**SUPPLEMENTAL DIGITAL CONTENT 3**

Appendix 3 Table 1. Sensitivity analysis: Baseline characteristics of study subjects and their outcomes at 24 and 48 weeks (+/- 3 month window) from starting ART by regimen (3rd drug) and study design for (i) ACTG5095 & ART-CC (N = 5363) (ii) ACTG5142 & ART-CC (N = 8710)

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **ABC** | |  | **EFV** | |  | **LPV** | |  | **EFV** | |
| **Characteristic** | **ACTG5095** | **Cohort** |  | **ACTG5095** | **Cohort** |  | **ACTG5142** | **Cohort** |  | **ACTG5142** | **Cohort** |
| **N (%) or median (IQR)** | **N=377** | **N=1694** |  | **N=376** | **N=2916** |  | **N=250** | **N=3871** |  | **N=248** | **N=4341** |
| Male | 305 (81) | 1146 (68) |  | 310 (82) | 2239 (77) |  | 191 (76) | 2827 (73) |  | 201 (81) | 3270 (75) |
| Age years | 38 (33-43) | 37 (31-44) |  | 38 (31-43) | 38 (32-45) |  | 37 (32-44) | 38 (32-45) |  | 39 (32-44) | 38 (32-45) |
| 16-29 | 57 (15) | 318 (19) |  | 68 (18) | 499 (17) |  | 41 (16) | 669 (17) |  | 41 (17) | 723 (17) |
| 30-39 | 163 (43) | 717 (42) |  | 149 (40) | 1202 (41) |  | 106 (42) | 1520 (39) |  | 89 (36) | 1755 (40) |
| 40-49 | 114 (30) | 444 (26) |  | 123 (33) | 773 (27) |  | 80 (32) | 1080 (28) |  | 90 (36) | 1213 (28) |
| ≥50 | 43 (11) | 215 (13) |  | 36 (10) | 442 (15) |  | 23 (9) | 602 (16) |  | 28 (11) | 650 (15) |
| IDU | 40 (11) | 286 (17) |  | 36 (10) | 373 (13) |  | 23 (9) | 423 (11) |  | 24 (10) | 577 (13) |
| HIV-1 RNA log10 copies/ml | 4.8 (4.4-5.3) | 4.6 (4.1-5.0) |  | 4.8 (4.4-5.4) | 5.0 (4.5-5.4) |  | 4.8 (4.4-5.2) | 5.1 (4.7-5.5) |  | 4.8 (4.4-5.2) | 5.0 (4.5-5.4) |
| <4 | 37 (10) | 358 (21) |  | 28 (7) | 311 (11) |  | 25 (10) | 363 (9) |  | 26 (10) | 460 (11) |
| 4-4.99 | 192 (51) | 908 (54) |  | 201 (52) | 1200 (41) |  | 137 (55) | 1224 (32) |  | 139 (56) | 1789 (41) |
| ≥5 | 148 (39) | 428 (25) |  | 147 (41) | 1405 (48) |  | 88 (35) | 2284 (59) |  | 83 (33) | 2092 (48) |
| CD4 cell count cells/L | 197 (79-343) | 250 (170-339) |  | 209 (77-331) | 198 (90-291) |  | 190 (70-300) | 146 (50-260) |  | 195 (48-314) | 191 (84-280) |
| 0-49 | 63 (17) | 104 (6) |  | 79 (21) | 489 (17) |  | 47 (19) | 950 (25) |  | 65 (26) | 741 (17) |
| 50-99 | 46 (12) | 101 (6) |  | 24 (6) | 285 (10) |  | 35 (14) | 570 (15) |  | 21 (8) | 467 (11) |
| 100-199 | 80 (21) | 370 (22) |  | 77 (20) | 690 (24) |  | 52 (21) | 887 (23) |  | 40 (16) | 1061 (24) |
| 200-349 | 103 (27) | 720 (43) |  | 112 (30) | 1012 (35) |  | 80 (32) | 960 (25) |  | 69 (28) | 1503 (35) |
| ≥350 | 85 (23) | 399 (24) |  | 84 (22) | 440 (15) |  | 36 (14) | 504 (13) |  | 53 (21) | 569 (13) |
| VL>200 copies/mL at 24 wks  N /N patients with VL (%) | 79/330  (23.9) | 351/1437  (24.4) |  | 55/363  (15.2) | 342/2529  (13.5) |  | 32/237  (13.5) | 532/3455  (15.4) |  | 22/230  (9.6) | 469/3794  (12.4) |
| VL>200 copies/mL at 48 wks  N /N patients with VL (%) | 51/193  (26.4) | 303/1336  (22.7) |  | 49/344  (14.2) | 308/2377  (13.0) |  | 23/220  (10.5) | 461/3235  (14.3) |  | 21/214  (9.8) | 433/3560  (12.2) |
| AIDS or death at 24 wks | 10 (2.65) | 50 (2.95) |  | 7(1.86) | 123 (4.22) |  | 7 (2.8) | 238 (6.15) |  | 7 (2.82) | 197 (4.54) |
| AIDS or death at 48 wks | 13 (3.45) | 82 (4.84) |  | 10 (2.66) | 176 (6.04) |  | 11 (4.40) | 312 (8.06) |  | 11 (4.44) | 279 (6.43) |
| Deaths at 24 wks | 3 (0.80) | 13 (0.77) |  | 0(0) | 31 (1.06) |  | 0(0) | 74 (1.91) |  | 3 (1.21) | 57 (1.31) |
| Deaths at 48 wks | 3 (0.80) | 26 (1.53) |  | 1 (0.27) | 57 (1.95) |  | 2 (0.80) | 114 (2.94) |  | 5 (2.02) | 97 (2.23) |

IQR = inter-quartile range

Appendix 3 Table 2: Sensitivity analysis: Crude and adjusted odds ratio (OR) for virological failure (HIV-1 RNA >200 copies/ml) with ratio of odds ratios at 24 and 48 weeks (+/- 3 month window) after starting treatment (i) between study design comparison of drug regimen (3rd drug) (ii) between drug regimen comparison of study design (white band ACTG5095 EFV v. ABC, grey band ACTG5142 EFV v.ABC

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Weeks of follow-up** | | **OR (95% CI) VL>200 copies/mL** | | | | | | |
| **Crude** | | |  | **Adjusted** | | |
| **Comparison of regimens** | | | **Trial** | **Cohort** | **Ratio of OR (cohort:trial)** |  | **Trial** | **Cohort** | **Ratio of OR (cohort:trial)** |
| EFV v. ABC (ACTG 5095) | | 24 | 0.57 (0.39, 0.83) | 0.48 (0.41, 0.57) | 0.85 (0.56,1.29) |  | 0.53 (0.36, 0.79) | 0.46 (0.39, 0.55) | 0.87 (0.56,1.35) |
| 48 | 0.46 (0.30, 0.72) | 0.51 (0.43, 0.60) | 1.10 (0.68,1.76) |  | 0.46 (0.28, 0.73) | 0.49 (0.40, 0.59) | 1.07 (0.64,1.77) |
| EFV v. LPV (ACTG 5142) | | 24 | 0.68 (0.38,1.21) | 0.77 (0.68,0.89) | 1.14 (0.63,2.07) |  | 0.71 (0.39,1.29) | 0.80 (0.70,0.93) | 1.13 (0.62,2.08) |
| 48 | 0.93 (0.50,1.74) | 0.83 (0.72,0.96) | 0.89 (0.47,1.70) |  | 0.97 (0.51,1.85) | 0.84 (0.72,0.98) | 0.87 (0.45,1.67) |
| **Comparison of study designs** | | | **Patients on EFV** | **Patients on ABC** |  |  | **Patients on EFV** | **Patients on ABC** |  |
| ACTG 5095 v. cohort | | 24 | 1.14 (0.84, 1.55) | 0.97 (0.74, 1.29) | 0.85 (0.56,1.29) |  | 1.14 (0.83, 1.57) | 0.77 (0.57, 1.05) | 0.68 (0.44,1.05) |
| 48 | 1.12 (0.81, 1.54) | 1.22 (0.87, 1.73) | 1.10 (0.68,1.76) |  | 1.06 (0.76, 1.49) | 0.99 (0.68, 1.45) | 0.93 (0.56,1.55) |
|  | |  | **Patients on EFV** | **Patients on LPV** |  |  | **Patients on EFV** | **Patients on LPV** |  |
| ACTG 5142 v. | | 24 | 0.75 (0.48,1.18) | 0.86 (0.58,1.26) | 1.14 (0.63,2.07) |  | 0.78 (0.49,1.23) | 0.92 (0.63,1.37) | 1.19 (0.65,2.17) |
| cohort | | 48 | 0.79 (0.50,1.25) | 0.70 (0.45,1.09) | 0.89 (0.47,1.70) |  | 0.83 (0.52,1.33) | 0.75 (0.48,1.18) | 0.91 (0.47,1.75) |

Adjusted models control for year of starting ART, age, sex, assumed transmission via injection drug use (IDU), AIDS diagnosis, CD4 count and HIV RNA at start of ART

Appendix 3 Table 3: Sensitivity analysis: Crude and adjusted odds ratio (OR) for virological failure (HIV-1 RNA >200 copies/ml) with ratio of odds ratios at 24 and 48 weeks (last viral load value carried forward)after starting treatment (i) between study design comparison of drug regimen (3rd drug) (ii) between drug regimen comparison of study design (white band ACTG5095 EFV v. ABC, grey band ACTG5142 EFV v.ABC.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Weeks of follow-up** | | **OR (95% CI) VL>200 copies/mL** | | | | | | |
| **Crude** | | |  | **Adjusted** | | |
| **Comparison of regimens** | | | **Trial** | **Cohort** | **Ratio of OR (cohort:trial)** |  | **Trial** | **Cohort** | **Ratio of OR (cohort:trial)** |
| EFV v. ABC (ACTG 5095) | | 24 | 0.57 (0.39, 0.83) | 0.51 (0.43, 0.60) | 0.90 (0.59,1.36) |  | 0.53 (0.36, 0.79) | 0.48 (0.41, 0.57) | 0.90 (0.58,1.39) |
| 48 | 0.55 (0.38, 0.81) | 0.52 (0.45, 0.61) | 0.94 (0.63,1.42) |  | 0.55 (0.38, 0.81) | 0.50 (0.43, 0.59) | 0.91 (0.59,1.40) |
| EFV v. LPV (ACTG 5142) | | 24 | 0.68 (0.38,1.21) | 0.77 (0.68,0.87) | 1.13 (0.63,2.04) |  | 0.71 (0.39,1.29) | 0.79 (0.69,0.91) | 1.12 (0.61,2.04) |
| 48 | 0.73 (0.42,1.27) | 0.81 (0.71,0.91) | 1.11 (0.63,1.97) |  | 0.73 (0.41,1.30) | 0.81 (0.71,0.93) | 1.11 (0.62,2.00) |
| **Comparison of study designs** | | | **Patients on EFV** | **Patients on ABC** |  |  | **Patients on EFV** | **Patients on ABC** |  |
| ACTG 5095 v. cohort | | 24 | 1.04 (0.77, 1.42) | 0.94 (0.71, 1.24) | 0.90 (0.59,1.36) |  | 1.06 (0.77, 1.45) | 0.76 (0.56, 1.02) | 0.72 (0.46,1.11) |
| 48 | 1.07 (0.79, 1.45) | 1.01 (0.77, 1.33) | 0.94 (0.63,1.42) |  | 1.03 (0.76, 1.41) | 0.81 (0.60, 1.08) | 0.78 (0.51,1.20) |
|  | |  | **Patients on EFV** | **Patients on LPV** |  |  | **Patients on EFV** | **Patients on LPV** |  |
| ACTG 5142 v. | | 24 | 0.69 (0.44,1.08) | 0.78 (0.53,1.14) | 1.13 (0.63,2.04) |  | 0.71 (0.45,1.12) | 0.84 (0.57,1.24) | 1.18 (0.65,2.16) |
| cohort | | 48 | 0.72 (0.47,1.11) | 0.80 (0.55,1.17) | 1.11 (0.63,1.97) |  | 0.75 (0.49,1.17) | 0.84 (0.57,1.24) | 1.11 (0.62,2.00) |

Adjusted models control for year of starting ART, age, sex, assumed transmission via injection drug use (IDU), AIDS diagnosis, CD4 count and HIV RNA at start of ART