SUPPLEMENTAL DIGITAL CONTENT

Methods for imputing missing baseline CD4 and HIV plasma viral load (pVL) values

Study-defined baseline CD4 and plasma viral load (pVL) values were measured within 6 months prior to integrase strand transfer inhibitor (INSTI) start date. If there was no measurement within this time window, missing values were imputed by the following data coding rules, where

- Most recent pre-INSTI value: most recent test result measured >6 months before INSTI start date.
- First post-INSTI value: first test result measured after INSTI start date.
- "On ART": person received continuous antiretroviral therapy between most recent pre-INSTI value and INSTI start date (by prescription records).
- Clinician review: Available CD4, pVL and ART data reviewed by study co-investigator KL (blinded to study outcome) and CD4 or pVL category assigned based on clinical decision.

Table S1. Data coding rules for imputation

CD4 imputation				
Most recent pre-INSTI value	**On ART between pre-INSTI value and INSTI start?**	**First post-INSTI value**	**Imputed CD4- category**	**Imputed N=33** n(%)
<200	yes or no	<200	<200	2 (6)
<200	no, and pVL>50	not available	<200	3 (9)
≥200	yes, and pVL <50	not available	≥200	6 (18)
≥200	yes or no	≥200	≥200	20 (61)
Other combination of variables, clinician review			≥200	1 (3)
Other combination of variables, clinician review			<200	1 (3)
pVL imputation				
Most recent pre-INSTI value	**On ART between pre-INSTI value and INSTI start?**	**First post-INSTI value**	**Imputed pVL category**	**Imputed N=8** n(%)
50 -100,000	yes or no	50 -100,000	50-100,000	2 (25)
50-100,000	no	not available	50-100,000	1 (13)
<50	yes	<50	<50	4 (50)
Other combination of variables, clinician review			<50	1 (13)

ART, antiretroviral therapy; INSTI integrase strand transfer inhibitor; CD4 cells/µL, pVL plasma viral load copies/mL

Table S2. Baseline characteristics in the subset of ART-experienced persons

Variable **n(%)** unless otherwise specified	**Raltegravir** **N= 218**	**Elvitegravir** **N= 248**	**Dolutegravir** **N= 334**	**p-value**
Time on ART, median (Q1-Q3) yr	5.6 (2.1-11.5)	4.6 (1.8-10.1)	5.3 (2.2-10.0)	0.450
Previous ART regimen				
PI + 2 NRTI	125 (57.3)	119 (48.0)	158 (47.3)	**<0.001**
NNRTI + 2 NRTI	77 (35.3)	102 (41.1)	95 (28.4)	
INSTI (±cobicistat) + 2 NRTI	5 (2.3)	20 (8.1)	64 (19.2)	
Other ART combination	11 (5.0)	7 (2.8)	17 (5.1)	
% Adherence, Previous ART				
median (Q1-Q3)	99.2 (87.4-99.7)	87.1 (44.4-99.5)	99.5 (89.0-99.7)	**<0.001**
≥80%	176 (80.7)	137 (55.2)	264 (79.0)	**<0.001**
Reason for regimen change to INSTI				
Treatment failure/ Drug resistance	3 (1.4)	9 (3.6)	7 (2.1)	**<0.001**
Adverse drug reaction	98 (45.0)	106 (42.7)	164 (49.1)	
Drug interaction	59 (27.1)	7 (2.8)	45 (13.5)	
Simplification	6 (2.8)	65 (26.2)	74 (22.2)	
Other/ Unspecified reason	52 (23.9)	61 (24.6)	44 (13.2)	

INSTI, integrase strand transfer inhibitor; NRTI, nucleoside(tide) reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; Time on antiretroviral therapy (ART): years between ART initiation and INSTI start date (total missing n=25). Previous ART, % adherence: days dispensed ART/follow-up days % (total missing n=6) . p-value: categorical variables calculated by Pearson's chi-squared or Fisher's exact tests, continuous variables by Wilcoxon rank sum test

Table S3 (a). Potential risk factors for emergent drug resistance mutations- whole cohort

Variable	category N	No new resistance n (% category N)	Emergent resistance n (% category N)	p-value
TOTAL	985	958 (97.3)	27 (2.7)	NA
Age median (Q1-Q3) years	985	46 (37-53)	51 (40-53)	0.559
Sex				**0.026**
male	759	743 (97.9)	16 (2.1)	
female	226	215 (95.1)	11 (4.9)	
Hepatitis C antibody status				0.089
negative or unknown	627	614 (97.9)	13 (2.1)	
positive	358	344 (96.1)	14 (3.9)	
HIV subtype				0.503
type B or unknown	894	868 (97.1)	26 (2.9)	
non-B	91	90 (98.9)	1 (1.1)	
Pre-INSTI pVL c/mL				**<0.001**
≤100,000 c/mL	874	856 (97.9)	18 (2.1)	
>100,000 c/mL	111	102 (91.9)	9 (8.1)	
Pre-INSTI CD4 cells/µL				**<0.001**
≥200	842	832 (98.8)	10 (1.2)	
<200	143	126 (88.1)	17 (11.9)	
Prior ART exposure				0.626
ART naive	185	181 (97.8)	4 (2.2)	
experienced, INSTI naive	685	664 (96.9)	21 (3.1)	
experienced, INSTI experienced	115	113 (98.4)	2 (1.9)	
Prior drug resistance				0.597
susceptible virus	831	809 (97.4)	22 (2.6)	
≥1 drug class resistance	154	149 (96.8)	5 (3.2)	
INSTI				**0.010**
raltegravir	270	256 (94.8)	14 (5.2)	
elvitegravir	323	315 (97.5)	8 (2.5)	
dolutegravir	392	387 (98.7)	5 (1.3)	
Concurrent ART at INSTI start				0.816
Tenofovir + emtricitabine/ lamivudine	599	582 (97.2)	17 (2.8)	
Abacavir+ lamivudine	386	376 (97.4)	10 (2.6)	
Regimen GSS				
≥3	935	910 (97.3)	25 (2.7)	0.643
<3	50	48 (96.0)	2 (4.0)	
% Adherence, INSTI				**0.002**
≥80%	848	831 (98.0)	17 (2.0)	
<80%	137	127 (92.7)	10 (7.3)	
% Adherence, Previous ART				**0.004**
≥80% or unknown*	768	753 (98.0)	15 (2.0)	
<80%	217	205 (94.5)	12 (5.9)	

ART, antiretroviral therapy; INSTI integrase strand transfer inhibitor; pVL plasma viral load; GSS genotypic sensitivity score; tenofovir supplied as tenofovir disoproxil fumarate. *Unknown adherence to previous ART includes persons who were ART naive or had previous ART regimen duration <30 days. p-value: categorical variables calculated by Pearson's chi-squared or Fisher's exact tests

Table S3 (b). Potential risk factors for emergent drug resistance mutations in the subset of ART-experienced persons

Variable	category N	No new resistance n (% category N)	Emergent resistance n (% category N)	p-value
TOTAL	800	777 (97.1)	23 (2.9)	NA
Previous ART regimen				
No PI	380	372 (97.9)	8 (2.1)	0.215
Included PI	420	405 (96.4)	15 (3.6)	
% Adherence, Previous ART				**0.006**
≥80% or unknown*	583	572 (98.1)	11 (1.9)	
<80%	217	205 (94.5)	12 (5.9)	
Reason for regimen change				0.502
Adverse drug reaction	368	359 (97.6)	9 (2.4)	
Other or unknown reason	432	418 (96.8)	14 (3.2)	

ART, antiretroviral therapy; PI, protease inhibitor; *Unknown adherence to previous ART includes persons who had previous ART regimen duration <30 days. p-value: categorical variables calculated by Pearson's chi-squared or Fisher's exact tests

Table S4 Frequency of emergent drug resistance mutations stratified by Integrase Strand Transfer Inhibitor and concurrently prescribed Nucleoside (tide) Reverse Transcriptase Inhibitors (NRTI)

Drug resistance mutations	Abacavir-Lamivudine	Tenofovir disoproxil fumarate-Emtricitabine/ Lamivudine	p-value
Raltegravir			
	N=102, n(%)	N=168, n(%)	
Any (IN or RT)	6 (5.9)	8 (4.8)	0.779
IN	2 (2.0)	4 (2.4)	0.999
RT	6 (5.9)	8 (4.8)	0.779
Elvitegravir			
	N=0	N=323, n(%)	
Any (IN or RT)	n/a	8 (2.5)	n/a
IN	n/a	5 (1.5)	n/a
RT	n/a	6 (1.9)	n/a
Dolutegravir			
	N=284, n(%)	N=108, n(%)	
Any (IN or RT)	4 (1.4)	1 (0.9)	0.999
IN	3 (1.1)	0	0.564
RT	3 (1.1)	1 (0.9)	0.999

Drug resistance mutations: Newly detected integrase (IN) or reverse transcriptase (RT) drug resistance mutations, p-value calculated by Fisher's Exact test, n/a not applicable.

Note that elvitegravir-cobicistat was available exclusively in a tablet co-formulated with tenofovir disoproxil fumarate and emtricitabine, therefore none of the persons in this cohort received elvitegravir-cobicistat with an abacavir-lamivudine NRTI backbone.