COMPARATIVE EFFICACY AND SAFETY OF A COMBINATION THERAPY OF DOLUTEGRAVIR AND LAMIVUDINE VS 3-DRUG ANTIRETROVIRAL REGIMENS IN TREATMENT-NAIVE HIV-1 INFECTED PATIENTS AT 96 WEEKS: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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Introduction

- Traditional antiretroviral therapy for patients living with HIV (PLHIV) includes combinations of 3 or more antiretroviral drugs (ARVs). Recent arrival of the 2-drug regimen (2DR) of DTG+3TC has demonstrated non-inferiority to 3-drug regimens (3DRs) in treatment-naive PLHIV up to Week 96 in the GEMINI-1 and GEMINI-2 studies.
- A previous Network Meta-analysis (NMA) showed DTG+3TC having comparable efficacy and safety to the guideline-recommended 3DRs at Week 48.[1]
- The objective of this analysis was to evaluate efficacy and safety of DTG+3TC compared to standard of care 3DRs up to Week 96 in treatment-naive PLHIV.

Methods

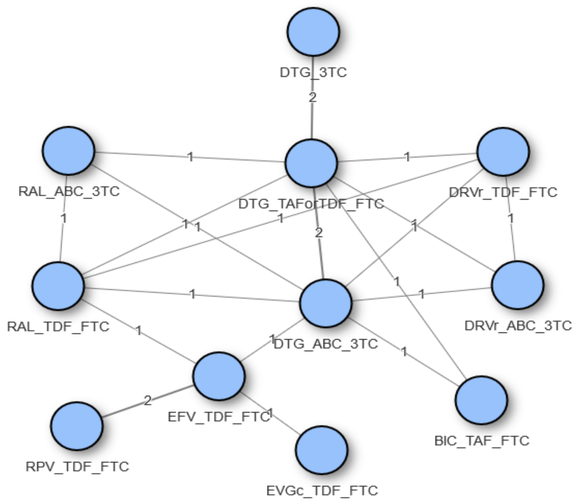
Systematic literature review

- The previously published SLR was updated on July 19, 2019, using PubMed, Embase and Cochrane databases to identify Phase 3/4 RCTs evaluating the efficacy and/or safety of DTG+3TC vs. guideline-recommended 3DRs among treatment-naive adult or adolescent (≥13 years) PLHIV.[1]
- Regimens of interest were core agents recommended by DHHS or EACS guidelines.[2,3]

Endpoints and statistical analysis

- Endpoints included in efficacy analyses were virologic suppression, defined as proportion of subjects with HIV-1 RNA ≤50 copies/mL and CD4 cell change, defined as mean CD4 cell change from baseline after initiating therapy.
- Endpoints included in the safety analysis were discontinuation rates, adverse events (AEs), drug-related AEs and serious AEs. Safety endpoints were reported as odds ratios.

Figure 1. Network of Studies

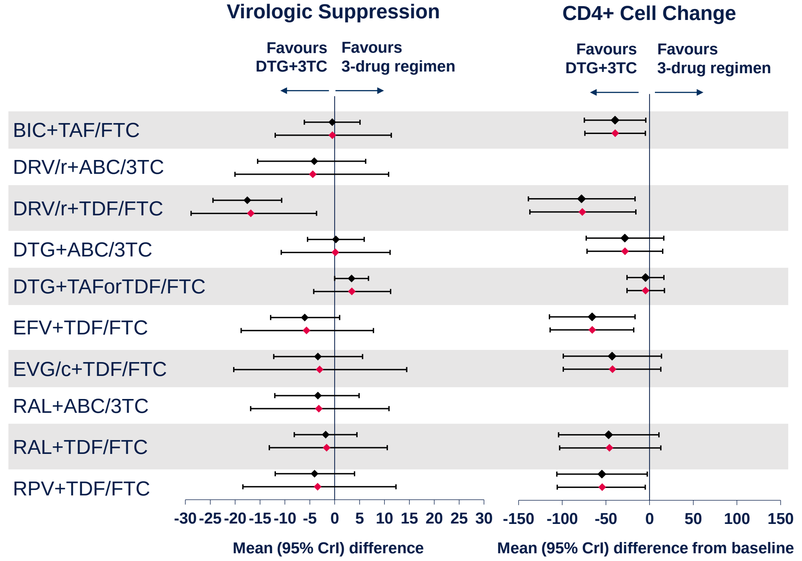


Results

Efficacy results (Figure 2)

- **Virologic suppression (VS)** achieved by DTG+3TC was superior to DRV/r+TDF/FTC and comparable to other 3DRs. The probability of DTG+3TC achieving better VS ranged from 2.5% with DTG+TAForTDF/FTC to 95.4% with EFV+TDF/FTC.
  - Stratified by baseline viral load of >100,000 RNA copies/mL and ≤100,000 RNA copies/mL or CD4 >200 cells/μL and ≤200cells/μL, DTG+3TC was broadly comparable to all the 3DRs also reporting those subgroup data with some significant differences.
- **Mean CD4 cell changes** with DTG+3TC were statistically significantly higher from baseline when compared to BIC+TAF/FTC, DRV/r+TDF/FTC, EFV+TDF/FTC and RPV+TDF/FTC. DTG+3TC was otherwise comparable with all other regimens.

Figure 2. Efficacy Endpoint Results for NMA Week 96



Fixed effects model is represented first, with a black filled symbol. Random effects model is represented below, with a red filled symbol. Error bars represent 95% credible intervals.

Safety results (See Table 1)

- **Discontinuation rates** were comparable between DTG+3TC and all other regimens, with no significant differences.
- **Any adverse event** rates for DTG+3TC were significantly lower than with EFV+TDF/FTC and comparable to other regimens.
- **Drug-related AEs** incidence in DTG+3TC patients were significantly lower when compared to DTG+TAForTDF/FTC and EFV+TDF/FTC. DTG+3TC drug-related AE rates were comparable to other regimens.
- **Serious adverse events** reported incidence in the DTG+3TC arm were significantly lower compared to BIC+TAF/FTC, DTG+ABC/3TC, EFV+TDF/FTC and RAL+TDF/FTC and comparable to other 3DRs.

Table 1. Safety Endpoint Results for NMA Week 96

Comparator	Discontinuations (Odds Ratio)	Any Adverse Events (Odds Ratio)	Drug-Related Adverse Events (Odds Ratio)	Serious Adverse Events (Odds Ratio)
BIC+TAF/FTC	1.04 (0.59, 1.83)	1.18 (0.67, 2.07)	0.87 (0.56, 1.35)	**1.94 (1.09, 3.5)**
DRV/r+TDF/FTC	1.47 (0.53, 4)	1.88 (0.44, 7.94)	Not reported	Not reported
DTG+ABC/3TC	0.87 (0.4, 1.86)	2.09 (0.85, 5.33)	1.49 (0.85, 2.57)	**2.12 (1.0, 4.57)**
DTG+TAF or TDF/FTC	0.74 (0.54, 1)	1.19 (0.9, 1.58)	**1.37 (1.07, 1.76)**	1.05 (0.73, 1.51)
EFV+TDF/FTC	1.45 (0.62, 3.31)	**3.35 (1.18, 9.98)**	**3.84 (2.06, 7.11)**	**2.48 (1.05, 5.95)**
EVG/c+TDF/FTC	1.24 (0.48, 3.11)	Not reported	Not reported	Not reported
RAL+TDF/FTC	0.99 (0.38, 2.54)	1.49 (0.36, 6.22)	0.95 (0.46, 1.96)	**3.01 (1.11, 8.26)**
RPV+TDF/FTC	1.02 (0.41, 2.48)	2.46 (0.76, 8.35)	Not reported	2.06 (0.8, 5.34)

*Results in bold are statistically significant; fixed effects model was selected for all analyses based on model diagnostics (Deviance Information Criterion). Numbers >1 in this table favoured the DTG+3TC arm. Numbers in parentheses represent 95% credible intervals.

Conclusions

- DTG+3TC provides an efficacious and durable long-term treatment alternative, with a good safety profile, for clinicians treating naive PLHIV.

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References:

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3. European AIDS Clinical Society. Guidelines, Version 10.0. 2019.

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