy, ⁵Infectious Diseases, Università degli Studi "Aldo Moro" di Bari, Italy, ⁶Clinic of Infectious Diseases, Azienda Ospedaliero-Universitaria Di Modena, Modena, Italy, ⁷Infectious Diseases Unit, Legnano General Hospital, ASST Ovest Milanese, Università degli studi Di Milano, Legnano, ⁸Department of Infectious Diseases, Grande Ospedale Metropolitano Niguarda, Milan, Italy, ⁹ASST Santi Paolo e Carlo, Department of Health Sciences, University of Milan, Milan, Italy, ¹⁰University College London, London, UK

Abstract

Background: Coinfection with viral hepatitis B and/or C (HBV and HCV) and HIV is common however, the impact of HBV and HCV coinfection on HIV viremia control during antiretroviral therapy (ART) has yet to be fully understood. The aim of this study was to investigate the impact of viral hepatitis coinfection (included potential occult hepatitis B infection) on the risk of viral rebound (VR) after achieving suppression in real-world data.

Methods: Patients living with HIV (PLWH) from the ICONA Foundation Cohort were prospectively evaluated with aim of assessing whether viral HBV and/or HCV coinfection influenced the risk of VR defined at the time of the first of two consecutive values >50 cp/mL, after achieving a HIV-RNA ≤ 50 cp / mL also in two consecutive occasions on their first line ART (baseline). Study population was divided in 5 exposure groups: HBsAg+/HIV+, HBsAg-/HBcAb+/HIV+, HCVAb+/HIV+, HCVAb+/HBcAb+/HIV+ and HIV mono-infected patients using all serological test results performed prior to baseline. Nationality, duration of viral suppression, history of virological failure prior to baseline and HIV-RNA at cART initiation ad mode of HIV transmission were identified a key confounders for the association of interest. Standard survival analysis by means of KM curves and Cox regression analysis with time-fixed covariates measured at baseline was employed.

Results: Of a total of 6,380 patients included (Table 1), 4,090 (64%) resulted HIV mono-infected, 308 (5%) HCVAb+, 1,342 (21%) HBcAb+, 410 (6%) HCVAb +/HBcAb+ and 230 (4%) HBsAg +. Regarding the immuno-virological status at baseline, all 4 co-infected groups had CD4+ cell counts lower and HIV-RNA values higher than those seen in HIV mono-infected PLWH. At baseline, almost all groups (98%) were on ART containing NRTIs active against HBV (lamivudine, tenofovir dipivoxil fumarate or alafenamide). Overall, 829 (13%) patients experienced VR over follow-up. By 48 months the risk of VR were the following: 4.8% in mono-infected HIV vs. 12.7% in HCVAb+, 5.9% in HBcAb+, 14.5% in HCVAb+/HBcAb+ and 6.0% in HBsAg+ (log-rank test p

Table 1 Main characteristics of patients by baseline HBV serology group.

| Characteristics | All neg N= 4090 | HCVAb+ N= 308 | HBcAb+ N= 1342 | HCVAb+/HBcAb+ N= 410 | HBsAg+ N= 230 | p-value ^a | Total N= 6380 |
|---|--------------------|-------------------|-------------------|-------------------------|-------------------|----------------------|-------------------|
| <i>Gender, n(%)</i> | | | | | | <.001 | |
| Female | 870 (21.3%) | 106 (34.4%) | 226 (16.8%) | 86 (21.0%) | 45 (19.6%) | | 1333 (20.9%) |
| <i>Age, years</i> | | | | | | <.001 | |
| Median (IQR) | 38 (31, 46) | 41 (35, 48) | 45 (38, 53) | 46 (40, 51) | 42 (35, 51) | | 40 (33, 48) |
| <i>Mode of HIV Transmission, n(%)</i> | | | | | | <.001 | |
| IDU | 82 (2.0%) | 157 (51.1%) | 22 (1.7%) | 269 (66.1%) | 9 (3.9%) | | 539 (8.5%) |
| Homosexual contacts | 1983 (48.8%) | 68 (22.1%) | 659 (49.8%) | 57 (14.0%) | 98 (42.8%) | | 2865 (45.3%) |
| Heterosexual contacts | 1770 (43.3%) | 76 (24.7%) | 578 (43.1%) | 72 (17.6%) | 116 (50.4%) | | 2612 (40.9%) |
| Other/Unknown | 226 (5.6%) | 6 (2.0%) | 65 (4.9%) | 9 (2.2%) | 6 (2.6%) | | 312 (4.9%) |
| <i>Nationality, n(%)</i> | | | | | | <.001 | |
| Not Italian | 730 (17.8%) | 30 (9.7%) | 396 (29.5%) | 56 (13.7%) | 77 (33.5%) | | 1289 (20.2%) |
| <i>AIDS diagnosis, n(%)</i> | | | | | | 0.011 | |
| Yes | 457 (11.2%) | 44 (14.3%) | 192 (14.3%) | 56 (13.7%) | 34 (14.8%) | | 783 (12.3%) |
| <i>CD4 count, cells/mm³</i> | | | | | | <.001 | |
| Median (IQR) | 543 (366, 740) | 480 (319, 679) | 497 (321, 700) | 437 (277, 631) | 455 (304, 678) | | 521 (344, 721) |
| <i>Viral load, log₁₀ copies/mL</i> | | | | | | <.001 | |
| Median (range) | 1.52 (0.00, 6.35) | 1.57 (0.00, 4.83) | 1.57 (0.00, 5.67) | 1.60 (0.00, 6.36) | 1.57 (0.00, 4.65) | | 1.56 (0.00, 6.36) |
| Median (IQR) | 1.52 (1.28, 1.60) | 1.57 (1.28, 1.70) | 1.57 (1.28, 1.62) | 1.60 (1.30, 1.70) | 1.57 (1.28, 1.69) | | 1.56 (1.28, 1.61) |
| <i>Antivirals started, n(%)</i> | | | | | | 0.002 | |
| Zidovudine | 206 (5.5%) | 33 (11.5%) | 96 (7.5%) | 62 (15.7%) | 13 (6.1%) | | 410 (6.9%) |
| Lamivudine | 940 (24.9%) | 92 (32.2%) | 377 (29.6%) | 145 (36.6%) | 39 (18.2%) | | 1593 (26.8%) |
| Abacavir | 662 (17.5%) | 42 (14.7%) | 242 (19.0%) | 53 (13.4%) | 10 (4.7%) | | 1009 (17.0%) |
| Tenofovir | 2512 (66.5%) | 183 (64.0%) | 807 (63.3%) | 235 (59.3%) | 169 (79.0%) | | 3906 (65.7%) |
| Emtricitabine | 2704 (71.6%) | 179 (62.6%) | 857 (67.3%) | 225 (56.8%) | 171 (79.9%) | | 4136 (69.5%) |
| TAF | 254 (6.7%) | 6 (2.1%) | 79 (6.2%) | 16 (4.0%) | 15 (7.0%) | | 370 (6.2%) |
| Rilpivirine | 553 (14.6%) | 30 (10.5%) | 143 (11.2%) | 34 (8.6%) | 21 (9.8%) | | 781 (13.1%) |
| Stribild | 250 (6.6%) | 13 (4.5%) | 75 (5.9%) | 9 (2.3%) | 17 (7.9%) | | 364 (6.1%) |
| Triumeq | 273 (7.2%) | 17 (5.9%) | 79 (6.2%) | 12 (3.0%) | 0 (0.0%) | | 381 (6.4%) |
| Genvoia | 143 (3.8%) | 4 (1.4%) | 44 (3.5%) | 7 (1.8%) | 8 (3.7%) | | 206 (3.5%) |
| Dolutegravir | 543 (14.4%) | 26 (9.1%) | 156 (12.2%) | 25 (6.3%) | 15 (7.0%) | | 765 (12.9%) |
| Elvitegravir | 393 (10.4%) | 17 (5.9%) | 119 (9.3%) | 16 (4.0%) | 25 (11.7%) | | 570 (9.6%) |
| Raltegravir | 248 (6.6%) | 20 (7.0%) | 83 (6.5%) | 19 (4.8%) | 16 (7.5%) | | 386 (6.5%) |
| <i>Follow-up time, months</i> | | | | | | 0.209 | |
| Median (IQR) | 46 (24, 78) | 44 (19, 78) | 48 (24, 84) | 52 (20, 89) | 51 (20, 85) | | 47 (23, 80) |

^aChi-square or Kruskal-Wallis test as appropriate

Table 2 Relative hazards (RH) of viral rebound >50 copies/mL from fitting a standard Cox regression model

| Exposure group | Unadjusted and adjusted relative hazards of viral rebound >50 copies/mL | | | | | | | |
|----------------|---|---------|--------------------------------------|---------|--------------------------------------|---------|--------------------------------------|---------|
| | Unadjusted RH (95% CI) | p-value | Adjusted ¹ RH (95% CI) | p-value | Adjusted ² RH (95% CI) | p-value | Adjusted ³ RH (95% CI) | p-value |
| HIV+ | 1 | | 1 | | 1 | | 1 | |
| Only HCVAb+ | 2.00 (1.54, 2.60) | <.001 | 1.65 (1.22, 2.22) | 0.001 | 1.79 (1.25-2.57) | 0.001 | 2.02 (1.55, 2.63) | <.001 |
| Only HBcAb+ | 1.23 (1.04, 1.47) | 0.018 | 1.23 (1.03, 1.46) | 0.022 | 1.26 (1.01-1.57) | 0.040 | 1.22 (1.02, 1.45) | 0.028 |
| HBcAb+/HCVAb+ | 2.55 (2.07, 3.14) | <.001 | 1.96 (1.48, 2.59) | <.001 | 1.73 (1.23-2.45) | 0.002 | 2.56 (2.08, 3.16) | <.001 |
| HBsAg+ | 1.49 (1.07, 2.08) | 0.020 | 1.45 (1.04, 2.04) | 0.029 | 1.57 (1.04-2.04) | 0.033 | 1.46 (1.04, 2.04) | 0.028 |

¹adjusted for duration of VL suppression and history of VF

²adjusted for duration of VL suppression and VL at cART and mode of transmission

³adjusted for nation of birth