# Supplementary material

**This appendix is a supplement to: Keene et al. *Virologic efficacy of tenofovir, lamivudine and dolutegravir as second-line in adults failing a tenofovir-based first-line regimen: a prospective cohort study***

Table 1a. Frequency of specific major nucleoside reverse-transcriptase inhibitor (NRTI) and non-nucleoside reverse-transcriptase inhibitor (NNRTI) mutations at baseline

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Table 9. Concomitant medications with potential for dolutegravir interaction taken at any point from baseline to week 24

Table 1a. Frequency of specific major nucleoside reverse-transcriptase inhibitor (NRTI) and non-nucleoside reverse-transcriptase inhibitor (NNRTI) mutations at baseline

|  |  |  |  |
| --- | --- | --- | --- |
| Major NRTI mutations (n/%) | N=54 | Major NNRTI mutations (n/%) | N=54 |
| M41L | 2 (4) | L100I | 2 (4) |
| K65R | 20 (37) | K101E | 5 (9) |
| K65N | 0 (0) | K101P | 0 (0) |
| K65E | 0 (0) | K103H | 0 (0) |
| D67N | 10 (19) | K103N | 31 (57) |
| T69Ins | 0 (0) | K103S | 1 (2) |
| T69Deletion | 1 (2) | K103T | 0 (0) |
| K70E | 4 (7) | V106A | 0 (0) |
| K70G | 0 (0) | V106M | 17 (31) |
| K70N | 0 (0) | E138K | 0 (0) |
| K70Q | 2 (4) | Y181C | 6 (11) |
| K70R | 7 (13) | Y181F | 0 (0) |
| K70S | 0 (0) | Y181G | 0 (0) |
| K70T | 2 (4) | Y181I | 0 (0) |
| L74I | 2 (4) | Y181S | 0 (0) |
| Y115F | 3 (6) | Y181V | 0 (0) |
| Q151L | 0 (0) | Y188C | 1 (2) |
| Q151M | 0 (0) | Y188F | 0 (0) |
| M184V | 45 (83) | Y188H | 0 (0) |
| M184I | 0 (0) | Y188L | 8 (15) |
| L210W | 0 (0) | G190A | 6 (11) |
| T215F | 0 (0) | G190C | 0 (0) |
| T215Y | 0 (0) | G190E | 1 (2) |
|  |  | G190Q | 0 (0) |
|  |  | G190S | 1 (2) |
|  |  | G190T | 0 (0) |
|  |  | G190V | 0 (0) |
|  |  | P225H | 16 (30) |
|  |  | F227C | 0 (0) |
|  |  | M230L | 1 (2) |
| Major mutations as defined by the Stanford university resistance database (last updated 2019-07-31)3 | | | |

Table 1b. Listing of major and minor nucleoside reverse-transcriptase inhibitor (NRTI) and non-nucleoside reverse-transcriptase inhibitor (NNRTI) mutations at baseline by participant

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| No | NRTI, major | NRTI, minor | NNRTI, major | NNRTI, minor |
| 1 | Y115F,M184V,K65R |  | Y181C | V108I |
| 2 | D67N,K70R,M184V | K219E | V106M | F227L |
| 3 |  |  | K103N |  |
| 4 | M184V,L74I | K219Q | P225H,K103N | A98G |
| 5 | K65R,M184V | V75I | K103N,L100I |  |
| 6 | M184V,K65R |  | K103N,Y188L |  |
| 7 | M184V,K65R | A62V,F77L,K219E | K103N,Y181C,G190A |  |
| 8 | D67N,K70E,M184V |  | K103N,Y188L | H221Y |
| 9 | K70R,D67N,M184V | K219E,T215I | K103N | V108I,K238T |
| 10 | K70E,D67DN,M184V | K219KR | K103N,P225H |  |
| 11 | M184V,K70Q |  | V106M,G190A,K101E |  |
| 12 | K70T,M41L,K65R,M184V |  | V106M,Y188L | E138A |
| 13 | M184V,M41L,K65R,K70T |  | V106M,Y188L | E138A |
| 14 | M184V |  | K103N | V108I |
| 15 | K65R,M184V,Y115F,L74LI,D67N | K219E | V106M,K103N |  |
| 16 | M184V | L74V | P225H,L100I,K103N | K238T |
| 17 | M184V,K70KR | K219E | V106M | V108I,F227FL |
| 18 | M184V,K70R,D67N | T215IV,K219E | Y188L | A98G |
| 19 | K70EQ,M184V |  | V106M | F227FL,E138A,V179D |
| 20 |  |  | K103N |  |
| 21 | M184V |  |  | E138A |
| 22 | M184V,K70R,D67N | K219Q | V106M | F227L,E138Q |
| 23 | M184V,K65R | A62V | V106M,K103S | F227L |
| 24 | M184V |  | P225H,K103N |  |
| 25 | D67N,M184V,K70E | K219R | K103N,P225H | H221Y,E138EG,F227FL,V108VI |
| 26 | M184V |  | Y188L,P225H | E138Q |
| 27 | K65R,M184V |  | K101E,Y181C,G190S |  |
| 28 | M184V | V75VM | K103N,P225H |  |
| 29 | D67N,K70R,M184V | K219E,T215I | G190E |  |
| 30 | M41ML,M184V,K65R,L74L |  | K103N | E138EG,V108I |
| 31 | K65R | A62AV | Y181C,V106M | H221Y,F227L |
| 32 | M184V | A62AV | G190GA,P225H,K103N | K238KT |
| 33 | K65R,M184V | A62AV | V106M | V179D |
| 34 | M184V,Y115F,K65R |  | V106M,K103N | F227L |
| 35 | M184V,K65R |  | P225H,K103N |  |
| 36 | K65R,M184V |  | V106M,M230L | V179D |
| 37 | K65R,M184V | A62V,K219E | K103N,G190A |  |
| 38 |  |  | K103N,P225H |  |
| 39 |  |  | K103N |  |
| 40 | K65R,D67DN |  | Y181C,K101E,G190A,V106VM |  |
| 41 |  |  | P225H,K103N |  |
| 42 | M184V,K70KT,K65R | V75M,A62AV | Y188C,V106M |  |
| 43 | M184V |  | P225H,K103N | V108I |
| 44 | M184V,K65R | A62V | Y188L,K103N |  |
| 45 | D67N,K70R,M184V | K219Q | G190A,V106M,K101E | F227L |
| 46 | M184V,K70KE |  | K101KE,Y188L,P225PH | V106VI |
| 47 | M184V |  | Y181C,K101E,V106M,G190A |  |
| 48 | L74I,M184V |  | K103N,P225H | A98G,H221Y,V108I |
| 49 | M184V |  | P225H,K103N |  |
| 50 | K65R, T69Deletion | K219R,A62V | K103N,V106M |  |
| 51 | M184V,K70Q |  | K103N | V108I,E138Q,L234LI |
| 52 | D67N,M184V,K70R | K219E | P225H,K103N |  |
| 53 |  |  |  |  |
| 54 | L74LI,M184V,K65KR,K70KN |  | K103N,P225H |  |
| Major and minor mutations as defined by the Stanford university resistance database (last updated 2019-07-31)3 | | | | |

Table 2. Outcomes for participants not suppressed (viral load [VL] <50 copies/mL) using the modified intention-to-treat analysis at week 24

|  |  |  |
| --- | --- | --- |
| Outcome | N(%) | Details |
| VL >1000 copies/ml | 0/60 (0%) |  |
| VL 50-1000 copies/ml | 7/60 (12%) | Six had a VL 50-99 copies/mL and one had a VL 100-999 copies/mL |
| Discontinued study drug (failure) | 0/60 (0%) |  |
| Discontinued study drug (other) | 1/60 (1.7%) | Participant discontinued the study drug due to a tenofovir-related adverse event |
| Missing data but still on study | 1/60 (1.7%) | Missed the study visit within the ±2 week VL window |

Table 3. Aggregated HIV viral load outcomes by study visit

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Participants analysed (n) | | Percentage suppressed (95% confidence interval) | | | |
| Week | mITT\* | Sensitivity analysis\*\* | <50cp/mL (mITT) | <50cp/mL (sensitivity) | <400cp/mL (mITT) | <400cp/mL (sensitivity) |
| 0 | 60 | 60 | 0.0 (0.0-6.0)† | 0.0 (0.0-6.0)† | 0.0 (0.0-6.0)† | 0.0 (0.0-6.0)† |
| 4 | 60 | 54 | 68.3 (55.0-79.7) | 75.9 (62.4-86.5) | 88.3 (77.4-95.2) | 98.1 (90.1-100.0) |
| 8 | 60 | 51 | 73.3 (60.3-83.9) | 86.3 (73.7-94.3) | 80.0 (67.7-89.2) | 94.1 (83.8-98.8) |
| **12** | **60** | **54** | **75.0 (62.1-85.3)** | **83.3 (70.7-92.1)** | **86.7 (75.4-94.1)** | **96.3 (87.3-99.5)** |
| 16 | 60 | 52 | 76.7 (64.0-86.6) | 88.5 (76.6-95.6) | 86.7 (75.4-94.1) | 100.0 (93.2-100.0)† |
| 20 | 60 | 48 | 63.3 (49.9-75.4) | 79.2 (65.0-89.5) | 80.0 (67.7-89.2) | 100.0 (92.6-100.0)† |
| **24** | **60** | **57** | **85.0 (73.4-92.9)** | **89.5 (78.5-96.0)** | **95.0 (86.1-99.0)** | **100.0 (93.7-100.0)**† |
| \* Modified intention-to-treat analysis (mITT) excludes those switching study drug for reasons of stopping contraception or wish to become pregnant, or becoming pregnant, transfer out for non-clinical reasons and death from non-HIV and non-drug causes  \*\* Sensitivity analysis excludes those excluded from mITT analysis, as well as lost to follow up, those missing a VL within the window, participants who stopped or were changed from the study drug for reasons other than failure of the regimen and those who had evidence of poor adherence (tenofovir diphosphate [TFV-DP] <350 fmol/punch). As TFV-DP was measured at weeks 12 and 24 only, it was assumed that individuals that were adherent/nonadherent at those visits were adherent/nonadherent respectively at the preceding visits (ie, weeks 4-12 for the week 12 adherence measure and weeks 16-24 for the week 24 adherence measure). Using this assumption, only one additional visit (at week 16) was excluded from the sensitivity population.  † One sided 97.5% confidence interval (CI) when 0 or 100% were successful | | | | | | |

## Table 4. HIV viral load (VL) data by participant

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Participant | VL result by week | | | | | | | | | | |
| Screening VL | Week 4 | | Week 8 | | Week 12 | Week 16 | | Week 20 | | Week 24 |
| 1 | 77425 | 314 | | 215 | | 69 | 102 | | 58 | | 49 |
| 2 | 4668 | <20 | | LDL | | 29 | LDL | | 23 | | LDL |
| 3 | 2113 | LDL | | LDL | | LDL | LDL | | <20 | | <20 |
| 4 | 2608 | 33 | | <20 | | LDL | LDL | | LDL | | LDL |
| 5 | 3097 | LDL | | <20 | | LDL | LDL | | <100 | | <20 |
| 6 | 1299 | 26 | | 31 | | 80 | 39 | | 50 | | <20 |
| 7 | 11178 | <20 | | <20 | | 70 | 22 | | MV | | LDL |
| 8 | 8320 | <20 | | <20 | | LDL | 24 | | <100 | | <20 |
| 9 | 17356 | 319 | | 22467 | | <20 | 107 | | LDL | | <20 |
| 10 | 61758 | 45 | | <20 | | <20 | LDL | | 32 | | 27 |
| 11 | 48765 | 73 | | <20 | | LDL | 39 | | LDL | | 75 |
| 12 | 22197 | 77 | | <20 | | 30 | <20 | | 30 | | 52 |
| 13 | 1040 | LDL | | LDL | | LDL | <20 | | LDL | | LDL |
| 14 | 44742 | <100 | | LDL | | LDL | MV | | LDL | | LDL |
| 15 | 2218 | <20 | | 21 | | <20 | LDL | | 37 | | 81 |
| 16 | 22794 | 34 | | LDL | | <20 | <20 | | 83 | | <100 |
| 17 | 79908 | 56 | | <20 | | 24 | 40 | | <20 | | 21 |
| 18 | 3323 | LDL | | LDL | | LDL | <20 | | LDL | | LDL |
| 19 | 6104 | 89 | | 62 | | 193 | 112 | | 109 | | 53 |
| 20 | 37243 | LDL | | 26 | | <20 | LDL | | LDL | | LDL |
| 21 | 6282 | <20 | | <20 | | <20 | LDL | | LDL | | LDL |
| 22 | 3432 | LDL | | 166 | | <20 | LDL | | LDL | | <20 |
| 23 | 4662 | <20 | | 33 | | 31 | 30 | | 21 | | 25 |
| 24 | 86446 | 71 | | <20 | | 26 | LDL | | 143 | | 21 |
| 25 | 24971 | 1816 | | 869 | | 5300 | 67 | | 97 | | <20 |
| 26 | 12649 | 23 | | <20 | | LDL | LDL | | LDL | | <50 |
| 27 | 7429 | <20 | | 21 | | <20 | <20 | | <100 | | LDL |
| 28 | 3163 | <20 | | LDL | | LDL | LDL | | <20 | | LDL |
| 29 | 25127 | LDL | | LDL | | LDL | LDL | | 162 | | <20 |
| 30 | 18081 | LDL | | LDL | | LDL | 45 | | LDL | | <20 |
| 31 | 16123 | <20 | | 20 | | LDL | LDL | | LDL | | LDL |
| 32 | 12661 | <20 | | <20 | | <20 | LDL | | MV | | LDL |
| 33 | 2138 | 29 | | 34 | | <20 | MV | | MV | | LDL |
| 34 | 64216 | 41 | | 68 | | 105 | 74038 | | MV | | 755 |
| 35 | 22809 | <20 | | <20 | | <20 | 38 | | MV | | <20 |
| 36 | 20846 | 32 | | LDL | | LDL | <20 | | MV | | LDL |
| 37 | 11414 | <20 | | 24 | | 21 | LDL | | MV | | 27 |
| 38 | 1952 | 66 | | LDL | | 221 | LDL | | MV | | LDL |
| 39 | 1147 | <20 | | 34 | | <20 | MV | | MV | | LDL |
| 40 | 92677 | <20 | | <20 | | MV | MV | | <50 | | <20 |
| 41 | 7383 | <20 | | <20 | | MV | 132 | | 22 | | LDL |
| 42 | 7027 | <20 | | 34 | | 1108 | MV | | <50 | | <50 |
| 43 | 39339 | 50 | | <20 | | MV | <20 | | <50 | | <20 |
| 44 | 18426 | 22 | | <20 | | MV | <20 | | LDL | | LDL |
| 45 | 9981 | LDL | | LDL | | LDL | <20 | | MV | | LDL |
| 46 | 2061 | LDL | | MV | | <20 | <20 | | LDL | | <20 |
| 47 | 9190 | LDL | | MV | | LDL | LDL | | LDL | | <20 |
| 48 | 57190 | LDL | | MV | | MV | <20 | | LDL | | LDL\* |
| 49 | 1834 | 21 | | MV | | <20 | LDL | | LDL | | LDL |
| 50 | 44757 | <20 | | MV | | <20 | <20 | | MV | | <20 |
| 51 | 124717 | 195 | | MV | | 35 | 33 | | <20 | | 20 |
| 52 | 40761 | 68 | | MV | | 206 | 107 | | MV | | MV |
| 53 | 1009 | LDL | | MV | | <20 | LDL | | <20 | | LDL |
| 54 | 2827 | MV | | LDL | | LDL | LDL | | <20 | | 21 |
| 55 | 6697 | MV | | MV | | 46 | 39 | | <20 | | <20 |
| 56 | 1923 | MV | | LDL | | <50 | 27 | | 44 | | 26 |
| 57 | 54005 | MV | | <20 | | <50 | <20 | | <20 | | <20 |
| 58 | 56219 | MV | | 48 | | MV | LDL | | 32 | | 63 |
| 59 | 1495 | LDL | | LDL | | MV | LDL | | LDL | | LDL |
| 60 | 2265 | MV | | 3216 | | 36 | MV | | <20 | | <50 |
| Key | VL suppressed <50 copies/mL | | VL 50-99 copies/mL | | VL 100-999 copies/mL | | | VL ≥ 1000 copies/mL | | MV: missed visit | |
| Result considered suppressed if the value is <50 copies/mL, or noted in the report as “<50”, “<20” or “LDL” (lower than detectable limit)  VL “<100”: Based on the low sample volume, the linear range of this assay in dilution was 100 - 10,000,000 copies/mL.  \* This participant was considered as a ‘virological failure’ in the modified intention-to-treat analysis as they were switched due to a tenofovir-related adverse event | | | | | | | | | | | |

Figure 1. Time to virologic suppression <50 copies/mL by modified intention-to-treat analysis

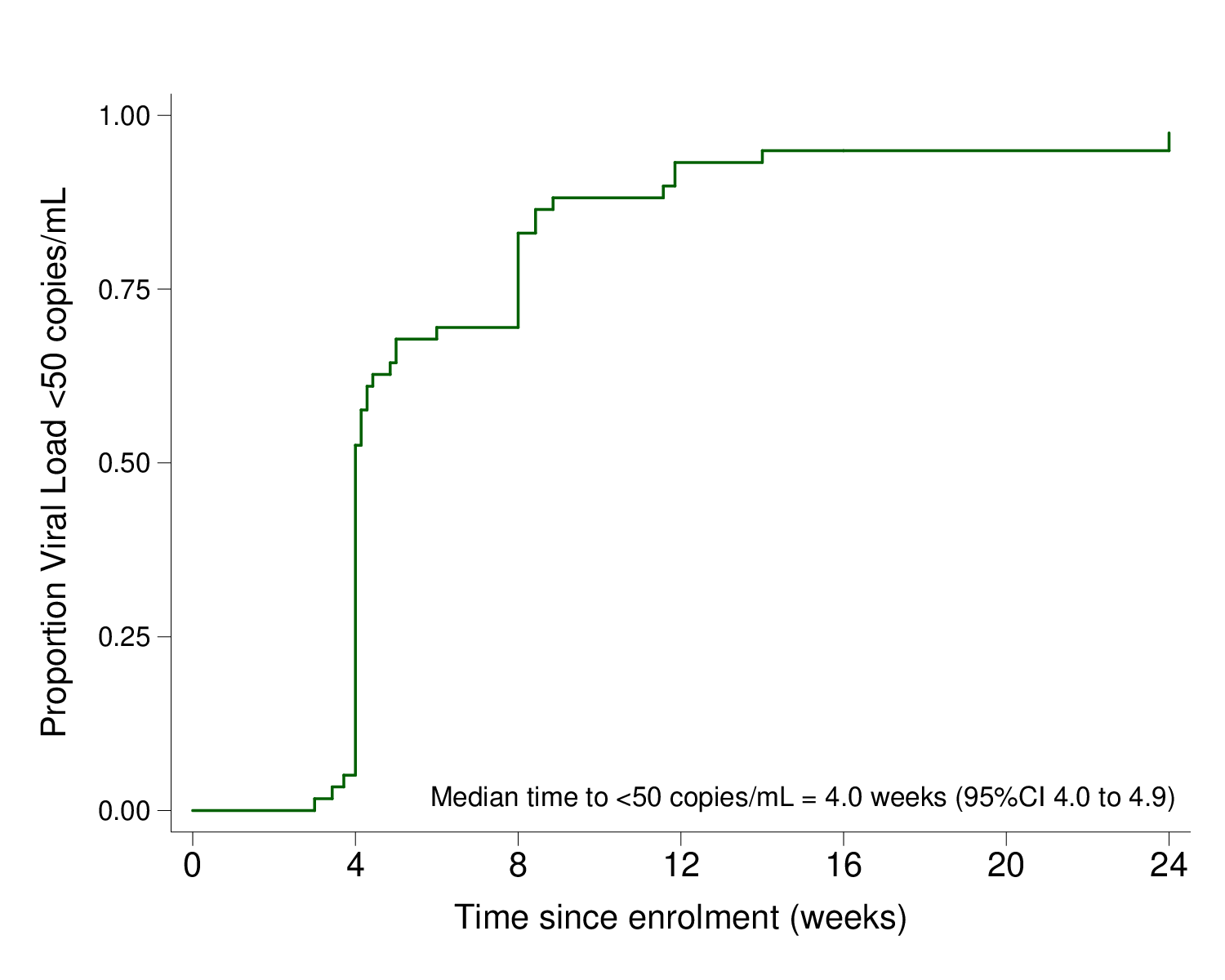
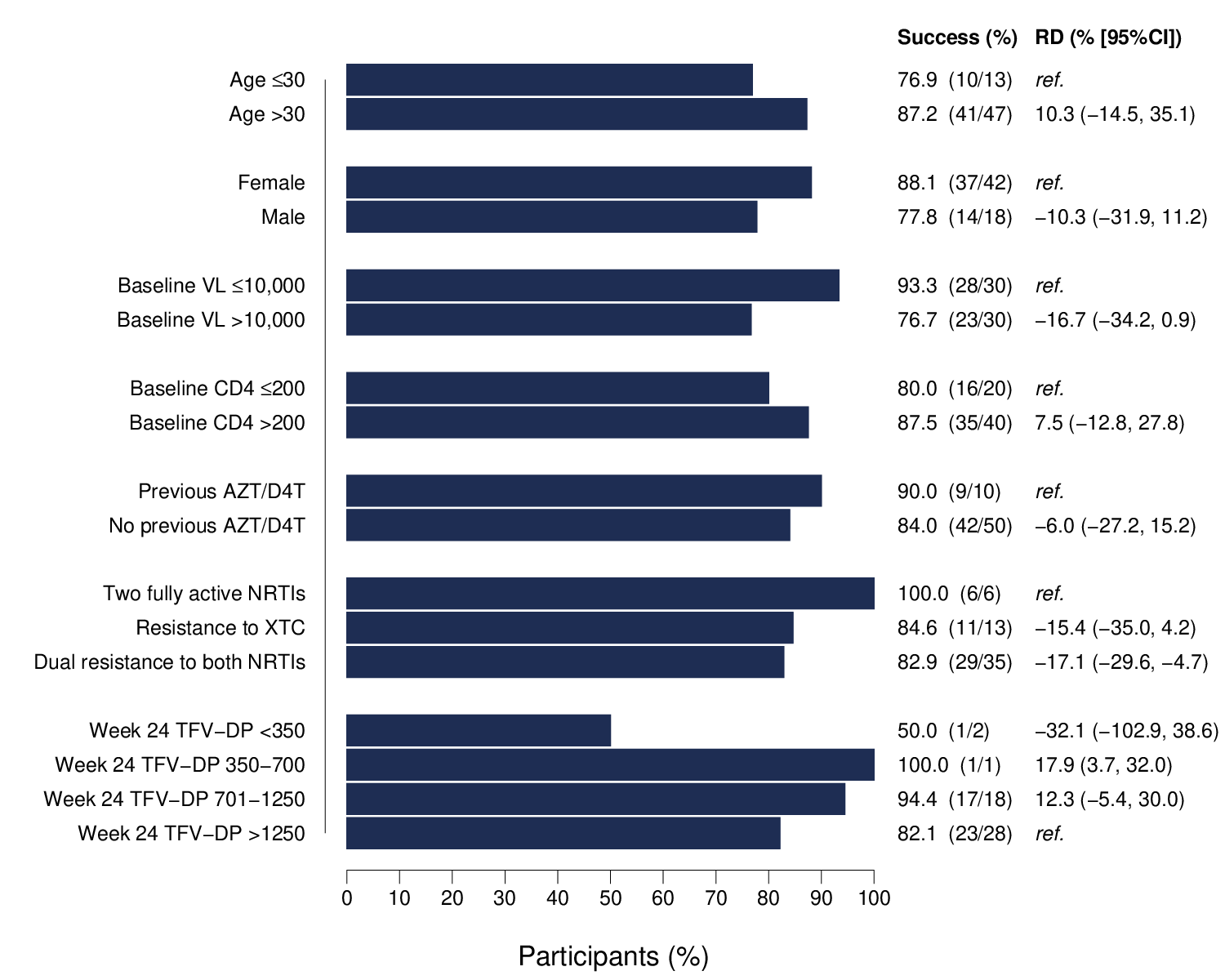


Table 5. Characteristics by primary outcome (viral load <50 copies/mL) at week 24 (modified intention-to-treat analysis, n=60)

|  |  |  |
| --- | --- | --- |
|  | Success at week 24  (VL<50 copies/mL)  (n=51) | Failure at week 24  (VL not <50 copies/mL)  (n=9) |
|  |  |  |
| **Participant characteristics** |  |  |
| Female, (n/%) | 37 (73%) | 5 (56%) |
| Age in years, (median/IQR) | 37 (31-46) | 36 (30-51) |
|  |  |  |
| **Baseline HIV characteristics** |  |  |
| CD4 count in cells/mm3 (median/IQR) | 294 (174-380) | 202 (175-236) |
| Viral load in copies/mL (median/IQR) | 8 320 (2 608-24 971) | 40 761 (22 197-56 219) |
|  |  |  |
| **ART history** |  |  |
| Previous ART duration in years (median/IQR) | 6.4 (3.0-8.5) | 3.4 (1.2-6.3) |
| Ever on zidovudine or stavudine (n/%) | 9/51 (18%) | 1/9 (11%) |
|  |  |  |
| **Baseline resistance\*, n(%)** |  |  |
| Tenofovir/ XTC resistance |  |  |
| Both <15 | 6/46 (13%) | 0/8 (0%) |
| Only tenofovir ≥15 | 0/46 (0%) | 0/8 (0%) |
| Only XTC ≥15 | 11/46 (24%) | 2/8 (25%) |
| Both ≥15 | 29/46 (63%) | 6/8 (75%) |
| Efavirenz and/or nevirapine resistance | 44/46 (96%) | 8/8 (100%) |
|  |  |  |
| **TFV-DP concentrations at week 24 (fmol/punch)\*\*** |  |  |
| <350, n (%) | 1/42 (2%) | 1/7 (14%) |
| 350-700, n (%) | 1/42 (2%) | 0 /7 (0%) |
| 701-1250, n (%) | 17/42 (41%) | 1/7 (14%) |
| >1250, n (%) | 23/42 (55%) | 5/7 (71%) |
|  |  |  |
| *ART (antiretroviral therapy), VL (viral load), XTC (lamivudine or emtricitabine)*  \* Resistance classified using Stanford interpretation, where a score <15 indicates susceptible or potential low-level resistance to a drug, and ≥15 indicate low-level, intermediate, or high-level resistance to a drug3  \*\* Tenofovir diphosphate (TFV-DP) concentration categorisation: <350 fmol/punch (equivalent of - men: <1.2 doses per week and women: <0.6 doses per week), 350-700 fmol/punch (men: 1.2 - 3.2 doses per week and women: 0.6 - 2.0 doses per week), 700-1250 fmol/punch (men: 3.2-6 doses per week and women: 2.0-5.3 doses per week) and > 1250 fmol/punch (men: >6 doses per week and women: >5.3 doses per week)4. | | |

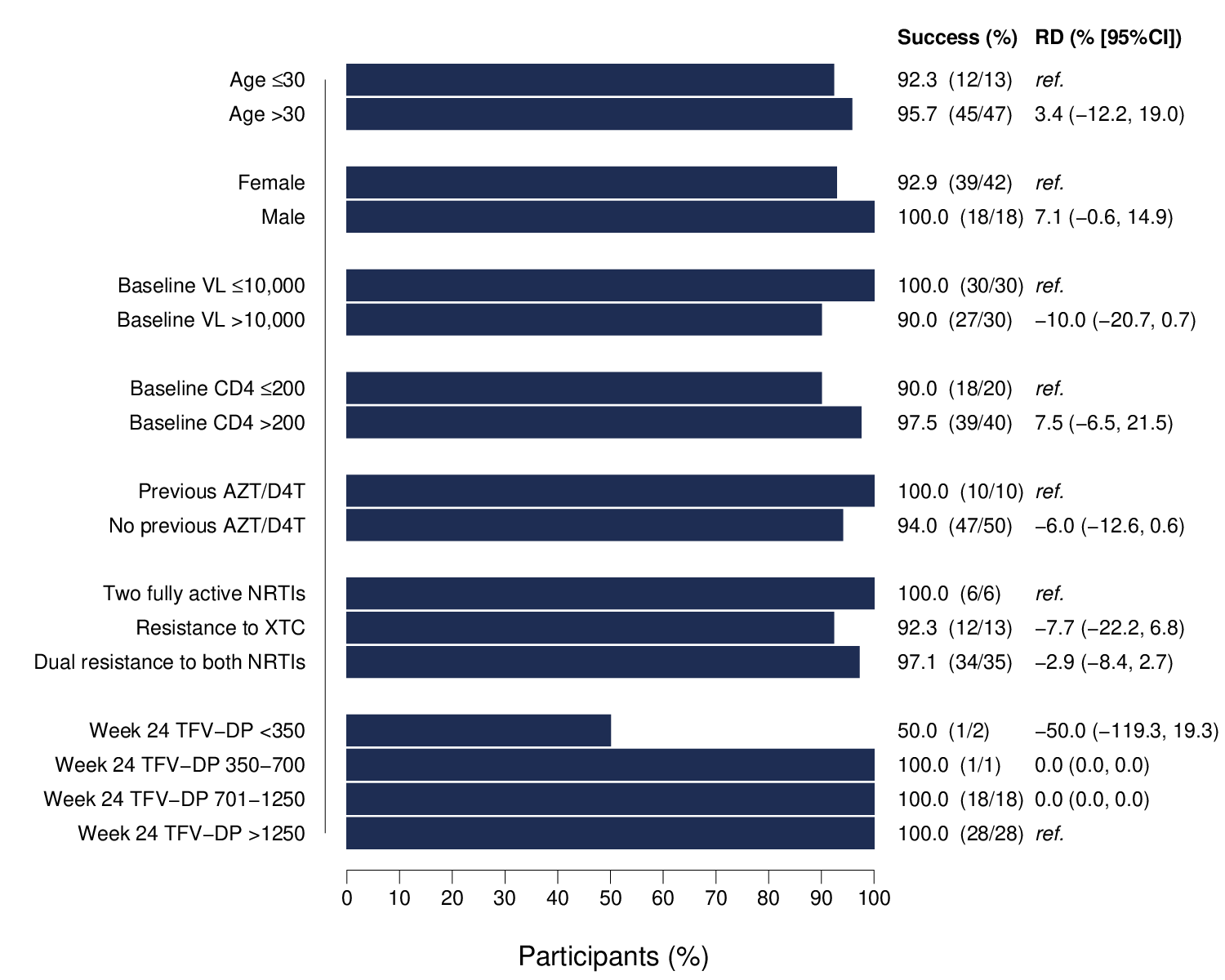
Table 6. Characteristics by viral load <400 copies/mL at week 24 (modified intention-to-treat analysis, n=60)

|  |  |  |
| --- | --- | --- |
|  | Success at week 24 (VL<400 copies/mL)  (n=57) | Failure at week 24  (VL not<400 copies/mL) (n=3) |
|  |  |  |
| **Participant characteristics** |  |  |
| Female, (n/%) | 39 (68) | 3 (100) |
| Age in years, (median/IQR) | 37 (31-46) | 34 (28-51) |
|  |  |  |
| **Baseline HIV characteristics** |  |  |
| CD4 count in cells/mm3 (median/IQR) | 263 (175-349) | 189 (110-241) |
| Viral load in copies/mL (median/IQR) | 9 190 (2 827-24 971) | 57 190 (40 761-64 216) |
|  |  |  |
| **ART history** |  |  |
| Previous ART duration in years (median/IQR) | 6.3 (3.0-8.3) | 2.7 (1.2-5.1) |
| Ever on zidovudine or stavudine (n/%) | 10 (18) | 0 (0) |
|  |  |  |
| **Baseline resistance\*, n(%)** | (n=52) | (n=2) |
| Tenofovir/ XTC resistance |  |  |
| Both <15 | 6 (12) | 0 (0) |
| Only tenofovir ≥15 | 0 (0) | 0 (0) |
| Only XTC ≥15 | 12 (23) | 1 (50) |
| Both ≥15 | 34 (65) | 1 (50) |
| Efavirenz and/or nevirapine resistance | 50 (96) | 2 (100) |
|  |  |  |
| **TFV-DP concentrations at week 24 (fmol/punch)\*\*** |  |  |
| <350, n (%) | 1/48 (4%) | 1/1 (100%) |
| 350-700, n (%) | 1/48 (4%) | 0/1 (0%) |
| 701-1250, n (%) | 18/48 (38%) | 0/1 (0%) |
| >1250, n (%) | 28/48 (58%) | 0/1 (0%) |
|  |  |  |
| *ART (antiretroviral therapy), VL (viral load), XTC (lamivudine or emtricitabine)*  \* Resistance classified using Stanford interpretation, where a score <15 indicates susceptible or potential low-level resistance to a drug, and ≥15 indicate low-level, intermediate, or high-level resistance to a drug3  \*\* Tenofovir diphosphate (TFV-DP) concentration categorisation: <350 fmol/punch (equivalent of - men: <1.2 doses per week and women: <0.6 doses per week), 350-700 fmol/punch (men: 1.2 - 3.2 doses per week and women: 0.6 - 2.0 doses per week), 700-1250 fmol/punch (men: 3.2-6 doses per week and women: 2.0-5.3 doses per week) and > 1250 fmol/punch (men: >6 doses per week and women: >5.3 doses per week)4. | | |

Figure 2. Subgroup analysis of primary endpoint stratified by baseline characteristics and adherence (tenofovir diphosphate concentration) at week 24 (VL < 50 copies/mL at week 24, modified intention-to-treat analysis)

*AZT (zidovudine), D4T (stavudine), NRTI (nucleoside reverse transcriptase inhibitor),* TFV-DP (tenofovir diphosphate), *VL (viral load), XTC (lamivudine or emtricitabine)*

Figure 3. Subgroup analysis of participants with viral load <400 copies/mL at week 24 stratified by baseline characteristics and adherence (tenofovir diphosphate concentration) at week 24 (modified intention-to-treat analysis)



*AZT (zidovudine), D4T (stavudine), NRTI (nucleoside reverse transcriptase inhibitor),* TFV-DP (tenofovir diphosphate), *VL (viral load), XTC (lamivudine or emtricitabine)*

Table 7. Categorised tenofovir diphosphate (TFV-DP) concentrations at baseline, week 12, and week 24, stratified by sex

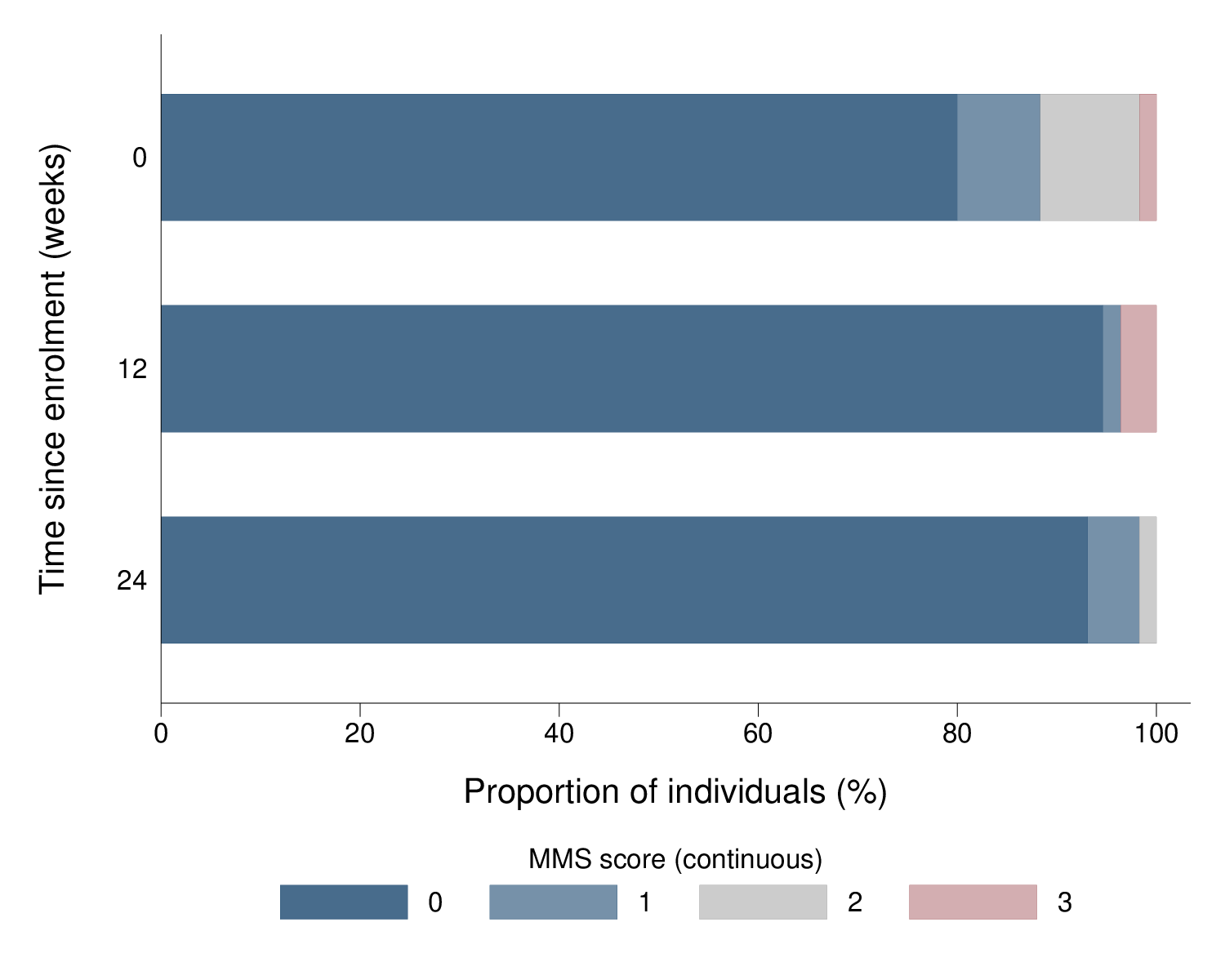
|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **TFV-DP (fmol/punch)\*** | **Baseline (N=60), n (%)** | | **Week 12 (N=55), n (%)** | | **Week 24 (N=49), n (%)** | |
|  | Women (N=42) | Men (N=18) | Women  (N=38) | Men  (N=17) | Women  (N=34) | Men (N=15) |
| **<350, n (%)** | 7 (16.7) | 1 (5.6) | 0 | 0 | 2 (5.9) | 0 |
| **350-700, n (%)** | 0 | 2 (11.1) | 1 (2.6) | 0 | 1 (2.9) | 0 |
| **701-1250, n (%)** | 18 (42.8) | 6 (33.3) | 11 (29) | 4 (23.5) | 14 (41.2) | 4 (26.7) |
| **>1250, n (%)** | 17 (40.5) | 9 (50) | 26 (68.4) | 13 (76.5) | 17 (50) | 11 (73.3) |

\* TFV-DP concentration categorisation: <350 fmol/punch (equivalent of - men: <1.2 doses per week and women: <0.6 doses per week), 350-700 fmol/punch (men: 1.2 - 3.2 doses per week and women: 0.6 - 2.0 doses per week), 700-1250 fmol/punch (men: 3.2-6 doses per week and women: 2.0-5.3 doses per week) and > 1250 fmol/punch (men: >6 doses per week and women: >5.3 doses per week)4.

Table 8. Summary of adverse events (AE) from baseline to week 24

|  |  |  |
| --- | --- | --- |
|  | Number of individuals (n/%) | Total number of events |
| Mortality (all-cause) | 0 (0%) | 0 |
| Serious AEs\* | 4 (7%) | 4 |
| Grade 3 and 4 AEs | 7 (12%) | 11 |
| Clinical | 5 (8%) | 7 |
| Grade 3 | 5 (8%) | 7 |
| Grade 4 | 0 (0%) | 0 |
| Laboratory | 4 (7%) | 4 |
| Grade 3 | 3 (5%) | 3 |
| Grade 4 | 1 (2%) | 1 |
| Adverse events requiring discontinuation of any ART medication\* | 1 (2%) | 1 |
| \* Serious AEs are defined as adverse events that result in death, a life-threatening incident, hospitalisation, disability, congenital abnormality or requires medical or surgical intervention to prevent permanent damage. | | |

Figure 4. Proportion of individuals with specific Modified Mini Screen (MMS) score over time (continuous score ranging from 0 to 22\*)



\* A score of ≥9 on the MMS has been validated to identify a DSM diagnosis of anxiety, mood or psychotic disorder with 82% specificity and 63% sensitivity1

Figure 5. Proportion of individuals with insomnia severity index (ISI) score at each timepoint (continuous measure ranging from 0 to 28\*)



\*A score of ≥11 on the ISI has been shown to detect severe insomnia with 97% sensitivity and 100% specificity2.

Table 9. Concomitant medications with potential for dolutegravir interaction taken at any point from baseline to week 24

|  |  |
| --- | --- |
| Concomitant medications | n=60 |
|  |  |
| **Key concomitant preventative medications, n(%)** | |
| Isoniazid\* | 40 (67%) |
| Cotrimoxazole | 21 (35%) |
|  |  |
| **Other concomitant medications with potential for dolutegravir interaction, n(%)** | |
| Ferrous sulphate | 5 (2%) |
| Metformin | 1 (0%) |
| Rifampicin | 1 (0%) |
| Zinc Sulfate Monohydrate | 1 (0%) |
| \*Participants received isoniazid as tuberculosis preventative therapy | |
|  |  |

**References**

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