

Using Climate-HIV to describe real-world clinical outcomes for people living with HIV taking dolutegravir-based regimens

International Journal of STD & AIDS
2021, Vol. 32(12) 1165–1173
© The Author(s) 2021




Article reuse guidelines:

sagepub.com/journals-permissions

DOI: 10.1177/09564624211027099

journals.sagepub.com/home/std



Chinyere Okoli¹ , Achim Schwenk², Matthew Radford^{1,*},
Melissa Myland³, Stephen Taylor⁴, Justine Barnes⁴, Ashini Fox⁵,
Alison Darley⁵, Fiona Grimson³, Iain Reeves⁶, Sajid Munshi⁶,
Adam Croucher⁶, Naomi Boxall³, Alistair Paice¹, Jean van Wyk¹
and Paul Benn¹

Abstract

Objectives: The objective of this study was to describe the real-world use and effectiveness of dolutegravir-based regimens (DBRs) in routine clinical practice in the United Kingdom.

Methods: Retrospective analysis was conducted using data from four National Health Service trusts using Climate-HIV, an electronic case record system. Eligible patients were aged ≥ 18 years with HIV-1 infection who were prescribed a DBR from December 2012 to March 2018. Outcome measurements were accessed at DBR initiation and at weeks 24, 48 and 96 and the last recorded visit up to the extraction date (last measurement). The primary endpoint was the proportion of patients with HIV-1 RNA <50 copies/mL at Week 48.

Results: The study cohort included 934 patients; 337 (36%) were female, 414 (47%) were white and 717 (77%) were treatment experienced (TE). The Kaplan–Meier estimated probability of achieving HIV-1 RNA <50 copies/mL at 48 weeks was 96% for treatment-naïve (TN) patients and 86% for TE patients. Median times to viral suppression (<50 copies/mL) were 49 and 57 days for TN and TE patients with detectable baseline viral load, respectively, according to Kaplan–Meier analysis. Median follow-up time was 377 days (interquartile range: 131–683). At last measurement, 87% (809/934) of patients remained on a DBR; among those patients, 681 (84%) had HIV-1 RNA <50 copies/mL.

Conclusions: High levels of virologic suppression and low rates of discontinuation of DBRs were seen in a large, diverse, UK-based population with HIV-1 infection. These findings are broadly consistent with efficacy data from phase III studies.

Keywords

Clinical practice data, HIV-1, dolutegravir, real-world outcomes, Climate-HIV

Date received: 8 January 2021; accepted: 17 May 2021

Introduction

Dolutegravir is a second-generation integrase strand transfer inhibitor indicated for treatment of HIV-1 infection in combination with other antiretroviral (ARV) agents.¹ The clinical efficacy and safety of dolutegravir-based 3-drug regimens (3DRs) have been demonstrated in phase III randomised control trials in treatment-naïve (TN)^{2–5} and treatment-experienced (TE)^{6–8} patients with HIV-1 infection. Following that, clinical studies with dolutegravir-based 2-drug regimens (2DRs) have demonstrated noninferiority of 2DRs in achieving or maintaining viral suppression compared with dolutegravir-based 3DRs.^{9–12} As a 3DR, dolutegravir demonstrated superior efficacy in five separate clinical studies versus various other non-dolutegravir-based 3DRs in TN

¹ ViiV Healthcare, Brentford, UK

² North Middlesex University Hospital NHS Trust, London, UK

³ IQVIA Real World Insights, UK & Ireland, London, UK

⁴ Birmingham Heartlands HIV Service, Birmingham Heartlands Hospital, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK

⁵ Nottingham University Hospitals NHS Trust, Nottingham, UK

⁶ Homerton University Hospital NHS Foundation Trust, London, UK

* Matthew Radford was an employee at ViiV Healthcare at the time of the study.

Corresponding author:

Chinyere Okoli, ViiV Healthcare, 980 Great West Road, Brentford Middlesex TW8 9GS, UK.

Email: chinyere.x.okoli@viivhealthcare.com

and TE patients.^{6,8} Dolutegravir has also been shown to be effective in patients with HIV-1 infection with multidrug ARV resistance.^{6,8} In addition, dolutegravir has a favourable safety profile, few drug–drug interactions and a high barrier-to-resistance profile.^{8,11,13} As a result of these clinical trials, dolutegravir-based regimens (DBRs) are listed as a preferred treatment option in international guidelines, including those from the US Department of Health and Human Services,¹⁴ the International Antiviral Society,¹⁵ the World Health Organization¹⁶ and the European AIDS Clinical Society.¹⁷

Real-world cohorts are essential to understanding how the results of clinical trials translate to real-world settings and diverse patient populations. Several cohort studies have assessed DBRs in real-world settings. In these cohorts, many patients remained on DBRs because of the high rates of achieving or maintaining virologic suppression and the low rates of discontinuation due to adverse events (AEs).^{18–22} Herein, we describe the real-world use and effectiveness of DBRs in a retrospective analysis of routine clinical practice in the United Kingdom from the Climate-HIV database.

Methods

Study design

This study is a retrospective analysis of data from the electronic case record system Climate-HIV, a database pooled from four participating hospitals in the United Kingdom (North Middlesex University Hospital National Health Service (NHS) Trust, Nottingham University Hospitals NHS Trust, Birmingham Heartlands Hospital and Homerton University Hospital NHS Foundation Trust). The study time period was from December 2012 to March 2018 (the first records of DBRs in Climate-HIV). Data were collected at the initiation of DBR (index date) and at follow-up time points of weeks 24, 48 and 96 as well as at the last recorded visit. To account for real-world data collection and lag in test data, a window of ± 6 weeks around each follow-up milestone (weeks 24, 48 and 96) was used to capture measurements. Patients were followed up until the earliest of last record, death, end of available data or switch/discontinuation of DBR (last measurement). The study protocol was approved by the Integrated Research Application System, which covers necessary approvals from the Research Ethics Committee (Project ID 225435; approved 20 July 2018) and the Health Research Authority (Project ID 225436). Because of the study design and data source, informed consent was not required.

Participants

Patients aged ≥ 18 years with a recorded diagnosis of HIV-1 infection prior to DBR initiation (index date), who were

treated at one of the Climate-HIV–participating hospitals, received their first DBR during the study period and had an HIV-1 RNA measurement recorded within the prior 9 months were eligible for the study. Patients were excluded if they had a diagnosis of HIV-2 infection.

Study endpoints

The primary endpoint was the proportion of patients with HIV-1 RNA < 50 copies/mL at 48 weeks (snapshot analysis). Secondary endpoints included changes in HIV-1 RNA and CD4⁺ cell count from baseline, mean time to achieve target HIV-1 RNA (< 50 copies/mL), treatment failure (switch/discontinuation of DBR) and virologic failure. Switching was defined as patients who switched to a non-DBR-containing regimen but did not include changing of regimens that used identical ARV drugs (e.g., change to/from a single-tablet regimen or generic formulation). Discontinuation was defined as patients who did not receive a subsequent prescription for ARVs for > 6 months; this may have been related to death, change to another clinic or lack of engagement (i.e., lost to follow-up). Virologic failure was defined as prior undetectable HIV-1 RNA measurement (i.e., < 50 copies/mL) in patients who switched/discontinued a DBR, viral load ≥ 50 copies/mL and subsequent measurement of ≥ 200 copies/mL; prior HIV-1 RNA < 50 copies/mL measurement and two consecutive viral load measurements ≥ 50 copies/mL or viral load ≥ 50 copies/mL with subsequent measurement ≥ 200 copies/mL and documented virologic failure as reason to switch/discontinue treatment, < 1 log decrease after 4 weeks of treatment with a DBR (TN patients only) or viral load > 400 copies/mL after 16 weeks of treatment with a DBR (TN patients only). Data for secondary endpoints were collected at last measurement as well as at weeks 24, 48 and 96 from the index date. Treatment persistence, defined as the probability of remaining on a DBR over time, was determined using Kaplan–Meier analysis. The probability of achieving HIV-1 RNA < 50 copies/mL over time for both TN and TE patients was also determined using Kaplan–Meier analyses.

Statistical analysis

Subpopulations for analysis included TN versus TE. Patients were considered to be TE if they had a record of receiving any prior ARV regimen. Data regarding demographics, ARV regimens, virologic outcomes and reasons for switch were summarised with descriptive statistics. Patients whose final record was extracted before the 24-, 48- and 96-week snapshots were not included in further analysis at these time points. Because of the retrospective non-interventional design of this study, only data that were already recorded in the database could be collated.

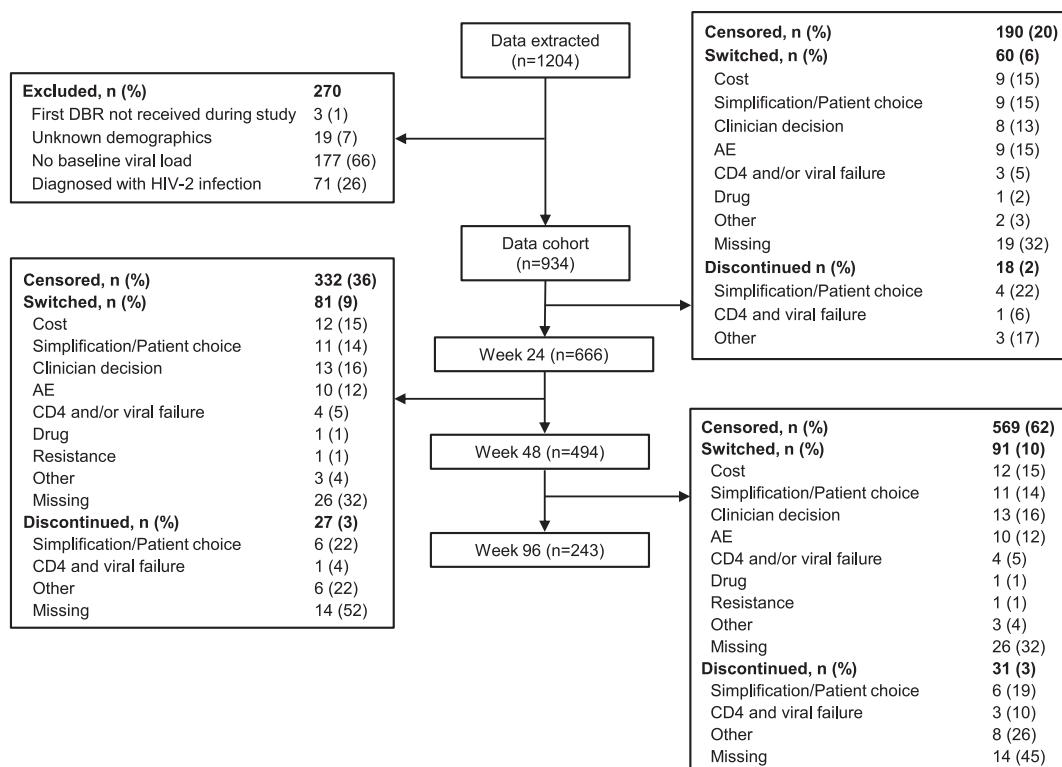


Figure 1. Disposition of all patients initiating a DBR from December 2012 to March 2018 at four climate-HIV-participating hospitals. AE: adverse event; DBR: dolutegravir-based regimen.

Results

Patient characteristics and disposition

Data for 1204 patients initiating a DBR at a participating site were extracted from Climate-HIV; 270 patients were excluded because they did not meet inclusion criteria (Figure 1). Therefore, the study cohort included 934 patients; of those, 217 were TN and 717 were TE. Of the overall population, 36% ($n = 337$) of patients were female (Table 1). The median age was 43 years; 71% of patients ($n = 667$) were aged <50 years. The majority of the population was white (47%); 34% of patients were Black African, 10% were Black Caribbean/other, 5% were of Asian descent and 5% were ≥ 1 race/ethnicity. Before the index date, median (interquartile range (IQR)) HIV-1 RNA was 23,897 copies/mL (3636–110,302) for TN patients and 40 copies/mL (40–89) for TE patients. The median times from HIV-1 diagnosis (or transfer into the system in the absence of a date of confirmed diagnosis) to the index date were 6 months for TN patients and 10 years for TE patients. For TE patients, the median number of regimens since diagnosis was 4 (IQR: 3–6) and 27% ($n = 193/717$) had previous exposure to integrase inhibitors. Resistance mutations were recorded in 17% ($n = 121/717$) of TE patients. The majority of patients (94% ($n = 880$)) initiated a once-daily DBR, with abacavir/dolutegravir/lamivudine being the most common regimen (61% ($n = 533$)). Twice-daily

DBRs were initiated in 3% of patients ($n = 27$), and 5% of patients ($n = 42$) were taking a 2DR.

Seven hundred forty-four patients remained in the cohort at 24 weeks; 190 patients were excluded due to their final records being extracted prior to the 24-week snapshot. Of these patients, 90% ($n = 666/744$) remained on a DBR. Among the patients who remained on a DBR at 24 weeks, excluding those with final records extracted prior to the 48-week snapshot ($n = 142$), 94% ($n = 494/524$) remained on a DBR. At 96 weeks, 237 patients were excluded because of premature data and 98% ($n = 243/247$) remained on a DBR. In addition to time point snapshots, data were collected at last measurement, the earliest last record, death, end of available data or at switch/discontinuation of DBR. The median follow-up time to last measurement was 377 days (IQR: 131–683; Supplementary Table). At the last recorded measurement, 87% ($n = 809/934$) of patients remained on a DBR, and Kaplan–Meier analysis indicated the rates of persistence of DBRs were 96% for TN and 86% for TE patients over a median follow-up period of 362 and 385 days, respectively (Figure 2). Switches and discontinuations infrequently occurred, with 13% of patients switching or discontinuing a DBR ($n = 125$; $n = 22$ TN and $n = 103$ TE). Switching off a DBR was more common among TE patients (11%) than TN patients (6%), with a median time (IQR) to switch or discontinuation of 101 (30–248) and 124 days (63–242), respectively. For TN

Table 1. Patient demographics and baseline disease characteristics.

Parameter	Overall (N = 934)	TN (n = 217)	TE (n = 717)
Sex, n (%)			
Female	337 (36)	58 (27)	279 (39)
Male	597 (64)	159 (73)	438 (61)
Ethnicity, n (%)			
Asian	42 (5)	14 (7)	28 (4)
Black African	305 (34)	46 (23)	259 (38)
Black Caribbean/other	87 (10)	21 (10)	66 (10)
≥1 Ethnicity/race	42 (5)	11 (5)	31 (5)
White	414 (47)	110 (54)	304 (44)
Age (y), median (IQR)	43 (34–51)	37 (30–45)	44 (35–52)
Age, n (%)			
<50 years	667 (71)	178 (82)	489 (68)
≥50 years	267 (29)	39 (18)	228 (32)
Time since HIV diagnosis to initiation of dolutegravir, median (IQR), y	8 (2–13)	<1 (<1–5)	10 (4–15)
Preindex HIV-1 RNA (c/mL), mean (IQR) ^a	40 (40–5157)	23,897 (3636–110,302)	40 (40–89)
Preindex HIV-1 RNA by category, n (%) ^a			
<50 c/mL	520 (56)	14 (6)	506 (71)
≥50 c/mL	414 (44)	203 (94)	211 (29)
Preindex CD4 ⁺ count (cells/mm ³), median (IQR) ^a	480 (286–662)	391 (236–535)	519 (321–706)
Resistance mutations at baseline, n (%)	144 (15)	23 (11)	121 (17)
Other with <6 patients overall	57 (40)	4 (17)	53 (44)
Non-nucleosides	43 (30)	9 (39)	34 (28)
Protease inhibitors (single mutation)	16 (11)	6 (26)	10 (8)
Lamivudine/emtricitabine (M184V)	8 (6)	1 (4)	7 (6)
Lamivudine/emtricitabine (M184V), non-nucleosides	7 (5)	1 (4)	6 (5)
Zidovudine/stavudine (TAMs)	6 (4)	1 (4)	5 (4)
Other	7 (5)	1 (4)	6 (5)

IQR: interquartile range; TAM: thymidine analogue mutation; TE: treatment experienced; TN: treatment naive.

^aLast measurement before index date (initiation of a dolutegravir-based regimen).

patients, the most common reason for switching when recorded was clinician decision ($n = 5$ (36%)), whereas cost reduction ($n = 13$ (16%)) was the most common for TE patients. Adverse events collected from the Climate-HIV database as reasons for switch included those that were gastrointestinal ($n = 4$), renal ($n = 3$) and central nervous system ($n = 2$) in nature; skin rash ($n = 2$); osteopenia ($n = 1$) and fatigue ($n = 2$).

Clinical outcomes

In patients with HIV-1 RNA ≥ 50 copies/mL at the index date, Kaplan–Meier analysis indicated that the probability of achieving HIV-1 RNA < 50 copies/mL at 48 weeks was 96% for TN patients (Day 350) and 86% for TE patients (Day 351; Figure 3). Median times to achieve HIV-1 RNA < 50 copies/mL were 49 days (IQR: 40–63) for TN patients and 57 days (IQR: 40–75) for TE patients according to Kaplan–Meier analysis. Of the 809 patients who remained on a DBR at last measurement, 84% ($n = 681$) had

HIV-1 RNA < 50 copies/mL (Table 2); this finding was generally similar across subgroups. At last measurement, median (IQR) decreases in viral load were 4.43 log₁₀ copies/mL (3.74–5.10) for TN patients ($n = 184$) and 2.5 log₁₀ copies/mL (1.7–4.0) for TE patients ($n = 208$). Median (IQR) increases in CD4⁺ count among patients with CD4 counts available at the index date were 182 cells/mm³ (74–325) for TN patients ($n = 169$) and 40 cells/mm³ (–51–140) for TE patients ($n = 469$). Overall, virologic failure occurred in 10% ($n = 22/217$) of TN and 5% ($n = 38/717$) of TE patients. Of the 60 patients (6%) experiencing virologic failure, 91% ($n = 20/22$) of TN patients and 87% ($n = 33/38$) of TE patients remained on a DBR at last measurement and 68% ($n = 15/22$) of TN and 61% ($n = 23/38$) of TE patients had HIV-1 RNA < 50 copies/mL at last measurement. Six percent ($n = 8/125$) of patients who switched or discontinued had a resistance test recorded during follow-up. Among the tested patients, no nucleoside reverse transcriptase inhibitor or integrase strand transfer inhibitor emergent resistance was observed.

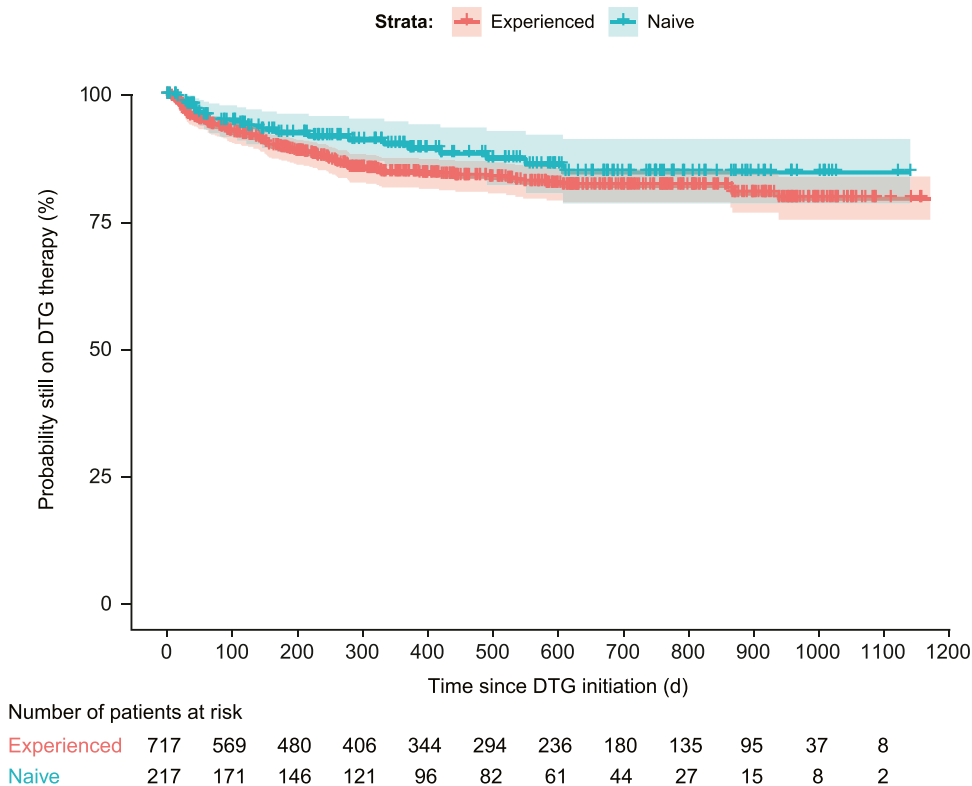


Figure 2. Kaplan–Meier analysis of time to switch/discontinuation. DTG: dolutegravir.

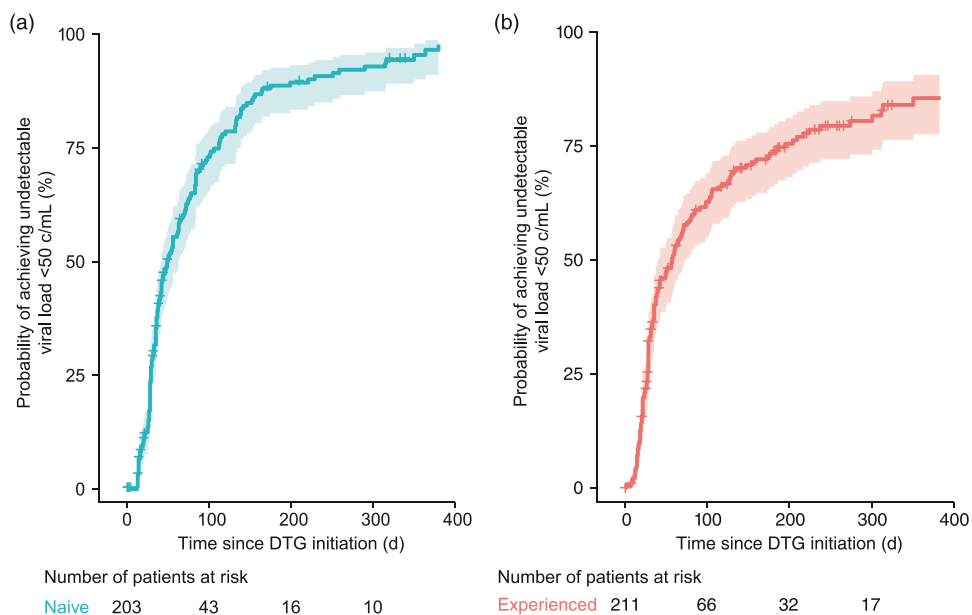


Figure 3. Kaplan–Meier curves for the probability of achieving undetectable viral load (<50 copies/mL) for (a) treatment-naive and (b) treatment-experienced patients with detectable viral load at dolutegravir initiation.

Among those who remained on dolutegravir at 48 weeks, similar proportions of patients aged <50 and ≥50 years had undetectable viral load (46.9% (*n* = 169) and 45.5% (*n* = 61), respectively; 48.9% (*n* = 176) and 46.3% (*n* = 62) had

no viral load data at 48 weeks, respectively). There were also no substantial differences in proportion of patients experiencing virologic failure (4.4% (*n* = 29) of those aged <50 years and 4.9% (*n* = 13) of those aged ≥50 years).

Table 2. Clinical characteristics.

Parameter	Overall (N = 934)	TN (n = 217)	TE (n = 717)
Days of follow-up available, median (IQR)	377 (131–683)	362 (124–642)	385 (136–700)
Still on DBR at last measurement, n (%)	809 (87)	195 (90)	614 (86)
Log decrease HIV-1 RNA from preindex ^a to last measurement among those whose load decreased, median (IQR)	4 (2–5)	4 (4–5)	2 (2–4)
Valid n	392	184	55
Time to HIV-1 RNA target, median (IQR)	33 (19–72)	44 (28–92)	30 (16–67)
Valid n	719	164	555
Virologic failure before last measurement, n (%)	60 (6)	22 (10)	38 (5)
Change in CD4 ⁺ cell count from DBR initiation to last measurement, median (IQR) ^b	73 (–27–192)	182 (74–325)	40 (–51–140)
Valid n	638	169	469

DBR: dolutegravir-based regimen; IQR: interquartile range; TE: treatment experienced; TN: treatment naive.

^aLast measurement before the index date (initiation of a DBR).

^bAmong patients with CD4 cell count available at DBR initiation.

Discussion

In this retrospective analysis of real-world clinical data, DBRs showed high levels of virologic suppression and low rates of discontinuation in a large, diverse, UK-based patient population with HIV-1 infection. At the last recorded measurement (median follow-up time of 377 days), 87% of patients remained on DBR and 6% of patients were classified in this study as having virologic failure; however, the majority continued DBR, and no recorded resistance to nucleoside reverse transcriptase inhibitors and integrase strand transfer inhibitors was recorded among patients who switched or discontinued treatment. One reason for switch was documented as ‘resistance’ by the clinician; however, no new emergence resistance was observed in documented notes (Table 2). Discontinuing and switching ARV regimens were infrequent (10% and 3%, respectively); the most common reasons for switch were clinical decision and cost reduction rather than AEs. The probability of achieving HIV-1 RNA <50 copies/mL at 48 weeks was 96% for TN patients and 86% for TE patients.

The real-world data in this heterogeneous population, in which >30% were women and more than 50% identified as non-white, are reassuringly consistent with phase III studies, the results of which show that dolutegravir is an effective and well-tolerated treatment option in both TN^{2–5} and TE patients.^{7,8,11} These results also agree with previously published real-world clinical data that show a high number of TN and TE patients remaining on DBRs with high rates of virologic suppression as well as low discontinuations due to AEs.^{18–22} For example, a retrospective study of patients in Australia showed that the probability of patients remaining on a DBR after 1 year was 95%, with few discontinuations due to AEs.¹⁹ Similarly, our results demonstrate that the probability of remaining on a DBR in a large, heterogeneous, UK-based patient population with HIV infection after approximately 1 year was 90% for TN patients and 86% for TE patients.

These results are also consistent with real-world evidence from DBR studies. In an observational multinational cohort of 490 patients with HIV-1 RNA <50 copies/mL while treated with efavirenz or a ritonavir-boosted protease inhibitor for ≥6 months and switched to a DBR, 32 (6.5%) patients experienced a detectable viral load and 44 (9.0%) patients switched or discontinued therapy by 1 year after the switch.²³ Use of dolutegravir in all TN (n = 22) and TE (n = 98) individuals at a single London HIV centre from 2014 to 2015 was associated with low rates of failure to achieve HIV-1 RNA <50 copies/mL and few discontinuations throughout the median follow-up period of 5.5 months.²⁴ These studies demonstrate how improvements in HIV therapy have led to effective and safe treatment options for both TN and TE patients, paving the way for dolutegravir-based 2DRs. Randomised control trials with dolutegravir-based 2DRs have demonstrated high rates of efficacy, high barrier-to-resistance and good tolerability profiles in both TN and TE patients.^{9–12} Real-world data studies on dolutegravir-based 2DRs are emerging to reflect this finding in those clinical trials.^{25–31} Although they were observed in a small number of patients in this study, real-world data on dolutegravir-based 2DRs from 2018 onwards report larger patient cohorts (332–1374 patients in 2020).^{27–31} The high rate of efficacy demonstrated in randomised control trials and observed in real-world data for dolutegravir-based 2DRs led to an increasing number of patients being switched from dolutegravir-based 3DRs and maintained on dolutegravir-based 2DRs. This seems to be more apparent because people living with HIV infection are ageing and are taking treatment for longer periods.³² Compared with the general population, individuals living with HIV are at increased risk of comorbidities and polypharmacy.^{33–35} Polypharmacy has been associated with increased risk of adverse health outcomes.^{36,37}

The ongoing COVID-19 pandemic has caused substantial worldwide disruptions to healthcare systems,

resulting in the reduced frequency of face-to-face consultations and routine monitoring at many clinics providing care to people living with HIV.³⁸ It is reassuring that the observations in this large cohort broadly mirror the efficacy and tolerability of DBRs in randomised control trials.

Databases like the Climate-HIV database that collect data on treatment outcomes in patients with HIV-1 infection provide valuable information for addressing evidence gaps not likely to be assessed in randomised control trials.^{37,39} Climate-HIV at the time of study design was the only single-point database with detailed patient-level data for individuals with HIV and was shared across four large separate NHS trusts with broad patient demographics. Climate-HIV was also the only database with single-point access as it was linked to the electronic patient record system so CD4⁺ cell count and viral load records were up-to-date. Such evidence is important for evaluating the real-world implementation of new treatment guidelines or interventions.^{39,40} Thus, the dissemination of HIV-1 treatment outcomes data from databases, including the real-world DBR clinical outcomes reported in this analysis, is critical for informing the real-world success of HIV-1 treatments.

This study has several limitations. Data are from four specialist clinical practices in England, so they may not be generalisable to other populations. Patients were followed up until the earliest of last record, death, end of available data or switch/discontinuation of DBR (last measurement). However, many patients' follow-up periods ceased before time point milestones, particularly at 48 and 96 weeks. At 48 and 96 weeks, 602 (64%) and 365 (39%) patients remained in the cohort, respectively, whereas 332 (36%) and 569 (61%) patients, respectively, were excluded due to their final record extraction occurring before the snapshot. This limits the conclusions that can be made regarding these endpoints. Kaplan–Meier curves provide a more reflective analysis of events with the time-to-event curves. More effective treatment, earlier initiation of ARV therapy and better tolerability have led to less need for repeat measures of treatment success markers such as HIV-1 RNA value and CD4⁺ count. In turn, these were reflected in the number of missing HIV-1 RNA values and CD4⁺ counts at the study milestones. For example, at weeks 24 and 48, a total of 56% and 48% of patients, respectively, did not have their HIV-1 RNA measurement recorded during the time period (assessed within a ± 6 -week time frame). Future studies may consider using time-varying analyses, which may be more appropriate for real-world settings because they take into account multiple measurements recorded within the time frame prior to milestones.⁴¹ In addition, because of the retrospective non-interventional design, we could only collate data that were already populated in the database. Data from the Climate-HIV database indicate specific AEs as reasons for switch or discontinuation; however, a full safety profile was unavailable for these patients. For example, 'Reason for start ART regimen' is listed in a drop-down menu in Climate-HIV, but

there is no further information that differentiates the reason to start one ART instead of another choice. Furthermore, in Climate-HIV, reasons for switch or discontinuation of a DBR were often marked as missing by clinicians, thereby limiting the conclusions to be drawn from these data. At the beginning of the study, patients were classified as TN or TE based on the presence of any prescribed ARV within their Climate-HIV record before DBR initiation. However, several individuals who were transferred from another clinic may have been initiated on DBR before entry into the Climate-HIV database.

Despite these limitations, the results of the present study suggest that DBR is an effective and tolerable treatment option for heterogeneous populations in both TN and TE patients based on achieving undetectable HIV-1 RNA and the low rates observed for discontinuing or switching therapy.

Acknowledgements

All listed authors meet the criteria for authorship set forth by the International Committee of Medical Journal Editors. Editorial assistance was provided under direction of the authors by Sherri Damlo, ELS, of MedThink SciCom and was funded by ViiV Healthcare.

Author's note

Data included in this manuscript have been previously presented at HIV Drug Therapy Glasgow; October 28-31, 2018; Glasgow, UK

Declaration of conflicting interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: C Okoli, A Paice, J van Wyk, and P Benn are employees of ViiV Healthcare and own stock in GlaxoSmithKline. M Radford was an employee of ViiV Healthcare at the time of the study. A Schwenk, J Barnes, A Darley, and S Munshi have nothing to disclose. M Myland and F Grimson are employees from IQVIA and have received grants from ViiV Healthcare. S Taylor has received grants from ViiV Healthcare, Gilead, and Merck. A Fox is employed by Nottingham University Hospitals NHS Trust, which received a grant from ViiV Healthcare before the conduct of the study to update clinical HIV databases. I Reeves has received grants from ViiV Healthcare. A Croucher is employed by the Jonathan Mann Clinic, Homerton University Hospital NHS Foundation Trust, which received a grant from ViiV Healthcare during the conduct of the study to update local patient records. N Boxall is employed by and has received personal fees from IQVIA.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by ViiV Healthcare.

Data availability statement

Anonymised data and study documents can be requested for further research from www.clinicalstudydatarequest.com.

ORCID iD

Chinyere Okoli  <https://orcid.org/0000-0002-9424-2873>

Supplementary material

Supplemental material for this article is available online.

References

- ViiV Healthcare. *Dolutegravir (Package Insert)*. Research Triangle Park, NC: ViiV Healthcare, 2018.
- Clotet B, Feinberg J, van Lunzen J, et al. Once-daily dolutegravir versus darunavir plus ritonavir in antiretroviral-naïve adults with HIV-1 infection (FLAMINGO): 48 week results from the randomised open-label phase 3b study. *Lancet* 2014; 383: 2222–2231.
- 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.
- Raffi F, Rachlis A, Stellbrink HJ, et al. Once-daily dolutegravir versus raltegravir in antiretroviral-naïve adults with HIV-1 infection: 48 week results from the randomised, double-blind, non-inferiority SPRING-2 study. *Lancet* 2013; 381: 735–743.
- Orrell C, Hagins DP, Belonosova E, et al. Fixed-dose combination dolutegravir, abacavir, and lamivudine versus ritonavir-boosted atazanavir plus tenofovir disoproxil fumarate and emtricitabine in previously untreated women with HIV-1 infection (ARIA): week 48 results from a randomised, open-label, non-inferiority, phase 3b study. *Lancet HIV* 2017; 4: e536–e546.
- Aboud M, Lombaard J, Zhang F, et al. Superior efficacy of dolutegravir (DTG) plus 2 nucleoside reverse transcriptase inhibitors (NRTIs) compared with lopinavir/ritonavir (LPV/RTV) plus 2 NRTIs in second-line treatment: interim data from the DAWNING study. In: 9th International AIDS society conference, Paris, France, 23–26 July 2017. abstract 5613.
- Trottier B, Lake JE, Logue K, et al. Dolutegravir/abacavir/lamivudine versus current ART in virally suppressed patients (STRIIVING): a 48-week, randomized, non-inferiority, open-label, Phase IIIb study. *Antivir Ther* 2017; 22: 295–305.
- Cahn P, Pozniak AL, Mingrone H, et al. Dolutegravir versus raltegravir in antiretroviral-experienced, integrase-inhibitor-naïve adults with HIV: week 48 results from the randomised, double-blind, non-inferiority SAILING study. *Lancet* 2013; 382: 700–708.
- Cahn P, Madero JS, Arribas JR, et al. Dolutegravir plus lamivudine versus dolutegravir plus tenofovir disoproxil fumarate and emtricitabine in antiretroviral-naïve adults with HIV-1 infection (GEMINI-1 and GEMINI-2): week 48 results from two multicentre, double-blind, randomised, non-inferiority, phase 3 trials. *Lancet* 2018; 393: 143–155.
- Cahn P, Madero JS, Arribas JR, et al. Durable efficacy of dolutegravir plus lamivudine in antiretroviral treatment-naïve adults with HIV-1 infection: 96-week results from the GEMINI-1 and GEMINI-2 randomized clinical trials. *J Acquir Immune Defic Syndr* 2020; 83: 310–318.
- Llibre JM, Hung CC, Brinson C, et al. Efficacy, safety, and tolerability of dolutegravir-rilpivirine for the maintenance of virological suppression in adults with HIV-1: phase 3, randomised, non-inferiority SWORD-1 and SWORD-2 studies. *Lancet* 2018; 391: 839–849.
- van Wyk J, Ajana F, Bisshop F, et al. Efficacy and safety of switching to dolutegravir/lamivudine fixed-dose 2-drug regimen vs continuing a tenofovir alafenamide-based 3- or 4-drug regimen for maintenance of virologic suppression in adults living with human immunodeficiency virus type 1: phase 3, randomized, noninferiority TANGO study. *Clin Infect Dis* 2020; 71: 1920–1929.
- Eron JJ, Clotet B, Durant J, et al. Safety and efficacy of dolutegravir in treatment-experienced subjects with raltegravir-resistant HIV type 1 infection: 24-week results of the VIKING study. *J Infect Dis* 2013; 207: 740–748.
- Panel on Antiretroviral Guidelines for Adults and Adolescents. *Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV*. Rockville, MD: Department of Health and Human Services, 2018. Report.
- Saag MS, Benson CA, Gandhi RT, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2018 recommendations of the International Antiviral Society-USA panel. *JAMA* 2018; 320: 379–396.
- World Health Organization (WHO). *Updated recommendations on first-line and second-line antiretroviral regimens and post-exposure prophylaxis and recommendations on early infant diagnosis of HIV, interim guidance*. Geneva, Switzerland: WHO, 2018. Report.
- European AIDS Clinical Society (EACS). *EACS Guidelines, Version 9.1*. London, UK: EACS, 2018. Report.
- Nance R, Vannappagari V, Smith K, et al. Clinical outcomes among persons living with HIV initiating dolutegravir-based vs. other recommended regimens in a clinical care from the centers for AIDS research network of integrated systems (CNICS). In: 16th European AIDS conference, Milan, Italy, 25–27 October 2017. Poster E987.
- Ferrer PE, Bloch M, Roth N, et al. A retrospective clinical audit of general practices in Australia to determine the motivation for switch to dolutegravir/abacavir/lamivudine and clinical outcomes. *Int J STD AIDS* 2018; 29: 300–305.
- Cid-Silva P, Llibre JM, Fernández-Bargiela N, et al. Clinical experience with the integrase inhibitors dolutegravir and elvitegravir in HIV-infected patients: efficacy, safety and tolerance. *Basic Clin Pharmacol Toxicol* 2017; 121: 442–446.
- Sörstedt E, Carlander C, Flamholz L, et al. Effect of dolutegravir in combination with nucleoside reverse transcriptase inhibitors (NRTIs) on people living with HIV who have pre-existing NRTI mutations. *Int J Antimicrob Agents* 2018; 51: 733–738.
- Mondi A, Cozzi-Lepri A, Tavelli A, et al. Effectiveness of dolutegravir-based regimens as either first-line or switch antiretroviral therapy: data from the Icona cohort. *J Int AIDS Soc* 2019; 22: e25227.
- Taramasso L, Tatarelli P, Ricci E, et al. Improvement of lipid profile after switching from efavirenz or ritonavir-boosted protease inhibitors to rilpivirine or once-daily integrase inhibitors: results from a large observational cohort study (SCOLTA). *BMC Infect Dis* 2018; 18: 357.
- Negedu O, Kim SH, Weston R, et al. Retrospective review of routine clinical patient experiences with dolutegravir; virological suppression, immunological recovery and adverse events. *HIV Med* 2017; 18: 709–710.

25. Ciccullo A, Baldin G, Capetti A, et al. A comparison between two dolutegravir-based two-drug regimens as switch strategies in a multicentre cohort of HIV-1-infected patients. *Antivir Ther* 2019; 24: 63–67.
26. Revuelta-Herrero JL, Chamorro-de-Vega E, Rodríguez-González CG, et al. Effectiveness, safety, and costs of a treatment switch to dolutegravir plus rilpivirine dual therapy in treatment-experienced HIV patients. *Ann Pharmacother* 2018; 52: 11–18.
27. Borghetti A, Ciccullo A, Baldin G, et al. Shall we dance? Extending TANGO's results to clinical practice. *Clin Infect Dis* 2020; 71: e200.
28. Deschanvres C, Raffi F, Reynes J, et al. Virologic failure and resistance in dolutegravir-based maintenance dual regimens. In: Conference on retroviruses and opportunistic infections, Boston, MA, 8–11 March 2020. Poster 490.
29. Fabbiani M, Rossetti B, Ciccullo A, et al. Efficacy and durability of 2-drug vs 3-drug INSTI-based regimens: data from real-life. In: Conference on retroviruses and opportunistic infections, Boston, MA, 8–11 March 2020. Poster 488.
30. Gagliardini R, Lorenzini P, Cozzi-Lepri A, et al. Effect of past virological failure on dolutegravir + lamivudine as maintenance regimen. In: Conference on retroviruses and opportunistic infections, Boston, MA, 8–11 March 2020. Poster 486.
31. Galizzi N, Poli A, Galli L, et al. Retrospective study on the outcome of two-drug regimens based on dolutegravir plus one reverse transcriptase inhibitor in virologically-suppressed HIV-infected patients. *Int J Antimicrob Agents* 2020; 55: 105893.
32. Smit M, Brinkman K, Geerlings S, et al. Future challenges for clinical care of an ageing population infected with HIV: a modelling study. *Lancet Infect Dis* 2015; 15: 810–818.
33. Guaraldi G, Orlando G, Zona S, et al. Premature age-related comorbidities among HIV-infected persons compared with the general population. *Clin Infect Dis* 2011; 53: 1120–1126.
34. Yang HY, Beymer MR and Suen SC. Chronic Disease onset among people living with HIV and AIDS in a large private insurance claims dataset. *Sci Rep* 2019; 9: 18514.
35. Greene M, Steinman MA, McNicholl IR, et al. Polypharmacy, drug-drug interactions, and potentially inappropriate medications in older adults with human immunodeficiency virus infection. *J Am Geriatr Soc* 2014; 62: 447–453.
36. Payne RA and Avery AJ. Polypharmacy: one of the greatest prescribing challenges in general practice. *Br J Gen Pract* 2011; 61: 83–84.
37. Okoli C, Schwenk A, Radford M, et al. Polypharmacy and potential drug-drug interactions for people with HIV in the UK from the climate-HIV database. *HIV Med* 2020; 21: 471–480.
38. Prabhu S, Poongulali S and Kumarasamy N. Impact of COVID-19 on people living with HIV: a review. *J Virus Erad* 2020; 6: 100019.
39. Sohn AH, Judd A, Mofenson L, et al. Using observational data to inform HIV policy change for children and youth. *J Acquir Immune Defic Syndr* 2018; 78(Suppl 1): S22–S26.
40. Ford N, Penazzato M, Vitoria M, et al. The contribution of observational studies in supporting the WHO 'treat all' recommendation for HIV/AIDS. *J Virus Erad* 2018; 4(Suppl 2): 5–8.
41. Dekker FW, de Mutsert R, van Dijk PC, et al. Survival analysis: time-dependent effects and time-varying risk factors. *Kidney Int* 2008; 74: 994–997.