**Supplemental Digital Content 1**

**Factors associated with baseline HIV drug resistance among HPTN 052 participants with virologic failure**

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| --- | --- |
|  | **Baseline resistance*****Univariate*** |
|  | **n/N (%)** | **OR (95% CI)** | **P**  |
| Study arm |  |  | 0.96 |
| Early ART arm | 6/128 (4.7%) | ref |  |
| Delayed ART arm | 4/83 (4.8%) | 1.03 (0.28-3.76) |  |
| Study groupa |  |  | 0.59 |
| Early ART arm | 6/128 (4.7%) | ref |  |
| Delayed ART arm (before 5/2011) | 2/22 (9.1%) | 2.03 (0.38-10.79) | 0.40 |
| Delayed ART arm (after 5/2011) | 2/61 (3.3%) | 0.69 (0.14-3.52) | 0.65 |
| Age at ART initiation |  |  | 0.13 |
| <25 years | 2/37 (5.4%) | ref |  |
| 25-39 years | 8/136 (5.9%) | 1.09 (0.22-5.38) | 0.91 |
| ≥40 years | 0/38 (0.0%) | - | 1.0 |
| Gender |  |  | 0.30 |
| Male | 3/96 (3.1%) | ref |  |
| Female | 7/115 (6.1%) | 2.01 (0.51-7.99) |  |
| CD4 at ART initiationb  |  | 0.83 (0.51-1.34) | 0.44 |
| VL at ART initiationc  |  | 0.47 (0.19-1.17) | 0.10 |
| Time to ART initiationd  |  | 0.67 (0.35-1.30) | 0.17 |
| HIV Subtype |  |  | 0.80 |
| C | 8/162 (4.9%) | ref |  |
| Non-C | 2/49 (4.1%) | 0.82 (0.17-3.99) |  |
| Region |  |  | 0.99 |
| Americas | 2/42 (4.8%) | ref |  |
| Asia | 3/59 (5.1%) | 1.07 (0.17-6.71) | 0.94 |
| Africa | 5/110 (4.5%) | 0.95 (0.18-5.11) | 0.95 |
| Regimene |  |  | 0.70 |
| EFV/3TC/ZDV | 8/158 (5.1%) | 1.36 (0.28-6.61) |  |
| Other | 2/53 (3.8%) | ref |  |
| Education |  |  | 0.34 |
| None | 3/32 (9.4%) | ref |  |
| Primary or secondary schooling | 7/171 (4.1%) | 0.41 (0.10-1.69) | 0.22 |
| Post-secondary schooling | 0/8 (0.0%) | - | 1.00 |
| Marital status |  |  | 0.32 |
| Married | 9/204 (4.4%) | ref |  |
| Not married | 1/7 (14.3%) | 3.61 (0.39-33.25) |  |
| Number of sex partnersf |  |  | 0.41 |
| 0-1 | 10/204 (4.9%) | ref |  |
| >1 | 0/7 (0.0%) | - |  |

**Footnotes**

Abbreviations: ART: antiretroviral therapy; N: number; OR: odds ratio; CI: confidence interval; ref: reference group; VL: viral load; EFV: efavirenz; 3TC: lamivudine; ZDV: zidovudine.

Odds ratios (OR) were calculated using logistic regression. An OR >1 indicates a higher risk of resistance. The OR could not be estimated if any cell was 0 for the categorical variable.

a Study group include participants in the early ART arm (ART initiated at enrollment), delayed ART arm (ART initiated before May, 2011), and delayed ART arm (ART initiated after May, 2011).

b Per CD4 cell count increment of 100 cells/mm3.

c Per viral load increment of 1 log10 HIV RNA copies/mL.

d Per 1 year increment.

e Among the 211 participants who failed ART, 158 (74.9%) were taking EFV/3TC/ZDV, 44 (20.9%) were taking protease inhibitor-based regimens and nine (4.3%) were taking a different EFV-based regimen.

f Number of sex partners in the 3 months prior to ART initiation.

**Supplemental Digital Content 2**

In HPTN 052, for participants with virologic failure, the follow-up period between ART initiation and ART failure was different in the two study arms (early ART arm: 177 person-years; delayed ART arm: 83 person-years). Additional analyses were performed to assess whether this biased the study findings.

First, data were stratified by study group (early ART arm; delayed ART arm with ART initiation before May 2011; delayed ART arm, with ART initiation after May 2011), recognizing that the two study arms had different sampling frames. An interaction term was included in the multivariate model, to explore potential interaction between study group and the following factors: CD4 cell count, HIV viral load, and ART regimen. As shown in the table below, none of the interaction terms was significant, indicating that there was no interaction between study group and any of the three variables associated with resistance at the time of failure.

**Results obtained with a multivariate model that included stratification by study group.**

|  |  |  |
| --- | --- | --- |
| Stratification Model | Variables analyzeda | Global p value |
|  No interaction terms | CD4 cell count | 0.50 |
|   | HIV viral load | **0.0003** |
|  | ART regimen | **0.021** |
|  Interaction terms | CD4 cell count \* study group | 1.00 |
|  | HIV viral load \* study group | 0.73 |
|  | ART regimen \* study group | 0.18 |

a CD4 cell count and HIV viral load were measured at the time of ART initiation. EFV/3TC/ZDV was compared to other regimens.

Second, the multivariate analyses were repeated after censoring data from participants in the early ART arm with virologic failure after the maximum time on ART in the delayed ART arm (2.7 years after ART initiation). The censored analysis included 102 participants with 106 person-years of follow-up in the early ART arm (reduced from 128 participants with 177 person-years of follow-up), and 83 participants with 83 person-years of follow-up in the delayed ART arm (no change). The original p values (from Table 2, without censoring) were similar to the p values obtained with censoring, as shown in the table below. These findings indicate that the difference in follow-up time after ART initiation in the two study arms did not significantly impact analysis of factors associated with resistance at the time of virologic failure.

P values obtained for different multivariate models with the outcome of resistance at the time of virologic failure.

|  |  |  |
| --- | --- | --- |
| Variablea | Original P value (from Table 2) | P value with censoring |
| Study group | 0.43 | 0.48 |
| CD4 cell count  | 0.98 | 0.95 |
| HIV viral load  | **0.0008** | **0.0009** |
| ART regimen | **0.024** | **0.01** |

a CD4 cell count and HIV viral load were measured at the time of ART initiation. EFV/3TC/ZDV was compared to other regimens.