Is DTG+3TC and DTG+RPV Effective and Safe in Clinical Practice? Evidence From Real World Data

MOPEB267

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Introduction

- Combinations of dolutegravir (DTG) with lamivudine (3TC) or rilpivirine (RPV) are attractive therapeutic options for PLHIV and healthcare providers because they provide a simplified and complete regimen with two well-established agents instead of three.
- DTG+3TC and DTG+RPV have been proven to be efficacious with good safety profiles in pivotal RCTs in naive and treatment-experienced HIV-infected patients, respectively.
- Several real-world studies have shown that DTG+3TC and DTG+RPV are also effective in virologically suppressed patients in clinical practice.

Objectives

- The objective of this study was to estimate the effectiveness and safety of DTG+3TC and DTG+RPV when initiated in virologically suppressed HIV-infected patients using meta-analysis techniques.

Methods

- A systematic literature review of PubMed and Embase along with 20 regional and international conferences was conducted between Jan 2013 and Mar 2019 to identify RWE studies of DTG+3TC or DTG+RPV in virologically suppressed HIV-infected patients. Eligible published articles presenting outcomes of interest were identified and extracted.
- Primary outcome of interest was the proportion of patients with virological suppression (<50 copies/mL) at Week 48 (W48) and Week 96 (W96). Other outcomes included viral failure and discontinuations, evaluated at W48 and W96.
- One-arm meta-analyses were conducted to estimate effect sizes for virological suppression as per snapshot (ITT-E population – viral failure - discontinuations) and per-protocol type analysis, viral failure and discontinuations for DTG+3TC and DTG+RPV separately. Dependent on the availability of published data, different sets of studies were included for different endpoints and timepoints. Meta-regression was used to estimate the effect of demographic and clinical characteristics on effectiveness and safety outcomes.
- The endpoint estimates were calculated using fixed effects and random effects model. The studies were weighed according to the inverse of variance estimates, which included inter and intra study variance. Forest plots were used 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, which was also used to select between fixed or random effects models. The selected model is reported here.

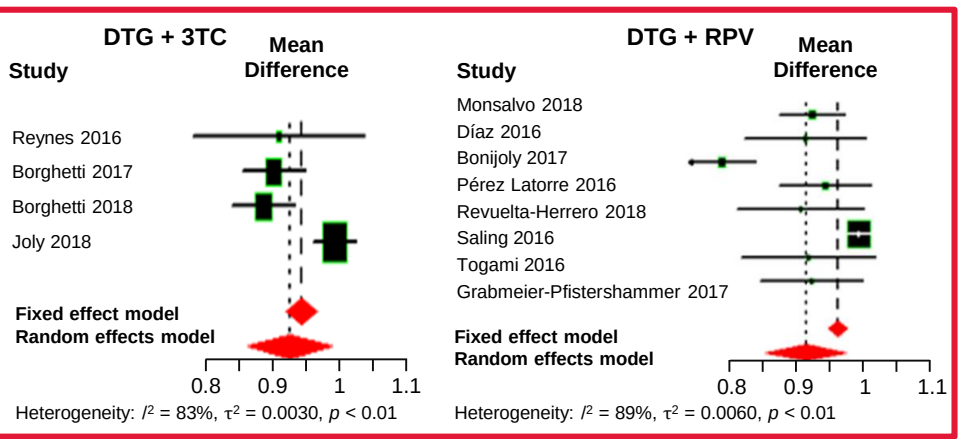
Results

- A total of 8 DTG+3TC studies (n=1,343) and 11 DTG+RPV studies (n=1,084) reported data on virologically suppressed HIV-infected patients with outcomes of interest at different time points. Two studies (n=140) reported data on DTG+3TC in treatment-naive patients. Most of the studies were from Europe while one each was conducted in the US and Japan.
- Studies of DTG+3TC and DTG+RPV in treatment-experienced patients were meta-analysed. No analysis was conducted in treatment-naive patients.

Snapshot analysis of viral suppression at Week 48 and Week 96

- In the snapshot analysis, random effects viral suppression rate at W48 was 90.6% (95% CI: 0.844, 0.967) for DTG+3TC regimen and 92.2% (95% CI: 0.863, 0.981) for DTG+RPV regimen (Figure 1). At W96, random effects viral suppression rate was 89.5% and 93.7% for DTG+3TC and DTG+RPV, respectively (Table 1).

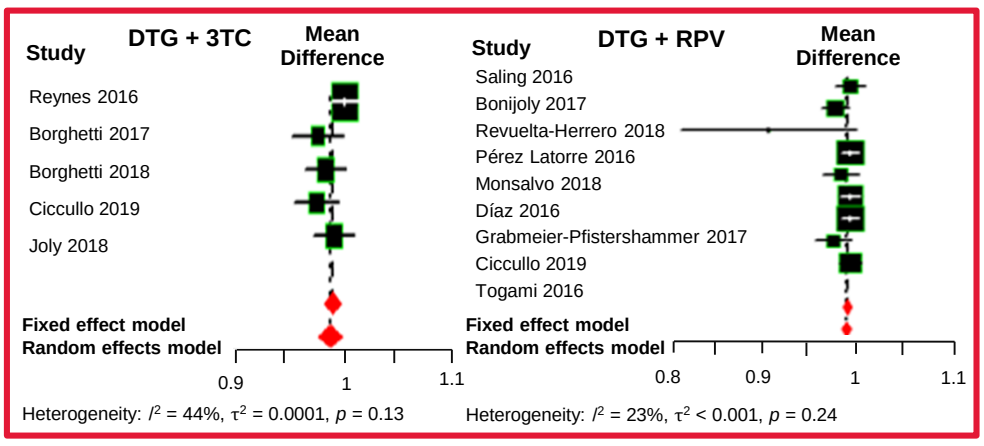
Figure 1. Snapshot Analysis for Viral Suppression at Week 48 - DTG+3TC and DTG+RPV



Viral suppression at Week 48 and Week 96

- Fixed effects pooled estimates for viral suppression at W48 were 98.9% (95% CI: 0.981, 0.997) in patients treated with DTG+3TC regimen and 99.7% (95% CI: 0.993, 1.00) in patients treated with DTG+RPV regimen (Figure 2).
- The results were sustained until W96, with 97.5% of patients maintaining suppression for DTG+3TC and 96.9% for DTG+RPV (fixed effect pooled estimate, Table 1).

Figure 2. Forest Plot – Viral Suppression at Week 48 - DTG+3TC and DTG+RPV



Viral failure at Week 48 and Week 96

- Results showed that at W48, there were 1.2% (95% CI: 0.004, 0.020) viral failures for DTG+3TC regimen in random effects analysis and 0.2% (95% CI: 0.0, 0.007) for DTG+RPV regimen in fixed effects analysis (Figure 3).
- Rates of viral failure at W96 for DTG+3TC (random effect model) was 1.8%, and for DTG+RPV (fixed effect model) was 1.5%.

Figure 3. Forest Plot – Viral Failure at Week 48 - DTG+3TC and DTG+RPV

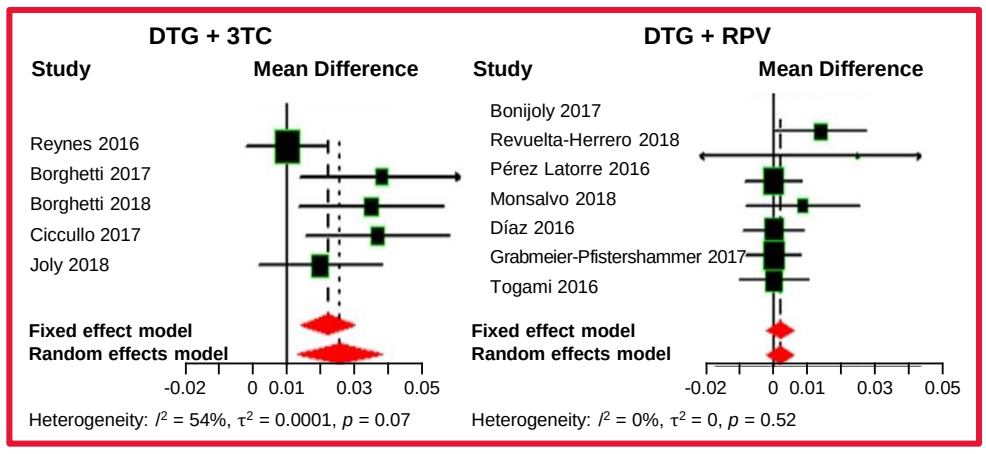
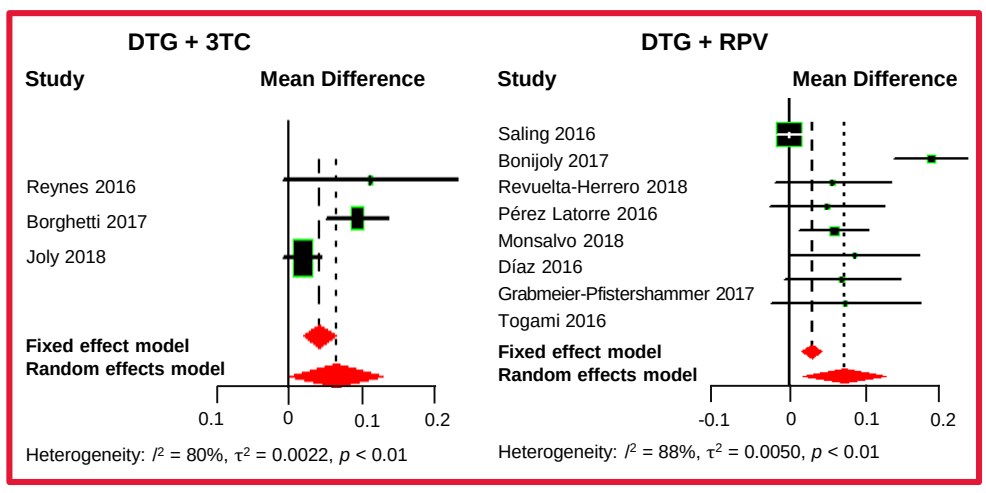


Figure 4. Forest Plot – Rate of Discontinuations at Week 48 - DTG+3TC and DTG+RPV



Rate of discontinuations at Week 48 and Week 96

- Random effects model estimated the rate of discontinuations for DTG+3TC regimen and DTG+RPV regimen at W48 to be 6.4% (95% CI: 0.001, 0.127) and 7.2% (95% CI: 0.018, 0.127), respectively (Figure 4).
- At W96, the rate of discontinuations observed for DTG+3TC and DTG+RPV (random effects model) was 9.2% and 4.7%, respectively (Table 1).

Table 1. Results of Viral Suppression, Viral Failure and Discontinuations for DTG+3TC and DTG+RPV at Week 96 (Random Effects Model)

Effect size (95% CI)	DTG+3TC	DTG+RPV
Snapshot analysis of viral suppression at W96	0.895 (0.842, 0.949)	0.937 (0.898, 0.976)
Viral suppression at W96	0.975 (0.958, 0.992)	0.969 (0.955, 0.984)*
Viral failure at W96	0.018 (0.005, 0.031)	0.015 (0.005, 0.024)*
Discontinuation at W96	0.092 (0.028, 0.155)	0.047 (0.014, 0.080)

*Fixed effects models were used

Meta-regression

- The results of meta-regression analysis showed that age and baseline CD4 count had no significant impact on viral suppression, viral failure and proportion of discontinuations at W48 for DTG+RPV regimen. There was insufficient data to conduct these analyses at W96.

Conclusion

- DTG+3TC and DTG+RPV are antiretroviral regimens that are effective and durable with low rates of virological failure and discontinuation when initiated in virologically suppressed treatment-experienced HIV patients in clinical practice

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