Effectiveness of Dolutegravir + Lamivudine in Real-world Studies in People With HIV-1 With M184V/I Mutations: A Systematic Review and Meta-analysis

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Key Takeaways

- Using real-world data from people with HIV-1 (PWH), a systematic literature review and a meta-analysis were performed to investigate the impact of historical or archived M184V/I on the effectiveness of dolutegravir + lamivudine (DTG + 3TC) in real-world switch populations; a sensitivity analysis was performed using data from interventional trials identified via a targeted literature search.

Introduction

- M184V/I is the most common RAM selected by DTG.
- Clinical development phase 3 interventional trials excluded participants with known or suspected RAMs.
- The presence of archived M184V/I mutations in phase 3 trials evaluating switch to DTG/3TC (TANGO, n=4; SALSA, n=2) did not impact viral efficacy.
- Absence of historical resistance results or availability of prior genotype (pooled TANGO/SALSA analyses, n=24) also had no impact on viral load response.
- Interim viral load (VL) >50 c/mL followed by Clotilde Allavena, 2019; Simon. Baseline RNA genotype
- For the secondary objective, sensitivity analyses were performed using interventional trial data.

Methods

- A systematic literature review was performed following Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (Figure 1A).
- Studies were screened for suppressed-switch populations reporting M184V/I mutations before DTG initiation.
- For the primary objective, common- and random-effects models analyses were conducted using RWE studies.
- Random-effects models provide estimates that were more generalizable to the overall population of interest.
- Common-effects (or fixed-effects) models assume that the included studies are the population of interest and are more informative when zero VF events are observed.

Results

- VF Outcomes in RWE Studies and Interventional Trials
- Of 3,942 publications and 198 conference abstracts identified via systematic literature review, 5 real studies met all search criteria and were analyzed (Table).
- The targeted literature search identified 5 relevant interventional trials.
- Proportions of PWH with historical M184V/I estimated to have VF at Week 24, 48, and 96 were low in real-world and interventional trial analyses based on reported VF outcomes at each time point.

- Table. Summary of VF Definitions and Outcomes for PWH With M184V/I RAMs Receiving DTG + 3TC in Real-world Studies and Interventional Trials

- VF Estimates
- Random-effects models are associated with greater uncertainty vs. common-effects models but can be used to provide results for the wide range of scenarios possible from the sample of studies used in the analysis.
- Common-effects (or fixed-effects) models assume that the included studies are the population of interest and are more appropriate and informative when true VF events are reported.

Conclusions

- Overall, pre-switch M184V/I prevalence was low in RWE studies.
- Real-world studies of PWH with historical or archived M184V/I receiving DTG + 3TC identified low incidence of VF through 96 weeks and no reported cases of INSTI treatment-emergent mutations; these findings were consistent with results from interventional trials.


Figure 1. PRISMA Flow Charts for (A) RWE Studies and (B) Interventional Trials

Figure 2. Meta-analysis Estimates of Proportions of VF at Weeks 24, 48, and 96 in PWH With Reported M184V/I Receiving DTG + 3TC From (A) Systematic Literature Review–Identified RWE Studies and (B) Targeted Literature-Identified Interventional Trials, Inclusive of All VF Definitions

A. RWE studies

B. Interventional trials

VF outcomes definitions: n/N (%).

- VF by real-world definition: n/N (%).
- VF by interventional trial definition: n/N (%).

Figure 3. Illustration of forest plots for VF at Week 96, excluding non-switch participants.

Study

VF prevalence (95% CI)

Hodgson-Tenzer 2019

Sali et al. 2020

LAMRES

100

Hocqueloux et al. EACS 2021; Virtual and London, UK. Slides OS1/2.

100

Effectiveness of Dolutegravir + Lamivudine in Real-world Studies and Interventional Trials

- Eligibility
- Screening
- Identification

Records identified through database searching

- Records excluded (n=1,831)
- Publications excluded (n=33)
- Studies excluded (n=1,810)

Figures: P015