Comparative Efficacy and Safety of Dolutegravir and Lamivudine in Treatment-Naïve HIV Patients

Poster P007

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Introduction

- Given the lifelong nature of HIV treatment, there is clinical interest in 2-drug antiretroviral therapy (ART) regimens that could minimise cumulative drug exposure while maintaining the efficacy of traditionally used 3-drug regimens (comprising a core agent + 2 nucleoside/nucleotide reverse transcriptase inhibitors)[1]
- In randomised controlled trials (RCTs), the 2-drug regimen dolutegravir (DTG) plus lamivudine (3TC) had similar efficacy to the traditional 3-drug regimen DTG plus tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) in treatment-naïve patients with HIV-1.[2] However, there are a number of other traditionally used 3-drug regimens for which no head-to-head study data are available
- **Objective**: To conduct an indirect comparison of the efficacy and safety of DTG + 3TC with commonly used 3-drug regimens in treatment-naïve patients with HIV-1, using a systematic review and network meta-analysis (NMA)

Methods

Systematic literature search and NMA

- A systematic review of the literature, clinicaltrials.gov and reimbursement documents was performed (4 December, 2018) to identify Phase III/IV RCTs for inclusion
  - Key inclusion criteria: studies in treatment-naïve patients ≥13 years of age with HIV-1 infection
- Treatment regimens of interest were those containing recommended core agents (as of October 2018[3,4]) plus the new core agent bictegravir (BIC). Efavirenz (EFV) + TDF/FTC was also included to facilitate the formation of a connected network

Outcomes

- **Efficacy**: the proportion of patients with virological suppression (VS) at Week 48 and change from baseline in CD4+ cell count at Week 48
- **Safety**: proportions of patients with adverse events (AE), serious AEs (SAE) and drug-related AEs by Week 48

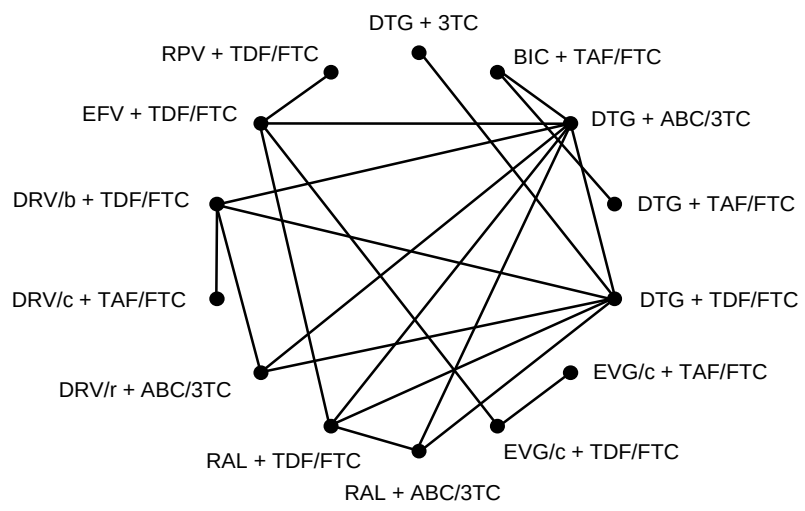
Statistical analysis

- A Bayesian NMA methodology was used to estimate relative treatment outcomes,[5,6] using a regimen approach where each regimen represented a unique node in the network. A likelihood function was defined for each outcome and treatment effects were modelled using a link function
- VS and change from baseline in CD4+ at Week 48 were analysed as continuous outcomes using normal distributions and are expressed as mean differences between the 3-drug regimens and DTG + 3TC with 95% credibility intervals (CrI). Safety outcomes were analysed as binary outcomes using binomial distributions and are expressed as odds ratios (OR) and 95% CrI for 3-drug regimens relative to DTG + 3TC

Results

- The network contained 14 unique ART regimens, including DTG + 3TC (**Figure 1**), based on data from 12 publications including 10,043 treatment-naïve patients with HIV-1
- Fixed-effect models were chosen based on model fit diagnostics (Deviance Information Criterion, convergence criteria, total residual deviations)

Figure 1. NMA network



3TC, lamivudine; ABC, abacavir; BIC, bictegravir; DRV/b, boosted daranuvir (cobistat or ritonavir); DRV/c, cobicistat-boosted darunavir; DRV/r, ritonavir-boosted daranuvir; DTG, dolutegravir; EFV, efavirenz; EVG/c, cobistat-boosted elvitegravir; FTC, emtricitabine; RAL, raltegravir; RPV, rilpivirine; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate

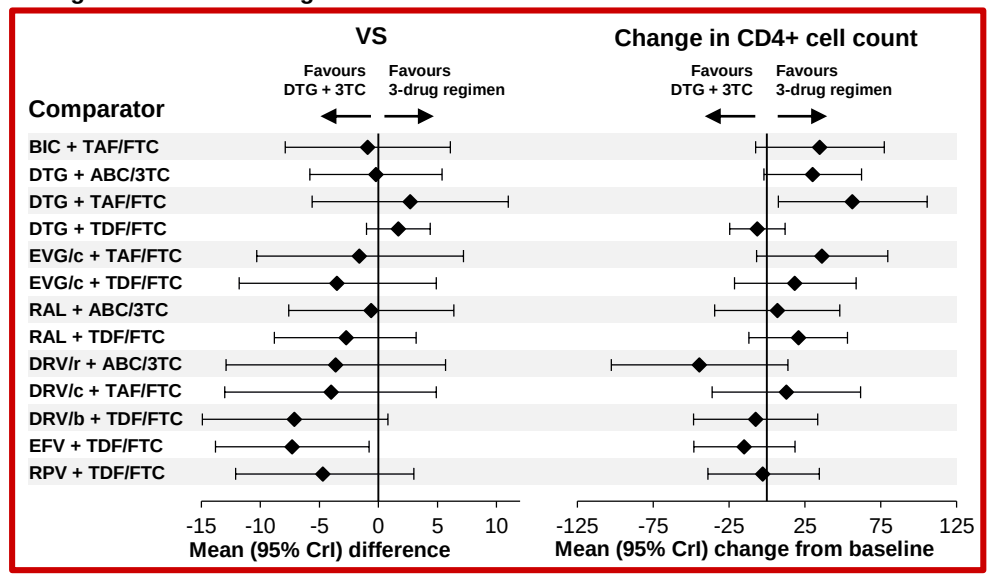
VS at Week 48

- DTG + 3TC was superior to EFV + TDF/FTC and similar to all other 3-drug regimens in terms of the proportion of patients achieving VS at Week 48 (**Figure 2**)
- Proportional difference for VS at Week 48 for 3-drug regimens versus DTG + 3TC ranged from -7.3% (95% CrI: -13.8, -0.8) for EFV + TDF/FTC to 2.7% (-5.6, 11.0) for DTG + TAF/FTC

CD4+ cell count change from baseline to Week 48

- DTG + 3TC induced similar increases in CD4+ cell count between baseline and Week 48 compared with all 3-drug regimens, except DTG + TAF/FTC, which was superior to DTG + 3TC (**Figure 2**)
- Mean between-treatment differences for 3-drug regimens versus DTG + 3TC ranged from -44 cells/μL for DRV/r + ABC/3TC to 56 cells/μL for DTG + TAF/FTC

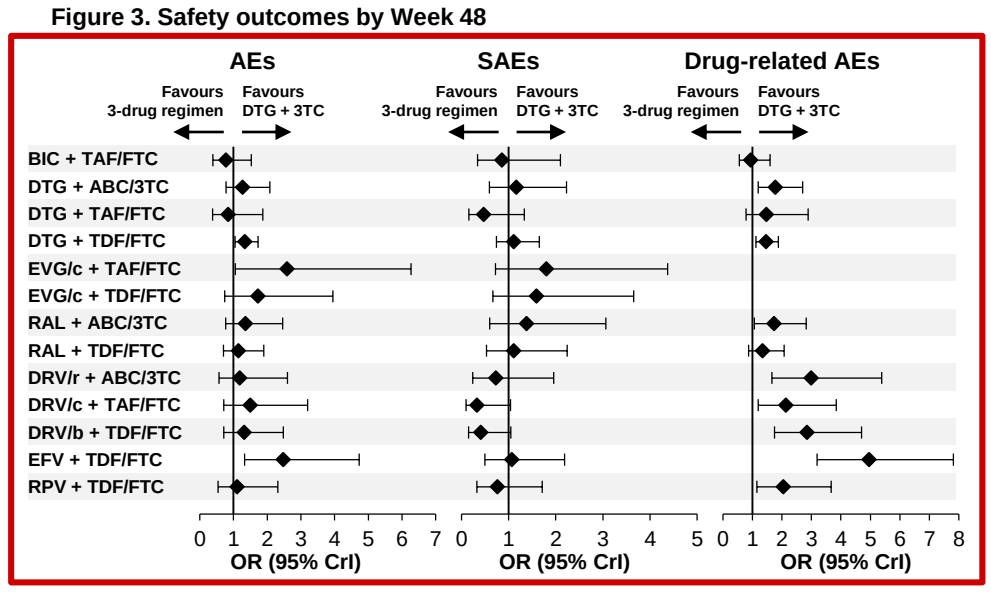
Figure 2. VS and change from baseline in CD4+ cell count at Week 48



Safety by Week 48

- AEs, SAEs and drug-related AEs were assessed for the same 3-drug regimens as the efficacy endpoints relative to DTG + 3TC, except for drug-related AEs with EVG/c + TAF/FTC and EVG/c + TDF/FTC, for which no data were available
- The odds of having an AE were similar with all 3-drug regimens and DTG + 3TC, except for DTG + TDF/FTC, EVG/c + TAF/FTC and EFV + TDF/FTC for which the odds of having an AE were significantly higher (**Figure 3**)
- The odds of having a SAE were similar with all 3-drug regimens and DTG + 3TC (**Figure 3**)
- The odds of having a drug-related AE were significantly higher for most 3-drug regimens versus DTG + 3TC, except BIC + TAF/FTC, DTG + TAF/FTC and RAL + TDF/FTC, for which the odds were similar (**Figure 3**)

Figure 3. Safety outcomes by Week 48



Conclusions

Through indirect comparisons over 48 weeks utilising a NMA, the 2-drug regimen DTG + 3TC demonstrated:

- Superior viral suppression compared with EFV + TDF/FTC and similar efficacy compared with all other 3-drug regimens analysed
- A reduced risk of drug-related AEs compared with several 3-drug regimens, with overall AEs and SAEs similar to the 3-drug regimens analysed

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