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ORIGINAL RESEARCH

Effectiveness and safety of dolutegravir two-drug regimens in virologically suppressed people living with HIV: a systematic literature review and meta-analysis of real-world evidence

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Objectives

Dolutegravir (DTG) is widely recommended within three-drug regimens. However, similar efficacy and tolerability have also been achieved with DTG within two-drug regimens in clinical trials. This study evaluated the real-world effectiveness and discontinuations in people living with HIV-1 (PLHIV) switching to DTG with lamivudine (3TC) or rilpivirine (RPV).

Methods

This was a one-arm meta-analysis utilizing data from a systematic literature review. Data from real-world evidence studies of DTG + RPV and DTG + 3TC were extracted, pooled and analysed. The primary outcome was the proportion of patients with viral failure (VF; ≥ 50 copies/mL in two consecutive measurements and/or ≥ 1000 copies/mL in a single measurement) at week 48 (W48) and week 96 (W96). Other outcomes included virological suppression (VS; < 50 copies/mL) and discontinuations (W48 and W96). Estimates were calculated for VF, VS as per snapshot (VSS) and on treatment analysis (VSOT), and discontinuations.

Results

Pooled mean estimates of VF for DTG + 3TC and DTG + RPV were 0.8% [95% confidence interval (CI): 0.4–1.3] and 0.6% (95% CI: 0.0–1.6), respectively, at W48. VSS rate at W48 was 85.0% (95% CI: 82.3–87.5) for DTG + 3TC regimen and 92.4% (95% CI: 85.0–97.7) in the DTG + RPV regimen. The DTG + 3TC and DTG + RPV regimens led to discontinuations in 13.6% (95% CI: 11.1–16.2) and 7.2% (95% CI: 2.1–14.4) of patients, respectively, at W48. Similar results were observed at W96.

Conclusions

Treatment with DTG + 3TC or DTG + RPV in clinical practice provides a low rate of VF and a high rate of VS when initiated in virologically suppressed PLHIV with diverse backgrounds.

Keywords: antiretroviral therapy, dolutegravir, lamivudine, meta-analysis, real-world clinical trials, rilpivirine, two-drug regimen

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Introduction

Current guidelines recommend a three-drug combined antiretroviral therapy (ART) regimen consisting of an integrase strand inhibitor (INSTI) and two nucleoside/nucleotide reverse transcriptase inhibitors for treatment-naïve and virologically suppressed people living with HIV-1 (PLHIV) [1–4]. However, the European Acquired Immune Deficiency Syndrome (AIDS) Clinical Society (EACS) and US Department of Health and Human Services (DHHS) guidelines now also recommend the use of two-drug regimens in switch patients due to their efficacy [1,4]. Furthermore, two-drug regimens are of interest as several ART agents are associated with the risk of well-established, long-term toxicities, including reduced bone

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mineral density, renal failure or chronic kidney disease, cardiovascular disease and diabetes [5–11]. In addition, the high prevalence of co-morbidities associated with HIV leads to polypharmacy, thus increasing the risk of drug–drug interactions and serious adverse drug events [12,13].

Considering the lifetime requirements for PLHIV, risks associated with long-term drug exposure [14] may be mitigated, at least partly, by reducing exposure to ART agents where possible. INSTIs have been shown to be the most efficacious core agents [15,16] and are the preferred agent according to EACS and DHHS guidelines, with dolutegravir (DTG) being the preferred INSTI according to the World Health Organization (WHO) for both first- and second-line therapy [1–4]. DTG is a once-daily INSTI approved for the treatment of adults with HIV-1 (who do not have documented or suspected resistance to INSTIs) in combination with other ART agents [16,17]. DTG is considered to be among the most effective INSTIs and, therefore, is the core agent for the majority of triple ART regimens [15,16,18]. In addition to the clinical value of DTG forming part of three-drug regimens, several clinical trials and meta-analyses have shown that DTG-containing two-drug ART regimens, particularly the combinations of DTG with lamivudine (3TC) or rilpivirine (RPV), have similar efficacy in achieving and maintaining virological suppression (VS) in PLHIV. This is achieved whilst reducing the number of ART agents and potential risk of drug–drug interactions owing to the simplified regimen compared with triple ART regimens [14,19–24].

Two multicentre, double-blind, randomized, phase III trials demonstrated non-inferiority of DTG + 3TC *vs.* DTG + tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) for achieving VS in treatment-naïve PLHIV (GEMINI-1 and GEMINI-2) [20,21]. In these 48-week studies, the tolerability profiles were considered similar between the two regimens [20]. The combination of DTG and RPV was non-inferior compared with the triple ART regimen in the maintenance of VS over 48 weeks in patients who switched to the two-drug ART regimen from their current triple ART regimen in the open-label, parallel-group, multicentre, phase III, randomized, non-inferiority studies, SWORD-1 and SWORD-2 [25]. In addition, a recent randomized phase III study evaluated the efficacy and safety of switching to DTG + 3TC from a tenofovir alafenamide (TAF)-based regimen (TANGO study). Results showed that switching to DTG + 3TC was not inferior to continuing a TAF-containing regimen at week 48 {W48; snapshot virological failure: < 1% *vs.* < 1%; adjusted difference= −0.6% [95% confidence interval (CI): −1.3–0.2]}. The safety profile of the DTG + 3TC regimen was similar to that seen with the TAF-based regimen [26,27].

These clinical trials are encouraging the use of these two-drug ART regimens in clinical practice, and the EACS and DHHS now recommend the use of DTG + 3TC for naïve patients and DTG with 3TC or RPV in virologically suppressed switch patients. Furthermore, a plethora of real-world evidence using cohort, case–control, claims-database studies, and case series have been conducted to investigate DTG two-drug regimens in routine clinical practice. Here we present the results of a one-arm meta-analysis with the objective of providing an estimate of the real-world effectiveness and tolerability (as measured by discontinuation rate) of DTG when used as part of a two-drug regimen with either 3TC or RPV in treatment-experienced PLHIV.

Methods

Study identification

A systematic search of Embase, MEDLINE, MEDLINE In-Process and Cochrane databases was performed to identify real-world studies evaluating the effectiveness and/or safety of DTG in virologically suppressed PLHIV switching to DTG with 3TC or RPV (published in any language between 1 January 2013 and 4 April 2020, inclusive). Abstracts published in major HIV/AIDS conference proceedings between and including 1 January 2013 and 4 April 2020 were hand-searched to supplement the literature searches. Full details of the search strategy (including search terms and strings) are presented in Table S1. Conferences included in these searches are presented in Table S2.

Following the identification and removal of duplicate publications, a two-step screening process was undertaken to identify suitable studies: step 1 – the titles and abstracts of all publications identified by the literature searches were reviewed for eligibility; step 2 – full-text copies of all relevant publications identified during step 1 were obtained and reviewed against the same eligibility criteria. Eligible populations included adult PLHIV (studies including only children were excluded); no limits were applied based on gender or race. Eligible studies included observational cohort studies (both retrospective and prospective), case–control studies, claims-database studies and case series. Eligible interventions included DTG-based drug regimens. Case reports detailing information for only one patient and case series providing evidence for four patients or less were excluded.

Linked publications were identified based on population, sites and study period. Alongside linking publications, studies were also reviewed by the team to assess whether there was potential duplication in cohorts and

populations for which results were being reported. Where duplication of cohort/population was suspected, only the publication reporting the highest number of people receiving DTG + 3TC or DTG + RPV, the overarching study, was included in the analysis.

The Downs and Black assessment tool was used to assess the methodological quality of the included studies [28].

Data were extracted from selected publications by two independent reviewers, with any discrepancies resolved by a third reviewer. Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) data extraction and reporting guidelines were observed [29–31].

Outcomes

Outcomes included in the meta-analysis were the proportion of patients with viral failure (VF), VS using a snapshot algorithm (VSS), VS on treatment (VSOT), and the proportion of patients discontinuing treatment at weeks 48 and 96. VSS was calculated as follows: intent-to-treat (ITT) population − (VF + discontinuations). This analysis was conducted to supplement the results reported in the identified publications, aiming to overcome potential biases of overestimating the proportion of virally suppressed population, as many of the studies did not account for participants who were lost to follow-up or discontinued. The VF was defined as plasma viral load ≥ 50 copies/mL obtained in two consecutive measurements and/or > 1000 copies/mL obtained in a single measurement. The VSOT was defined as the proportion of patients achieving a specific reduction in HIV RNA copies/mL (usually < 50 copies/mL in accordance with FDA guidance [32]), over the number patients who remain on DTG + 3TC or RPV group at weeks 48 and 96.

Data analysis and quality assessments

Extracted data (including VS) were analysed using a fixed-effects model assuming asymptotically normally distributed variance and a random-effects model using restricted maximum likelihood or Bayesian methods to estimate variance. Root mean square error (RMSE) criteria were used to determine the best-fit model and guided the choice of the model used for the estimates. Statistical heterogeneity between studies was assessed using the following equation: $I^2 = (Q - \mathrm{df}/Q) \times 100\%$, where I is the level of inconsistency, Q is the χ^2 statistic and df the degrees of freedom. Publication bias for each outcome was analysed using a funnel plot (sample size *vs.* estimated effect size) and effect modification (i.e. between-study variations in treatment duration, dosage) analysed using meta-regression. Data are presented as the proportion of patients (percentage), standard error (SE; for study data), 95% CI (for meta-analysis data), weighting (for fixed and random effects), funnel plot asymmetry (*P*-value) and heterogeneity (I^2).

Results

Studies included

In total, the systematic literature review identified 394 studies from 530 publications that investigated DTG in PLHIV (Fig. 1). Of these, a total of 118 studies assessed DTG as a dual therapy (with 3TC or RPV) and reported data for effectiveness and/or discontinuations. Of the 118 studies, 82 studies were excluded as they included treatments other than DTG + 3TC and DTG + RPV, reported data at time points other than 48 or 96 weeks, or investigated treatment-naïve patients. Only two studies were identified investigating dual therapy in treatment-naïve patients; therefore, this analysis focused on treatment-experienced patients. Of the 36 studies in treatment-experienced suppressed patients, only seven studies reported effectiveness and/or discontinuation data for DTG + 3TC and 11 studies for DTG + RPV in cohorts believed to be unique and distinct from each other. Outcomes of interest (meta-analysis inputs) for studies providing W48 data are presented in Table 1 and those for studies providing W96 data are presented in Table S3. Results from a quality evaluation using the Downs and Black assessment tool can be found in Table S4.

Dual therapy with DTG + 3TC

Study and patient characteristics for the selected six studies with 48-week data are presented in Table 1. Males comprised 68.4–77.4% of the PLHIV. The mean age of PLHIV ranged from 48.5 to 59 years and all PLHIV were treatment-experienced suppressed. Most PLHIV switched from triple therapy [33–35]. Some populations also had PLHIV with resistance mutations including the M184I/V mutation for 3TC resistance [33–36]. PLHIV in Reynes *et al.* [36] were considered heavily pre-treated, whereas Hidalgo-Tenorio *et al.* [35] and Gagliardini *et al.* [37] included a population with no history of VF.

Outcomes

Five publications reported VF and VS data at W48; three publications reported data that enabled the calculation of VSS at W48 (Table 1). Overall, the meta-analysis showed that treatment of virologically suppressed patients with

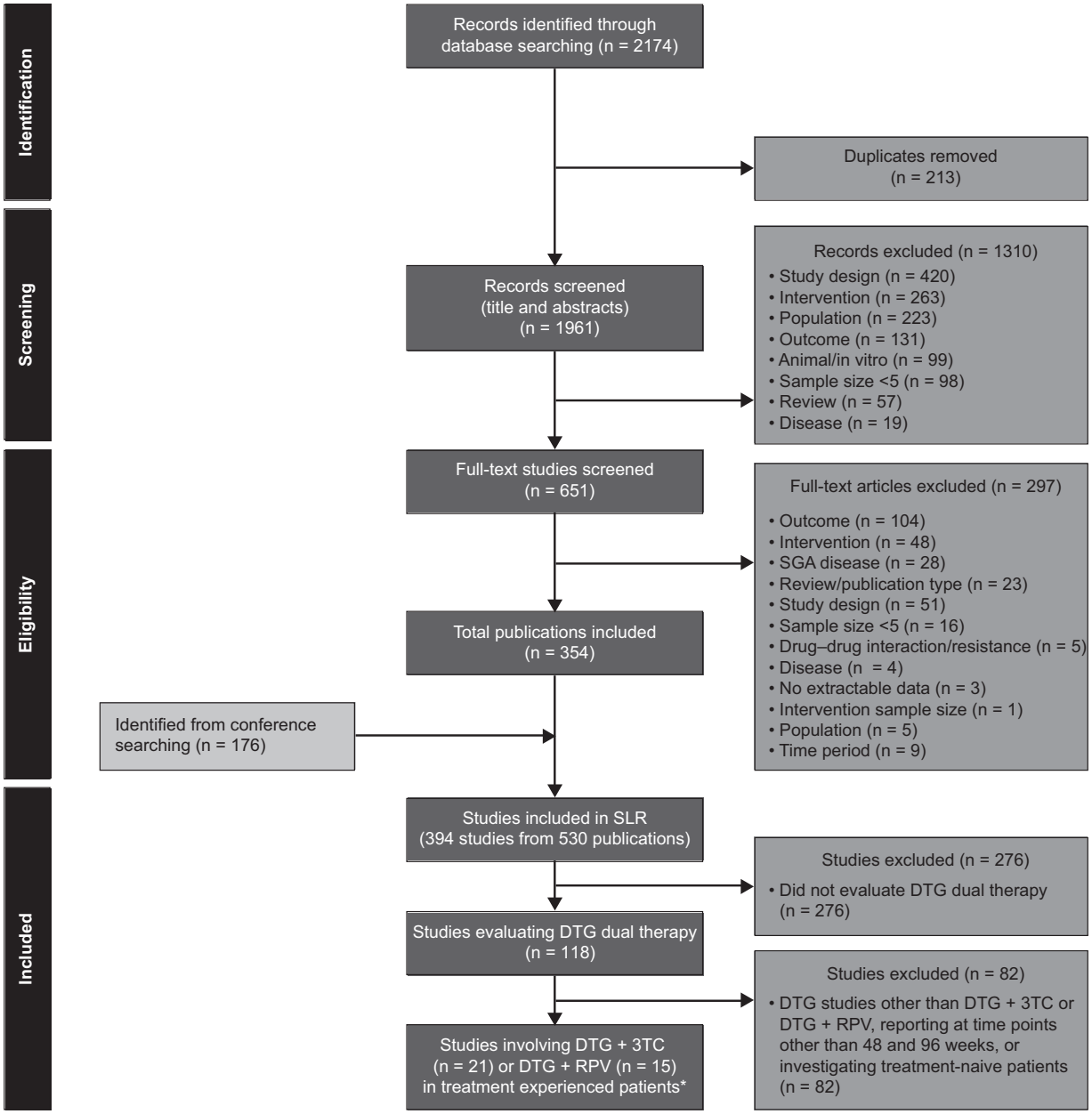

Fig. 1 PRISMA flow chart showing studies published from 2013 to 2019 investigating the use of dolutegravir (DTG) + lamivudine (3TC) and DTG + rilpivirine (RPV) in people living with HIV-1 (PLHIV). *One study evaluated both DTG + 3TC and DTG + RPV. ART, antiretroviral therapy; SGA, subgroup available; SLR, systematic literature review.

DTG + 3TC resulted in VF in 1.0% (95% CI: 0.3–2.0) of patients at W48 (Fig. 2a), with similar results reported at W96 (1.0%; 95% CI: 0.2–2.2; Fig. S1a). The VSS value was 85.0% (95% CI: 82.3–87.5) and 87.9% (95% CI: 76.6–96.0) at W48 (Fig. 2b) and W96 (Fig. S1b), respectively. The VSOT was 98.8% (95% CI: 97.7–99.7) at W48 (Fig. 2c), and 98.4% (95% CI: 96.4–99.7) at W96 (Fig. S1c). Heterogeneity between studies was assessed and found to be not significant enough to affect the analysis. Funnel plot analyses indicated that no publication bias was present in VF, VSOT and VSS data (P = 0.340, 0.228 and 0.706, respectively, at W48). Three publications reported data for discontinuations at W48. Overall, the meta-analysis showed that treatment with

Table 1 Summary of outcomes and patient characteristics for studies investigating dolutegravir (DTG) + lamivudine (3TC) or DTG + rilpivirine (RPV) in people living with HIV-1 (PLHIV) at week 48

Study (first author, year)	Mean age (years)	Male gender (%)	ITT* (*n*)	VSOT [% (95% CI)]	VF [% (95% CI)]	VSS [% (95% CI)]	Discontinuations [% (95% CI)]
DTG + 3TC							
Galizzi, 2020 [34]	52.5	68.4	307	97.7 (95.4–99.1)	2.3 (0.9–4.6)	_	_
Hidalgo-Tenorio, 2019 [35]	48.5	77.4	177	96.6 (92.8–98.7)	2.8 (0.9–6.5)	82.5 (76.1–87.8)	14.7 (9.8–20.8)
Balidin, 2019 [33]	51.0	68.8	556	98.7 (97.4–99.5)	1.3 (0.5–2.6)	84.7 (81.4–87.6)	13.8 (11.1–17.0)
Gagliardini, 2020 (no previous VF) [37]	50.0	75.5	772	99.6 (98.9–99.9)	0.4 (0.1–1.1)	_	_
Gagliardini, 2020 (previous VF) [37]	53.0	69.6	194	98.5 (95.5–99.7)	1.0 (0.1–3.7)	_	_
Reynes, 2016/2017 [36,48]	59	74	27	100.0 (87.2–100.0)	0 (0–1.3)	88.9 (70.8–97.6)	11.1 (2.4–29.2)
DTG + RPV							
Casado, 2019 [39]	54	72	102	96.1 (90.3–98.9)	1.0 (0.0–5.3)	93.1 (86.4–97.2)	5.9 (2.2–12.4)
Galizzi, 2020 [34]	53.5	80.6	67	98.5 (92.0–100)	_	_	_
Deschanvres, 2020 [49]	54.5	69.1	799	97.2 (95.9–98.3)	_	_	_
Bonijoly, 2017[50]	55	67	268	_	1.5 (0.4–3.8)	75.0 (69.4–80.1)	23.5 (18.6–29.0)
Diaz, 2016 [38]	53	66	38	100 (90.7–100.0)	0 (0–9.3)	92.1 (78.6–98.3)	7.9 (1.7–21.4)
Saling, 2016 [41]	-	50	14	100 (76.8–100.0)	–	100 (76.8–100.0)	0 (0–23.2)
Revuelta-Hererro, 2018 [40]	49	63	35	97.1 (85.1–99.9)	2.9 (0.1–14.9)	91.4(76.9–98.2)	5.7 (0.7–19.2)
Togami, 2016 [51]	57	96	25	100 (87.2–100.0)	0 (0–12.8)	96.3 (81.0–99.9)	7.4 (0.9–24.3)
Ciccullo, 2019 [52]	52	72	187	98.4 (95.4–99.7)	1.6 (0.3–4.6)	95.2 (91.1–97.8)	3.7 (1.5–7.6)
Grabmeier-Pfistershammer, 2016 [53]	54	81	43	100 (91.8–100.0)	0 (0–8.2)	93.0 (3.9)	7.0 (1.5–19.1)

ITT, intent to treat; SE, standard error; VF, viral failure; VSOT, viral suppression on treatment; VSS, viral suppression using snapshot algorithm.
*ITT population receiving DTG dual therapy.

DTG + 3TC in virologically suppressed PLHIV led to discontinuations in 13.6% (95% CI: 11.1–16.2) of patients at W48 (Fig. 2d). The proportion of discontinuations at W96 was 11.6% (95% CI: 4.50; 21.1); Fig. S1d). At W48, heterogeneity was 0% and funnel plot analyses indicated no publication bias ($P = 0.877$).

Dual therapy with DTG + RPV

Study and patient characteristics for the selected 10 studies included in the W48 analyses are presented in Table 1. In general, males accounted for 50–96% of the participants. The mean age of participants ranged from 49 to 57 years and all PLHIV were treatment-experienced and suppressed on current therapy. Some of the studies reported patient populations that could be considered heavily pre-treated (Diaz *et al.* [38] median 4.3 ARTs; Casado *et al.*: mean 6.1 prior regimens; and Revuelta-Hererro *et al.*: median 5 prior regimens (median 4 prior ARTs). In Diaz *et al.* [38], patients had a long history of ART (median 19.4 years). Some studies reported populations that contained patients with known resistance mutations [34,38–41].

Outcomes

Of DTG + RPV studies, eight publications reported VF and VSS data, and nine publications reported VSOT at W48 (Table 1). Overall, the meta-analysis showed that treatment with DTG + RPV in virologically suppressed PLHIV resulted in VF in 0.6% (95% CI: 0.0–1.6) of patients at W48 (Fig. 3a), with similar results reported at W96 (1.4%; 95% CI: 0.4–2.7%; Fig. S2a). The VSS values were 92.4% (95% CI: 85.0–97.7) and 92.8% (95% CI: 90.1–95.1) at weeks 48 (Fig. 3b) and 96 (Fig. S2b), respectively. The VSOT values were 98.5% (95% CI: 97.6–99.2) at W48 (Fig. 3c) and 97.3% (95% CI: 94.7–99.1) at W96 (Figure S2c). At W48, heterogeneity values for VF, VSS and VSOT were 0%, 86.6%, and 0%, respectively, at W48. Funnel plot analyses indicated that no publication bias was present in VF, VSOT and VSS data ($P = 0.591$, 0.214, and 0.190, respectively), at W48. Eight publications reported data for discontinuations at W48. Overall, the meta-analysis showed that treatment with DTG + RPV in virologically suppressed PLHIV led to discontinuations in 7.2% (95% CI: 2.1–14.4) of PLHIV at W48 (Fig. 3d). Slightly lower results were reported at W96 (5.7%; 95% CI: 3.7–8.2; Fig. S2d). Heterogeneity was 86.5% and funnel plot analyses indicated no publication bias ($P = 0.265$).

Discussion

The results of this real-world evidence meta-analysis support the use of DTG + 3TC or DTG + RPV as an effective maintenance therapy alternative to three-drug regimens in virologically suppressed treatment-experienced PLHIV. These results are consistent with a recent randomized phase III study evaluating the efficacy and safety of

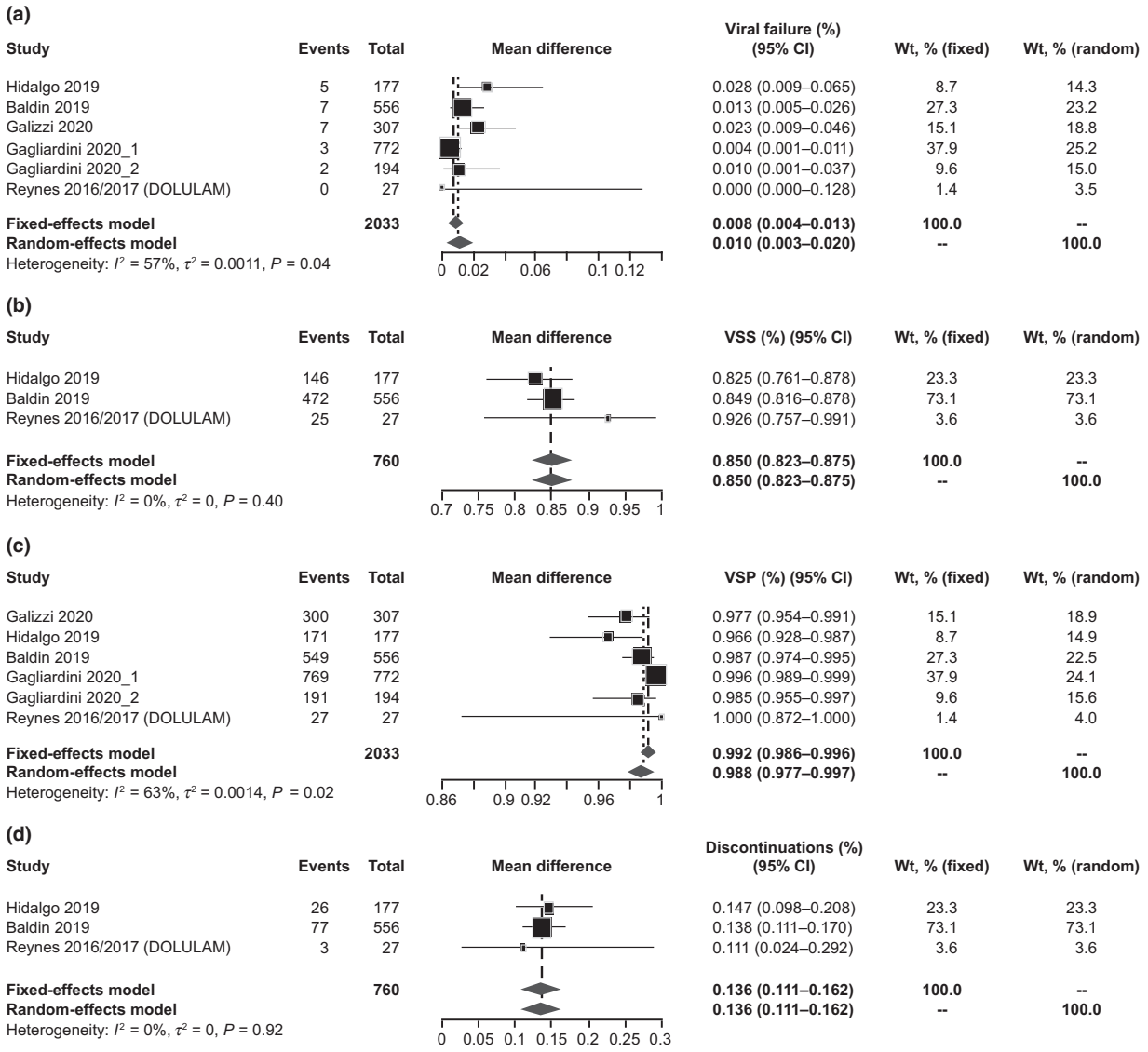

Fig. 2 Summary of week 48 meta-analysis data for dolutegravir (DTG) + lamivudine (3TC) treatment in people living with HIV-1 (PLHIV): (a) viral failure (VF); (b) viral suppression using snapshot algorithm (VSS); (c) viral suppression on treatment (VSOT); and (d) discontinuations. CI, confidence interval; Wt, weight.

switching to DTG + 3TC from a TAF-based regimen (TANGO study) and the randomized pilot clinical trial (ASPIRE), which investigated the efficacy of switching from triple therapy to DTG + 3TC. At W48, VF was 0% and VSS was 93% in TANGO while VF was 2% and VSS 91% in ASPIRE, which are comparable to the estimates determined in this meta-analysis. In addition, for DTG + RPV, the results from this meta-analysis are comparable to those reported in the SWORD-1 and SWORD-2 studies (VSS was 95% at W48) [25]. The SWORD-1 and SWORD-2 studies demonstrated non-inferiority of the dual regimen *vs*. current triple regimens and a similar safety profile in patients who had VS for the 6 months before screening. Moreover, our results for VF are comparable to real-world VF reported for DTG-based triple therapy (0.5–2.8%) [44–46].

The results of this analysis also support those of previous meta-analyses evaluating both randomized controlled trials and real-world evidence studies, which report a high virological efficacy with DTG-based dual maintenance therapy and a low potential for drug–drug interactions and toxicity [14,19]. Interestingly, in the

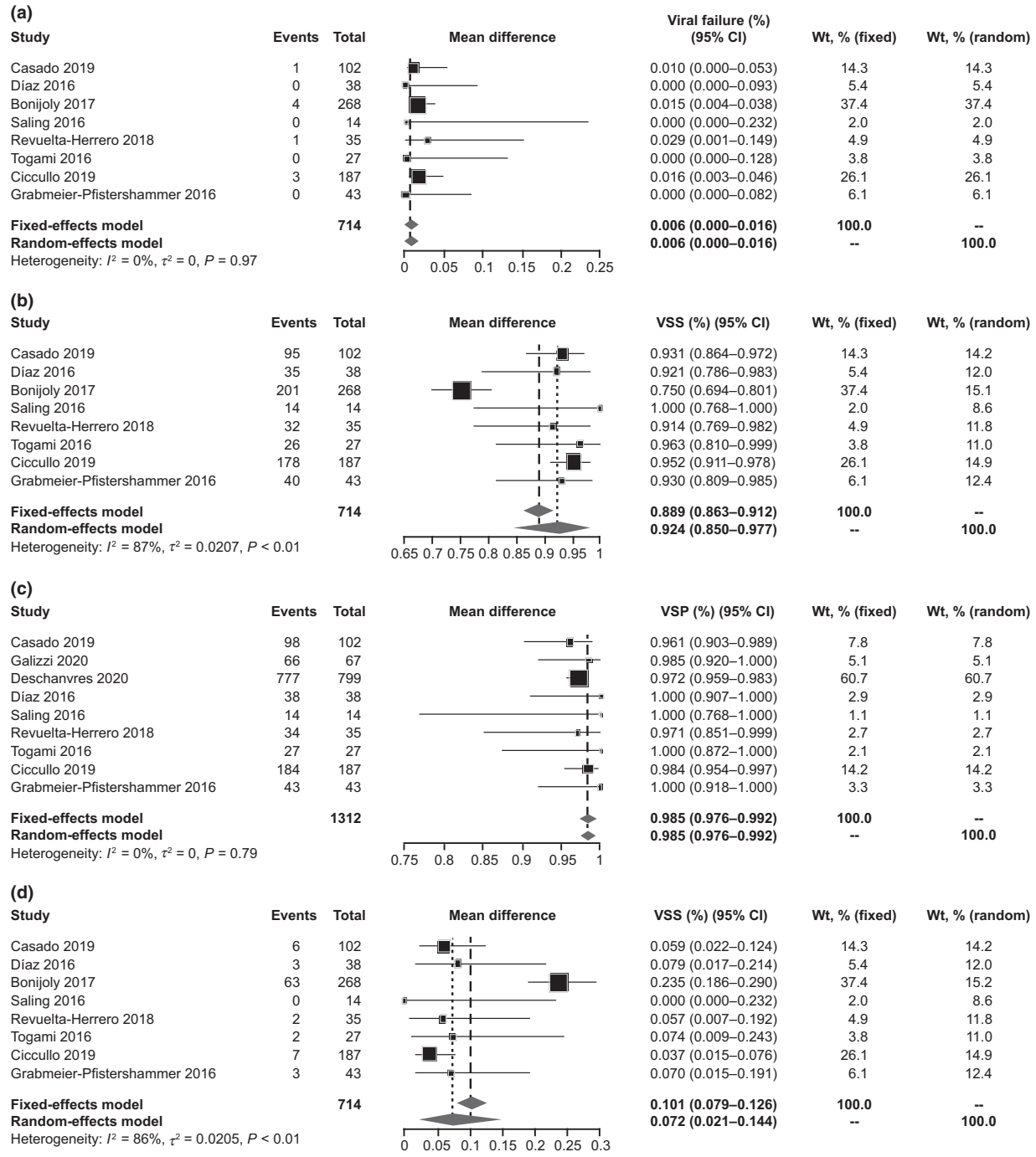

Fig. 3 Summary of week 48 meta-analysis data for dolutegravir (DTG) + rilpivirine (RPV) treatment in people living with HIV-1 (PLHIV): (a) viral failure (VF); (b) viral suppression using snapshot algorithm (VSS); (c) viral suppression on treatment (VSOT); and (d) discontinuations. CI, confidence interval; Wt, weight.

meta-analysis by Achhra *et al.* [14] no substantial difference in VF rate between dual ART and triple ART regimens was observed, although a higher rate was observed in treatment-naïve than in pre-treated suppressed patients. Unlike these previous meta-analyses, our study focused completely on real-world evidence, with broadly balanced patient populations across studies (i.e. results were not skewed by the population of a single study, e.g.

SWORD [19]), included published data up to March 2019 (published after approval of DTG + RPV), and specifically distinguished between DTG-containing dual ART regimens, thereby providing novel information to support clinicians with real-world treatment decisions.

Strengths of this meta-analysis include long-term evidence (up to 96 weeks) in a real-world setting, making it applicable to patients in clinical practice. Furthermore, there were no restrictions with regard to geographical region, and although most studies were conducted in Europe, this meta-analysis provides a more global picture of the use of DTG-containing, two-drug, ART regimens than previous studies of this kind [19]. It is also important to note that the lack of restrictions on inclusion criteria in real-word studies leads to substantial variations in patient populations, including multiple treatment backgrounds, different durations of treatment exposure, the presence of resistance mutations, experience of previous treatment failures and other characteristics that would normally exclude patients from randomized clinical trials, but may be more representative of real-world clinical settings. Some patients included in this analysis were heavily pre-treated (maximum reported median of nine prior regimens), had long treatment histories (maximum reported mean = 19.4 years), had experienced prior VFs, or had detectable resistance mutations. Despite this variability in treated patients, our results were consistent with those observed in DTG + 3TC or DTG + RPV RCTs.

Despite the potential variability of real-world data, the effectiveness and tolerability outcomes for DTG + 3TC or DTG + RPV were generally consistent across studies included in this meta-analysis. These results should provide reassurance to clinicians that treatment of HIV with DTG + 3TC or DTG + RPV can be effective in diverse virologically suppressed, treatment-experienced patients outside of a clinical trial environment. Moreover, the endpoints reported in this meta-analysis are consistent with those used in randomized controlled trials and are widely used in clinical practice. This meta-analysis also included snapshot data, which considers the ITT population, including the proportion of discontinuations or those lost to follow-up in the analysis. This provides a more stringent view of treatment success than simply reporting proportions of VS among patients who remained in the study up to W48 and W96 and ignoring patients who have discontinued treatment for various reasons.

This study was a single-arm meta-analysis and was thus associated with limitations such as lack of a control group and publication bias. Additional limitations of this analysis include those inherent to real-world studies, such as non-randomization, no control for confounding factors, coding errors and determination of causality. As this meta-analysis focused on outcomes at W48 and W96, and the studies pertaining to data at these two time points varied, there is a potential for inconsistent results, with outcomes, such as VF, being higher at W48 than at W96. Furthermore, safety and tolerability data (adverse events, mortality), drug–drug interactions, and co-morbidities were not included in the meta-analysis as the information was not consistently reported across studies. Likewise, 96 weeks may not be a long enough follow-up to capture some co-morbidities. Snapshot data were not consistently reported across real-world studies; however, this outcome could be calculated based on study data in many cases for the purpose of this meta-analysis [32]. Furthermore, while the two-drug regimens DTG + 3TC and DTG + RPV may provide a suitable treatment option for most patients, physicians should always evaluate the suitability of such regimens when considering a regimen switch in virologically suppressed patients including factors such as pre-existing resistance and hepatitis B virus coinfection.

Conclusions

Overall, the results of this one-arm meta-analysis show that treatment with a two-drug regimen of DTG + 3TC or DTG + RPV in clinical practice provides a low rate of VF and a high rate of viral suppression in pre-treated PLHIV who were suppressed at treatment initiation. Furthermore, viral suppression was shown to be maintained across patient populations and treatment histories of the individual studies included in this meta-analysis.

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Conflict of interest: YP, DP, LE, VC, JvW, and AdR are employees of ViiV Healthcare. YP and LE hold shares in GSK. AdR holds shares in GSK and ViiV Healthcare. MJ, DJ and SF are employees of GSK. SK and SS are employees of Parexel, who was commissioned by ViiV Healthcare to conduct this study. MR is a former employee of ViiV Healthcare and holds stock in GSK and ViiV Healthcare.

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review, data analysis, data interpretation, and writing of the report.

Author contributions

The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors, take responsibility for the integrity of the work as a whole, contributed to the writing and reviewing of the manuscript, and have given final approval for the version to be published. All authors had full access to the data in this study and take complete responsibility for the integrity of the data and accuracy of the data analysis.

Ethics approval and informed consent

Ethics approval and patient consent were not required, because this was a meta-analysis based on previously published study data.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1 Search terms, strings and strategy for systematic literature review in (A) Embase and MEDLINE databases, (B) Cochrane database, and (C) PubMed platform.

Table S2 Conference proceedings searched to supplement the literature review.

Table S3 Summary of outcomes and patient characteristics for studies investigation DTG + 3TC or DTG + RPV in PLWHIV at Week 96.

Table S4 Results of the Downs and Black assessment tool (11)

Fig. S1 Summary of Week 96 meta-analysis data for DTG + 3TC treatment in PLWHIV: (A) viral failure, (B) VSS, (C) VSP, and (D) discontinuations.

Fig. S2 Summary of Week 96 meta-analysis data for DTG + RPV treatment in PLWHIV: (A) viral failure, (B) VSS, (C) VSP, and (D) discontinuations.