|  |  |
| --- | --- |
| N | 57 |
| Age | 41 [38-44] |
| Gender (% women) | 15 (26%) |
| HIV-1 acquisition (% sexual transmission) | 30 (53%) |
| Hepatitis C virus coinfection (%) | 29 (51%) |
| CD4 T cell count (cells/mm3) | 947 [650-1194] |
| Nadir CD4 T cell count (cells/mm3) | 337 [234-375] |
| Time on ART | 7.7 [ 6.2-11.3] |
| Time on suppressive ART (years) | 4.9 [3.1-5.5] |
| Pre-ART HIV-1 load (log10 copies/mL) | 4.2 [3.3-4.8] |

**Supplemental Digital Content 1**: Baseline characteristics of the HIV-1-infected participants.

**Supplemental Digital Content 2**. Baseline characteristics of the 57 individuals included in the study, and association between covariates and plasma HIV-1 RNA rebound after four weeks of treatment discontinuation.

\* No recorded data in two donors.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **HIV-1 RNA rebound (log10 copies/mL)** | | |
|  |  | **Frequency**  **N (%)** | Median [IQ25-75] | **Mann-Whitney U-test**  **p** |
| Route of HIV-1 transmission\* |  |  |  |  |
| Sexual intercourse |  | 30 (52.6) | 3.2 [1.7-5.0] | 0.17 |
| Injecting drug use |  | 25 (43.9) | 4.3 [2.0-5.4] |
| Hepatitis C virus infection\* |  |  |  |  |
| No |  | 27 (47.4) | 3.1 [1.8-5.0] | 0.29 |
| Yes |  | 29 (50.9) | 4.3 [1.9-5.2] |
| TLR9 1635 SNP AG+GG |  | 44 (77.2%) | 3.0 [1.8-4.9] | **0.007** |
| AA |  | 13 (22.8%) | 5.1 [3.8-5.4] |
| TLR2  1892 SNP AA+CC  AC  2258 SNP GG+AA  GA |  | 50 (87.7%)  3 (5.3%)  52 (91.2%)  1 (1.8%) | 3.4 [1.8-5.1]  2.7 [2.2-n/a]  3.3 [1.8-5.1]  [n/a] | 0.18 |
| n/a |
| TLR4 |  |  |  |  |
| 896 SNP AA+GG |  | 40 (70.2%) | 3.4 [1.9-5.1] | 0.74 |
| AG |  | 13 (22.8%) | 3.1 [1.7-5.3] |
| 1196 SNP CC+TT |  | 39 (68.4%) | 3.4 [1.8-5.1] | 0.4 |
| CT |  | 14 (24.6%) | 3.0 [1.7-5.3] |
| CCR5 WT |  | 53 (93) | 3.4 [2.0-5.1] | 0.42 |
| Δ32 |  | 4 (7) | 2.8 [1.7-4.8] |

**Supplemental Digital Content 3.** **A)** HLA-A and **B)** HLA-B allele frequency distribution, and comparison among 57 donors for HIV-1 RNA load after 4 weeks of ART interruption (rebound), HIV-1 RNA load set point (mean HIV-1 RNA load from weeks 8 to 72 of follow-up, and CD4 count set point (mean CD4 cells/mm3 measurements from weeks 8 to 72 of follow up).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **p value (Mann Whitney U-test)** | | |
| **A)** | N (%) | **HIV-1 RNA load rebound** | **HIV-1 RNA load set point** | **CD4 count set point** |
| HLA-A01 |  |  |  |  |
| YES | 10 (17.5) | 0.34 | 0.49 | 0.12 |
| NO | 47 (82.5) |
| HLA-A02 |  |  |  |  |
| YES | 35 (61.4) | 0.42 | 0.20 | 0.47 |
| NO | 22 (38.6) |
| HLA-A03 |  |  |  |  |
| YES | 11 (19.3) | 0.45 | 0.83 | 0.52 |
| NO | 46 (80.7) |
| HLA-A11 |  |  |  |  |
| YES | 7 (12.3) | 0.98 | 0.24 | 0.32 |
| NO | 50 (87.7) |
| HLA-A23 |  |  |  |  |
| YES | 5 (8.8) | 0.31 | 0.45 | 0.39 |
| NO | 52 (91.2) |
| HLA-A24 |  |  |  |  |
| YES | 8 (14.0) | 0.16 | 0.11 | 0.13 |
| NO | 49 (86.0) |
| HLA-A25 |  |  |  |  |
| YES | 2 (3.5) | n/a | n/a | n/a |
| NO | 55 (96.5) |
| HLA-A26 |  |  |  |  |
| YES | 8 (14.0) | **0.02** | 0.74 | **0.04** |
| NO | 49 (86.0) |
| HLA-A29 |  |  |  |  |
| YES | 6 (10.5) | 0.76 | 0.55 | 0.89 |
| NO | 51 (89.5) |
| HLA-A30 |  |  |  |  |
| YES | 5 (8.8) | 0.65 | 0.20 | 0.96 |
| NO | 52 (91.2) |
| HLA-A32 |  |  |  |  |
| YES | 6 (10.5) | 0.38 | 0.62 | 0.15 |
| NO | 51 (89.5) |
| HLA-A33 |  |  |  |  |
| YES | 1 (1.8) | n/a | n/a | n/a |
| NO | 56 (98.2) |
| HLA-A68 |  |  |  |  |
| YES | 3 (5.2) | 0.14 | **0.04** | 0.31 |
| NO | 54 (94.7) |
| HLA-A74 |  |  |  |  |
| YES | 0 (0) | n/a | n/a | n/a |
| NO | 57 (100) |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **p value (Mann Whitney U-test)** | | |
| **B)** | N (%) | **HIV-1 RNA load rebound** | **HIV-1 RNA load set point** | **CD4 count set point** |
| HLA-B7 |  |  |  |  |
| YES | 9 (15.8) | 0.71 | 0.06 | 0.26 |
| NO | 48 (84.2) |
| HLA-B8 |  |  |  |  |
| YES | 9 (15.8) | 0.70 | 0.96 | 0.84 |
| NO | 48 (84.2) |
| HLA-B14 |  |  |  |  |
| YES | 12 (21.1) | 0.42 | 0.85 | 0.36 |
| NO | 45 (78.9) |
| HLA-B15 |  |  |  |  |
| YES | 6 (10.5) | 0.19 | 0.55 | 0.29 |
| NO | 51 (89.5) |
| HLA-B18 |  |  |  |  |
| YES | 10 (17.5) | 0.13 | 0.13 | 0.34 |
| NO | 47 (82.5) |
| HLA-B27 |  |  |  |  |
| YES | 3 (5.2) | 0.42 | 0.25 | 0.61 |
| NO | 54 (94.7) |
| HLA-B35 |  |  |  |  |
| YES | 10 (17.5) | 0.65 | 0.27 | 0.53 |
| NO | 47 (82.5) |
| HLA-B40 |  |  |  |  |
| YES | 3 (5.2) | 0.48 | 0.76 | 0.20 |
| NO | 54 (94.7) |
| HLA-B44 |  |  |  |  |
| YES | 37 (64.9) | 0.63 | 0.98 | 0.65 |
| NO | 20 (35.1) |
| HLA-B45 |  |  |  |  |
| YES | 1 (1.8) | n/a | n/a | n/a |
| NO | 56 (98.2) |
| HLA-B51 |  |  |  |  |
| YES | 10 (17.5) | 0.11 | 0.68 | 0.55 |
| NO | 47 (82.5) |
| HLA-B50/56 |  |  |  |  |
| YES | 3 (5.2) | 0.77 | 0.28 | 0.53 |
| NO | 54 (94.7) |
| HLA-B57 |  |  |  |  |
| YES | 6 (10.5) | 0.10 | 0.07 | 0.13 |
| NO | 51 (89.5) |
| HLA-B53 |  |  |  |  |
| YES | 2 (3.5) | n/a | n/a | n/a |
| NO | 55 (96.5) |

n/a, not applicable. Comparison between groups was performed when groups had at least three participants to compare.

**Supplemental** **Digital Content 4**. Men’s baseline characteristics and association between covariates and plasma HIV rebound after four weeks of treatment discontinuation.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **HIV-1 RNA rebound (log10 copies/mL)** | | |
|  |  | **Frequency**  **N (%)** | **Median [IQ25-75]** | **Mann-Whitney U test**  **p** |
| Route of HIV-1 transmission\* |  |  |  |  |
| Sexual intercourse |  | 19 (45%) | 3.4 [2.6-5.1] | 0.47 |
| Injecting drug use |  | 21 (50%) | 4.3 [2.0-5.4] |
| Hepatitis C virus infection\* |  |  |  |  |
| No |  | 20 (48%) | 3.4 [2.3-5.1] | 0.14 |
| Yes |  | 21 (50%) | 4.7 [2.7-5.5] |
| CCR5 Δ32 |  | 39 (93%)  3 (7%) | 4.3 [2.6-5.2]  3.9 [1.7-n/a] | 0.64 |
| TLR9 1635 SNP AG+GG |  | 31 (74%) | 3.3 [1.9-5.1] | **0.007** |
| AA |  | 11 (26%) | 5.1 [4.7-5.5] |
| TLR2  1892 SNP AA+CC  AC  2258 SNP GG+AA  GA |  | 37 (94.8%)  2 (5.1%)  38 (97.5%)  1 (2.5%) | 3.9 [2.4-5.2]  3.7 [2.2-n/a]  3.7 [2.2-5.2]  5.5 [n/a] | 0.97 |
| 0.31 |
| TLR4 |  |  |  |  |
| 896 SNP AA+GG |  | 30 (71%) | 4.1 [2.5-5.2] | 0.76 |
| AG |  | 9 (21%) | 3.4 [1.9-5.4] |
| 1196 SNP CC+TT |  | 29 (69%) | 4.3 [2.7-5.2] | 0.37 |
| CT |  | 10 (24%) | 3.1 [1.7-5.4] |

\* No recorded data in two donors.

**Supplemental Digital Content 5.** **A)** HLA-A and **B)** HLA-B allele frequency distribution and comparison within men for HIV-1 RNA load after 4 weeks of ART interruption (rebound), HIV-1 RNA load set point (mean HIV-1 RNA load from weeks 8 to 72 of follow-up, and CD4 count set point (mean CD4 cells/mm3 measurements from weeks 8 to 72 of follow up).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **p value (Mann Whitney U-test)** | | |
| **A)** | N (%) | **HIV-1 RNA load rebound** | **HIV-1 RNA load set point** | **CD4 count set point** |
| HLA-A01 |  |  |  |  |
| YES | 8 (19) | 0.64 | 0.42 | 0.08 |
| NO | 34 (81) |
| HLA-A02 |  |  |  |  |
| YES | 16 (38) | 0.59 | 0.54 | 0.54 |
| NO | 26 (62) |
| HLA-A03 |  |  |  |  |
| YES | 9 (21) | 0.21 | 0.29 | 0.48 |
| NO | 33 (79) |
| HLA-A11 |  |  |  |  |
| YES | 4 (10) | 0.44 | 0.49 | 0.81 |
| NO | 38 (90) |
| HLA-A23 |  |  |  |  |
| YES | 3 (7) | n/a | 0.93 | 0.49 |
| NO | 39 (93) |
| HLA-A24 |  |  |  |  |
| YES | 7 (16) | 0.43 | 0.52 | 0.25 |
| NO | 35 (84) |
| HLA-A25 |  |  |  |  |
| YES | 1 (2) | n/a | n/a | n/a |
| NO | 41 (98) |
| HLA-A26 |  |  |  |  |
| YES | 6 (14) | 0.07 | 0.94 | 0.26 |
| NO | 36 (86) |
| HLA-A29 |  |  |  |  |
| YES | 6 (14) | 0.34 | 1.00 | 0.91 |
| NO | 36 (86) |
| HLA-A30 |  |  |  |  |
| YES | 3 (7) | n/a | n/a | n/a |
| NO | 39 (93) |
| HLA-A32 |  |  |  |  |
| YES | 4 (10) | n/a | n/a | n/a |
| NO | 38 (90) |
| HLA-A33 |  |  |  |  |
| YES | 1 (2) | n/a | n/a | n/a |
| NO | 41 (98) |
| HLA-A68 |  |  |  |  |
| YES | 1 (2) | n/a | n/a | n/a |
| NO | 41 (98) |
| HLA-A74 |  |  |  |  |
| YES | 0 (0) | n/a | n/a | n/a |
| NO | 42 (100) |
|  |  | **p value (Mann Whitney U-test)** | | |
| **B)** | N (%) | **HIV-1 RNA load rebound** | **HIV-1 RNA load set point** | **CD4 count set point** |
| HLA-B7 |  |  |  |  |
| YES | 9 (21) | 0.36 | 0.17 | 0.14 |
| NO | 33 (79) |
| HLA-B8 |  |  |  |  |
| YES | 6 (14) | 0.97 | 0.85 | 0.67 |
| NO | 36 (86) |
| HLA-B14 |  |  |  |  |
| YES | 8 (19) | 0.64 | 0.41 | 0.67 |
| NO | 34 (81) |
| HLA-B15 |  |  |  |  |
| YES | 6 (14) | 0.52 | 0.97 | 0.18 |
| NO | 36 (86) |
| HLA-B18 |  |  |  |  |
| YES | 5 (12) | **0.038** | 0.11 | 0.89 |
| NO | 37 (88) |
| HLA-B27 |  |  |  |  |
| YES | 2 (5) | n/a | n/a | n/a |
| NO | 40 (95) |
| HLA-B35 |  |  |  |  |
| YES | 6 (14) | 0.18 | 0.76 | 0.64 |
| NO | 36 (86) |
| HLA-B40 |  |  |  |  |
| YES | 2 (5) | n/a | n/a | n/a |
| NO | 40 (95) |
| HLA-B44 |  |  |  |  |
| YES | 24 (57) | 0.83 | 0.47 | 0.79 |
| NO | 18 (43) |
| HLA-B45 |  |  |  |  |
| YES | 0 (0) | n/a | n/a | n/a |
| NO | 42 (100) |
| HLA-B51 |  |  |  |  |
| YES | 8 (19) | 0.23 | 0.71 | 0.51 |
| NO | 34 (81) |
| HLA-B50/56 |  |  |  |  |
| YES | 2 (5) | n/a | n/a | n/a |
| NO | 40 (95) |
| HLA-B57 |  |  |  |  |
| YES | 4 (10) | 0.15 | 0.065 | 0.35 |
| NO | 38 (90) |
| HLA-B27/57 |  |  |  |  |
| YES | 6 (14) | 0.14 | **0.037** | 0.37 |
| NO | 36 (86) |

n/a, not applicable. Comparison between groups was performed when groups had at least three participants to compare.

**Supplemental Digital Content 6**: Univariate and multivariate linear regression analyses to assess factors independently associated with HIV-1 RNA load and CD4 T cell count set point after ART interruption.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **HIV-1 RNA load set point** | | | |  |  | **CD4 T cell count set point** | | | |
|  | Univariate |  | Multivariate | |  |  | Univariate |  | Multivariate | |
|  | p |  | p | Regression coefficient  [95% Confidence interval] |  |  | p |  | p | Regression coefficient  [95% Confidence interval] |
| TLR41196C/T | 0.027 |  | ns |  |  | HLA-A01 | 0.050 |  | **0.027** | 0.316 [20.34-313.26] |
| Pre-ART viral load | <0.001 |  | **0.001** | 0.456 [0.20-0.71] |  | Nadir CD4 count | 0.002 |  | **0.001** | 0.691 [0.29-1.09] |
| Nadir CD4 count | 0.030 |  | ns |  |  |  |  |  |  |  |
| Time with viral load <50 copies/mL | <0.001 |  | **0.002** | -0.173 [-0.27- -0.07] |  |  |  |  |  |  |

ns; not significant.



**Supplemental Digital Content 7: Sex but not TLR9 1635A/G SNP or HLA-A26 allele, is associated with a lower HIV-1 plasma load during the follow up.** A) Women had lower viral load than men during the 72 weeks of follow up (p<0.05). B) TLR9 1635A/G SNP and C) HLA-A26 allele are not directly associated with the HIV-1 load during the follow up (p=not significant, NS).



**Supplemental Digital Content 8. Variables associated with the establishment of a viral load and CD4 T cell count set point.** HIV-1 RNAload positively correlates with A) pre-ART HIV-1 RNA (r=0.69, p<0.001), and B) HIV-1 RNA rebound at week four after interruption (r=0.52, p<0.001). Women are represented with open triangles and men with filled circles. C) CD4 T cell count set point positively correlated with nadir CD4 T cell count (r=0.48, p=0.001).



**Supplemental Digital Content 9. Comparison between women and men according to HIV-1 RNA load and CD4 cell count set points.** A) Women and men showed similar levels of pre-ART HIV-1 RNA load while women had lower levels of HIV-1 RNA load at the set point (p=0.002). B) Similar levels of both nadir CD4 cell count and CD4 cell count set point. W, women and M, men.