**SUPPLEMENTAL DIGITAL CONTENT 2**

Appendix 2 Table 1: Sensitivity analysis: stratified by baseline viral load (upper VL≥100,000, lower VL<100,000 copies /mL) 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 after starting treatment (i) between study design comparison of drug regimen (ii) between drug regimen comparison of study design (white band ACTG5095 EFV v. ABC, grey band ACTG5142 EFV v.ABC).

**Baseline VL≥100,000 copies /mL EFV v. ABC N=2128; EFV v. LPV N=4547**

|  |  |  |
| --- | --- | --- |
|  | **Weeks of follow-up** | **OR (95% CI) VL>200 copies/mL** |
| **Crude** |  | **Adjusted** |
| **Comparison of regimens** | **Trial** | **Cohort** | **Ratio of OR** |  | **Trial** | **Cohort** | **Ratio of OR** |
| EFV v. ABC (ACTG 5095) | 24 | 0.60 (0.33, 1.08) | 0.36 (0.26, 0.49) | 0.60 (0.31,1.17) |  | 0.54 (0.29, 1.00) | 0.36 (0.26, 0.49) | 0.66 (0.32,1.35) |
| 48 | 0.33 (0.15, 0.68) | 0.37 (0.26, 0.52) | 1.14 (0.50,2.57) |  | 0.31 (0.14, 0.69) | 0.35 (0.25, 0.51) | 1.15 (0.47,2.84) |
| EFV v. LPV (ACTG 5142) | 24 | 0.55 (0.21, 1.47) | 0.79 (0.64, 0.97) | 1.43 (0.53,3.88) |  | 0.60 (0.21, 1.75) | 0.80 (0.65, 0.99) | 1.33 (0.48,3.66) |
| 48 | 0.38 (0.12, 1.25) | 0.85 (0.69, 1.05) | 2.24 (0.67,7.52) |  | 0.44 (0.12, 1.64) | 0.87 (0.69, 1.09) | 1.99 (0.58,6.78) |
| **Comparison of study designs** | **Patients on EFV** | **Patients on ABC** |  |  | **Patients on EFV** | **Patients on ABC** |  |
| ACTG 5095 v. cohort | 24 | 1.45 (0.90, 2.34) | 0.87 (0.54, 1.39) | 0.60 (0.31,1.17) |  | 1.51 (0.92, 2.47) | 0.74 (0.44, 1.25) | 0.49 (0.24,1.01) |
| 48 | 0.97 (0.55, 1.72) | 1.10 (0.61, 1.98) | 1.14 (0.50,2.57) |  | 0.97 (0.54, 1.74) | 1.08 (0.55, 2.14) | 1.12 (0.45,2.74) |
|  |  | **Patients on EFV** | **Patients on LPV** |  |  | **Patients on EFV** | **Patients on LPV** |  |
| ACTG 5142 v. | 24 | 0.74 (0.34, 1.64) | 1.06 (0.58, 1.95) | 1.43 (0.53,3.88) |  | 0.71 (0.32, 1.60) | 1.00 (0.54, 1.85) | 1.41 (0.51,3.89) |
| cohort | 48 | 0.45 (0.16, 1.25) | 1.01 (0.53, 1.93) | 2.24 (0.67,7.52) |  | 0.45 (0.16, 1.28) | 0.96 (0.49, 1.85) | 2.10 (0.62,7.18) |

**Baseline VL<100,000 copies /mL EFV v. ABC N=3235; EFV v. LPV N=4163**

|  |  |  |
| --- | --- | --- |
|  | **Weeks of follow-up** | **OR (95% CI) VL>200 copies/mL** |
| **Crude** |  | **Adjusted** |
| **Comparison of regimens** | **Trial** | **Cohort** | **Ratio of OR** |  | **Trial** | **Cohort** | **Ratio of OR** |
| EFV v. ABC (ACTG 5095) | 24 | 0.55 (0.33, 0.90) | 0.56 (0.44, 0.72) | 1.03 (0.59,1.80) |  | 0.53 (0.31, 0.90) | 0.56 (0.44, 0.73) | 1.06 (0.59,1.93) |
| 48 | 0.56 (0.33, 0.98) | 0.54 (0.41, 0.70) | 0.95 (0.52,1.75) |  | 0.58 (0.31, 1.06) | 0.54 (0.41, 0.71) | 0.94 (0.49,1.81) |
| EFV v. LPV (ACTG 5142) | 24 | 0.76 (0.37, 1.56) | 0.73 (0.58, 0.92) | 0.96 (0.45,2.03) |  | 0.75 (0.35, 1.60) | 0.71 (0.55, 0.92) | 0.95 (0.43,2.08) |
| 48 | 1.43 (0.66, 3.11) | 0.79 (0.62, 1.00) | 0.55 (0.24,1.25) |  | 1.38 (0.61, 3.11) | 0.83 (0.64, 1.08) | 0.60 (0.26,1.41) |
| **Comparison of study designs** | **Patients on EFV** | **Patients on ABC** |  |  | **Patients on EFV** | **Patients on ABC** |  |
| ACTG 5095 v. cohort | 24 | 1.09 (0.72, 1.66) | 1.12 (0.77, 1.62) | 1.03 (0.59,1.80) |  | 0.99 (0.64, 1.53) | 0.97 (0.65, 1.44) | 0.98 (0.54,1.77) |
| 48 | 1.49 (0.98, 2.26) | 1.42 (0.91, 2.21) | 0.95 (0.52,1.75) |  | 1.32 (0.86, 2.04) | 1.26 (0.77, 2.08) | 0.96 (0.49,1.85 |
|  |  | **Patients on EFV** | **Patients on LPV** |  |  | **Patients on EFV** | **Patients on LPV** |  |
| ACTG 5142 v. | 24 | 0.94 (0.54, 1.63) | 0.90 (0.54, 1.49) | 0.96 (0.45,2.03) |  | 1.00 (0.56, 1.79) | 0.99 (0.59, 1.66) | 0.99 (0.45,2.17) |
| cohort | 48 | 1.11 (0.65, 1.89) | 0.62 (0.33, 1.14) | 0.55 (0.24,1.25) |  | 1.17 (0.67, 2.05) | 0.71 (0.37, 1.34) | 0.60 (0.26,1.41) |

Appendix 2 Table 2: Sensitivity analysis: stratified by baseline CD4 count (upper CD4<200, lower CD4≥200) 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 after starting treatment (i) between study design comparison of drug regimen (ii) between drug regimen comparison of study design (white band ACTG5095 EFV v. ABC, grey band ACTG5142 EFV v.ABC).

**CD4 count <200 copies/mL EFV v. ABC N=2408; EFV v. LPV N=4936**

|  |  |  |
| --- | --- | --- |
|  | **Weeks of follow-up** | **OR (95% CI) VL>200 copies/mL** |
| **Crude** |  | **Adjusted** |
| **Comparison of regimens** | **Trial** | **Cohort** | **Ratio of OR** |  | **Trial** | **Cohort** | **Ratio of OR** |
| EFV v. ABC (ACTG 5095) | 24 | 0.69 (0.41, 1.17) | 0.38 (0.28, 0.52) | 0.56 (0.30,1.02) |  | 0.64 (0.37, 1.11) | 0.34 (0.25, 0.47) | 0.53 (0.28,1.03) |
| 48 | 0.35 (0.19, 0.67) | 0.40 (0.29, 0.55) | 1.14 (0.56,2.30) |  | 0.36 (0.18, 0.72) | 0.36 (0.26, 0.51) | 0.99 (0.46,2.14) |
| EFV v. LPV (ACTG 5142) | 24 | 0.69 (0.33, 1.43) | 0.77 (0.63, 0.94) | 1.12 (0.52,2.37) |  | 0.73 (0.34, 1.56) | 0.79 (0.64, 0.98) | 1.08 (0.50,2.34) |
| 48 | 0.68 (0.29, 1.58) | 0.90 (0.73, 1.12) | 1.32 (0.55,3.17) |  | 0.70 (0.29, 1.69) | 0.89 (0.71, 1.12) | 1.28 (0.52,3.11) |
| **Comparison of study designs** | **Patients on EFV** | **Patients on ABC** |  |  | **Patients on EFV** | **Patients on ABC** |  |
| ACTG 5095 v. cohort | 24 | 1.67 (1.08, 2.57) | 0.93 (0.60, 1.42) | 0.56 (0.30,1.02) |  | 1.60 (1.02, 2.50) | 0.69 (0.43, 1.11) | 0.43 (0.22,0.83) |
| 48 | 1.25 (0.76, 2.04) | 1.42 (0.85, 2.36) | 1.14 (0.56,2.30) |  | 1.21 (0.73, 2.00) | 1.09 (0.61, 1.95) | 0.90 (0.42,1.95) |
|  |  | **Patients on EFV** | **Patients on LPV** |  |  | **Patients on EFV** | **Patients on LPV** |  |
| ACTG 5142 v. | 24 | 1.05 (0.59, 1.88) | 1.17 (0.72, 1.91) | 1.12 (0.52,2.37) |  | 1.08 (0.60, 1.96) | 1.24 (0.75, 2.03) | 1.14 (0.53,2.48) |
| cohort | 48 | 0.78 (0.40, 1.53) | 1.04 (0.59, 1.82) | 1.32 (0.55,3.17) |  | 0.85 (0.43, 1.68) | 1.07 (0.60, 1.89) | 1.26 (0.52,3.05) |

**CD4 count ≥200 copies/mL EFV v. ABC N=2955; EFV v. LPV N=3774**

|  |  |  |
| --- | --- | --- |
|  | **Weeks of follow-up** | **OR (95% CI) VL>200 copies/mL** |
| **Crude** |  | **Adjusted** |
| **Comparison of regimens** | **Trial** | **Cohort** | **Ratio of OR** |  | **Trial** | **Cohort** | **Ratio of OR** |
| EFV v. ABC (ACTG 5095) | 24 | 0.46 (0.27, 0.81) | 0.59 (0.46, 0.76) | 1.27 (0.69,2.34) |  | 0.43 (0.24, 0.77) | 0.60 (0.46, 0.78) | 1.39 (0.73,2.63) |
| 48 | 0.60 (0.32, 1.11) | 0.54 (0.42, 0.71) | 0.91 (0.46,1.78) |  | 0.55 (0.29, 1.07) | 0.55 (0.42, 0.73) | 1.00 (0.49,2.06) |
| EFV v. LPV (ACTG 5142) | 24 | 0.68 (0.26, 1.76) | 0.73 (0.58, 0.93) | 1.08 (0.41,2.88) |  | 0.68 (0.25, 1.84) | 0.73 (0.56, 0.95) | 1.07 (0.39,2.95) |
| 48 | 1.41 (0.54, 3.66) | 0.71 (0.56, 0.90) | 0.51 (0.19,1.35) |  | 1.55 (0.56, 4.27) | 0.82 (0.63, 1.06) | 0.53 (0.19,1.48) |
| **Comparison of study designs** | **Patients on EFV** | **Patients on ABC** |  |  | **Patients on EFV** | **Patients on ABC** |  |
| ACTG 5095 v. cohort | 24 | 0.89 (0.56, 1.42) | 1.13 (0.76, 1.68) | 1.27 (0.69,2.34) |  | 0.90 (0.55, 1.45) | 1.03 (0.68, 1.57) | 1.15 (0.61,2.17) |
| 48 | 1.31 (0.83, 2.06) | 1.19 (0.72, 1.96) | 0.91 (0.46,1.78) |  | 1.20 (0.75, 1.93) | 1.15 (0.67, 1.99) | 0.96 (0.46,1.97) |
|  |  | **Patients on EFV** | **Patients on LPV** |  |  | **Patients on EFV** | **Patients on LPV** |  |
| ACTG 5142 v. | 24 | 0.63 (0.30, 1.32) | 0.68 (0.36, 1.30) | 1.08 (0.41,2.88) |  | 0.67 (0.31, 1.45) | 0.72 (0.37, 1.40) | 1.07 (0.39,2.95) |
| cohort | 48 | 0.94 (0.49, 1.81) | 0.48 (0.23, 1.00) | 0.51 (0.19,1.35) |  | 0.92 (0.47, 1.80) | 0.54 (0.25, 1.17) | 0.59 (0.21,1.65) |

Appendix 2 Table 3: Sensitivity analysis: stratified by baseline viral load (upper VL≥100,000, lower VL<100,000 copies /mL) Crude and adjusted hazard ratio (HR) for AIDS or death with ratio of hazard ratios at 24 and 48 weeks after starting treatment (i) between study design comparison of drug regimen (ii) between drug regimen comparison of study design (white band ACTG5095 EFV v. ABC, grey band ACTG5142 EFV v.ABC).

**Baseline VL≥100,000 copies /mL EFV v. ABC N=2128; EFV v. LPV N=4547**

|  |  |  |
| --- | --- | --- |
|  | **Weeks of follow-up** | **HR (95% CI) AIDS or death** |
| **Crude** |  | **Adjusted** |
| **Comparison of regimens** | **Trial** | **Cohort** | **Ratio of HR** |  | **Trial** | **Cohort** | **Ratio of HR** |
| EFV v. ABC (ACTG 5095) | 24 | 0.56 (0.19, 1.66) | 0.86 (0.51, 1.45) | 1.55 (0.46,5.19) |  | 0.37 (0.12, 1.15) | 0.73 (0.43, 1.25) | 1.95 (0.56,6.82) |
| 48 | 0.58 (0.23, 1.48) | 0.61 (0.40, 0.92) | 1.04 (0.38,2.89) |  | 0.41 (0.16, 1.07) | 0.53 (0.35, 0.81) | 1.31 (0.46,3.71) |
| EFV v. LPV (ACTG 5142) | 24 | 1.06 (0.31, 3.66) | 0.77 (0.60, 0.99) | 0.73 (0.20,2.57) |  | 0.78 (0.20, 2.99) | 0.88 (0.68, 1.15) | 1.14 (0.32,4.08) |
| 48 | 1.21 (0.44, 3.34) | 0.79 (0.64, 0.99) | 0.66 (0.23,1.85) |  | 0.99 (0.32, 3.00) | 0.88 (0.70, 1.10) | 0.89 (0.31,2.54) |
| **Comparison of study designs** | **Patients on EFV** | **Patients on ABC** |  |  | **Patients on EFV** | **Patients on ABC** |  |
| ACTG 5095 v. cohort | 24 | 1.02 (0.42, 2.50) | 0.78 (0.32, 1.91) | 0.77 (0.22,2.71) |  | 0.88 (0.35, 2.18) | 0.82 (0.33, 2.01) | 0.93 (0.26,3.34) |
| 48 | 1.16 (0.57, 2.37) | 0.84 (0.39, 1.77) | 0.72 (0.26,2.02) |  | 1.04 (0.51, 2.15) | 0.87 (0.41, 1.86) | 0.83 (0.29,2.38) |
|  |  | **Patients on EFV** | **Patients on LPV** |  |  | **Patients on EFV** | **Patients on LPV** |  |
| ACTG 5142 v. | 24 | 0.62 (0.25, 1.53) | 1.18 (0.54, 2.56) | 1.91 (0.58,6.28) |  | 0.49 (0.19, 1.21) | 0.99 (0.42, 2.32) | 2.04 (0.58,7.11) |
| cohort | 48 | 0.61 (0.28, 1.31) | 0.86 (0.45, 1.65) | 1.41 (0.52,3.85) |  | 0.49 (0.23, 1.06) | 0.74 (0.37, 1.50) | 1.52 (0.53,4.32) |

**Baseline VL<100,000 copies /mL EFV v. ABC N=3235; EFV v. LPV N=4163**

|  |  |  |
| --- | --- | --- |
|  | **Weeks of follow-up** | **HR (95% CI) AIDS or death** |
| **Crude** |  | **Adjusted** |
| **Comparison of regimens** | **Trial** | **Cohort** | **Ratio of HR** |  | **Trial** | **Cohort** | **Ratio of HR** |
| EFV v. ABC (ACTG 5095) | 24 | 2.01 (0.18, 22.15) | 1.36 (0.83, 2.24) | 0.68 (0.06,7.88) |  | 2.00 (0.16, 24.62) | 1.01 (0.60, 1.69) | 0.50 (0.04,5.98) |
| 48 | 3.01 (0.31, 28.97) | 1.27 (0.85, 1.91) | 0.42 (0.04,4.21) |  | 3.39 (0.33, 35.25) | 0.96 (0.63, 1.47) | 0.28 (0.03,2.88) |
| EFV v. LPV (ACTG 5142) | 24 | 0.98 (0.14, 6.93) | 0.70 (0.50, 0.98) | 0.72 (0.10,5.26) |  | 0.81 (0.11, 5.84) | 0.86 (0.60, 1.23) | 1.06 (0.14,7.83) |
| 48 | 0.73 (0.16, 3.28) | 0.77 (0.58, 1.02) | 1.05 (0.23,4.80) |  | 0.79 (0.17, 3.67) | 0.89 (0.66, 1.21) | 1.13 (0.24,5.25) |
| **Comparison of study designs** | **Patients on EFV** | **Patients on ABC** |  |  | **Patients on EFV** | **Patients on ABC** |  |
| ACTG 5095 v. cohort | 24 | 0.28 (0.07, 1.16) | 0.19 (0.03, 1.39) | 0.68 (0.06,7.81) |  | 0.31 (0.07, 1.28) | 0.12 (0.02, 0.92) | 0.40 (0.03,4.75) |
| 48 | 0.27 (0.09, 0.87) | 0.12 (0.02, 0.88) | 0.44 (0.04,4.36) |  | 0.29 (0.09, 0.93) | 0.07 (0.01, 0.53) | 0.25 (0.02,2.52) |
|  |  | **Patients on EFV** | **Patients on LPV** |  |  | **Patients on EFV** | **Patients on LPV** |  |
| ACTG 5142 v. | 24 | 0.36 (0.09, 1.47) | 0.26 (0.06, 1.05) | 0.72 (0.10,5.22) |  | 0.37 (0.09, 1.55) | 0.28 (0.07, 1.16) | 0.76 (0.10,5.60) |
| cohort | 48 | 0.36 (0.12, 1.15) | 0.38 (0.14, 1.03) | 1.04 (0.23,4.76) |  | 0.37 (0.12, 1.19) | 0.41 (0.15, 1.13) | 1.10 (0.24,5.11) |

Appendix 2 Table 4: Sensitivity analysis: stratified by baseline CD4 count (upper CD4<200, lower CD4≥200) Crude and adjusted hazard ratio (HR) for AIDS or death with ratio of hazard ratios at 24 and 48 weeks after starting treatment (i) between study design comparison of drug regimen (ii) between drug regimen comparison of study design (white band ACTG5095 EFV v. ABC, grey band ACTG5142 EFV v.ABC).

**CD4 count <200 copies/mL EFV v. ABC N=2408; EFV v. LPV N=4936**

|  |  |  |
| --- | --- | --- |
|  | **Weeks of follow-up** | **HR (95% CI) AIDS or death** |
| **Crude** |  | **Adjusted** |
| **Comparison of regimens** | **Trial** | **Cohort** | **Ratio of HR** |  | **Trial** | **Cohort** | **Ratio of HR** |
| EFV v. ABC (ACTG 5095) | 24 | 0.70 (0.25, 1.96) | 1.11 (0.73, 1.69) | 1.59 (0.52,4.85) |  | 0.45 (0.16, 1.31) | 0.92 (0.59, 1.42) | 2.03 (0.64,6.40) |
| 48 | 0.76 (0.31, 1.89) | 0.83 (0.59, 1.17) | 1.09 (0.41,2.89) |  | 0.51 (0.20, 1.30) | 0.69 (0.49, 0.98) | 1.36 (0.50,3.67) |
| EFV v. LPV (ACTG 5142) | 24 | 0.75 (0.24, 2.36) | 0.86 (0.69, 1.07) | 1.15 (0.36,3.69) |  | 0.60 (0.18, 2.00) | 0.98 (0.78, 1.23) | 1.63 (0.50,5.28) |
| 48 | 0.57 (0.21, 1.54) | 0.90 (0.74, 1.09) | 1.58 (0.57,4.35) |  | 0.51 (0.18, 1.46) | 1.00 (0.81, 1.22) | 1.94 (0.70,5.38) |
| **Comparison of study designs** | **Patients on EFV** | **Patients on ABC** |  |  | **Patients on EFV** | **Patients on ABC** |  |
| ACTG 5095 v. cohort | 24 | 0.46 (0.20, 1.05) | 0.79 (0.38, 1.64) | 1.71 (0.57,5.15) |  | 0.44 (0.19, 1.01) | 0.59 (0.27, 1.31) | 1.34 (0.43,4.24) |
| 48 | 0.44 (0.21, 0.89) | 0.55 (0.29, 1.06) | 1.27 (0.49,3.32) |  | 0.41 (0.20, 0.84) | 0.41 (0.20, 0.80) | 0.99 (0.37,2.68) |
|  |  | **Patients on EFV** | **Patients on LPV** |  |  | **Patients on EFV** | **Patients on LPV** |  |
| ACTG 5142 v. | 24 | 0.53 (0.22, 1.28) | 0.62 (0.29, 1.31) | 1.17 (0.36,3.75) |  | 0.52 (0.21, 1.29) | 0.72 (0.34, 1.53) | 1.37 (0.42,4.44) |
| cohort | 48 | 0.45 (0.20, 1.01) | 0.76 (0.41, 1.38) | 1.68 (0.61,4.62) |  | 0.45 (0.20, 1.02) | 0.88 (0.48, 1.61) | 1.95 (0.70,5.42) |

 **CD4 count ≥200 copies/mL EFV v. ABC N=2955; EFV v. LPV N=3774**

|  |  |  |
| --- | --- | --- |
|  | **Weeks of follow-up** | **HR (95% CI) AIDS or death** |
| **Crude** |  | **Adjusted** |
| **Comparison of regimens** | **Trial** | **Cohort** | **Ratio of HR** |  | **Trial** | **Cohort** | **Ratio of HR** |
| EFV v. ABC (ACTG 5095) | 24 | 0.96 (0.06, 15.38) | 0.81 (0.04, 15.55) | 0.99 (0.06,17.33) |  | 0.96 (0.47, 1.92) | 0.81 (0.39, 1.68) | 1.00(0.05,18.28) |
| 48 | 0.96 (0.14, 6.81) | 0.98 (0.56, 1.70) | 1.02 (0.13,7.82) |  | 0.82 (0.11, 6.11) | 0.84 (0.47, 1.49) | 1.02 (0.13,8.17) |
| EFV v. LPV (ACTG 5142) | 24 | NE | 0.53 (0.32, 0.87) | NE |  | NE | 0.51 (0.29, 0.87) | NE |
| 48 | NE | 0.57 (0.39, 0.85) | NE |  | NE | 0.51 (0.33, 0.79) | NE |
| **Comparison of study designs** | **Patients on EFV** | **Patients on ABC** |  |  | **Patients on EFV** | **Patients on ABC** |  |
| ACTG 5095 v. cohort | 24 | 0.38 (0.05, 2.87) | 0.36 (0.05, 2.72) | 0.94 (0.05,16.24) |  | 0.30 (0.04, 2.26) | 0.23 (0.03, 1.82) | 0.78 (0.04,14.25) |
| 48 | 0.45 (0.11, 1.86) | 0.45 (0.11, 1.91) | 1.02 (0.13,7.73) |  | 0.38 (0.09, 1.62) | 0.30 (0.07, 1.32) | 0.79 (0.10,6.31) |
|  |  | **Patients on EFV** | **Patients on LPV** |  |  | **Patients on EFV** | **Patients on LPV** |  |
| ACTG 5142 v. | 24 | 1.12 (0.27, 4.70) | NE | NE |  | 1.44 (0.32, 6.39) | NE | NE |
| cohort | 48 | 1.73 (0.69, 4.35) | NE | NE |  | 2.32 (0.87, 6.14) | NE | NE |

NE not estimated due to sparse data