Appendix Table 1: Availability of baseline and 6-month follow-up inflammation data

|  |  |  |
| --- | --- | --- |
|  | Available | Missing |
| sCD4 | 269 (95%) | 13 (5%) |
| sCD163 | 269 (95%) | 13 (5%) |
| D-dimer | 271 (96%) | 11 (4%) |
| HLA-DR+/CD8+ | 199 (71%) | 83 (29%) |
| IL-6 | 267 (95%) | 15 (5%) |
| K:T ratio | 270 (96%) | 12 (4%) |

Appendix Table 2: Secondary models assessing the effect of average percentage adherence on inflammatory biomarkers. Both sets of models adjust for potential confounders (baseline inflammation level, use of a Nevirapine versus Efavirenz based regimen, duration of viral suppression, age, gender, baseline log viral load, depression[27, 29][27, 29][26, 28], and heavy alcohol use); the second model also adjusts for adherence interruptions.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Effect of average adherence on biomarkers of inflammation | | | |
| Biomarker | Without adjustment for adherence interruptions | | With adjustment for adherence interruptions | |
|  | **Effect (95% CI)** | **P** | **Effect (95% CI)** | **P** |
| **sCD14** | -0.14 (-0.4, 0.1) | 0.28 | 0.24 (-0.2, 0.7) | 0.28 |
| **sCD163** | -0.16 (-0.6, 0.3) | 0.45 | 0.7 (0.1, 1.3) | 0.027 |
| **D-dimer** | -1.2 (-2.1, -0.3) | 0.008 | -1.0 (-2.5, 0.6) | 0.22 |
| **HLA-DR+/CD8+** | -0.4 (-0.7, -0.1) | 0.023 | -0.3 (-0.8, 0.2) | 0.23 |
| **IL-6** | -1.6 (-2.5, -0.6) | 0.003 | -1.0 (-2.5, 0.4) | 0.16 |
| **K/T ratio** | -0.3 (-0.7, 0.1) | 0.17 | 0.5 (-0.2, 1.1) | 0.17 |

Appendix Table 3a: Sensitivity analysis: Effect of adherence interruptions on inflammatory biomarkers adjusting for confounders (baseline inflammation, use of a Nevirapine versus Efavirenz based regimen, age, gender, baseline log viral load, depression[27, 29][27, 29][26, 28], heavy alcohol use, and duration of viral suppression) excluding participants without Month 3 viral suppression data.

|  |  |  |
| --- | --- | --- |
| Biomarker | Primary model excluding participants without Month 3 viral suppression data. | |
|  | **Effect (95% CI)** | **P** |
| **sCD14** | 2.6 (0.3, 5.0) | 0.029 |
| **sCD163** | 4.9 (1.0, 8.9) | 0.013 |
| **D-dimer** | 7.3 (-2.9, 18.5) | 0.17 |
| **HLA-DR+/CD8+** | 2.3 (0.1, 4.6) | 0.041 |
| **IL-6** | 16.7 (6.2, 28.3) | 0.001 |
| **K/T ratio** | 5.0 (1.6, 8.6) | 0.004 |

Appendix Table 3b: Sensitivity analyses: Effect of adherence interruptions on inflammatory biomarkers considering the time in an interruption as the percentage of days with <20, <30 and <50% adherence, as well as the number of >72 hour interruptions.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Threshold** | | | | | |  | |
|  | **<20%** | | **<30%** | | **<50%** | | **# > 72 hr interruptions** | |
| **Biomarker** | **Effect (95% CI)** | **P** | **Effect (95% CI)** | **P** | **Effect (95% CI)** | **P** | **Effect (95% CI)** | **P** |
| **sCD14** | 1.7 (0.3, 3.2) | 0.019 | 1.3 (-0.1, 2.6) | 0.057 | 0.4 (-0.8, 1.6) | 0.51 | 0.9 (-1.1, 2.9) | 0.37 |
| **sCD163** | 3.4 (1.1, 5.8) | 0.004 | 2.8 (0.6, 5.0) | 0.014 | 1.3 (-5.3, 3.2) | 0.17 | 1.5 (-2.1, 5.2) | 0.43 |
| **D-dimer** | 8.2 (2.5, 14.20) | 0.004 | 7.07 (2.0, 12.4) | 0.006 | 4.3 (-0.3, 9.1) | 0.065 | 11.1 (3.1, 19.8) | 0.006 |
| **HLA-DR+/CD8+** | 2.4 (0.7, 4.2) | 0.007 | 2.2 (0.7, 3.8) | 0.005 | 1.6 (0.3, 2.9) | 0.015 | 2.8 (0.7, 5.0) | 0.011 |
| **IL-6** | 11.4 (3.3, 20.3) | 0.005 | 9.7 (2.5, 17.4) | 0.008 | 7.1 (1.9, 12.4) | 0.007 | 10.5 (1.1, 20.9) | 0.028 |
| **K/T ratio** | 4.1 (1.9, 6.3) | <0.001 | 3.3 (1.0, 5.6) | 0.005 | 1.8 (-0.2, 3.9) | 0.078 | 3.3 (-0.9, 7.7) | 0.13 |

Appendix Table 4a: Computation of running average corresponding to the data in Figure 1. In this table, the symbols “√” and “-” from Figure 1 are represented by 100% and 0% respectively. In computing the running averages, we assumed perfect (100%) adherence in the days proceeding and those following the 28 days.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Pattern | A | | B | | C | | D | | E | |
| Day | Daily Adh | Running Average | Daily Adh | Running Average | Daily Adh | Running Average | Daily Adh | Running Average | Daily Adh | Running Average |
| … | … | … | … | … | … | … | … | … | … | … |
| 1 | 100 | 100 | 100 | 67 | 100 | 67 | 100 | 89 | 100 | 100 |
| 2 | 100 | 100 | 0 | 56 | 100 | 56 | 100 | 78 | 100 | 89 |
| 3 | 100 | 100 | 0 | 56 | 0 | 44 | 100 | 67 | 100 | 78 |
| 4 | 100 | 100 | 100 | 44 | 0 | 33 | 100 | 56 | 100 | 67 |
| 5 | 100 | 100 | 0 | 33 | 0 | 22 | 0 | 44 | 100 | 56 |
| 6 | 100 | 100 | 0 | 33 | 0 | 11 | 0 | 33 | 0 | 44 |
| 7 | 100 | 100 | 100 | 33 | 0 | 0 | 0 | 22 | 0 | 33 |
| 8 | 100 | 100 | 0 | 33 | 0 | 11 | 0 | 11 | 0 | 22 |
| 9 | 100 | 100 | 0 | 33 | 0 | 22 | 0 | 0 | 0 | 11 |
| 10 | 100 | 100 | 100 | 33 | 0 | 33 | 0 | 11 | 0 | 0 |
| 11 | 100 | 100 | 0 | 33 | 0 | 44 | 0 | 22 | 0 | 0 |
| 12 | 100 | 100 | 0 | 33 | 100 | 56 | 0 | 22 | 0 | 0 |
| 13 | 100 | 100 | 100 | 33 | 100 | 67 | 0 | 22 | 0 | 0 |
| 14 | 100 | 100 | 0 | 33 | 100 | 67 | 100 | 22 | 0 | 0 |
| 15 | 100 | 100 | 0 | 33 | 100 | 67 | 100 | 22 | 0 | 0 |
| 16 | 100 | 100 | 100 | 33 | 100 | 67 | 0 | 22 | 0 | 0 |
| 17 | 100 | 100 | 0 | 33 | 100 | 56 | 0 | 22 | 0 | 0 |
| 18 | 100 | 100 | 0 | 33 | 0 | 44 | 0 | 22 | 0 | 0 |
| 19 | 100 | 100 | 100 | 33 | 0 | 33 | 0 | 11 | 0 | 0 |
| 20 | 100 | 100 | 0 | 33 | 0 | 22 | 0 | 0 | 0 | 11 |
| 21 | 100 | 100 | 0 | 33 | 0 | 11 | 0 | 11 | 0 | 22 |
| 22 | 100 | 100 | 100 | 33 | 0 | 0 | 0 | 22 | 0 | 33 |
| 23 | 100 | 100 | 0 | 33 | 0 | 11 | 0 | 33 | 0 | 44 |
| 24 | 100 | 100 | 0 | 33 | 0 | 22 | 0 | 44 | 100 | 56 |
| 25 | 100 | 100 | 100 | 44 | 0 | 33 | 100 | 56 | 100 | 67 |
| 26 | 100 | 100 | 0 | 56 | 0 | 44 | 100 | 67 | 100 | 78 |
| 27 | 100 | 100 | 0 | 56 | 100 | 56 | 100 | 78 | 100 | 89 |
| 28 | 100 | 100 | 100 | 67 | 100 | 67 | 100 | 89 | 100 | 100 |
| … | ... | … | ... | ... | ... | ... | … | … | … | … |

Appendix Table 4b: Percentage of days with running average less than a given threshold.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Pattern | | | | |
| Threshold | A | B | C | D | E |
| <10 | 0/28 (0%) | 0/28 (0%) | 2/28 (7%) | 2/28 (7%) | 10/28 (36%) |
| <20 | 0/28 (0%) | 0/28 (0%) | 6/28 (21%) | 6/28 (21%) | 12/28 (43%) |
| <30 | 0/28 (0%) | 0/28 (0%) | 10/28 (36%) | 16/28 (57%) | 14/28 (50%) |
| <40 | 0/28 (0%) | 20/28 (71%) | 14/28 (50%) | 18/28 (64%) | 16/28 (57%) |
| <50 | 0/28 (0%) | 24/28 (86%) | 24/28 (86%) | 2028 (71%) | 18/28 (64%) |
| <60 | 0/28 (0%) | 26/28 (93%) | 22/28 (79%) | 22/28 (79%) | 20/28 (71%) |