

Metabolic Effects of Switching From DTG/3TC to BIC/FTC/TAF in PWH With Neuropsychiatric Conditions

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BACKGROUND

- People with HIV (PWH) and neuropsychiatric comorbidities face an elevated cardiovascular risk, often exacerbated by the metabolic effects of both psychotropic medications and certain antiretrovirals.
- The metabolic consequences of switching between DTG/3TC and BIC/FTC/TAF in this population remain poorly characterized.
- We report the 48-week changes in fasting lipids and body weight observed in the MIND clinical trial (Gesida 11920. IN-ES-380-5729. EUDRACT: 2021-005927-19).

METHODS

- **Study Design:** Phase IV, randomized, double-blinded, placebo-controlled, multicenter trial. (figure 1).
- **Study Population:** Virologically suppressed PWH with stable neuropsychiatric comorbidities (figure 2) on DTG/3TC.
- **Secondary Objectives (Pre-specified):** 48-week changes in body weight and fasting lipids (TC, LDL, HDL, and TG) were defined as secondary safety endpoints in the original protocol and Statistical Analysis Plan.
- **Statistical Analysis:** Comparisons were performed on an intention-to-treat (ITT) basis using generalized estimating equation (GEE) models to evaluate longitudinal changes.

Figure 1: Study Design and Randomization Schema

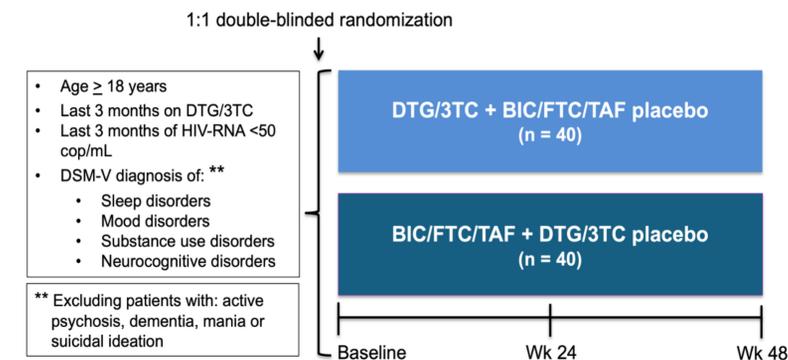
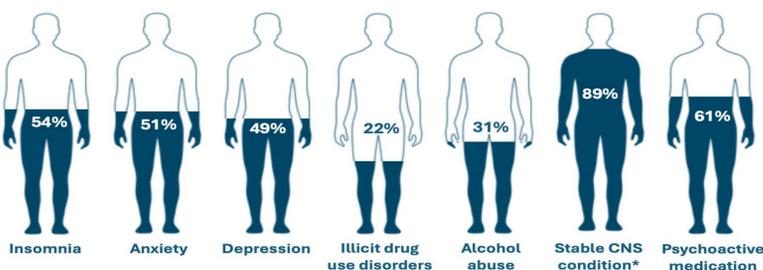


Figure 2: Baseline Neuropsychiatric Comorbidities



- **Metabolic optimization:** In this randomized, double-blind, placebo-controlled trial, switching to BIC/FTC/TAF effectively limited weight gain and improved the overall lipid profile compared to DTG/3TC at 48 weeks.
- **Cardiovascular risk reduction:** The reduction in total cholesterol and LDL resulted in a more favorable atherogenic index in the switch arm, despite divergent HDL trends between groups.
- **Clinical Stability:** The switch strategy to BIC/FTC/TAF demonstrated a balance between sustained virologic efficacy and the maintenance of neuropsychiatric and metabolic stability in this vulnerable population.

RESULTS

- **Weight and lipid profile dynamics:** A significantly lower weight increase and a longitudinal decline in pro-atherogenic cholesterol (TC and LDL) were observed in the switch arm compared to the continuation group throughout the 48-week period (see table 2).
- **Net atherogenic impact:** The improvement in the TC/HDL ratio in the BIC/FTC/TAF arm remained significant, effectively counterbalancing the HDL evolution observed in the control group (see table 2).
- **Adjusted Metabolic Outcomes:** The differences in weight and lipid trajectories between groups persisted in multivariate analyses after adjusting for the baseline burden of weight-modifying psychotropic medications and lipid-lowering agents.
- **Virologic Efficacy and Safety:** High rates of virologic control were sustained throughout the 48-week period, with 100% of participants in the switch arm maintaining suppression in the Per-Protocol analysis. BIC/FTC/TAF showed no investigator-led discontinuations for neuropsychiatric adverse events or weight gain. The three discontinuations for neuropsychiatric events reported during the study resulted from patient withdrawal of consent.

Table 2. Evolution of Metabolic Parameters from Baseline through Week 48 by Treatment Arm (ITT Population)

Variable	Treatment Arm	Baseline	Week 48	Mean Change	P-value*
Weight (Kg)	BIC/FTC/TAF	76.6	77.1	+0.5	0.04
	DTG/3TC	73.4	75.6	+2.2	
Total Cholesterol (mg/dL)	BIC/FTC/TAF	183.0	175.7	-7.3	0.02
	DTG/3TC	174.1	183.5	+9.4	
LDL Cholesterol (mg/dL)	BIC/FTC/TAF	113.6	106.5	-7.1	0.05
	DTG/3TC	103.1	110.4	+7.3	
HDL Cholesterol (mg/dL)	BIC/FTC/TAF	49.7	48.3	-1.4	0.02
	DTG/3TC	45.2	48.6	+3.4	
TC/HDL ratio	BIC/FTC/TAF	3.53	3.47	-0.06	0.04
	DTG/3TC	3.64	3.65	+0.01	
Triglycerides (mg/dL)	BIC/FTC/TAF	108.1	106.2	-1.9	0.69
	DTG/3TC	128.9	131.9	+3.0	

*P-value corresponds to the interaction term (treatment*time) from the GEE model, assessing the difference in change between arms.

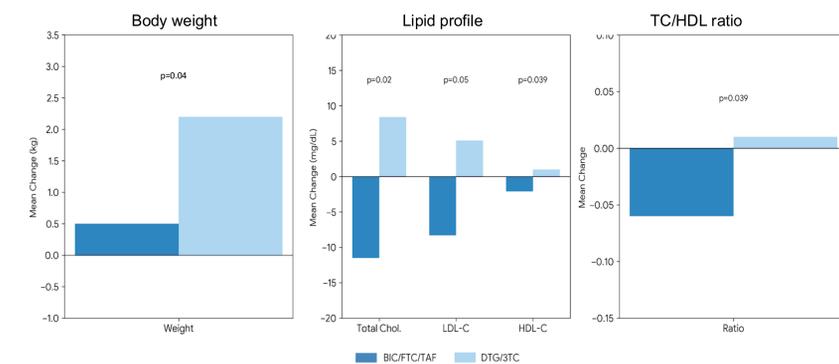
** Results remained consistent after adjusting for the use of weight-modifying psychotropic medications or lipid-lowering agents.

BASELINE CHARACTERISTICS

	BIC/FTC/TAF (+ DTG/3TC placebo) (n=41)	DTG/3TC (+ BIC/FTC/TAF placebo) (n=39)
Sex at birth: female; n (%)	9 (22)	10 (26)
Age (years); mean (SD)	48.2 (11.6)	49.3 (9.0)
Ethnicity: Caucasian; n (%)	31 (76)	27 (69)
Way of transmission: Intravenous drug user; n (%)	10 (24)	8 (21)
Years living with HIV since diagnosis; mean (SD)	14.0 (10.3)	15.0 (10.5)
Years treated with DTG/3TC; mean (SD)	1.9 (0.8)	2.2 (1.2)
Body mass Index; mean (SD)	26.07 (5.19)	26.06 (4.13)
Use of psychotropic medication; n (%)	26 (63.4)	23 (59.0)
Use of statins; n (%)	12 (29.3)	10 (25.6)

* Baseline characteristics were balanced between treatment arms. No statistically significant differences were observed between groups in these baseline parameters (P>0.05).

Figure 3. Changes in body weight and lipid profiles



CONCLUSIONS

- These results provide supportive evidence for BIC/FTC/TAF as a metabolically favorable alternative in individuals with mental health comorbidities. The consistency of these outcomes, even when accounting for comedications, suggests that this switch may contribute to improved long-term weight and lipid management in this specific population.

PLAIN LANGUAGE SUMMARY

Switching to BIC/FTC/TAF helped limit weight gain and improve cholesterol levels in people living with HIV and mental health conditions. These benefits were independent of the psychiatric medications used. This switch is a safe option to improve metabolic health without compromising viral control or mental health stability.

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