P044

Efficacy of dolutegravir plus lamivudine in treatment-naïve people living with HIV without baseline drug-resistance testing available: 48-week results from the randomized D2ARLING study

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Key takeaway

DTG+3TC demonstrated non-inferior efficacy compared with DTG+TDF/XTC in treatment-naïve PHIV **without the information of baseline resistance testing.**

Introduction

- DTG-3TC two-drug regimen is indicated as one of the preferred regimens for treatment-naïve people with HIV (PHIV).
- Efficacy data in PHIV without baseline HIV-1 drug-resistance testing is limited.
- Some guidelines do not recommend initiating DTG-3TC without baseline resistance testing information.
- The aim of this study was to evaluate the efficacy of DTG+3TC in the absence of information on baseline resistance testing in treatment-naïve people with HIV.

Methods

D2ARLING was a randomized, non-inferiority, open-label, single-centre, phase IV study designed to assess the efficacy and safety of DTG+3TC in treatment-naïve PHIV with no available baseline resistance testing.

Participants were randomized 1:1 (stratified by screening plasma HIV-1 RNA and CD4+ T-cell count) to DTG+3TC or DTG+TDF/XTC. Per protocol, a genotypic drug-resistance test was performed on day 1 and remained double-blinded throughout the study, simulating a scenario of inaccessibility of baseline resistance testing (figure 1). Additionally, genotypic drug-resistance testing was done in participants experiencing protocol-defined virological failure (PDVF).

Primary endpoint: proportion of participants with HIV-1 RNA <50 copies/mL at week 48 (ITT-exposed analysis, snapshot algorithm, non-inferiority 95%CI margin=10%). Week-24 interim analysis was presented at IAS 2023. Week-48 results are reported here (ClinicalTrials.gov: NCT04549467).

Results

- Out of 244 subjects screened, 214 were randomized and treated with DTG+3TC (n=106) or DTG+TDF/XTC (n=108).
- Baseline characteristics were similar between arms (table 1). None of the participants had previously been on pre-exposure prophylaxis (PrEP).
- At week 48 in the ITT-exposed snapshot, 91.5% of participants in the DTG+3TC arm and 88.9% in the DTG+TDF/XTC arm achieved HIV-1 RNA <50 copies/mL (difference 2.6%; 95%CI -5.3%, 10.6%), demonstrating non-inferiority of dolutegravir plus lamivudine to the three-drug regimen (figures 2 and 3).
- Among participants with baseline HIV-1 RNA of >100,000 copies/mL, 31 (94%) of 33 participants in the DTG+3TC group and 28 (85%) of 33 in the DTG+TDF/XTC group achieved virological success at week 48 (ITT-E population).
- Among participants with CD4+ <200 cells/mL, 17 (81%) of 21 participants in the DTG+3TC group achieved HIV-1 RNA <50 copies per mL at week 48 compared with 22 (96%) of 23 in the DTG+TDF/XTC group (ITT-E analysis).
- No participants in the DTG+3TC arm and two in the DTG+TDF/XTC arm met PDVF. No treatment-emergent mutations to any of the study drugs were observed in the virological failure genotypic resistance test.
- Adverse event (AE) rates were similar (DTG+3TC n=61, DTG+TDF/XTC n=59), and rates of withdrawals due to AEs were low (<1%) in both arms.
- All serious AEs were unrelated: DTG+3TC (2.8%) vs. DTG+TDF/XTC (5.6%).
- Median weight change was 3.5 kg and 1.8 kg in the DTG+3TC and DTG+TDF/XTC arms, respectively (p=0.01).
- After the last participant completed the study, baseline genotypic resistance testing results were unblinded. No lamivudine, emtricitabine, or tenofovir resistance-associated mutations were identified.

Figure 1. D2ARLING study design

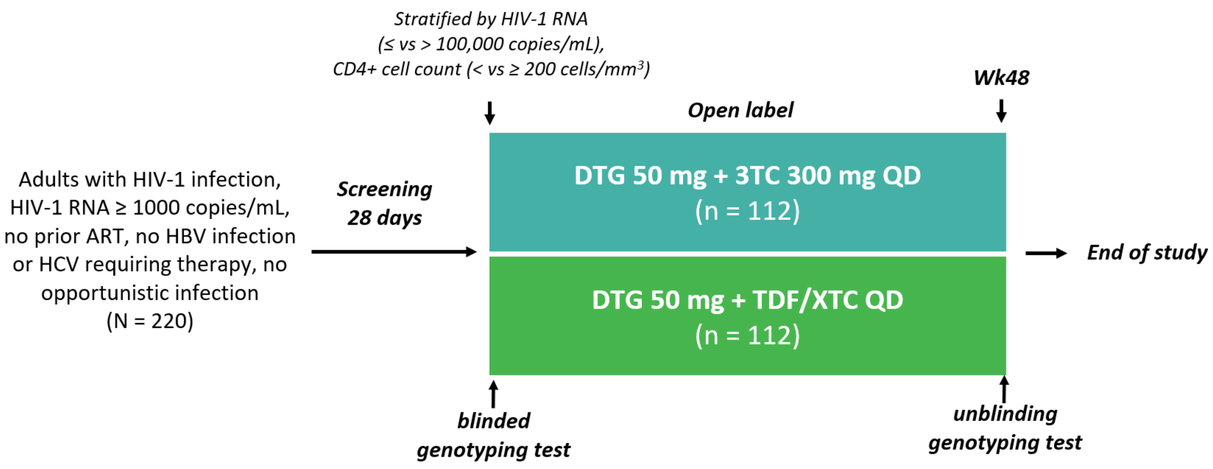


Table 1. Demographics and clinical baseline characteristics in the ITT-exposed population.

Characteristic	3TC-DTG (n=106)	XTC/TDF-DTG (n=108)	Total (N=214)
Female sex	24 (22.6%)	25 (23.1%)	49 (22.9%)
Median age, y (IQR)	31.50 (27-41)	31(26-37)	31 (26-39)
Hispanic Latin, n (%)	106 (100%)	108 (100%)	214 (100%)
HIV-1 RNA >100 000 c/mL	33 (31.1%)	33 (30.6%)	66 (30.8%)
CD4 T <200 cells/µL	21 (19.8%)	23 (21.3%)	44 (20.6%)
CDC stage 3	21 (19.8%)	23 (21.3%)	44 (20.6%)

Figure 2. Virologic Snapshot Outcomes at week 48 (ITT-E Population)

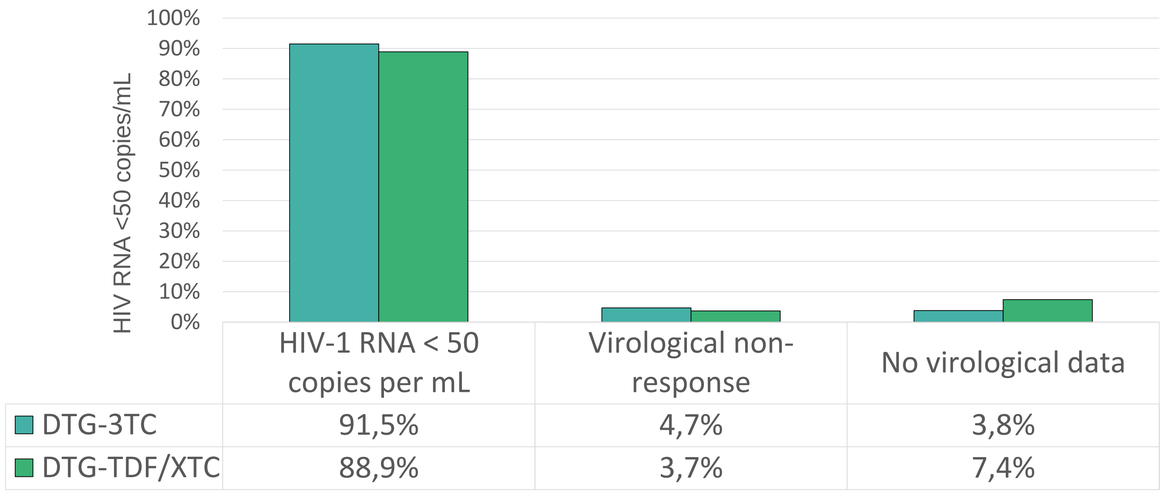
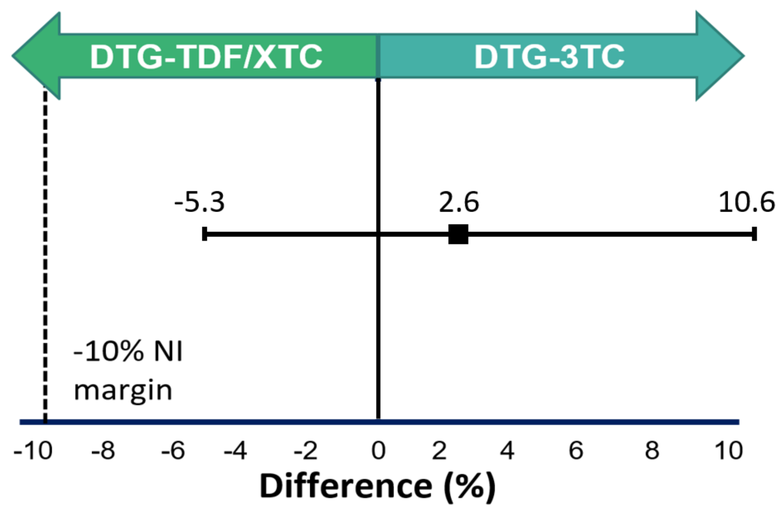


Figure 3. Adjusted treatment difference (95%CI)



Endpoint (<50 c/mL)

DTG-3TC is non-inferior to DTG-TDF/XTC (week 48)

Conclusions

This study provides evidence supporting the non-inferiority of dolutegravir plus lamivudine compared to a preferred three-drug regimen in treatment-naïve individuals without baseline resistance testing. These findings suggest that baseline resistance testing may not be a requirement for initiating treatment with dolutegravir plus lamivudine in settings with low frequency or suspicion of transmitted drug resistance to these drugs.

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