**Supplemental Appendix**

**Figure S1 Study profile**

**Supplemental Table S1 Primary treatment outcomes of Thai HIV-infected children**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **N** | **All children** | **Children who switched to second line regimen** |
| **4,120** | **1,054** |
| **Duration on ART (years)** | **Median (IQR)** | 3.7 (2.1-5.5) | 2.1 (1.3-3.3) |
| **Total person years** |  | 17,950 | 4,970 |
|  |  |  |  |
| **No. of death** | **N (%)** | 181 (4) | 84 (8) |
| **Mortality rate per 100 PYFU** | **Rate (95%CI)** | 1.01 (0.87-1.17) | 1.69 (1.36-2.09) |
| **No. of loss to follow up** | **N (%)** | 270 (7) | 79 (8) |
| **LTFU rate per 100 PYFU** | **Rate(95%CI)** | 1.51 (1.34-1.7) | 1.59 (1.28-1.99) |
|  |  |  |  |
| **Achieved immunological recovery (IMR)** | **N (%)** | 3,118 (76) | 486 (46) |
| **CD4%** | **Median (IQR)** | 24 (18-29) | 21 (14-27) |
| **CD4 cell count at age ≥ 5 years** | **Median (IQR)** | 609 (483-800) | 554 (262-733) |
| **Time from baseline to IMR (years)** | **Median (IQR)** | 1.1 (0.8-2.1) | 2.2 (1.0-4.5) |
|  |  |  |  |
| **No. of immunological failure (IMF)** | **N (%)** | 449 (11) | 197 (19) |
| **IMF rate per 100 PYFU** | **(95%CI)** | 16.3 (15.0-18.0) | 26.8 (23.3-30.8) |
| **Time from baseline to IMF (months)** | **Median (IQR)** | 48 (26-66) | 48 (30-66) |
| **Time from IMF to switch (months)** | **Median (IQR)** | 12.83 (6.3-27.77) | 8.4 (3.3-15.4) |
|  |  |  |  |
| **No of virological failure (VF)** | **N (%)** | 1,412 (34) | 887 (84) |
| **VF rate per 100 PYFU** | **(95%CI)** | 11 (10-12) | 42 (39-44) |
| **Time from baseline to VF (months)** | **Median (IQR)** | 35 (16 -58) | 19 (11-34) |
| **Time from VF to switch (months)** | **Median (IQR)** | 11 (4-21) | 6 (3 -15) |
|  |  |  |  |
| **Virological status at censored** | **N (%)** | 3,559 (86) | 900 (22) |
| **VL at censored** | **Median (IQR)** | 40 (20-7,280) | 14,970 (5,976-34,600) |
| **log VL at censored** | **Median (IQR)** | 1.6 (1.3-3.86) | 4.18 (3.78-4.54) |

**Table S2 Characteristics associated with immunological failure (IMF) and virological failure (VF)**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Characteristics (N=4120)** | **N of IMF** | **PY** | **IMF rate**  **(95% CI) per 100 FU** | **IMF** | | | |  | **N of VF** | **PY** | **VF rate**  **(95% CI) per 100 FU** | **VF** | | | |
| **Univariate** | | **Multivariate** | |  | **Univariate** | | **Multivariate** | |
| **HR (95% CI)** | **p** | **aHR (95% CI)** | **p** |  | **HR (95% CI)** | **p** | **aHR (95% CI)** | **p** |
| **Gender** |  |  |  |  | 0.033 |  | 0.067 |  |  |  |  |  | 0.258 |  |  |
| Male | 223 | 1,211 | 18 (16-21) | 1.23 (1.02-1.48) |  | 1.19 (0.99-1.43) |  |  | 645 | 5,562 | 12 (11-13) | 1.06 (0.96-1.18) |  |  |  |
| Female | 226 | 1,530 | 15 (13-17) |  |  |  |  |  | 767 | 7,019 | 11 (10-12) | ref |  |  |  |
| **Age at ART initiation** |  |  |  |  | <0.001 |  | <0.001 |  |  |  |  |  | <0.001 |  | <0.001 |
| < 5 years | 72 | 524 | 14 (11-17) | 1.20 (0.88-1.63) |  | 1.54 (1.12-2.11) |  |  | 280 | 2,453 | 11 (10-13) | 1.30 (1.1-1.52) |  | 1.48 (1.26-1.74) |  |
| 5- < 9 years | 87 | 699 | 12 (10-15) | ref |  | ref |  |  | 322 | 3,689 | 9 (8-10) | ref |  | ref |  |
| 9- < 12 years | 128 | 772 | 17 (14-20) | 1.49 (1.13-1.95) |  | 1.50 (1.14-1.97) |  |  | 407 | 3,515 | 12 (11-13) | 1.31 (1.13-1.52) |  | 1.31 (1.13-1.52) |  |
| ≥ 12 years | 162 | 744 | 22 (19-25) | 2.24 (1.72-2.90) |  | 2.29 (1.76-2.98) |  |  | 403 | 2,924 | 14 (13-15) | 1.53 (1.32-1.77) |  | 1.59 (1.37-1.84) |  |
| **Calendar Year** |  |  |  |  | <0.001 |  | <0.001 |  |  |  |  |  | <0.001 |  | <0.001 |
| 2008 | 11 | 7 | 148 (82-267) | 2.53 (1.28-4.98) |  | 3.33 (1.69-6.59) |  |  | 36 | 133 | 27 (19-37) | 4.56 (3.15-6.59) |  | 5.47 (3.77-7.92) |  |
| 2009 | 70 | 49 | 143 (114-181) | 2.11 (1.45-3.08) |  | 2.45 (1.68-3.59) |  |  | 186 | 930 | 20 (17-23) | 1.74 (1.43-2.12) |  | 1.93 (1.59-2.36) |  |
| 2010 | 85 | 83 | 102 (83-126) | 1.77 (1.25-2.51) |  | 1.80 (1.27-2.55) |  |  | 230 | 1,679 | 14 (12-16) | 1.05 (0.88-1.26) |  | 1.13 (0.94-1.35) |  |
| 2011 | 53 | 68 | 78 (59-102) | ref |  | ref |  |  | 274 | 2,223 | 12 (11-14) | ref |  | ref |  |
| 2012 | 94 | 193 | 49 (40-60) | 1.57 (1.11-2.21) |  | 1.48 (1.05-2.09) |  |  | 281 | 2,596 | 11 (10-12) | 0.95 (0.81-1.13) |  | 0.93 (0.79-1.10) |  |
| 2013 | 79 | 421 | 19 (15-23) | 1.25 (0.86-1.81) |  | 1.16 (0.80-1.68) |  |  | 229 | 2,589 | 9 (8-10) | 0.86 (0.72-1.04) |  | 0.81 (0.68-0.98) |  |
| 2014 | 57 | 1,918 | 3 (2-4) | 1.10 (0.72-1.68) |  | 0.98 (0.64-1.50) |  |  | 176 | 2,431 | 7 (6 -8) | 0.68 (0.55-0.84) |  | 0.64 (0.52-0.79) |  |
| **Baseline HIV clinical stage** |  |  |  |  | 0.425 |  |  |  |  |  |  |  | 0.193 |  |  |
| N or A | 332 | 2,110 | 16 (14-18) | 0.90 (0.67-1.22) |  |  |  |  | 1096 | 9,515 | 12 (11-12) | 1.17 (0.98-1.41) |  |  |  |
| B | 68 | 352 | 19 (15-25) | 1.06 (0.74-1.54) |  |  |  |  | 187 | 1,726 | 11 (9-13) | 1.12 (0.89-1.40) |  |  |  |
| C | 49 | 279 | 18 (13-23) | ref |  |  |  |  | 129 | 1,339 | 10 (8-11) | ref |  |  |  |
| **First regimen** |  |  |  |  | 0.326 |  |  |  |  |  |  |  | 0.882 |  |  |
| NNRTI based ART | 416 | 2,489 | 17 (15-18) | 1.19 (0.83-1.70) |  |  |  |  | 1290 | 11,523 | 11 (10 -12) | 0.99 (0.82-1.19) |  |  |  |
| PI based ART | 33 | 251 | 13 (9-19) | ref |  |  |  |  | 122 | 1,058 | 12 (10-14) | ref |  |  |  |
| **Baseline CD4%** |  |  |  |  | <0.001 |  | <0.001 |  |  |  |  |  | <0.001 |  | <0.001 |
| <10% | 243 | 928 | 26 (23-30) | 6.90 (4.5-10.59) |  | 7.19 (4.66-11.09) |  |  | 545 | 3,852 | 14 (13-15) | 1.78 (1.51-2.10) |  | 1.89 (1.60-2.24) |  |
| 10- <16% | 42 | 409 | 10 (8-14) | 2.56 (1.54-4.25) |  | 2.78 (1.67-4.64) |  |  | 224 | 1,727 | 13 (11-15) | 1.63 (1.35-1.98) |  | 1.72 (1.42-2.09) |  |
| ≥16% | 23 | 495 | 5 (3-7) | ref |  | ref |  |  | 196 | 2,555 | 8 (7-9) | ref |  | ref |  |
| unknown | 141 | 908 | 16 (13-18) | 3.56 (2.29-5.53) |  | 3.70 (2.38-5.76) |  |  | 447 | 4,447 | 10 (9-11) | 1.3 (1.1-1.54) |  | 1.32 (1.11-1.56) |  |
| **Region** |  |  |  |  | 0.011 |  | 0.089 |  |  |  |  |  | <0.001 |  | 0.001 |
| Bangkok | 31 | 243 | 13 (9-18) | ref |  | ref |  |  | 108 | 1,321 | 8 (7-10) | ref |  | ref |  |
| Central | 62 | 277 | 22 (17-29) | 2.19 (1.42-3.37) |  | 1.78 (1.15-2.76) |  |  | 148 | 1,166 | 13 (11-15) | 1.49 (1.16-1.91) |  | 1.46 (1.14-1.87) |  |
| Northern | 92 | 600 | 15 (13-19) | 1.28 (0.85-1.92) |  | 1.12 (0.74-1.69) |  |  | 297 | 3,055 | 10 (9-11) | 1.17 (0.94-1.46) |  | 1.16 (0.93-1.45) |  |
| Southern | 60 | 399 | 15 (12-19) | 1.50 (0.97-2.31) |  | 1.25 (0.81-1.93) |  |  | 212 | 1,702 | 12 (11-14) | 1.47 (1.17-1.85) |  | 1.46 (1.16-1.85) |  |
| Eastern | 54 | 274 | 20 (15-26) | 1.65 (1.06-2.57) |  | 1.31 (0.84-2.03) |  |  | 150 | 1,349 | 11 (9-13) | 1.32 (1.03-1.70) |  | 1.25 (0.97-1.60) |  |
| Western | 19 | 111 | 17(11-26) | 1.49 (0.84-2.64) |  | 1.27 (0.71-2.26) |  |  | 56 | 539 | 10. (8-14) | 1.25 (0.91-1.73) |  | 1.23 (0.89-1.70) |  |
| North eastern | 131 | 836 | 16 (13-19) | 1.46 (0.99-2.16) |  | 1.13 (0.76-1.68) |  |  | 441 | 3,450 | 13 (12-14) | 1.51 (1.22-1.87) |  | 1.46 (1.18-1.81) |  |

Note: PY-Person-years; CI- confidence interval; HR- hazard ratio; aHR-adjusted hazard ratio