

Introduction

- Evidence from randomized clinical trials has shown that dolutegravir+lamivudine (DTG+3TC) is an efficacious and durable regimen with an acceptable safety profile for treatment-naïve and treatment-experienced people living with HIV (PLHIV)
- DTG+3TC is also recommended in treatment guidelines as first line treatment for naïve patients
- With its potential benefits as a simplified regimen with high barrier to resistance and favourable drug-drug interaction profile, DTG+3TC is a treatment alternative to established 3-drug regimens
- The aim of the current study was to extend the findings from a previously conducted meta-analysis, which had demonstrated the effectiveness and durability of DTG+3TC in a real-world population (Punekar 2019)

Objective

- The objective of this meta-analysis was to estimate the effectiveness and safety of DTG+3TC in treatment-experienced PLHIV by combining real-world evidence (RWE) from clinical practice

Methods

- A systematic literature review of PubMed and Embase along with 20 regional and international conferences between January 2013 and April 2020 was conducted to identify RWE studies of DTG+3TC in PLHIV
- Eligible published articles presenting outcomes of interest were identified and data extracted
- Primary outcome: Proportion of patients with virological suppression (<50 copies/mL) at Week 48 (W48) and Week 96 (W96)
- Secondary outcomes: Viral failure and discontinuations at W48 and W96
- One-arm meta-analysis was used to estimate effect sizes for (a) virological suppression as per snapshot (ITT-E population – viral failure – discontinuations) and on-treatment type analysis, (b) viral failure, and (c) discontinuations from DTG+3TC
- Based on the information available in the publications, studies including duplicate patient populations were removed
- Based on the availability of published data, different sets of studies were included for different endpoints and time points
- The endpoint estimates were calculated using fixed effects and random effects models. 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 I² (inconsistency) statistic. An I² value of >50% or a low p value (<0.05) indicated heterogeneity among studies wherein a random effects model is preferred

Results

- A total of 12 DTG+3TC studies (n=3039) reporting data on virologically suppressed PLHIV on outcomes of interest at different time points were identified
- Studies of DTG+3TC in treatment-experienced PLHIV were used in meta-analysis. Only one study was identified in treatment-naïve PLHIV; therefore, no analysis was conducted in this population
- Since the I² value of >50% and p value of <0.05 were observed in all the analysis, random effect was considered as the representative model. However, results of fixed effect model were also presented in the respective forest plots

Snapshot Analysis of Viral Suppression

- In the snapshot analysis, random effects viral suppression rate for DTG+3TC at W48 was 87.8% (95% CI: 83.1, 91.8) and, at W96, was 85.5% (95% CI: 79.4%, 90.7; Figure 1)
- Results from fixed-effect model are presented in Table 1

Viral Suppression Among On-Treatment Population

- Random effects pooled estimates for viral suppression at W48 and W96 were 98.6% (95% CI: 97.7, 99.3) and 97.5% (95% CI: 95.8, 98.8), respectively, in patients treated with DTG+3TC regimen (Figure 2)
- Results from fixed effects model are presented in Table 1

Viral Failure

- Results showed that, at W48, there were 1.3% (95%CI: 0.6, 2.1) viral failures for DTG+3TC regimen in the random effects model. At W96 analysis, 2.0% (95% CI: 0.9, 3.5) viral failure was reported for the DTG+3TC regimen in random effects analysis (Figure 3)
- No study reported presence of treatment emergent resistance

Figure 1. Viral Suppression – Snapshot Analysis

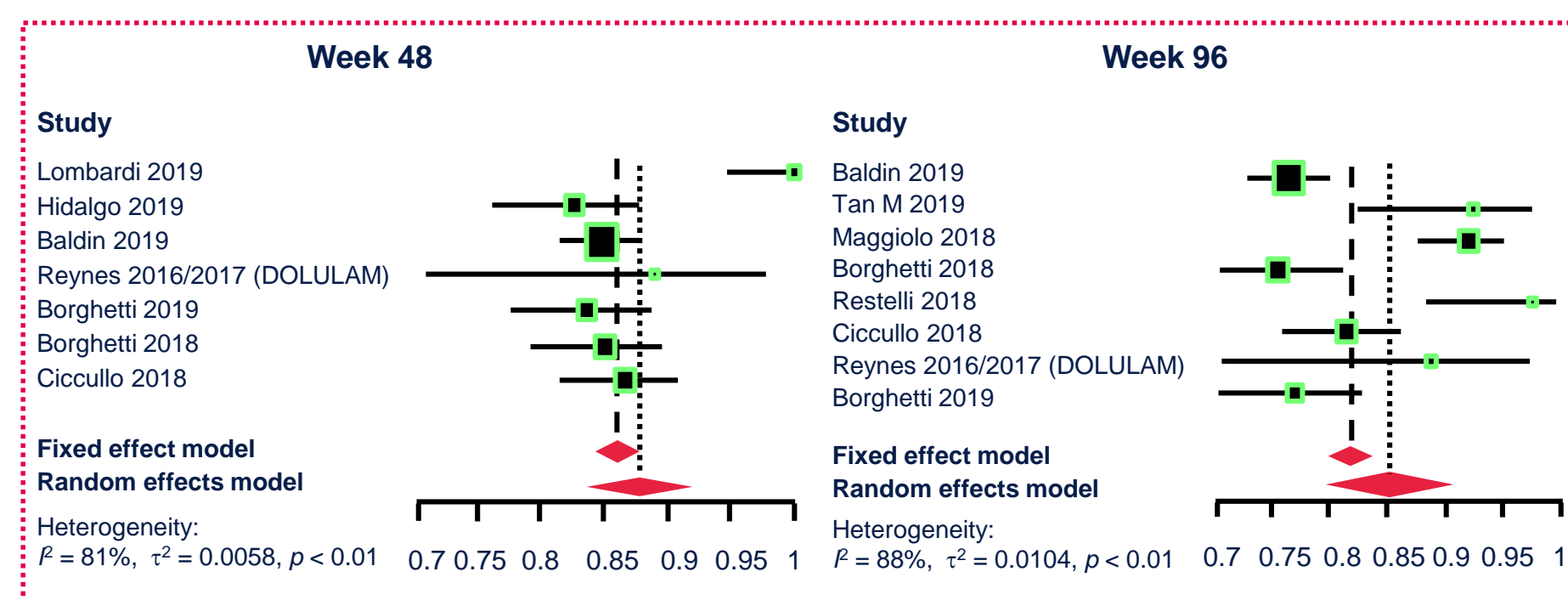


Figure 2. Viral Suppression – On-Treatment Analysis

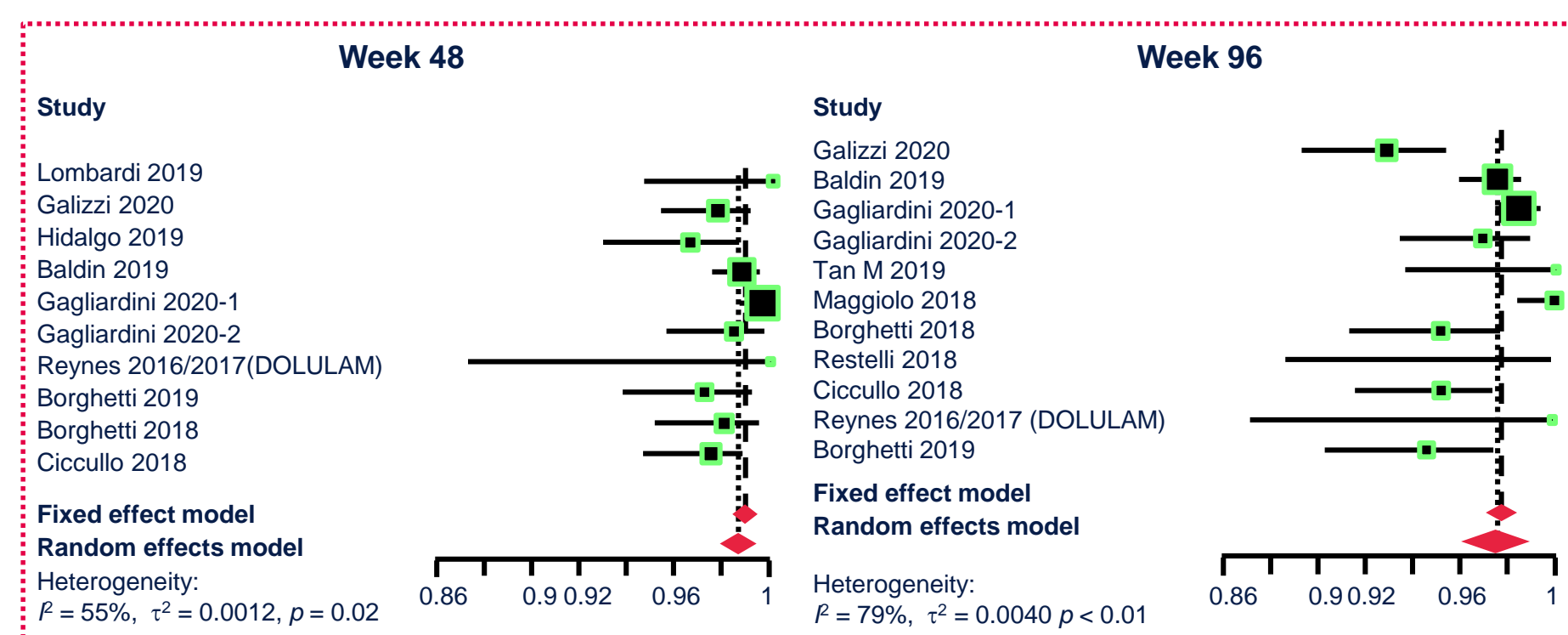
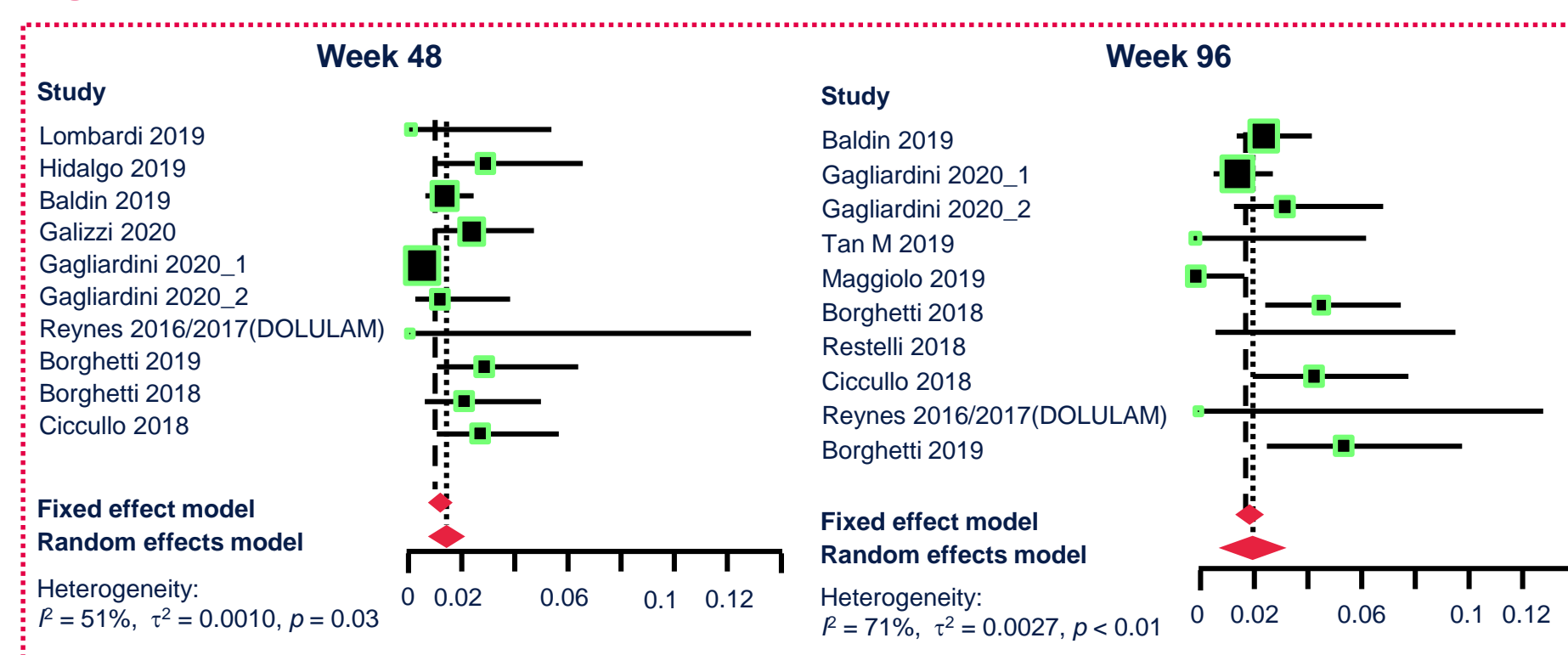


Figure 3. Viral Failure



Rate of Discontinuations

- Random effects model estimated the rate of discontinuations for DTG+3TC regimen at W48 and W96 as 10.4% (95% CI: 6.9, 14.4) and 11.8% (95% CI: 0.7.3, 17.2), respectively (Figure 4)
- Results from fixed effects model are presented in Table 1

Figure 4. Discontinuation Rate

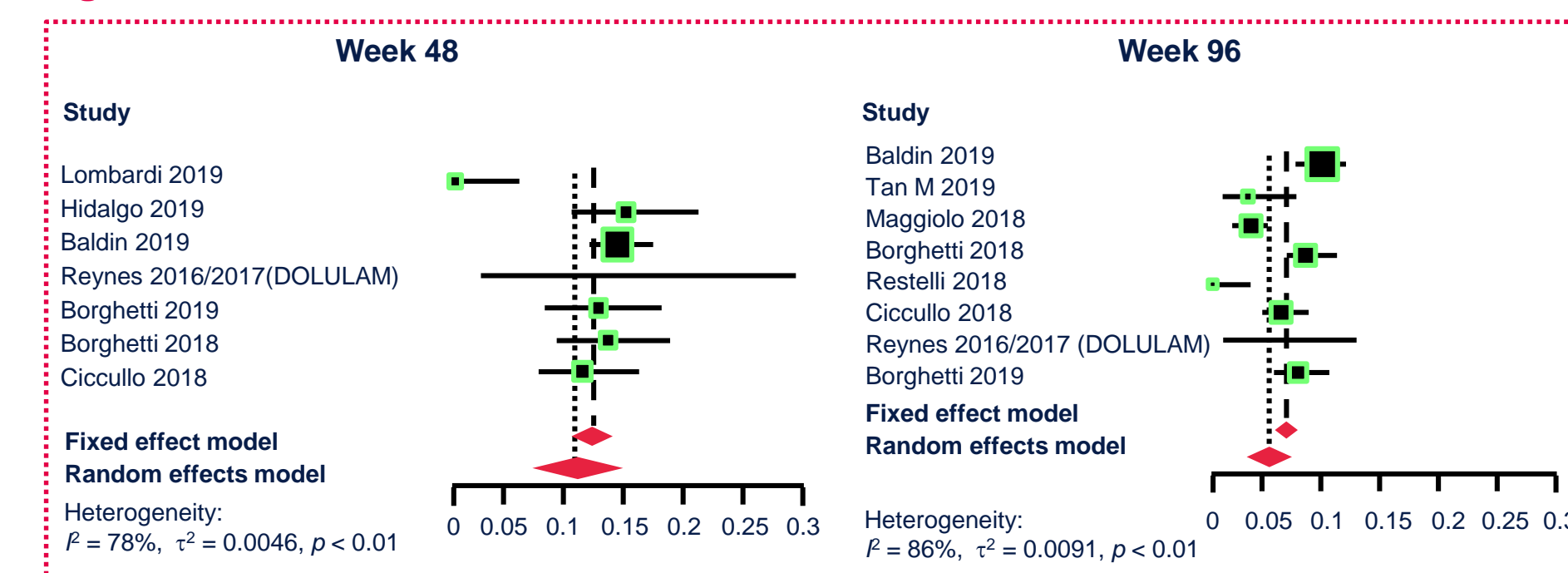


Table 1. Results of Viral Suppression, Viral Failure, and Discontinuations (Fixed Effects Model)

| Effect size (95% CI) | Week 48 | Week 96 |
|----------------------------------|--------------------|--------------------|
| Viral suppression – Snapshot | 86.1% [84.2; 87.8] | 81.9% [79.9; 83.8] |
| Viral suppression – On treatment | 98.9% [98.4; 99.3] | 97.6% [97.0; 98.2] |
| Viral failure | 1.0% [0.6; 1.5] | 1.9% [1.4; 2.6] |
| Discontinuation | 11.8% [10.2; 13.6] | 15.2% [13.4; 17.0] |

Limitations

- This was a single arm non-comparative analysis with inherent clinical heterogeneity between included studies
- A few studies included in the analysis had a small sample size (n≤50)
- Subgroup analysis and meta-regression were not conducted to explore the sources of potential heterogeneity as part of current meta-analysis

Conclusions

- DTG+3TC is an effective and durable antiretroviral regimen with low rates of discontinuation in virologically suppressed treatment experienced PLHIV in clinical practice
- Present results support findings from previous RWE meta-analysis and phase 3 clinical trials
- Further data are required to assess the translation of clinical trial results to clinical practice in treatment-naïve PLHIV

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