OPEN

# Virologic Impact of the Dolutegravir Transition: Prospective Results From the Multinational African Cohort Study

*Allahna Esber, PhD, MSPH,[a,b] Nicole Dear, MPH,[a,b] Neha Shah, MD, MPH,[a] Hannah Kibuuka, MBChB,[c] Jonah Maswai, MBChB, MPH,[a,d] John Owuoth, MBChB,[e,f] Valentine Singoei, MBChB,[e,f] Emmanuel Bahemana, MD,[a,g] Michael Iroezindu, MB, BS, MPH,[a,h] Trevor A. Crowell, MD, PhD,[a,b] Christina S. Polyak, MD, MPH,[a,b] Joseph S. Cavanaugh, MD,[a] and Julie A. Ake, MD, MSc,[a] on behalf of the AFRICOS Study Group*

**Background:** The real-world impact on viral suppression of switching from non–dolutegravir-based therapy to tenofovir/lamivudine/dolutegravir (TLD) is not thoroughly characterized in Africa. We described the virologic consequences of switching regimens in the African Cohort Study (AFRICOS), an observational cohort in Nigeria, Kenya, Uganda, and Tanzania.

**Methods:** Among antiretroviral-experienced people living with HIV (PLWH) in AFRICOS, we compared viral load (VL) non-suppression (VL $\geq$ 1000 copies/mL) among those who switched with those who never switched to TLD, restricting to participants who had at least 1 visit with a recorded VL after the countrywide rollout of TLD. We calculated Kaplan–Meier curves and conducted Cox proportional hazards modeling to estimate adjusted hazard ratios and 95% confidence intervals for factors potentially associated with nonsuppression.

**Results:** As of September 1, 2021, there were 3108 PLWH enrolled. Among 1576 participants who switched to TLD, 1486 (94.3%) remained suppressed after transition, 12 (0.8%) remained unsuppressed, and 38 (2.4%) lost suppression, compared with 652 (82.1%), 75 (9.4%), and 46 (5.8%), respectively, of 797 participants who did not switch ($P < 0.001$). After adjustment for sex, age, study site, and self-reported antiretroviral therapy adherence, virally suppressed participants who did not switch to TLD had significantly higher rates of losing viral suppression compared with those who switched (adjusted hazard ratio: 4.26; 95% confidence interval: 2.72 to 6.68).

**Conclusions:** PLWH transitioning to TLD had higher rates of viral suppression compared with those who remained on other regimens. Even within a highly suppressed population, TLD transition provided significant benefits for achieving or maintaining viral suppression.

**Key Words:** dolutegravir, virologic response, HIV integrase inhibitors

(*J Acquir Immune Defic Syndr* 2022;91:285–289)

Received for publication March 14, 2022; accepted June 20, 2022.

From the [a]US Military HIV Research Program, Walter Reed Army Institute of Research, Silver Spring, MD; [b]Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., Bethesda, MD; [c]Makerere University Walter Reed Project, Kampala, Uganda; [d]US Army Medical Research Directorate—Africa, Kericho, Kenya; [e]US Army Medical Research Directorate—Africa, Kisumu, Kenya; [f]HJF Medical Research International, Kisumu, Kenya; [g]HJF Medical Research International, Mbeya, Tanzania; and [h]HJF Medical Research International, Abuja, Nigeria.

Supported by the President's Emergency Plan for AIDS Relief through a cooperative agreement between the Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., and the US Department of Defense (W81XWH-11-2-0174 and W81XWH-18-2-0040).

The authors have no conflicts of interest to disclose.

Presented, in part, at IAS 2021 (virtual), July 18–21, 2021.

J.S.C. and J.A.A. are co-last authors.

The views expressed are those of the authors and should not be construed to represent the positions of the US Army or the Department of Defense. The investigators have adhered to the policies for protection of human subjects as prescribed in AR 70-25.

The Henry M. Jackson Foundation for the Advancement of Military Medicine (HJF) and the Water Reed Army Institute of Research (WRAIR) are committed to safeguarding the privacy of research participants. Distribution of data will require compliance with all applicable regulatory and ethical processes, including establishment and approval of an appropriate data-sharing agreement. To request a minimal data set, please contact the Data Coordinating and Analysis Center (DCAC) at PubRequest@hivresearch.org and indicate the RV329 study along with the name of the manuscript.

Correspondence to: Allahna Esber, PhD, MSPH, Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., 6720A Rockledge Drive, Suite 400, Bethesda, MD 20817 (e-mail: aesber@global-id.org).

Copyright © 2022 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

## INTRODUCTION

Dolutegravir (DTG)-based antiretroviral therapy (ART) has a high genetic barrier to resistance and causes fewer adverse events, resulting in higher rates of viral suppression.[1–7] Consequently, in 2018, tenofovir disoproxil fumarate–lamivudine–DTG (TLD) was recommended as a preferred first-line treatment by the World Health Organization (WHO)[8] and rolled out as the preferred regimen in programs supported by the President's Emergency Plan for AIDS Relief (PEPFAR).

However, there are limited data on the real-world effectiveness of TLD among ART-experienced people living

with HIV (PLWH), particularly in African settings, where treatment may be less individualized than in more resource-rich settings. Questions remain about the comparable effectiveness of TLD in people transitioning from other regimens. We examined viral nonsuppression [viral load (VL) ≥ 1000 copies/mL], as well as time to viral nonsuppression across 12 PEPFAR-supported clinical sites in Africa.

## METHODS

### Study Design and Setting

The African Cohort Study (AFRICOS) is an ongoing observational study that began enrolling PLWH in January 2013 from 12 clinics in Kayunga, Uganda; South Rift Valley and Kisumu West, Kenya; Mbeya, Tanzania; and Lagos and Abuja, Nigeria.[9] Nonpregnant PLWH aged 18 years and older have been eligible for enrollment since 2013; participation was expanded to include clinic clients as young as 15 years in 2020. Every 6 months, participants answer a behavioral questionnaire, extensive medical record reviews are conducted, and laboratory testing including VL quantification is performed.

### Analytic Population

For these analyses, we compared outcomes of interest among participants who switched to TLD at any time with participants who never switched to TLD over the course of follow-up. Only participants who had at least 2 VLs and at least 1 visit with available VL data after the country rollout of TLD through September 1, 2021, were included. Nigeria began TLD rollout in October 2018 and Kenya and Uganda began rollout in December 2018. All 3 required a VL < 1000 copies/mL to start TLD; that requirement was removed by Kenya in March 2019. Tanzania began rollout in March 2019 without the requirement for VL suppression. To assess the effects of TLD, participants who switched to TLD were excluded if they had been on TLD for less than 3 months. To compare time to viral nonsuppression, survival analyses were further restricted to participants with a VL < 1000 copies/mL at the visit before TLD switch or the first visit during the analysis period among nonswitchers. All participants had 2 VLs included in this analysis. For those who switched to TLD, the first VL was the VL performed at the visit before transitioning to TLD. For those who did not switch to TLD, the first VL was their first available VL after the country rollout of TLD through September 1, 2021. The second VL for both groups was either the VL from the most recent visit (through September 1, 2021) or first visit with virologic nonsuppression and was at least 3 months after a switch.

### Measures

The main outcome was viral nonsuppression, defined as a VL ≥ 1000 copies/mL to be consistent with PEPFAR programming and WHO guidelines.[10,11] Standard polymerase chain reaction (PCR)-based clinical tests were used at each site.[12] The main exposure was TLD use, which was abstracted from medication record review. Available data from documented visits were used; visit adherence was not determined. ART adherence was based on the self-reported number of doses missed and dichotomized as missing zero or any doses in the 30 days before the study visit.

### Analytic Methods

Descriptive statistics were performed using the Fisher exact test for categorical variables and the Kruskal–Wallis test for continuous variables, comparing participants who did and did not transition to TLD. Among all participants with available VL data, we descriptively examined change in VL after TLD transition. For participants who did not switch, we compared their first eligible VL to the most recent VL. We used Cox proportional hazards modeling to estimate hazard ratios and 95% confidence intervals (CIs) to estimate time to viral nonsuppression by regimens. Only visits occurring after the respective country began transitioning to TLD were included. Confounders were selected a priori based on the literature. Models were adjusted for study site, age, sex, and self-reported ART adherence.

### Ethical Considerations

The study was approved by institutional review boards of the Walter Reed Army Institute of Research and all collaborating institutions. All participants provided written informed consent before enrollment.

## RESULTS

Of the 3108 PLWH enrolled in AFRICOS, 2382 completed a visit after their respective country adopted TLD as first-line ART, and 2342 had VL data available. Of participants with VL data, 797 remained on their current regimen while 1868 switched to a DTG-based regimen, including 1782 who switched to TLD, of whom 1576 had been on TLD for at least 3 months and were included in these analyses. TLD switch was more common among men than women (77.1% vs. 59.0%; $P < 0.001$), and the median age was higher for PLWH who had switched to TLD compared with PLWH who had not [45.6 years (interquartile range: 37.5–53.5) vs. 40.1 years (33.5–47.2)]. TLD transition varied by site with a higher percentage of participants switching to TLD in Nigeria (78.4%); Kisumu West, Kenya (73.9%); and Tanzania (70.4%) compared with Uganda (39.8%) and South Rift Valley, Kenya (40.8%, $P < 0.001$). Among those who remained on their regimen, 107 (13.6%) reporting missing one or more doses, compared with 187 (11.9%) of those who did switch ($P = 0.25$). Most participants transitioned from tenofovir-lamivudine-efavirenz (TLE) (64.4%), while 15.2% transitioned from azidothymidine–lamivudine–nevirapine. Only 12 (<1%) participants transitioned to TLD from a protease inhibitor-based regimen.

### Change in Viral Load

Among the 1576 participants who switched to TLD, 1486 (94.3%) had VLs < 1000 copies/mL at the visit before


Copyright © 2022 The Author(s). Published by Wolters Kluwer Health, Inc.

switch and remained suppressed after transition, compared with only 652 of 797 (81.8%) participants who did not switch to TLD (Fig. 1). Among the participants who switched to TLD, 12 (0.8%) had and maintained VLs ≥ 1000 copies/mL and 38 (2.4%) participants with VLs < 1000 copies/mL had VLs rise above 1000 copies/mL. Comparatively, among those who did not switch, 75 (9.4%) had and maintained VLs ≥ 1000 copies/mL and 46 (5.8%) participants with VLs < 1000 copies/mL had VLs rise above 1000 copies/mL ($P < 0.001$). Examining finer changes in VLs by including a category for low-level viremia (VL 50–999 copies/mL), 84.0% of participants who switched to TLD maintained a VL < 50 copies/mL compared with 69.8% of participants who did not switch to TLD ($P < 0.001$).

There were 37 participants with a VL ≥ 1000 copies/mL on TLE at the time of TLD transition and who had a VL measured at least 3 months after switching; 33 (89.2%) had a VL < 1000 copies/mL after switching, whereas 4 remained with VLs ≥ 1000 copies/mL. Of the 12 participants previously on a protease inhibitor-based regimen, 8 remained virally suppressed after switching to TLD (66.7%), 1 became suppressed (8.3%), and 3 were unsuppressed at transition and remained unsuppressed (25.0%).

### Time to Viral Nonsuppression (Viral Loads ≥1000 Copies/mL)

Among the 2085 participants with a VL < 1000 copies/mL at the time of TLD switch or the first eligible study visit, there was a combined total of 83 (4.0%) participants who developed viral nonsuppression. The mean time between the 2 VLs was 1.55 years for the 1505 participants who switched to TLD (median = 1.73 years; IQR = 1.03–2.05 years) and 1.41 years for the 580 participants who did not switch to TLD (median = 1.51 years; IQR = 0.66–2.00 years).

Thirty-seven (2.5%) of those who switched to TLD developed viral nonsuppression, compared with 46 (7.9%) of those who did not switch to TLD ($P < 0.001$).

In the unadjusted proportional hazards model, participants who did not switch to TLD had 3.59 times the hazard of developing viral nonsuppression compared with those who transitioned to TLD (95% CI: 2.33 to 5.55; Table 1). After adjustment for sex, age, study site, and self-reported ART adherence, virally suppressed participants who did not switch to TLD had significantly higher rates of losing viral suppression compared with those who switched (adjusted hazard ratio: 4.26; 95% CI: 2.72 to 6.68).

## DISCUSSION

We found that among ART-experienced, virally suppressed PLWH, those who switched to TLD maintained viral suppression better than those individuals who continued on other regimens. These findings support the programmatic intention to switch all PLWH to TLD to maximize viral suppression and reduce individual and community VLs.

Our findings are similar, and additive, to what has been reported in the literature. A study among key populations in Nigeria demonstrated that a greater proportion of participants who switched to TLD had a VL < 200 copies/mL after 3 months compared with a similar group of patients maintained on TLE for another 6 months before switching (88% vs. 76.3%).[13] Similarly, a study in Lesotho showed that after switching to TLD, the proportion of participants with a VL < 100 copies/mL increased from 96% to 98%, and the percentage with pill count-based adherence >95% improved from 82% to 90%.[14]

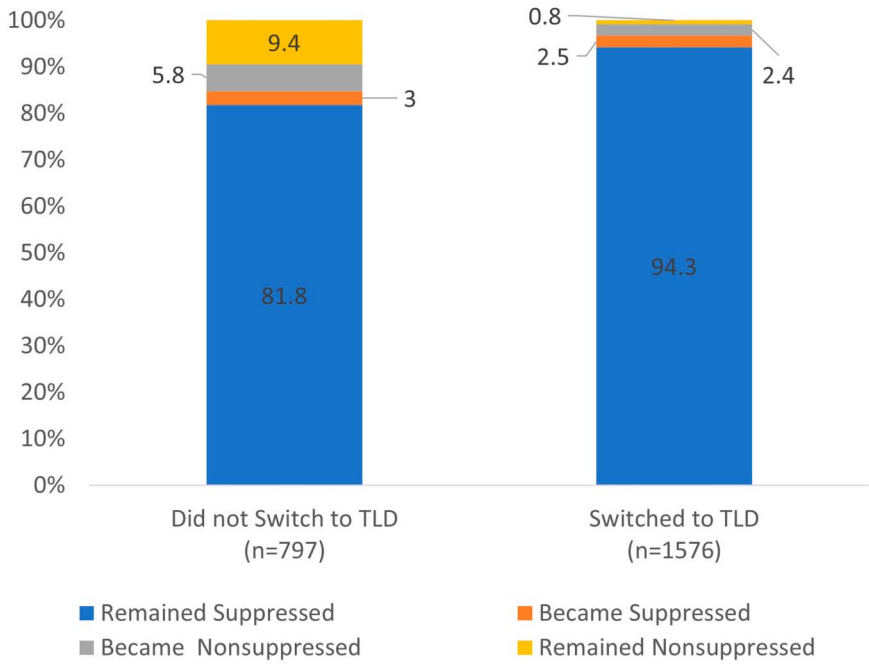


**FIGURE 1.** VL category by antiretroviral therapy switch status. VL suppression defined as a VL < 1000 copies/mL, and nonsuppressed defined as a VL ≥ 1000 copies/mL. For participants who did not transition to TLD, the preswitch VL was the first available VL after the country began rollout of TLD.

Copyright © 2022 The Author(s). Published by Wolters Kluwer Health, Inc.

**TABLE 1.** Unadjusted and Adjusted Hazard Ratios for Time to Viral Non-suppression (Viral Load ≥ 1000 Copies/mL)

| | | Unadjusted | | Adjusted | |
|---|---|---|---|---|---|
| | N (%) | Hazard Ratio | 95% CI | Hazard Ratio | 95% CI |
| On TLD | | | | | |
| Yes | 1576 (66.4%) | Ref | | — | |
| No | 797 (33.6%) | 3.59 | 2.33 to 5.55 | 4.26 | 2.72 to 6.68 |
| Sex | | | | | |
| Male | 970 (40.9%) | Ref | | — | |
| Female | 1403 (59.1%) | 0.80 | 0.51 to 1.23 | 0.55 | 0.35 to 0.88 |
| Age | | | | | |
| 18–29 | 301 (12.7%) | Ref | | — | |
| 30–39 | 514 (21.7%) | 0.93 | 0.41 to 2.08 | 1.08 | 0.46 to 2.51 |
| 40–49 | 872 (36.7%) | 1.10 | 0.48 to 2.10 | 1.22 | 0.57 to 2.60 |
| 50+ | 686 (28.9%) | 0.69 | 0.32 to 1.50 | 1.00 | 0.44 to 2.24 |
| Study site | | | | | |
| Kayunga, Uganda | 397 (16.7%) | Ref | | — | |
| South Rift Valley, Kenya | 823 (34.7%) | 1.44 | 0.72 to 2.88 | 1.52 | 0.76 to 3.06 |
| Kisumu West, Kenya | 463 (19.5%) | 1.06 | 0.48 to 2.37 | 1.18 | 0.53 to 2.66 |
| Mbeya, Tanzania | 412 (17.4%) | 1.84 | 0.82 to 4.13 | 1.98 | 0.87 to 4.53 |
| Abuja and Lagos, Nigeria | 278 (11.7%) | 1.72 | 0.80 to 3.71 | 1.59 | 0.71 to 3.56 |
| Missed ART | | | | | |
| None | 2062 (87.5%) | Ref | | — | |
| Missed ≥1 | 294 (12.5%) | 2.80 | 1.73 to 4.53 | 2.68 | 1.58 to 4.56 |

Missed ART was based on participant self-reported number of doses in the last 30 days.

Current WHO guidelines recommend changing nucleoside reverse transcriptase inhibitors (NRTIs) at the time of transition from a failing first-line regimen to minimize the risk of developing resistance.[10] However, we found that nearly 90% of participants unsuppressed on TLE were able to suppress on TLD despite not changing the NRTI backbone. Previously, we found among a subset of ART-experienced AFRICOS participants that 68% had an NRTI mutation suggesting high levels of resistance in this cohort.[15] These data add to a growing body of literature documenting that even when PLWH have viral nonsuppression on tenofovir or other NRTIs, TLD is an effective regimen.[16,17] The NADIA trial showed high levels of viral suppression, defined as a VL < 400 copies/mL, after switching to TLD among those with a K65R viral mutation or intermediate-level to high-level tenofovir resistance.[1] Similarly, the DO-REAL study in Lesotho showed that among 44 participants with a VL above 100 copies/mL at transition, 42 (95%) dropped their VLs to below 100 copies/mL at follow-up.[14] These findings suggest that maintaining a tenofovir backbone rather than switching to zidovudine may be an appropriate option when switching to DTG-based therapy, allowing for continued 1 pill, once-a-day dosing and sparing the substantial adverse events associated with prolonged zidovudine therapy.

This study is not without a few limitations. Most countries required viral suppression as a requirement to initiate TLD; therefore, we were unable to perform formal modeling with this group given the small sample size. We focused this analysis on 2 VLs and used a VL cutoff of 1000 copies/mL; although a single VL above that threshold is notable, the design of this study prohibits us from commenting on persistent nonsuppression and low-level viremia, both of which are more established clinical considerations. Participants enrolled in the study received additional attention and diagnostic services beyond the standard of care, which may limit generalizability to individuals not enrolled in AFRICOS. In addition, VL testing as part of the study visit was scheduled independently from routine HIV care visits when ART regimen changes were made, so there were varying durations between regimen changes and VL measurements across participants. Some countries required viral suppression in the 6 or 12 months before TLD initiation, so the populations who did and did not switch may not be equivalent in viral suppression and ART adherence, which could bias the results. However, given that we restricted our survival analysis to only participants who were suppressed below 1000 copies/mL we believe this bias to be minimal. Finally, there may be other confounders which were not measured or included in this analysis, which could further limit comparability of the groups. If, for example, providers used some unrecorded judgment to decide who was and was not switched to TLD (eg, a perceived adherence issue), that could have biased these results.

These data provide insights into the real-world impact of the TLD transition in Africa, demonstrating that even among PLWH with high rates of viral suppression, TLD provides an additional benefit and can further reduce rates of viral nonsuppression and community VLs.

## ACKNOWLEDGMENTS

*The authors thank the study participants, local implementing partners, and hospital leadership at Kayunga*


*Copyright © 2022 The Author(s). Published by Wolters Kluwer Health, Inc.*

*District Hospital, Kericho District Hospital, AIC Litein Mission Hospital, Kapkatet District Hospital, Tenwek Mission Hospital, Kapsabet District Hospital, Nandi Hills District Hospital, Kisumu West District Hospital, Mbeya Zonal Referral Hospital, Mbeya Regional Referral Hospital, Defence Headquarters Medical Center, and the 68th Nigerian Army Reference Hospital.*

*The authors would also like to thank the AFRICOS Study team—from the US Military HIV Research Program Headquarters team: Danielle Bartolanzo, Alexus Reynolds, Rory Eustace, Mark Milazzo, Leilani Francisco, Badryah Omar, Steven Schech, Tsedal Mebrahtu, Elizabeth Lee, Kimberly Bohince, Ajay Parikh, Jaclyn Hern, Emma Duff, Kara Lombardi, Michelle Imbach, and Leigh Anne Eller; from the AFRICOS Uganda team: Michael Semwogerere, Prossy Naluyima, Godfrey Zziwa, Allan Tindikahwa, Hilda Mutebe, Cate Kafeero, Enos Baghendaghe, William Lwebuge, Freddie Ssentogo, Hellen Birungi, Josephine Tegamanyi, Paul Wangiri, Christine Nabanoba, Phiona Namulondo, Richard Tumusiime, Ezra Musingye, Christina Nanteza, Joseph Wandege, Michael Waiswa, Evelyn Najjuma, Olive Maggaga, Isaac Kato Kenoly, and Barbara Mukanza; from the AFRICOS South Rift Valley, Kenya team: Rither Langat, Aaron Ngeno, Lucy Korir, Raphael Langat, Francis Opiyo, Alex Kasembeli, Christopher Ochieng, Japhet Towett, Jane Kimetto, Brighton Omondi, Mary Leelgo, Michael Obonyo, Linner Rotich, Enock Tonui, Ella Chelangat, Joan Kapkiai, Salome Wangare, Zeddy Bett Kesi, Janet Ngeno, Edwin Langat, Kennedy Labosso, Joshua Rotich, Leonard Cheruiyot, Enock Changwony, Mike Bii, Ezekiel Chumba, Susan Ontango, Danson Gitonga, Samuel Kiprotich, Bornes Ngtech, Grace Engoke, Irene Metet, Alice Airo, and Ignatius Kiptoo; from the AFRICOS Kisumu, Kenya team: Valentine Sing'oei, Winne Rehema, Solomon Otieno, Celine Ogari, Elkanah Modi, Oscar Adimo, Charles Okwaro, Christine Lando, Margaret Onyango, Iddah Aoko, Kennedy Obambo, Joseph Meyo, and George Suja; from the AFRICOS Abuja, Nigeria team: Yakubu Adamu, Nnamdi Azuakola, Mfreke Asuquo, Abdulwasiu Bolaji Tiamiyu, Afoke Kokogho, Samirah Sani Mohammed, Ifeanyi Okoye, Sunday Odeyemi, Aminu Suleiman, Lawrence Umejo, Onome Enas, Miriam Mbachu, Ijeoma Chigbu-Ukaegbu, Wilson Adai, Felicia Anayochukwu Odo, Rabi Abdu, Rosemary Akiga, Helen Nwandu, CHisara Okolo, Ndubuisis Okeke; from the AFRICOS Lagos, Nigeria team: Zahra Parker, Asogwa Ugochukwu Linus, Concilia Amaka Agbaim, Tunde Adegbite, Nkenchiere Harrison, Adewale Adelakun, Ekeocha Chioma, Victoria Idi, Rachel Eluwa, Jumoke Nwalozie, Igiri Faith, Blessing Okanigbuan, Achugwo Emmanuel, Nkiru Nnadi, Ndubuisi Rosemary, Uzoegwu Amaka Natalie, Obende Theresa Owanza, Falaju Idowu Francis, Jacintal Elemere, Obilor Ifeoma Lauretta, Edward Akinwale, and Inalegwu Ochai; and from the AFRICOS Mbeya, Tanzania team: Lucas Maganga, Samoel Khamadi, John Njegite, Connie Lueer, Abisai Kisinda, Jaquiline Mwamwaja, Faraja Mbwayu, Gloria David, Mtasi Mwaipopo, Reginald Gervas, Doroth Mkondoo, Nancy Somi, Paschal Kiliba, Gwamaka Mwaisanga, Johnisius Msigwa, Hawa Mfumbulwa, Peter Edwin, and Willyhelmina Olomi.*

## REFERENCES

1. Paton NI, Musaazi J, Sc M, et al. Dolutegravir or darunavir in combination with zidovudine or tenofovir to treat HIV. *N Engl J Med.* 2021;385:330–341.
2. Aboud M, Kaplan R, Lombaard J, et al. Dolutegravir versus ritonavir-boosted lopinavir both with dual nucleoside reverse transcriptase inhibitor therapy in adults with HIV-1 infection in whom first-line therapy has failed (DAWNING): an open-label, non-inferiority, phase 3b trial. *Lancet Infect Dis.* 2019;19:253–264.
3. Walmsley S, Baumgarten A, Berenguer J, et al. Dolutegravir plus abacavir/lamivudine for the treatment of HIV-1 infection in antiretroviral therapy-naive patients: week 96 and week 144 results from the SINGLE randomized clinical trial. *J Acquir Immune Defic Syndr.* 2015; 70:1–3.
4. Venter WDF, Moorhouse M, Sokhela S, et al. Dolutegravir plus two different prodrugs of tenofovir to treat HIV. *N Engl J Med.* 2019;381: 803–815.
5. Walmsley SL, Antela A, Clumeck N, et al. Dolutegravir plus abacavir–lamivudine for the treatment of HIV-1 infection. *N Engl J Med.* 2013;369:1807–1818.
6. Kanters S, Vitoria M, Zoratti M, et al. Comparative efficacy, tolerability and safety of dolutegravir and efavirenz 400 mg among antiretroviral therapies for first-line HIV treatment: a systematic literature review and network meta-analysis. *EClinicalMedicine*. 2020;28:100573.
7. Parienti JJ, Fournier AL, Cotte L, et al. Forgiveness of dolutegravir-based triple therapy compared with older antiretroviral regimens: a prospective multicenter cohort of adherence patterns and HIV-RNA replication. *Open Forum Infect Dis.* 2021;8:ofab316.
8. World Health Organization. *Updated Recommendations on First-Line and Second-Line Antiretroviral Regimens and Post-Exposure Prophylaxis and Recommendations on Early Infant Diagnosis of HIV*. World Health Organization; 2018. https://www.who.int/publications/i/item/WHO-CDS-HIV-18.51.
9. Esber A, Polyak C, Kiweewa F, et al. Persistent low-level viremia predicts subsequent virologic failure: is it time to change the third 90? *Clin Infect Dis.* 2019;69:805–812.
10. World Health Organization. *Update of Recommendations on First- and Second-Line Antiretroviral Regimens*. World Health Organization; 2019. https://apps.who.int/iris/handle/10665/325892.
11. Presidents Emergency Plan for AIDS Relief (PEPFAR). *PEPFAR 2021 Country and Regional Operational Plan (COP/ROP) Guidance for All PEPFAR Countries*. US State Department; 2021. https://www.state.gov/wp-content/uploads/2020/12/PEPFAR-COP21-Guidance-Final.pdf.
12. Kibuuka H, Musingye E, Mwesigwa B, et al. Predictors of all-cause mortality among people with HIV in a prospective cohort study in East Africa and Nigeria. *Clin Infect Dis*. 2021:ciab995.
13. Moses K, Adefisayo OA, Maryam B, et al. Virologic response among key populations living with HIV following a switch to dolutegravir-based regimen in Southern Nigeria. *Int J Virol AIDS.* 2020;7:069.
14. Brown JA, Nsakala BL, Mokhele K, et al. Viral suppression after transition from nonnucleoside reverse transcriptase inhibitor- to dolutegravir-based antiretroviral therapy: a prospective cohort study in Lesotho (DO-REAL study). *HIV Med.* 2022;23:287–293.
15. Crowell TA, Danboise B, Parikh A, et al. Pretreatment and acquired antiretroviral drug resistance among persons living with HIV in four African countries. *Clin Infect Dis.* 2021;73:e2311–e2322.
16. Calmy A, Sanchez TT, Kouanfack C, et al. Dolutegravir-based and low-dose efavirenz-based regimen for the initial treatment of HIV-1 infection (NAMSAL): week 96 results from a two-group, multicentre, randomised, open label, phase 3 non-inferiority trial in Cameroon. *Lancet HIV*. 2020; 7:677–687.
17. Keene CM, Griesel R, Zhao Y, et al. Virologic efficacy of tenofovir, lamivudine and dolutegravir as second-line antiretroviral therapy in adults failing a tenofovir-based first-line regimen. *AIDS.* 2021;35:1423–1432.

*Copyright © 2022 The Author(s). Published by Wolters Kluwer Health, Inc.*