# Supplementary Material

## Figure S1 Flow chart showing inclusion/exclusion process



## Table S1 Associations between baseline characteristics and choice of INSTIs – univariable analysis

|  |  |  |
| --- | --- | --- |
|  | **Raltegravir vs Dolutegravir** | **Elvitegravir vs Dolutegravir** |
| **Variable** | **Reference** | **Group** | **RR\*** | **(95% CI)** | **p-value** | **RR\*** | **(95% CI)** | **p-value** |
| INSTI start, per 1-year increase |  | 0.30 | (0.28, 0.31) | <0.001 | 0.81 | (0.77, 0.85) | <0.001 |
| Geographical region1 | Western Europe/Australia | Southern Europe | 1.60 | (1.42, 1.79) | <0.001 | 1.35 | (1.20, 1.52) | <0.001 |
| Northern Europe | 4.45 | (3.88, 5.11) |  | 0.78 | (0.69, 0.96) |  |
| Eastern Europe | 2.80 | (2.32, 3.38) |  | 1.10 | (0.87, 1.41) |  |
| Age, per 10-year increase |  | 1.05 | (1.01, 1.09) | 0.03 | 0.83 | (0.80, 0.87) | <0.001 |
| Gender | Male | Female | 1.06 | (0.95, 1.17) | 0.32 | 0.70 | (0.61, 0.80) | <0.001 |
| Ethnic origin† | White | Black | 1.33 | (1.14, 1.54) | <0.001 | 1.30 | (1.10, 1.55) | <0.001 |
| Smoking status† | Never | Current | 1.04 | (0.91, 1.20) | 0.08 | 1.00 | (0.87, 1.15) | 0.96 |
| Previous | 1.23 | (1.03, 1.48) |  | 0.98 | (0.80, 1.19) |  |
| ART experience | Experienced, VL<400 cps/mL | Naive | 0.92 | (0.82, 1.04) | <0.001 | 1.44 | (1.28, 1.62) | <0.001 |
| Experienced, VL≥400 cps/mL | 2.11 | (1.80 ,2.48) |  | 1.13 | (0.91, 1.40) |  |
| HIV risk† | MSM | IDU | 1.25 | (1.09, 1.44) | <0.001 | 0.62 | (0.52, 0.74) | <0.001 |
| Heterosexual | 1.09 | (0.98, 1.22) |  | 0.79 | (0.70, 0.89) |  |
| CD4 nadir, cells/mm³ | <200 | 200-349 | 0.76 | (0.68, 0.85) | <0.001 | 1.41 | (1.24, 1.60) | <0.001 |
| 350-499 | 0.67 | (0.58, 0.79) |  | 1.68 | (1.44, 1.96) |  |
| ≥500 | 0.70 | (0.59, 0.83) |  | 1.67 | (1.42, 1.98) |  |
| CD4 at INSTI start, cells/mm³ | <200 | 200-349 | 0.87 | (0.73, 1.04) | <0.001 | 1.79 | (1.41, 2.26) | <0.001 |
| 350-499 | 0.71 | (0.60 ,0.83) |  | 1.85 | (1.49, 2.30) |  |
| ≥500 | 0.60 | (0.52 ,0.69) |  | 1.55 | (1.28, 1.89) |  |
| Hepatitis C† | No | Yes | 1.29 | (1.16, 1.45) | <0.001 | 0.69 | (0.59, 0.79) | <0.001 |
| Hepatitis B† | No | Yes | 1.60 | (1.28, 2.00) | <0.001 | 1.59 | (1.24, 2.04) | <0.001 |
| Hypertension† | No | Yes | 0.92 | (0.82, 1.04) | 0.20 | 0.80 | (0.70, 0.92) | 0.002 |
| Diabetes† | No | Yes | 1.16 | (0.98, 1.37) | 0.09 | 0.87 | (0.70, 1.07) | 0.18 |
| Prior AIDS† | No | Yes | 1.40 | (1.25, 1.56) | <0.001 | 0.65 | (0.56, 0.76) | <0.001 |
| Prior NADM† | No | Yes | 1.14 | (0.91, 1.43) | 0.24 | 0.56 | (0.39, 0.79) | 0.001 |
| Prior ESLD† | No | Yes | 1.22 | (0.78, 1.93) | 0.38 | 0.52 | (0.22, 1.24) | 0.14 |
| Prior CVD† | No | Yes | 1.90 | (1.50, 2.40) | <0.001 | 0.84 | (0.59, 1.18) | 0.31 |
| Prior fracture† | No | Yes | 0.84 | (0.68, 1.05) | 0.13 | 0.92 | (0.70, 1.21) | 0.56 |
| Prior CKD† | No | Yes | 1.17 | (0.93, 1.47) | 0.18 | 0.60 | (0.42, 0.85) | 0.004 |

Abbreviations: RR-risk ratio; CI-confidence interval; INSTI-integrase inhibitor; ART-antiretroviral treatment; VL-viral load; MSM-men who have sex with men; IDU-intravenous drug user; NADM-non-AIDS defining malignancies; ESLD-end stage liver disease; CVD-cardiovascular disease; CKD-chronic kidney disease

\*Results from a univariable, multinomial logistic regression

1Due to low counts, Australia is grouped with Northern Europe and Eastern Central Europe is grouped with Eastern Europe.

†Missing data fitted as an unknown category (data not shown)

## Figure S2 Association between gender and INSTI uptake, by age



Abbreviations: EVG-elvitegravir; DTG-dolutegravir; RAL-raltegravir; RR-risk ratio; CI-confidence interval

\*Log RR comparing females to males estimated from a multinomial logistic regression model including an interaction between age and gender, adjusted for year of starting INSTI, geographical region, ethnicity, smoking status, HIV risk group, antiretroviral treatment experience, CD4 nadir, CD4 at INSTI start, hepatitis B, hepatitis C, hypertension, diabetes, prior AIDS, non-AIDS malignancies, end stage liver disease, cardiovascular disease, fracture, chronic kidney disease

## Table S2 Associations between baseline characteristics and INSTI discontinuation in the first 6 months after INSTI start

|  |  |  |
| --- | --- | --- |
|  | **Univariable model\*** | **Multivariable model\*** |
| **Variable** | **Reference** | **Group** | **HR** | **(95% CI)** | **p-value** | **HR** | **(95% CI)** | **p-value** |
| INSTI type | Dolutegravir | Raltegravir | 2.27 | (1.94, 2.64) | <0.001 | 3.03 | (2.47, 3.71) | <0.001 |
| Elvitegravir | 1.17 | (0.95, 1.44) |  | 1.37 | (1.10, 1.70) |  |
| INSTI start, per 1 year later |  | 0.89 | (0.85, 0.94) | <0.001 | 1.11 | (1.04, 1.18) | 0.001 |
| Geographical region1 | Western Europe/Australia | Southern Europe | 0.83 | (0.70, 0.98) | <0.001 | 0.58 | (0.43, 0.78) | <0.001 |
| Northern Europe | 1.03 | (0.84, 1.27) |  | 0.89 | (0.64, 1.25) |  |
| Eastern Europe | 0.43 | (0.28, 0.66) |  | 0.31 | (0.20, 0.50) |  |
| Age category | <30 | 30-39 | 1.07 | (0.81, 1.41) | 0.32 | 1.04 | (0.78, 1.39) | 0.19 |
| 40-49 | 0.88 | (0.67, 1.16) |  | 0.84 | (0.63, 1.12) |  |
| ≥50 | 0.98 | (0.75, 1.27) |  | 0.95 | (0.70, 1.28) |  |
| Gender | Male | Female | 1.34 | (1.15, 1.56) | <0.001 | 1.28 | (1.06, 1.56) | 0.01 |
| Ethnic origin† | White | Black | 1.14 | (0.92, 1.42) | 0.36 | 0.96 | (0.74, 1.25) | 0.47 |
| Other | 0.88 | (0.60, 1.27) |  | 0.79 | (0.54, 1.15) |  |
| HIV risk† | MSM | IDU | 1.18 | (0.96, 1.46) | 0.06 | 0.89 | (0.67, 1.19) | 0.65 |
| Heterosexual | 1.24 | (1.06, 1.45) |  | 1.01 | (0.82, 1.25) |  |
| Other | 1.05 | (0.66, 1.67) |  | 0.75 | (0.46, 1.22) |  |
| Smoking status† | Never | Current | 1.04 | (0.85, 1.27) | 0.79 | 0.96 | (0.77, 1.19) | 0.49 |
| Previous | 1.10 | (0.84, 1.44) |  | 1.13 | (0.86, 1.50) |  |
| ART experience | Experienced, VL<400 cps/mL | Naive | 1.15 | (0.98, 1.36) | <0.001 | 1.10 | (0.87, 1.39) | 0.046 |
| Experienced, VL≥400 cps/mL | 1.68 | (1.36, 2.08) |  | 1.36 | (1.07, 1.73) |  |
| CD4 nadir, cells/mm³ | <200 | 200-349 | 0.87 | (0.74, 1.03) | 0.41 | 1.05 | (0.86, 1.28) | 0.68 |
| 350-499 | 0.91 | (0.73, 1.13) |  | 1.13 | (0.86, 1.47) |  |
| ≥500 | 1.00 | (0.80, 1.25) |  | 1.20 | (0.88, 1.64) |  |
| CD4 at INSTI start, cells/mm³ | <200 | 200-349 | 0.70 | (0.54, 0.91) | <0.001 | 0.76 | (0.58, 1.01) | 0.06 |
| 350-499 | 0.63 | (0.50, 0.80) |  | 0.69 | (0.51, 0.91) |  |
| ≥500 | 0.63 | (0.52, 0.77) |  | 0.71 | (0.54, 0.95) |  |
| Hepatitis C† | No | Yes | 1.18 | (1.00, 1.36) | 0.005 | 1.32 | (1.06, 1.66) | 0.01 |
| Hepatitis B† | No | Yes | 0.96 | (0.68, 1.36) | 0.83 | 0.93 | (0.66, 1.33) | 0.70 |
| Hypertension† | No | Yes | 0.87 | (0.73, 1.05) | 0.14 | 0.92 | (0.75, 1.11) | 0.37 |
| Diabetes† | No | Yes | 0.82 | (0.62, 1.08) | 0.15 | 0.82 | (0.62, 1.10) | 0.19 |
| Prior AIDS† | No | Yes | 1.08 | (0.92, 1.28) | 0.35 | 1.01 | (0.84, 1.21) | 0.90 |
| Prior NADM† | No | Yes | 1.47 | (1.08, 1.99) | 0.01 | 1.55 | (1.13, 2.12) | 0.006 |
| Prior ESLD† | No | Yes | 1.11 | (0.53, 2.36) | 0.78 | 0.99 | (0.46, 2.11) | 0.97 |
| Prior CVD† | No | Yes | 1.16 | (0.82, 1.66) | 0.40 | 1.15 | (0.79, 1.68) | 0.46 |
| Prior fracture† | No | Yes | 0.84 | (0.59, 1.20) | 0.35 | 0.85 | (0.59, 1.22) | 0.38 |
| Prior CKD† | No | Yes | 0.83 | (0.56, 1.24) | 0.36 | 0.79 | (0.52, 1.19) | 0.26 |

Abbreviations: HR-hazard ratio; CI-confidence interval; INSTI-integrase inhibitor; ART-antiretroviral treatment; VL-viral load; MSM-men who have sex with men; IDU-intravenous drug user; NADM-non-AIDS defining malignancies; ESLD-end stage liver disease; CVD-cardiovascular disease; CKD-chronic kidney disease

\*Results from a Cox proportional hazards model; all variables were fitted simultaneously in the multivariable model

1Due to low counts, Australia is grouped with Northern Europe and Eastern Central Europe is grouped with Eastern Europe.

†Missing data fitted as an unknown category (data not shown)

## Figure S3 Risk of INSTI discontinuation, by age category



Abbreviations: EVG-elvitegravir; DTG-dolutegravir; RAL-raltegravir; HR-hazard ratio; CI-confidence interval

\*Log HR comparing INSTI types estimated from a Cox proportional hazards model including an interaction between INSTI type and age category, adjusted for year of starting INSTI, geographical region, gender, ethnicity, smoking status, HIV risk group, antiretroviral treatment experience, CD4 nadir, CD4 at INSTI start, hepatitis B, hepatitis C, hypertension, diabetes, prior AIDS, non-AIDS malignancies, end stage liver disease, cardiovascular disease, fracture, chronic kidney disease