EFFECTIVENESS AND TOLERABILITY OF DTG+3TC IN CLINICAL PRACTICE: EVIDENCE IN PLHIV FROM REAL-WORLD DATA

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Introduction

- Clinical trials have shown dolutegravir (DTG) + lamivudine (3TC) to be an efficacious, well-tolerated and durable regimen for therapy-experienced and therapy-naive people living with HIV (PLHIV)[1-6]
- DTG+3TC is recommended by major regional and international guidelines as a switch strategy for virologically suppressed PLHIV[7-9] and for the initial treatment of naive PLHIV
- This is an update of previously published analyses to include more recently published data[10,11]

Objective

- The objective of this project was to identify published real-world evidence (RWE) for DTG+3TC in PLHIV and conduct a meta-analysis to estimate effectiveness and tolerability of DTG+3TC in PLHIV by combining RWE from clinical practice

Methods

- A systematic literature review of PubMed and Embase along with 24 regional and international conferences was conducted between January 2013 and August 2021 to identify RWE studies of DTG+3TC in PLHIV
- Eligible published articles presenting outcomes of interest for therapy-experienced (suppressed and non-suppressed at switch) and therapy-naive PLHIV were identified, and data were extracted. Note, studies would be included if contributing >1 endpoint at timepoint of interest. Therefore, differences in studies and populations included in each analysis may differ
- Meta-analysis primary outcome: proportion of patients with virological suppression (<50 copies/mL) at week 48 (W48) and week 96 (W96). Secondary outcomes: virological failure and discontinuations at W48 and W96
- One-arm meta-analysis was used to estimate effect sizes for (a) virological suppression (VS) as per snapshot (ITT-E population – virological failure - discontinuations) and on-treatment analysis, (b) virological failure (defined as ≥50 copies/mL in two consecutive measurements and/or ≥1000 copies/mL in a single measurement), and (c) discontinuations from DTG+3TC
- Based on the information available in the publications, studies including duplicate patient populations were removed to avoid double counting of PLHIV
- The endpoint estimates were calculated using fixed effects and random effects models, and the model with the best fit was reported. The studies were weighted according to the inverse of variance estimates, which included inter and intra study variance. Forest plots were constructed to report the effect size and 95% confidence intervals (CIs) for each study, as well as overall estimated summary effect size and 95% CI for each outcome variable
- The heterogeneity among the studies was assessed using the I^2 (inconsistency) statistic. A low P value (<0.05) would provide statistical evidence of heterogeneity among studies and indicate a random effects model is more appropriate than fixed effects
- For further information on methods please refer to previous reporting[10,11]

Results

Systematic Literature Review

- A total of 89 RWE studies, comprising >5,000 PLHIV using DTG+3TC in a real-world setting, were identified
- The studies identified included >200 ART-naive PLHIV reporting effectiveness in total

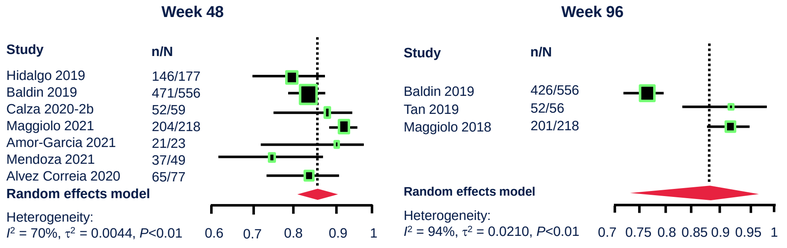
Meta-analysis

- A total of 11 DTG+3TC studies (n=3,021 PLHIV) reported data on therapy-experienced virologically suppressed PLHIV with at least one outcome of interest at a timepoint of interest.[12-22] Three studies were identified meeting the same criteria in therapy-naive PLHIV (n=152)[23-25]
- Studies were included in each analysis if relevant data were reported (not all studies are included in each analysis)

Therapy-Experienced Patients

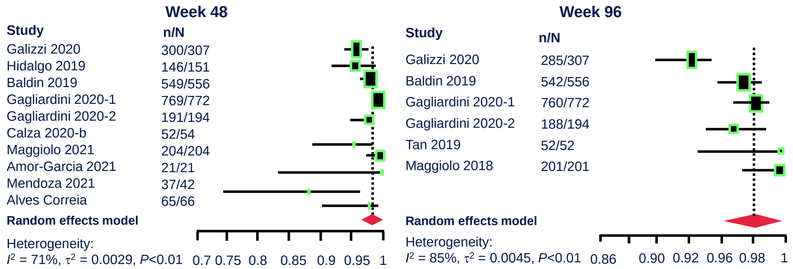
- For therapy-experienced PLHIV, results from random effects models were reported due to high heterogeneity demonstrated in the analysis
- In the snapshot analysis, the viral suppression rate for DTG+3TC was 86.4% (95% CI: 81.7, 90.5) and 87.6% (95% CI: 74.2, 96.7) at W48 and 96, respectively; Figure 1
- For on-treatment analysis, the viral suppression rate for DTG+3TC was 98.7% (95% CI: 97.3, 99.6) and 98.1% (95% CI: 96.0, 99.5) at W48 and 96, respectively; Figure 2
- Of the 8 studies (n=1976) in therapy-experienced patients that reported baseline resistance testing, no cases of treatment-emergent resistance were reported[12-19]

Figure 1. Snapshot Viral Suppression Rates in Therapy-Experienced PLHIV



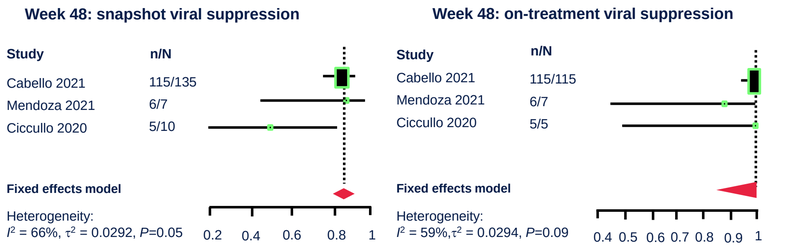
I^2 and τ^2 are measures of quantification of heterogeneity, P<0.05 is significant heterogeneity, n = Number of events, N = Total patients evaluated for the event.

Figure 2. On-Treatment Viral Suppression Rates in Therapy-Experienced PLHIV



I^2 and τ^2 are measures of quantification of heterogeneity, P<0.05 is significant heterogeneity, n = Number of events, N = Total patients evaluated for the event.

Figure 3. Snapshot and On-Treatment Viral Suppression Rates in Therapy-Naive PLHIV



I^2 and τ^2 are measures of quantification of heterogeneity, P<0.05 is significant heterogeneity, n = Number of events, N = Total patients evaluated for the event.

Therapy-Naive PLHIV

- For therapy-naive PLHIV, data points of interest were available only for timepoint W48. Fixed-effects model results are reported due to low heterogeneity (Figure 3, Table 1)
- In the snapshot analysis, viral suppression rate for DTG+3TC at W48 was 85.4% (95% CI: 78.6, 91.3); Figure 3
- For on-treatment analysis, viral suppression rate for DTG+3TC at W48 was 100% (95% CI: 100.0, 100.0); Figure 3
- None of the three studies in therapy-naive patients reported therapy-emergent resistance

Table 1. Results of Virological Failure and Discontinuation Rates in Therapy-Experienced and Therapy-Naive PLHIV

Effect size (95% CI)	n/N	Week 48	n/N	Week 96
Therapy-experienced patients				
Virological failure	44/2965	1.2% [0.4; 2.2]	58/2329	1.7% [0.5; 3.4]
Discontinuations	145/1159	11.9% [8.5; 15.6]	137/830	11.7% [3.8; 23.0]
Therapy-naive patients				
Virological failure	1/152	0% [0.0; 0.0]	NA	NA
Discontinuations	25/152	13.6% [0.079; 0.203]	NA	NA

n = Number of events, N = Total patients evaluated for the event.

Limitations

- This was a single-arm, non-comparative analysis with inherent clinical heterogeneity between included studies; several studies included in the analysis had a small sample size (n ≤50)

Conclusions

- Data from over 5,000 PLHIV using DTG+3TC in a real-world setting are available including >200 therapy-naive PLHIV reporting effectiveness outcomes
- DTG+3TC is an effective, tolerable and durable antiretroviral regimen with low rates of discontinuation in therapy-naive and -experienced PLHIV in clinical practice
- In studies with baseline resistance testing, no cases of treatment-emergent resistance reported in therapy-naive and -experienced PLHIV in clinical practice
- These results support findings from phase 3 clinical trials both in therapy-naive and -experienced PLHIV
- High rates of effectiveness, long-term durability (RWE reporting up to 5 years), low rates of discontinuations, high barrier to resistance

Acknowledgments

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