**SUPPLEMENTAL TABLES**

**Supplemental Table S1. Cohort demographics and HIV-1 status.** All times are in years.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **#** | **Gender** | **Race** | **Latino** | **Risk** | **B\*57** | **HCV****Ab** | **HCV****PCR** | **F/U****Start Age** | **SCV F/U****Duration****(Years)** | **CD4+ T cells****at Start****(cells/ul)** | **Est. Time****HIV+****At Start** | **Est.****Age****Infected** | **SCV****F/U End** |
| 1 | M | White | N | \*\* | \*\* | N | \*\* | 61.8 | 7.2 | 1495 | 0.0 | 61.8 | ART |
| 2 | F | White | N | CSW/FSM | N | N | \*\* | 36.9 | 13.7 | 659 | 0.0 | 36.8 | IC |
| 3 | M→F | White | N | MSM | \*\* | N | \*\* | 24.3 | 11.3  | 550 | 0.0\*\*\* | 24.3 | **Viremia (a)** |
| 4 | F | Black | \*\* | IVDU | \*\* | Y | Y | 62.5 | 3.4 | 1071 | 0.0 | 62.5 | OOC |
| 5\* | F | Black | N | \*\* | \*\* | \*\* | \*\* | 44.8 | 9.4  | 1128 | 2.5 | 42.2 | **Viremia (b)** |
| 6 | M | Black | \*\* | MSM | N | N | \*\* | 36.7 | 8.6 | 801 | 11.0 | 25.7 | OOC |
| 7 | M | White | N | \*\* | \*\* | N | \*\* | 52.1 | 5.2 | 547 | 25.1 | 27.0 | IC |
| 8 | M | Black | N | \*\* | N | Y | N | 50.4 | 5.6 | 746 | 15.3 | 35.1 | IC |
| 9 | F | Black | \*\* | FSM | \*\* | N | \*\* | 24.5 | 9.7  | 1074 | 2.2 | 22.3 | **Viremia (a)** |
| 10 | M | Black | \*\* | \*\* | \*\* | N | \*\* | 50.6 | 7.2 | 709 | 0.3 | 50.3 | IC |
| 11 | F | Black | N | \*\* | \*\* | \*\* | N | 50.4 | 9.5 | 1111 | 13.6 | 36.8 | IC |
| 12 | F | Black | N | \*\* | \*\* | N | \*\* | 36.6 | 6.7 | 1105 | 7.3 | 29.3 | IC |
| 13 | M | Black | N | \*\* | \*\* | \*\* | Y | 51.3 | 9.4 | 904 | 0.0 | 51.3 | IC |
| 14\* | F | Black | N | \*\* | \*\* | N | \*\* | 45.3 | 3.1  | 619 | 18.3 | 27.0 | **Viremia (b)** |
| 15 | F | Black | N | \*\* | \*\* | N | \*\* | 45.8 | 5.0 | 674 | 2.0 | 43.9 | IC |
| 16 | F | Black | N | \*\* | \*\* | N | \*\* | 48.9 | 4.8 | 743 | 20.4 | 28.5 | IC |
| 17 | M | White | N | MSM | \*\* | N | \*\* | 51.1 | 2.5 | 491 | 8.7 | 42.4 | OOC |
| 18 | F | Black | N | FSM | N | N | \*\* | 44.3 | 4.1 | 1032 | 3.9 | 40.4 | IC |
| 19 | M | Black | N | \*\* | \*\* | N | \*\* | 38.1 | 1.9 | 851 | 0.6 | 37.5 | OOC |
| 20 | F | Black | N | \*\* | \*\* | N | \*\* | 43.0 | 0.6 | 1122 | 20.0 | 22.9 | OOC |
| 21 | F | White | Y | \*\* | N | N | \*\* | 21.3 | 3.0 | 804 | 0.0 | 21.3 | IC |
| 22 | F | Black | N | IVDU | \*\* | Y | \*\* | 54.9 | 1.4 | 1350 | 30.4 | 24.5 | IC |
| 23 | F | Black | Y | \*\* | \*\* | \*\* | \*\* | 34.8 | 2.4 | 1785 | 0.1 | 34.7 | IC |
| 24 | F | Black | N | \*\* | N | N | \*\* | 37.2 | 1.7 | 507 | 5.2 | 32.0 | IC |
| 25\* | F | Black | N | FSM | \*\* | \*\* | \*\* | 59.8 | 1.6 | 1363 | 17.3 | 42.6 | IC |
| 26 | F | Black | N | FSM | \*\* | \*\* | \*\* | 29.2 | 1.7 | 914 | 2.4 | 26.8 | IC |
| 27 | M | Black | N | MSM | \*\* | N | \*\* | 63.6 | 1.7 | 955 | 24.0 | 39.6 | IC |
| 28 | M | White | \*\* | MSM | \*\* | N | \*\* | 48.9 | 3.0 | 1243 | 8.3 | 40.6 | IC |
| 29 | M | Black | N | \*\* | \*\* | N | \*\* | 33.7 | 9.2 | 333 | 0.0 | 33.7 | ART |
| 30\* | F | White | N | CSW/FSM | Y | Y | Y | 50.2 | 14.1 | 279 | 3.7 | 46.4 | IC |
| 31 | M | Black | N | \*\* | \*\* | N | \*\* | 48.9 | 3.4  | 1351 | 0.0 | 48.9 | **Viremia (b)** |
| 32 | M | \*\* | \*\* | MSM | \*\* | N | \*\* | 40.8 | 3.6 | 480 | 0.0\*\*\* | 40.8 | OOC |
| 33 | M | White | \*\* | MSM | \*\* | N | \*\* | 57.7 | 2.5 | 676 | 5.3 | 52.4 | OOC |
| 34 | M | White | \*\* | MSM/IVDU | \*\* | N | \*\* | 46.8 | 2.3 | 858 | 0.2 | 46.6 | OOC |
| 35\* | M | Black | N | \*\* | \*\* | N | \*\* | 47.4 | 1.9 | 317 | 20.9 | 26.5 | OOC |
| 36 | M→F | Black | N | \*\* | \*\* | Y | Y | 44.8 | 7.9 | 733 | 23.8 | 21.0 | OOC |
| 37 | F | Black | \*\* | FSM | N | N | \*\* | 29.4 | 4.2 | 1010 | 0.1\*\*\* | 29.3 | OOC |
| 38 | M | \*\* | \*\* | MSM | \*\* | N | \*\* | 36.0 | 3.0 | 948 | 0.1\*\*\* | 35.9 | OOC |
| 39 | M | White | Y | MSM | Y | N | \*\* | 30.2 | 3.4  | 378 | 0.0\*\*\* | 30.2 | **Viremia (b)** |
| 40 | F | White | N | \*\* | N | Y | Y | 58.0 | 5.2 | 446 | 20.1 | 37.9 | IC |
| 41 | F | Black | N | \*\* | \*\* | N | \*\* | 37.8 | 5.1 | 1863 | 8.4 | 29.4 | IC |
| 42 | M | Black | N | MSM | N | N | \*\* | 28.4 | 2.3 | 977 | 1.3\*\*\* | 27.1 | OOC |
| 43 | M | White | Y | MSM | N | N | \*\* | 27.7 | 2.5 | 931 | 0.0\*\*\* | 27.7 | IC |
| 44 | F | Black | N | FSM | N | N | \*\* | 48.1 | 1.3 | 822 | 0.4 | 47.6 | OOC |
| 45\* | F | Black | N | \*\* | N | N | \*\* | 31.3 | 1.1 | 717 | 11.8 | 19.5 | IC |
| 46 | M | White | Y | MSM | N | N | \*\* | 47.9 | 0.5 | 1025 | 0.0 | 47.9 | IC |
| 47 | M | Black | N | MSM | N | \*\* | \*\* | 50.7 | 1.1 | 722 | 33.3 | 17.4 | ART |
| 48 | F | White | Y | \*\* | \*\* | N | \*\* | 32.6 | 13.3 | 1105 | 0.9 | 31.8 | IC |
| 49\* | M→F | Black | N | MSM | N | Y | N | 42.2 | 8.2  | 1302 | 10.3 | 32.0 | **Viremia (b)** |
| 50 | F | Black | N | \*\* | \*\* | N | \*\* | 27.6 | 5.5  | 552 | 0.1 | 27.5 | **Viremia (b)** |
| 51 | F | Asian | N | \*\* | N | N | \*\* | 47.7 | 1.5  | 902 | 0.1 | 47.6 | **Viremia (b)** |
| 52 | M | White | N | MSM | \*\* | Y | Y | 38.5 | 9.6 | 944 | 0.0 | 38.5 | IC |
| 53 | M | White | \*\* | \*\* | \*\* | N | \*\* | 42.3 | 7.6 | 712 | 0.0 | 42.3 | ART |

\* History of limited course of ART before viremic control

\*\*Not specified or not tested

\*\*\*Reported HIV-1 seronegative test within 2 years of first seropositive test

“M”: Male

“F”: Female

“M→F”: Transgender from male to female

“N/S”: Not specified

“CSW”: Commercial sex work

“FSM”: Female sex with male

“MSM”: Male sex with male

“IVDU”: Intravenous drug (illicit) use

“ART”: Started on ART while aviremic; follow-up duration reflects time until start of ART

“IC”: Was still in care at AHF at the time of this study

“Viremia”: Became viremic during follow-up; observed loss of SCV due to a) viremia>1000 or b) three consecutive levels ≥50

“OOC”: Out of care at AHF; censored for loss to follow-up

**Supplemental Table S2. Frequencies and magnitudes of intermittently detectable viremia “blips” in persons with sustained or non-sustained SCV during observation period of SCV.**

|  |  |
| --- | --- |
|  | **Estimated Years Infected** |
| **0 to <5** | **5 to <10** | **10 to <15** | **15 to <20** | **20 to <25** | **25 to <30** | **30 to <35** | **All** |
| **%****Detectable****(Fraction)** | **Detectable****Median****(Range)** | **%****Detectable****(Fraction)** | **Detectable****Median****(Range)** | **%****Detectable****(Fraction)** | **Detectable****Median****(Range)** | **%****Detectable****(Fraction)** | **Detectable****Median****(Range)** | **%****Detectable****(Fraction)** | **Detectable****Median****(Range)** | **%****Detectable****(Fraction)** | **Detectable****Median****(Range)** | **%****Detectable****(Fraction)** | **Detectable****Median****(Range)** | **%****Detectable****(Fraction)** | **Detectable****Median****(Range)** |
| **Sustained****SCV (44)** | 4.2%(8/189) | 2.08(1.78-2.44) | 9.1%(10/110) | 1.90(1.85-2.34) | 2.2%(1/46) | 1.96(1.96-1.96) | 2.5%(1/40) | 2.20(2.20-2.20) | 11.3%(6/53) | 1.81(1.78-2.20) | 6.3%(2/32) | 2.15(1.97-2.32) | 7.1%(1/14) | 2.26(2.26-2.26) | 5.8%(28/484)\*\* | 1.97(1.78-2.44) |
| **Non-Sustained****SCV (9)** | 16.7%(6/36) | 2.03(1.82-2.88) | 16.7%(1/6) | 2.89(2.89-2.89) | 12.5%(1/8) | 2.04(2.04-2.04) | 18.2%(2/11) | 1.81(1.78-1.85) | 0%(0/2) | - | - | - | - | - | 15.9%(10/63)\*\* | 1.98(1.78-2.89) |
| **All****Subjects (53)** | 6.2%(14/225) | 2.08(1.78-2.88) | 8.6%(10/116) | 1.90(1.85-2.89) | 3.7%(2/54) | 2.00(1.96-2.04) | 5.9%(3/51) | 1.85(1.78-2.20) | 10.9%(6/55) | 1.81(1.78-2.00) | 6.3%(2/32) | 2.15(1.97-2.32) | 7.1%(1/14) | 2.26(2.26-2.26) | 6.9%(38/547) | 1.97(1.78-2.89) |

Percentages of viremia tests that were ≥50 RNA copies/mL versus <50 RNA copies/mL, and median values of detectable viremia tests (log10 RNA copies/mL plasma) are indicated for the indicated time periods in relationship to estimated duration of infection. Viremia measurements before qualification of SCV were excluded, to avoid tests before stable viremia was established in chronic infection.

**Supplemental Table S3. Frequencies and magnitudes of intermittent viremia “blips” in relationship to loss of SCV.**

|  |
| --- |
| **Years to Loss of SCV** |
| **-10 to >-5** | **-5 to >0** |
| **% Detectable****(Fraction)** | **Detectable****Median****(Range)** | **% Detectable****(Fraction)** | **Detectable****Median****(Range)** |
| 33.3%(5/15) | 2.15(1.82-2.89) | 10.4%(5/48) | 1.85(1.78-2.88) |

For the nine persons with non-sustained SCV, percentages of viremia tests that were ≥50 RNA copies/mL versus <50 RNA copies/mL, and median values of detectable viremia tests (log10 RNA copies/mL plasma) are indicated for the indicated time periods in relationship to loss of SCV. Viremia measurements before qualification of SCV were excluded, to avoid tests before stable viremia was established in chronic infection.

**Supplemental Table S4. Mixed effects model for blood CD4+ T cell slopes.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Effect** | **Estimate** | **95% Confidence****Interval** | **P-value** |
| Intercept | 882.27 |  |  |
| Age at estimated infection time (years)a | 6.15 | -0.10, 12.39 | 0.054 |
| Baseline blood CD4+ T-cell level (cells/μl)a | 0.97 | 0.80, 1.15 | <0.0001 |
| Female genderb | 105.23 | -17.37, 227.84 | 0.091 |
| Black racec | -4.87 | -135.23, 125.48 | 0.940 |
| Observed loss of SCV | 18.05 | -153.65, 189.74 | 0.833 |
| Estimated duration of infection at entrya | -1.11 | -8.44, 6.23 | 0.763 |
| Follow-up time from entry (years) | -9.79 | -28.68, 9.10 | 0.309 |
| Follow-up time to observed loss of SCV\* (years) | -17.65 | -45.49, 10.19 | 0.213 |
| Duration of infection at entry\*follow-up time (years) | -1.28 | -2.63, 0.06 | 0.062 |
| Baseline CD4\* follow-up time (years) | -0.02 | -0.04, -0.006 | 0.008 |
| Black race\* follow-up time (years) | 3.46 | -14.05, 20.96 | 0.698 |
| Age at infection\* follow-up time (years) | -1.89 | -2.68, -1.09 | <0.0001 |
| Female\* follow-up time (years) | 8.98 | -7.83, 25.79 | 0.294 |

The rate of blood CD4+ T-cell level decline during the observation period was estimated in the SCV cohort (n=50, excluding 3 transgender patients) using linear mixed effects modeling with random intercept and fixed effect covariates of age at time of infection, initial blood CD4+ T-cell level, duration of infection at entry, race, gender, viremic status (loss of SCV versus persistent SCV during observation), and follow-up time. The interaction of each covariate with follow-up time was included in the model to assess the effect of each covariate on the slope of CD4+ T-cell decline. The overall slope in CD4+ T-cell blood level (assuming mean values in the cohort for age at the time of infection, baseline blood CD4+ T cell level, duration of infection, White race, male gender, and persistent SCV) is given by the estimate for follow-up time (-9.79 cells/μL/year). The estimates for the interactions provide the difference from this overall slope associated with each covariate.

aCentered at mean

bReference = male

cReference = White race

\*Interaction term

**Supplemental Table S5. Selected studies estimating the prevalence of SCV within populations of persons with HIV-1 infection.**

|  |  |  |  |
| --- | --- | --- | --- |
|  |  |  | **SCV/Total (%)** |
| **Authors** | **Definition of SCV****(“Elite Control”)** | **Median Age****Diagnosed** | **All** | **Males** | **Females** | **Whites** | **Blacks** | **Asians** |
| Olson *et al*[[1](#_ENREF_1)] | Viremia <75 for three consecutive testsover >1 year without “blips” >1000from persons with known seroconversion timein 28 cohorts across Europe, Canada, Australia,and sub-Saharan Africa | 32 | 95/17,334\*(0.55%) | 60/13,506\*(0.44%) | 35/3,828\*(0.92%) | NR/NR(?) | NR/NR(?) | NR/NR(?) |
| Grabar *et al*[[2](#_ENREF_2)] | Infected ≥10 years, asymptomatic, ART-naïve,with 90% tests of viremia <500 and last viremia <50from persons with chronic infection in France | 28 | 69/27,257\*\*(0.25%) | 43/NR(?) | 26/NR(?) | 64/NR(?) | 4/NR(?) | NR |
| Lambotte *et al*[[3](#_ENREF_3)] | Infected ≥10 years, ART-naïve,with 90% tests of viremia <400from persons with chronic infection in France | 40 | 15/2,851(0.53%) | 11/NR(?) | 4/NR(?) | NR | NR | NR |
| Okulicz *et al*\*\*\*[[4](#_ENREF_4)] | Viremia below detection (400, 200, or 50)for three consecutive tests over ≥1 yearwithout “blips”>1000from persons with chronic infection in USA | 27 | 25/4,468(0.56%) | 20/4,045(0.49%) | 5/423(1.18%) | 13/1,965(0.66%) | 11/2,000(0.55%) | 0/73(0.0%) |
| Current Study | Viremia <50 for three consecutive tests over >1 yearfrom persons with chronic infection in USA | 35 | 53/29,811(0.18%) | 24/24,603(0.10%) | 26/4,517(0.58%) | 17/16,559(0.10%) | 33/10,089(0.33%) | 1/430(0.23%) |

All viremia level definitions in the absence of ART.

NR= Not Reported

\*Denominator numbers were inferred from adding persons with versus without SCV, and reported percentages of men in each group

\*\*Denominator reflects only persons infected at least 8 years with ≥ three viremia tests in past 5 years (27,257 of 46,880 in the total cohort); demographics were not reported for this group.

\*\*\*This study classified a cohort of 4,586 persons as 25 “elite controllers,” 153 “viremic controllers,” 52 “long term nonprogressors” for 7 years, 101 “long term nonprogressors” for 10 years, and 4,290 “other subjects.” Because the elite and viremic controller groups did not overlap with each other or the “other subjects” but did overlap with the nonprogressor groups, the denominators are calculated from the reported numbers of elite and viremic controller groups combined with “other subjects,” totaling 4,468 persons within the total cohort of 4,586 persons. Numbers of females are inferred from reported numbers of males versus these totals.

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4. Okulicz JF, Marconi VC, Landrum ML, et al. Clinical outcomes of elite controllers, viremic controllers, and long-term nonprogressors in the US Department of Defense HIV natural history study. J Infect Dis **2009**; 200(11): 1714-23.

**SUPPLEMENTAL FIGURE LEGENDS**

**Supplemental Figure S1. Racial and gender demographics of 53 HIV-1-infected persons with SCV.** The plot indicates the breakdown of the cohort by race and gender.

**Supplemental Figure S2. Censored observation normal fitting for viremia measurements.** Maximum likelihood estimates were done for viremia tests using both censored (<50 RNA copies/mL plasma, indicated by the horizontal dotted line) and observed (≥50 RNA copies/mL plasma) values in A. persons with sustained SCV throughout observation and B. persons with observed loss of SCV during observation. Frequencies of detectable viremia (≥50 RNA copies/mL plasma) are plotted as bars for comparisons to the best-fit distribution curves. The means for the sustained and non-sustained SCV groups were 0.65 and 0.83 respectively (95% confidence intervals 0.26 - 1.03 and 0.40 - 1.34 respectively).