

Switch to DTG/3TC vs B/F/TAF (PASO-DOBLE Study): Efficacy & Weight Changes by Predefined Subgroups

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Background: The PASO-DOBLE study (ClinicalTrials.gov NCT04884139) demonstrated non-inferior efficacy and less weight gain when switching to DTG/3TC vs BIC/FTC/TAF in virologically suppressed people with HIV (PWH). We planned to assess subgroup analyses of efficacy (HIV RNA <50 copies/mL at 48 weeks) and clinically meaningful weight changes (>5% from baseline) by predefined baseline demographic, clinical and treatment characteristics.

Methods: Clinically stable, virologically suppressed PWH on regimens containing ≥1 pill/day, boosters, or drugs with cumulative toxicity such as EFV or TDF were randomized (1:1) to switch to DTG/3TC or BIC/FTC/TAF stratifying by sex at birth and TAF at baseline. According to the statistical analysis plan, we calculated unadjusted differences with 95% confidence intervals DTG/3TC minus BIC/FTC/TAF in the proportions of PWH with: 1) HIV RNA <50 copies/mL, and 2) weight gain >5% in the exposed intention-to-treat population between study arms at 48 weeks according to sex at birth, age, race/ethnicity, previous AIDS, CD4 cells, and antiretrovirals at baseline.

Results: Between 14-July-2021 and 24-March-2023, 553 PWH switched to DTG/3TC (n=277) or BIC/FTC/TAF (n=276), including 147 (27%) women and 155 (28%) with TAF at baseline. In general, there were consistent effects on efficacy across major subgroups. Significant differences in viral suppression favoured DTG/3TC vs BIC/FTC/TAF in the following subgroups: age 35-50 years (9.6%, 95%CI 0.3 to 18.9), Latin-American ethnicity (11.8%, 95%CI 1.0 to 22.7), **185**

and TDF at baseline (8.2%, 95%CI 0.1 to 16.2). There were significant lower proportions of PWH with >5% weight gain with DTG/3TC vs BIC/F/TAF in the following subgroups (**Figure**): females (-22.5%, 95%CI -37.9 to -7.1), age 35-50 years (-15.5%, 95%CI -29.0 to -2.1), Latin-American ethnicity (-16.9%, 95%CI -33.3 to -0.4), no prior AIDS (-9.5%, 95%CI -17.9 to -1.1), and pre-switch CD4 cells ≥500/mm³ (-10.4%, 95%CI -18.9 to -1.8), TDF- (-21.1%, 95%CI -34.2 to -8.0), FTC- (-13.0%, 95%CI -22.0 to -3.9), and NNRTI-containing regimens (-16.9%, 95%CI -27.8 to -6.0).

Conclusions: Although these results should be interpreted with caution as analyses were unadjusted, non-inferiority of DTG/3TC vs BIC/FTC/TAF and the difference in favour of less weight gain with DTG/3TC were generally consistent across all subgroups analysed.

Figure. Proportions of PWH with weight gain >5% in the exposed intention-to-treat population in each study arm at 48 weeks according to predefined subgroups.

