

Supplemental Table 1 Factors associated with baseline QTcB (Bazett), QTcF (Fridericia) and PR in the fully adjusted linear regression model\*

| Factor                      | QTcB (Bazett)<br>Coef. (SE) | p     | QTcF (Fridericia)<br>Coef. (SE) | p     | PR Duration<br>Coef. (SE) | p     |
|-----------------------------|-----------------------------|-------|---------------------------------|-------|---------------------------|-------|
| Heart Rate                  |                             |       |                                 |       | −0.42 (0.0)               | <0.01 |
| Age (year)                  | 0.35 (0.04)                 | <0.01 | 0.39 (0.04)                     | <0.01 | 0.23 (0.04)               | <0.01 |
| Gender (F vs. M)            | 11.69 (0.73)                | <0.01 | 9.79 (0.72)                     | <0.01 | −4.81 (0.90)              | <0.01 |
| Race                        |                             |       |                                 |       |                           |       |
| Black (vs. White)           | −0.61 (0.76)                | 0.42  | −0.98 (0.76)                    | 0.19  | 6.83 (0.93)               | <0.01 |
| Asian (vs. White)           | 6.62 (1.80)                 | <0.01 | 3.35 (1.78)                     | 0.06  | 6.64 (2.23)               | <0.01 |
| Other Races (vs. White)     | −1.04 (0.97)                | 0.28  | −1.26 (0.96)                    | 0.19  | −1.47 (1.20)              | 0.22  |
| Smoking Status              |                             |       |                                 |       |                           |       |
| Current (vs. Never)         | 0.03 (0.72)                 | 0.97  | −0.78 (0.72)                    | 0.28  | −3.40 (0.89)              | <0.01 |
| Past (vs. Never)            | −0.33 (0.79)                | 0.67  | 0.35 (0.78)                     | 0.66  | −1.91 (0.97)              | 0.05  |
| Total/HDL Cholesterol Ratio | 0.21 (0.13)                 | 0.11  | −0.31 (0.13)                    | 0.02  | 0.36 (0.16)               | 0.03  |
| Baseline BMI                | 0.26 (0.06)                 | <0.01 | 0.09 (0.06)                     | 0.16  | 0.34 (0.08)               | <0.01 |
| Prior CVD (Y vs. N)         | 1.79 (1.22)                 | 0.14  | −3.45 (1.21)                    | <0.01 | 0.34 (1.52)               | 0.82  |
| Diabetes (Y vs. N)          | 2.20 (1.64)                 | 0.18  | 4.66 (1.63)                     | <0.01 | −0.83 (2.03)              | 0.68  |
| Use of BP-lowering drugs    | 4.29 (0.85)                 | <0.01 | 3.52 (0.84)                     | <0.01 | 2.28 (1.05)               | 0.03  |
| Use of lipid lowering drugs | −0.14 (0.84)                | 0.86  | −0.63 (0.83)                    | 0.45  | 0.67 (1.03)               | 0.52  |
| Years since HIV dx          | −0.00 (0.07)                | 0.98  | −0.04 (0.07)                    | 0.57  | −0.05 (0.08)              | 0.57  |
| Baseline CD4 (per 100)      | −0.03 (0.12)                | 0.82  | −0.03 (0.12)                    | 0.83  | −0.21 (0.15)              | 0.16  |
| Baseline HIV-RNA ≤ 400      | 0.21 (0.85)                 | 0.81  | 1.39 (0.84)                     | 0.10  | 0.10 (1.04)               | 0.92  |
| NRTI backbone regimen       |                             |       |                                 |       |                           |       |
| AZT + 3TC (without ABC)     | Ref.                        | –     | Ref.                            | –     | Ref.                      | –     |
| TNV (without ABC)           | −3.13 (0.91)                | <0.01 | −2.55 (0.90)                    | <0.01 | 1.29 (1.11)               | 0.25  |
| ABC (without TNV)           | −0.92 (0.95)                | 0.33  | −1.26 (0.94)                    | 0.18  | 2.06 (1.16)               | 0.08  |
| 3TC + d4T                   | −2.57 (0.94)                | <0.01 | −3.50 (0.93)                    | <0.01 | 0.06 (1.16)               | 0.96  |
| Other NRTI regimens         | −1.28 (0.95)                | 0.18  | −1.88 (0.94)                    | 0.05  | 2.58 (1.17)               | 0.03  |

\*All variables are included in the model in addition to ART use. Multivariable association of ART use with QTcB, QTcF and PR are listed in Table 3 in the main article.

Supplemental Table 2 Change in baseline QT duration and PR interval after 12 months of continuous versus interrupted use of HIV medications (Intention-to-treat analysis)

| Measure                 | DC Group |                       |                              |      | VS Group |                       |                              |      |      |
|-------------------------|----------|-----------------------|------------------------------|------|----------|-----------------------|------------------------------|------|------|
|                         | N        | Baseline<br>Mean (SD) | Change (M12-BL)<br>Mean (SD) | p*   | N        | Baseline<br>Mean (SD) | Change (M12-BL)<br>Mean (SD) | p*   | p ** |
| QTcB (Bazett)           |          |                       |                              |      |          |                       |                              |      |      |
| Any PI/r                | 406      | 414.3 (17.66)         | 0.48 (15.67)                 | 0.54 | 435      | 415.7 (18.85)         | 0.69 (18.00)                 | 0.43 | 0.74 |
| SQV/r                   | 100      | 419.7 (19.31)         | −0.24 (15.80)                | 0.88 | 106      | 422.0 (19.11)         | −0.60 (20.83)                | 0.77 | 0.91 |
| LPV/r                   | 189      | 412.2 (16.56)         | 2.26 (15.27)                 | 0.04 | 201      | 413.9 (18.38)         | 1.17 (16.93)                 | 0.33 | 0.43 |
| Other PI/r <sup>s</sup> | 117      | 413.3 (17.12)         | −1.79 (15.99)                | 0.23 | 128      | 413.4 (18.34)         | 1.00 (17.17)                 | 0.51 | 0.41 |
| Non-boosted PI          | 293      | 417.1 (20.64)         | −0.30 (20.42)                | 0.80 | 270      | 416.3 (20.47)         | 1.43 (18.69)                 | 0.21 | 0.24 |
| QTcF (Fridericia)       |          |                       |                              |      |          |                       |                              |      |      |
| Any PI/r                | 406      | 405.7 (17.40)         | −0.64 (15.27)                | 0.40 | 435      | 407.6 (18.38)         | 0.72 (17.96)                 | 0.41 | 0.10 |
| SQV/r                   | 100      | 410.7 (18.16)         | −0.54 (14.88)                | 0.72 | 106      | 412.2 (18.00)         | 0.49 (19.80)                 | 0.80 | 0.55 |
| LPV/r                   | 189      | 404.7 (16.90)         | 0.11 (15.00)                 | 0.92 | 201      | 405.5 (18.37)         | 1.66 (17.00)                 | 0.17 | 0.57 |
| Other PI/r <sup>s</sup> | 117      | 403.2 (16.84)         | −1.95 (16.06)                | 0.19 | 128      | 407.0 (18.17)         | −0.57 (17.90)                | 0.72 | 0.18 |
| Non-boosted PI          | 293      | 408.7 (21.52)         | −1.91 (19.91)                | 0.10 | 270      | 408.0 (19.32)         | 0.29 (17.13)                 | 0.78 | 0.14 |
| PR Interval             |          |                       |                              |      |          |                       |                              |      |      |
| Any PI/r                | 480      | 161.5 (24.94)         | −0.92 (15.19)                | 0.18 | 509      | 161.6 (24.04)         | −1.54 (16.08)                | 0.03 | 0.52 |
| SQV/r                   | 104      | 160.1 (21.41)         | −0.79 (12.06)                | 0.51 | 113      | 155.1 (19.92)         | −0.94 (11.91)                | 0.40 | 0.51 |
| LPV/r                   | 230      | 162.4 (23.19)         | −1.36 (12.65)                | 0.10 | 231      | 163.3 (26.49)         | −1.54 (14.81)                | 0.12 | 0.76 |
| Other PI/r <sup>s</sup> | 146      | 161.2 (29.60)         | −0.33 (20.15)                | 0.84 | 165      | 163.7 (22.29)         | −1.96 (19.90)                | 0.21 | 0.87 |
| Non-boosted PI          | 335      | 160.0 (21.86)         | −0.69 (12.56)                | 0.32 | 305      | 160.6 (23.49)         | −0.45 (13.45)                | 0.56 | 0.59 |

SQV/r, LPV/r, ATV/r, and PI/r = Saquinavir, Lopinavir, Atazanavir and Protease Inhibitors boosted with Ritonavir; NNRTI = Non-nucleoside Reverse Transcriptase Inhibitor; NRTI = Nucleoside Reverse Transcriptase Inhibitor. \* p-value obtained from paired T test comparing baseline and month 12 mean values of PR and QT. \*\* p-value for comparison between mean changes in the DC group versus VS group after adjusting for baseline value, age, gender, race, smoking status, total cholesterol/HDL ratio, BMI, prior CVD, diabetes, use of blood pressure lowering drugs, use of lipid lowering drugs, duration of HIV infection, and baseline CD4 and HIV-RNA (plus heart rate in the PR models); NNRTI = Non-nucleoside Reverse Transcriptase Inhibitor. <sup>s</sup> Including atazanavir boosted with ritonavir.

Supplemental Table 3 Change in baseline QTc and PR interval durations after 24 months of continuous versus interrupted use of HIV medications (Intention-to-treat analysis)

| Measure                 | DC Group |                    |                           |      | VS Group |                    |                           |      |      |
|-------------------------|----------|--------------------|---------------------------|------|----------|--------------------|---------------------------|------|------|
|                         | N        | Baseline Mean (SD) | Change (M24-BL) Mean (SD) | p*   | N        | Baseline Mean (SD) | Change (M24-BL) Mean (SD) | p*   | p**  |
| QTcB (Bazett)           |          |                    |                           |      |          |                    |                           |      |      |
| Any PI/r                | 235      | 412.1 (16.98)      | 0.71 (16.13)              | 0.50 | 253      | 414.7 (17.11)      | 1.03 (16.06)              | 0.31 | 0.90 |
| SQV/r                   | 27       | 410.9 (15.09)      | -3.06 (12.36)             | 0.21 | 30       | 419.3 (13.10)      | 1.04 (15.09)              | 0.71 | 0.06 |
| LPV/r                   | 121      | 411.8 (17.20)      | 2.97 (18.41)              | 0.08 | 142      | 414.0 (17.42)      | 1.12 (16.59)              | 0.42 | 0.17 |
| Other PI/r <sup>§</sup> | 87       | 412.9 (17.37)      | -1.26 (13.15)             | 0.37 | 81       | 414.1 (17.79)      | 0.87 (15.65)              | 0.62 | 0.83 |
| Non-boosted PI          | 206      | 417.2 (19.78)      | -2.13 (20.16)             | 0.13 | 192      | 414.2 (18.96)      | 1.26 (17.93)              | 0.33 | 0.20 |
| QTcF (Fridericia)       |          |                    |                           |      |          |                    |                           |      |      |
| Any PI/r                | 235      | 404.2 (16.83)      | -0.59 (17.26)             | 0.60 | 253      | 406.3 (16.99)      | 1.38 (15.99)              | 0.17 | 0.20 |
| SQV/r                   | 27       | 402.5 (18.19)      | -4.27 (14.83)             | 0.15 | 30       | 409.9 (16.64)      | 1.50 (16.05)              | 0.61 | 0.02 |
| LPV/r                   | 121      | 405.1 (16.56)      | 0.83 (19.72)              | 0.64 | 142      | 405.1 (16.42)      | 2.48 (16.29)              | 0.07 | 0.97 |
| Other PI/r <sup>§</sup> | 87       | 403.4 (16.88)      | -1.42 (13.91)             | 0.34 | 81       | 407.0 (18.06)      | -0.59 (15.43)             | 0.73 | 0.92 |
| Non-boosted PI          | 206      | 408.0 (20.70)      | -2.98 (19.68)             | 0.03 | 192      | 406.2 (19.06)      | 1.30 (17.31)              | 0.30 | 0.02 |
| PR Interval             |          |                    |                           |      |          |                    |                           |      |      |
| Any PI/r                | 279      | 162.4 (26.40)      | -1.55 (17.78)             | 0.15 | 300      | 162.9 (24.38)      | 0.77 (14.40)              | 0.35 | 0.07 |
| SQV/r                   | 31       | 162.0 (25.64)      | -2.65 (14.60)             | 0.32 | 35       | 156.2 (20.97)      | 0.46 (15.81)              | 0.87 | 0.79 |
| LPV/r                   | 145      | 163.4 (21.07)      | -1.17 (15.87)             | 0.38 | 165      | 164.1 (25.77)      | 1.28 (14.05)              | 0.24 | 0.17 |
| Other PI/r <sup>§</sup> | 103      | 161.1 (32.79)      | -1.77 (21.03)             | 0.40 | 100      | 163.3 (22.92)      | 0.05 (14.56)              | 0.97 | 0.15 |
| Non-boosted PI          | 237      | 159.4 (21.96)      | -1.31 (19.05)             | 0.29 | 228      | 161.6 (23.56)      | -0.10 (14.16)             | 0.92 | 0.20 |

SQV/r, LPV/r, ATV/r, and PI/r = Saquinavir, Lopinavir, Atazanavir and Protease Inhibitors boosted with Ritonavir; NNRTI = Non-nucleoside Reverse Transcriptase Inhibitor; NRTI = Nucleoside Reverse Transcriptase Inhibitor. \*p-value obtained from paired T test comparing baseline and month -24 mean values of PR and QT. \*\*p-value for comparison between mean changes in the DC group versus VS group after adjusting for baseline value, age, gender, race, smoking status, total cholesterol/HDL ratio, BMI, prior CVD, diabetes, use of blood pressure lowering drugs, use of lipid lowering drugs, duration of HIV infection, and baseline CD4 and HIV-RNA (plus heart rate in the PR models); NNRTI = Non-nucleoside Reverse Transcriptase Inhibitor. <sup>§</sup>Including atazanavir boosted with ritonavir.