**SUPPLEMENTARY FILE**

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## Details of HIV drug resistance testing

We attempted sequencing of HIV-1 *pol* (protease [PR], reverse transcriptase [RT] and integrase [IN]) for all samples with VL ≥500 copies/mL. Following RNA extraction (Chemagic 360; Perkin Elmer, Germany), we amplified PR, RT and IN genes using the amplification module of the Applied Biosystems HIV-1 Genotyping Kit with Integrase (Thermo Fisher Scientific, Waltham, MA); and sequenced on the Illumina MiSeq platform (Illumina, San Diego, CA). We used FastQC in Genome Detective (<http://krisp.ukzn.ac.za/app/typingtool/virus/>) to filter low-quality reads and remove potential adapters. We imported the resulting bam files into Geneious 8.0.3 (https://www.geneious.com) for read assembly and aligned to a subtype C annotated reference. We identified major drug resistance mutations (DRMs) at >20% frequency using Stanford HIVdb (version 9.1).

## Table S1: Baseline characteristics by ART regimen at enrolment

| **Variable** | **Levels** | **Dolutegravir,****n = 43** | **Efavirenz,****n = 37** | **Total** |
| --- | --- | --- | --- | --- |
| Age, years  | Median (IQR)  | 40.0 (34.0 to 48.0)  | 38.0 (33.0 to 41.0)  | 38.5 (33.0 to 45.0)  |
| Gender  | Female  | 24 (55.8)  | 23 (62.2)  | 47 (58.8)  |
|  | Male  | 19 (44.2)  | 14 (37.8)  | 33 (41.2)  |
| Time since ART initiation, years  | Median (IQR)  | 2.5 (0.6 to 6.0)  | 4.1 (1.4 to 5.2)  | 3.2 (1.0 to 6.0)  |
| NRTI backbone  | ABC  | 1 (2.3)  |  | 1 (1.2)  |
|  | TDF  | 42 (97.7)  | 37 (100.0)  | 79 (98.8)  |
| Time on current regimen, years  | Median (IQR)  | 0.7 (0.5 to 1.1)  | 3.2 (1.1 to 5.0)  | 1.1 (0.6 to 2.9)  |
| History of other chronic medical conditions  | No  | 37 (86.0)  | 34 (91.9)  | 71 (88.8)  |
|  | Yes  | 6 (14.0)  | 3 (8.1)  | 9 (11.2)  |
| Current ART side effects  | No  | 41 (95.3)  | 37 (100.0)  | 78 (97.5)  |
|  | Yes  | 2 (4.7)  |  | 2 (2.5)  |
| Last time participant missed a dose of ART  | Within past the week  | 10 (23.3)  | 7 (18.9)  | 17 (21.2)  |
|  | 1-2 weeks ago  | 3 (7.0)  | 1 (2.7)  | 4 (5.0)  |
|  | 2-4 weeks ago  | 7 (16.3)  | 5 (13.5)  | 12 (15.0)  |
|  | 1-3 months ago  | 5 (11.6)  | 5 (13.5)  | 10 (12.5)  |
|  | >3 months ago  | 1 (2.3)  | 1 (2.7)  | 2 (2.5)  |
|  | Never  | 17 (39.5)  | 18 (48.6)  | 35 (43.8)  |
| Hazardous drinking (AUDIT-C)  | No  | 30 (69.8)  | 24 (64.9)  | 54 (67.5)  |
|  | Yes  | 13 (30.2)  | 13 (35.1)  | 26 (32.5)  |
| Smoking status  | Current smoker  | 8 (18.6)  | 5 (13.5)  | 13 (16.2)  |
|  | Never smoked  | 35 (81.4)  | 31 (83.8)  | 66 (82.5)  |
|  | Ex-smoker  |  | 1 (2.7)  | 1 (1.2)  |
| Body mass index, kg/m2  | Median (IQR)  | 28.4 (24.5 to 32.2)  | 25.4 (22.2 to 31.5)  | 27.3 (22.9 to 31.7)  |
| Ethnicity  | Black African  | 43 (100.0)  | 36 (97.3)  | 79 (98.8)  |
|  | Other  |  | 1 (2.7)  | 1 (1.2)  |
| Highest level of education completed  | None  | 0 (0.0)  | 0 (0.0)  | 0 (0.0)  |
|  | Primary school only  | 1 (2.3)  | 0 (0.0)  | 1 (1.2)  |
|  | Secondary school but not matric  | 22 (51.2)  | 17 (45.9)  | 39 (48.8)  |
|  | Matriculation  | 16 (37.2)  | 16 (43.2)  | 32 (40.0)  |
|  | Tertiary  | 4 (9.3)  | 4 (10.8)  | 8 (10.0)  |
| Employment status  | Unemployed  | 13 (30.2)  | 15 (40.5)  | 28 (35.0)  |
|  | Informal employment  | 5 (11.6)  | 1 (2.7)  | 6 (7.5)  |
|  | Part time employment  | 7 (16.3)  | 2 (5.4)  | 9 (11.2)  |
|  | Full-time employment  | 15 (34.9)  | 12 (32.4)  | 27 (33.8)  |
|  | Student  | 1 (2.3)  | 4 (10.8)  | 5 (6.2)  |
|  | Self-employed  | 2 (4.7)  | 3 (8.1)  | 5 (6.2)  |
| Monthly personal income, ZAR  | <1000  | 16 (37.2)  | 20 (54.1)  | 36 (45.0)  |
|  | 1000-4000  | 14 (32.6)  | 9 (24.3)  | 23 (28.8)  |
|  | 4001-8000  | 8 (18.6)  | 8 (21.6)  | 16 (20.0)  |
|  | >8000  | 5 (11.6)  | 0 (0.0)  | 5 (6.2)  |
| Enrolment CD4 count category, cells/µL  | <200  | 6 (14.0)  | 15 (40.5)  | 21 (26.2)  |
|  | 200-349  | 12 (27.9)  | 9 (24.3)  | 21 (26.2)  |
|  | 350-499  | 14 (32.6)  | 4 (10.8)  | 18 (22.5)  |
|  | >=500  | 11 (25.6)  | 9 (24.3)  | 20 (25.0)  |

## Table S2: HIV drug resistance mutations among participants with viraemia\*

| **ENROLMENT** | **FOLLOW-UP** | **EXIT** |
| --- | --- | --- |
| **ART** | **VL** | **NRTI mutations** | **NNRTI mutations** | **VL** | **NRTI mutations** | **NNRTI mutations** | **New Regimen** | **VL** | **NRTI mutations** | **NNRTI mutations** |
| TEE  | 3530  | None  | V108I  | 91  | NA  | NA  | TLD | 100  | NA  | NA  |
| TEE  | 2550  | None  | None  | 231  | NA  | NA  | Not switched  | <20  | NA  | NA  |
| TEE  | 128000  | A62V,K65R,M184V  | L100I,K103N,Y188L  | 5490000  | A62V,K65R,M184V  | L100I,K103N,V106VI,Y188L  | ZLD  | 384  | NA  | NA  |
| TEE  | 1450  | K219E  | None  | 82600  | K65KR,M184MIV  | K103N,V106M  | ZLD  | <20  | NA  | NA  |
| TEE  | 13500  | D67N,K70E,M184V  | K101E,V106M,G190A,F227L  | 69276  | D67N,K70EQ,M184V  | K101E,V106M,G190A,F227L  | ZLD  | 64.7  | NA  | NA  |
| TEE  | 116000  | D67N,M184V,K219R  | A98G,K103N,P225H  | 124215  | K65R,M184I  | K103N,L234I  | TDF / ZLD  | 41.7  | NA  | NA  |
| TEE  | 6320  | K65R,D67G  | V106M,G190A  | 9020  | A62V,K65R,D67G,Y115F,M184V  | V106M,G190A  | ZLD  | <20  | NA  | NA  |
| TEE  | 10900  | M184V  | K101P,K103N  | 5000  | M184V  | K101P,K103N  | ZLD  | TND  | NA  | NA  |
| TEE†  | 939  | K65R,M184V  | A98G,K101E,V108I,Y181C  | 1222  | HIVDR testing unsuccessful  | HIVDR testing unsuccessful  | AZT / 3TC / LPVr  | <20  | NA  | NA  |
| TEE  | 6410  | K70R,M184V,K219Q  | K103N,P225H,K238T  | 2030  | HIVDR testing unsuccessful  | HIVDR testing unsuccessful  | AZT / 3TC / LPVr  | 85  | NA  | NA  |
| TEE  | 8810  | D67N,K70E,L74I,M184V  | K103N,V106M,V179T  | 3638  | D67N,K70E,L74LI,M184V  | K103N,V106M,V179T  | ZLD  | <20  | NA  | NA  |
| TEE  | 59500  | K65R,D67N,M184I  | A98G,K103N,L234I  | 20839  | None  | K103N  | ZLD  | 99.5  | NA  | NA  |
| TEE  | 94100  | L74I,M184V  | K103N,G190S  | 21600  | L74LI,M184V  | K103N,V179IT,G190S  | TDF / ZLD  | NA  | NA  | NA  |
| TEE  | 284000  | K70E,L74I,M184V,K219R  | A98G,K103N,P225H,F227L  | 419846  | K70E,M184V,K219R  | A98G,K103N,P225H,F227L  | TDF / ZLD  | 42.4  | NA  | NA  |
| TEE  | 1190  | K219R  | K103N  | 0  | NA  | NA  | TLD | TND  | NA  | NA  |
| TEE  | 5130  | A62V,K65R,K70Q,M184V  | K101P,Y181C,G190A  | 1388  | A62V,K65R,K70Q,M184V  | K101P,Y181C,G190A  | ZLD  | <20  | NA  | NA  |
| TEE  | 439  | NA  | NA  | 937  | A62AV,K65R,K70T,M184V  | V106M,V108I,Y188C,F227L  | ZLD  | TND  | NA  | NA  |
| TEE  | 297  | NA  | NA  | 1390  | K65R,M184V  | L100I,K103N  | ZLD  | TND  | NA  | NA  |
| TEE  | 352000  | T69D,M184V  | V179D,Y188L  | 235000  | T69D,M184V  | V179D,Y188L  | ZLD  | 23.7  | NA  | NA  |
| TEE  | 1420  | D67N,M184V,K219R  | K103N,V108I  | 615  | HIVDR testing unsuccessful  | HIVDR testing unsuccessful  | Not switched  | NA  | NA  | NA  |
| TEE  | 6320  | D67T,K70R,M184V,T215V,K219E  | A98G,K103N,V108I,P225H  | 10934  | D67T,K70R,M184V,T215V,K219E  | A98G,K103N,V108I,P225H  | TDF / ZLD  | TND  | NA  | NA  |
| TEE  | 22300  | K65R  | V106M,V179D  | 1630  | M184V  | V106M,V179D  | ZLD  | <20  | NA  | NA  |
| TEE  | 534  | HIVDR testing unsuccessful  | HIVDR testing unsuccessful  | 4690  | HIVDR testing unsuccessful  | HIVDR testing unsuccessful  | TDF / FTC / LPVr  | TND  | NA  | NA  |
| TEE  | 18900  | A62V,K65R,K70T,M184V  | V106M,V179D,Y181C,H221Y,F227I  | 64000  | A62V,K65R,K70T,M184V  | V106M,V179D,Y181C,H221Y,F227I  | ZLD  | TND  | NA  | NA  |
| TEE  | 1180  | None  | K103N,V106M,G190A  | 7140  | M184V  | K103N,V106M,G190A  | ZLD  | <20  | NA  | NA  |
| TEE  | 2200  | D67N,M184V,K219E  | K103N,V108I  | 2225  | D67N,K70R,M184V,K219E  | K103N,V108I  | ZLD  | 109  | NA  | NA  |
| TEE  | 267000  | None  | V106M  | 586  | None  | V106M  | TLD | TND  | NA  | NA  |
| TEE  | 21900  | None  | None  | 40  | NA  | NA  | TLD | TND  | NA  | NA  |
| TEE  | 1360  | K70R,M184V,K219Q  | K103N,P225H,K238T  | 251  | NA  | NA  | TLD | TND  | NA  | NA  |
| TEE  | 6050  | K70Q,L74I,M184V  | K103S,V106M  | 422320  | K70KQ,L74I,M184V  | K103NS,V106M  | ZLD  | 5810  | K70KQ,L74LI,M184V  | K103NS,V106M  |
| TEE  | 20100  | None  | K103N  | 1660  | HIVDR testing unsuccessful  | HIVDR testing unsuccessful  | ZLD  | 4370  | D67N,M184V,K219E  | K103N,P225H  |
| TEE  | 959  | M41L,M184V,T215Y  | A98AG,K103N,E138Q,P225H  | 191  | NA  | NA  | TLD | 802  | M41L,M184V,T215Y  | K103N,E138Q,P225H  |
| TLD | 177827  | NA  | NA  | 148000  | None  | None  | Not switched  | NA  | NA  | NA  |
| TLD | 18600  | None  | K103N  | 84  | NA  | NA  | Not switched  | 22.1  | NA  | NA  |
| TLD | 2180  | None  | None  | NA  | NA  | NA  | Not switched  | <20  | NA  | NA  |
| TLD | 515  | None  | V106M,V179VD  | 0  | NA  | NA  | Not switched  | 23.9  | NA  | NA  |
| TLD | 3950  | M184V  | K103N,V106M  | 40  | NA  | NA  | Not switched  | 82.9  | NA  | NA  |
| TLD | 27  | NA  | NA  | 41  | NA  | NA  | Not switched  | 7980  | None  | None  |
| TLD | 738  | None  | None  | 40  | NA  | NA  | Not switched  | 24.3  | NA  | NA  |
| TLD | 13400  | None  | None  | 0  | NA  | NA  | Not switched  | 220  | NA  | NA  |
| TLD | 327  | NA  | NA  | 20  | NA  | NA  | Not switched  | 676  | HIVDR testing unsuccessful  | HIVDR testing unsuccessful  |
| TLD | 18000  | None  | None  | 86700  | None  | None  | Not switched  | TND  | NA  | NA  |
| TLD | 4910  | None  | None  | 20  | NA  | NA  | Not switched  | TND  | NA  | NA  |
| TLD | 2980  | None  | Y188L  | 40  | NA  | NA  | Not switched  | 52600  | None  | Y188L  |
| TLD | 333000  | None  | None  | 34  | NA  | NA  | Not switched  | TND  | NA  | NA  |
| TLD | 296000  | None  | None  | 40  | NA  | NA  | Not switched  | 33.3  | NA  | NA  |
| TLD | <20  | NA  | NA  | 1280  | None  | None  | Not switched  | TND  | NA  | NA  |
| TLD | 11700  | None  | None  | 40  | NA  | NA  | Not switched  | TND  | NA  | NA  |
| TLD | 14900  | None  | K103N,E138A  | 72  | NA  | NA  | Not switched  | 16900  | K65KR  | K103N,E138A  |
| TLD | 3260  | None  | Y188L  | 5760  | None  | Y188L  | Not switched  | 47600  | None  | Y188L  |
| TLD | 238  | NA  | NA  | 40  | NA  | NA  | Not switched  | 10100  | None  | None  |
| TLD | 23400  | None  | None  | 50  | NA  | NA  | Not switched  | NA  | NA  | NA  |
| TLD | 215000  | None  | A98G  | 25  | NA  | NA  | Not switched  | 33.9  | NA  | NA  |
| TLD | 35800  | None  | A98G  | 1215  | None  | None  | Not switched  | 25.10  | NA  | NA  |
| TLD | 48.1  | NA  | NA  | NA  | NA  | NA  | Not switched  | 3520  | HIVDR testing unsuccessful  | HIVDR testing unsuccessful  |
| TLD | 3600  | None  | V106M,Y188C  | 53  | NA  | NA  | Not switched  | 42.2  | NA  | NA  |
| ALD | 95100  | L74I,M184V  | K103N,G190S  | 6243  | None  | None  | Not switched  | <20  | NA  | NA  |

\* No major PI or INSTI mutations detected throughout follow-up. † One participant had been transitioned from TDF / FTC / EFV to TDF / 3TC / DTG 15 days before enrolment, on the same day that the pre-enrolment viral load was viraemic. At the enrolment visit, they were changed back to TDF / FTC / EFV because they should not have been transitioned with a viral load >1000 copies/mL. TLD = tenofovir disoproxil fumarate, lamivudine and dolutegravir, ZLD = zidovudine, lamivudine and dolutegravir, TDF = tenofovir disoproxil fumarate, ALD = abacavir, lamivudine and dolutegravir. TND = not detected.