Supplemental Digital Content Table 1. Baseline characteristics of study population by country and by changing NRTI from first-line to second-line vs. remaining on same NRTI in second-line.

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|  | **South Africa** | **Zambia** |
|   | No change in NRTI (N=205) | Change in NRTI (N=4070) | No change in NRTI (N=347) | Change in NRTI (N=1668) |
| Female | 151 (73.7%) | 2560 (62.9%) | 196 (56.5%) | 932 (55.9%) |
| Age group (years) |   |   |  |  |
| 18-29 | 72 (35.1%) | 1222 (30.0%) | 77 (22.2%) | 384 (23.0%) |
| 30-39 | 94 (45.9%) | 1796 (44.1%) | 151 (43.5%) | 753 (45.1%) |
| 40-49 | 32 (15.6%) | 814 (20.0%) | 85 (24.5%) | 372 (22.3%) |
| 50+ | 7 (3.4%) | 238 (5.9%) | 34 (9.8%) | 159 (9.3%) |
| CD4 (cells/mm3) at first-line initiation | 81.0 (37.0-160.0) | 87.0 (32.5-161.0) | 91.0 (38.0-175.0) | 85.5 (37.0-156.0) |
| ALT (IU/L) at first-line initiation | 22.0 (15.5-31.5) | 24.0 (17.0-35.0) | 21.9 (13.1-34.6) | 21.0 (14.0-33.0) |
| Hemoglobin (g/dL) at first-line initiation | 11.5 (10.2-12.7) | 11.6 (10.2-13.0) | 10.9 (9.2-12.5) | 11.1 (9.8-12.4) |
| Weight (kg) at first-line initiation | 60.0 (50.7-70.0) | 60.0 (53.0-69.4) | 55.0 (49.0-62.0) | 55.2 (49.4-63.0) |
| Months on first-line | 29.2 (17.3) | 30.5 (19.6) | 32.7 (16.6) | 34.2 (15.2) |
| Viral load (copies/mL) at second-line switch | 2300 (49-32000) | 12047 (3657-55000) | -- | -- |
| CD4 (cells/mm3) count at second-line switch | 261.5 (137.5-443.0) | 190.0 (101.0-300.0) | 101.0 (28.0-229.0) | 118.0 (53.0-207.0) |

Statistics reported as median (IQR), mean (standard deviation), or N (%)

Supplemental Digital Content Table 2. Summary of propensity scores for propensity to change NRTI in second-line vs. remain on same NRTI for each model, using patient data from South Africa.

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| **First-line NRTI:** | **Remain on AZT** | **Change to TDF** |
| **AZT** | 0.62 (0.43-0.83) | 0.88 (0.76-0.94) |
|  | **Remain on AZT** | **Change to ABC** |
| **AZT** | 0.27 (0.10-0.62) | 0.94 (0.86-0.98) |
|  | **Remain on d4T** | **Change to AZT** |
| **d4T** | 0.80 (0.75-0.85) | 0.87 (0.80-0.93) |
|  | **Remain on d4T** | **Change to TDF** |
| **d4T** | 0.63 (0.50-0.81) | 0.86 (0.73-0.93) |
|  | **Remain on TDF** | **Change to AZT** |
| **TDF** | 0.89 (0.83-0.94) | 0.97 (0.94-0.98) |

Propensity scores displayed as median (IQR)

Supplemental Digital Content Table 3. Hazard ratios and 95% confidence intervals of second-line immunologic failure among Zambian patients, using Cox proportional hazards models adjusted for propensity scores.

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| --- | --- |
|  | **Second-line NRTI** |
| **First-line NRTI** | **AZT** | **d4T** | **TDF** | **ABC** |
| **AZT** | (ref) |  (x) | 0.52 (0.17, 1.62) | 0.62 (0.16, 2.40) |
| **d4T** | 0.95 (0.18, 4.89) | (ref) | 0.82 (0.24, 2.88) | 0.63 (0.11, 3.63) |
| **TDF** | 1.05 (0.38, 2.95) |  (x) | (ref) | 0.83 (0.23, 3.06) |

AZT = zidovudine; d4T = stavudine; TDF = tenofovir; ABC = abacavir

ref = Reference category, compared to other estimates in the row

x = Sample size too small