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Impact of Switching From Dual to Triple Therapy on Inflammation: INSTINCT Study

Sergio Serrano-Villar[1,2], **Laura Martín-Pedraza***[1,2], Carmen Busca[3], Juan Manuel Tiraboschi[4], Jesús Santos[5], Luis López-Cortés[6], Carmen Hidalgo-Tenorio[7], Vicente Estrada[8], María José Crusells[9], Alfonso Cabello[10], Alberto Díaz de Santiago[11], María Novella[12], Miguel Torralba[13], Marta de Miguel[14], Santiago Moreno[1,2]

[1] Infectious Diseases Department, Hospital Universitario Ramón y Cajal, Universidad de Alcalá, IRYCIS, Madrid, Spain; [2] CIBERINFEC, Instituto de Salud Carlos III, Madrid, Spain; [3] Hospital Universitario La Paz, Madrid, Spain; [4] Hospital Universitario de Bellvitge, Barcelona, Spain; [5] Hospital Virgen de la Victoria, Málaga, Spain; [6] Hospital Universitario Virgen del Rocío, Sevilla, Spain; [7] Hospital Universitario Virgen de las Nives, Granada, Spain; [8] Hospital Clínico San Carlos, Madrid, Spain; [9] Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain; [10] Fundación Jimenez Díaz, Madrid, Spain; [11] Hospital Puerta de Hierro, Madrid, Spain; [12] Hospital Universitario Principe de Asturias, Madrid, Spain; [13] Hospital Universitario de Guadalajara, Guadalajara, Spain; [14] Fundación SEIMC-GeSIDA, Madrid, Spain

BACKGROUND

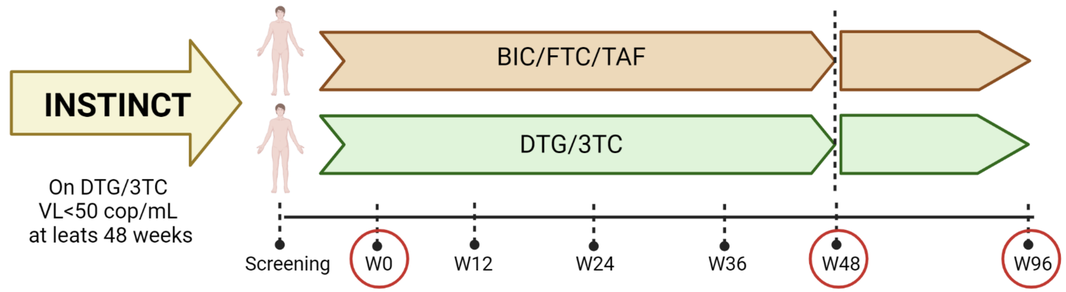
Because inflammation is associated with morbidity and mortality and has been linked to HIV transcription in lymphoid tissues during ART, it is necessary to address the impact of switching ART regimens on inflammation.

METHODS

- Interim analysis of the randomized, open-label, multicenter INSTINCT trial (clinicaltrial.gov: NCT04076423).
- We evaluated the effect of switching from DTG/3TC to BIC/FTC/TAF vs. remaining on DTG/3TC on systemic inflammation up to 48 weeks. We included 117 participants. Participants were adults with confirmed, virologically suppressed HIV, on stable ART with DTG/3TC for a minimum of 48 weeks.
- Exclusion criteria: previous virological failure, drug resistance, and autoimmune conditions.
- IL-6 levels measured in triplicate (Kit Human IL-6 HS Bio-techne®), samples carefully located on plates to avoid batch-effects.
- We focused on IL-6 changes from baseline to week 48 using high-sensitivity ELISA.
- Statistical analysis: Mann-Whitney and linear regression.

Table 1

	DTG/3TC (N=60)	BIC/FTC/TAF (N=57)	Overall (N=117)
Gender			
Male	53 (88.3%)	46 (80.7%)	99 (84.6%)
Female	7 (11.7%)	10 (17.5%)	17 (14.5%)
Age (y) (years)			
Mean (SD)	43.6 (11.0)	45.1 (11.4)	44.3 (11.1)
Ethnicity			
White Caucasian	49 (81.7%)	43 (75.4%)	92 (78.6%)
Latino	11 (18.3%)	13 (22.8%)	24 (20.5%)
Afroamerican	0 (0%)	1 (1.8%)	1 (0.9%)
Other	0 (0%)	0 (0%)	0 (0%)
Risk Factor			
Heterosexual	12 (20.0%)	18 (31.6%)	30 (25.6%)
MSM	42 (70.0%)	31 (54.4%)	73 (62.4%)
IDU	2 (3.3%)	2 (3.5%)	4 (3.4%)
Transfusion	0 (0%)	0 (0%)	0 (0%)
Unknown	4 (6.7%)	3 (5.3%)	7 (6.0%)
Other	0 (0%)	3 (5.3%)	3 (2.6%)
AIDS Past			
	7 (11.7%)	4 (7.0%)	11 (9.4%)
CD4 Nadir (cells/uL)			
Median (Q1, Q3)	370 (214, 484)	325 (219, 457)	338 (215, 466)
CD4 counts (cells/uL)			
Median (Q1, Q3)	776 (611, 974)	779 (593, 1010)	776 (606, 991)
CD8 counts (cells/uL)			
Median (Q1, Q3)	786 (638, 1020)	666 (536, 906)	742 (591, 948)
Years HIV Dx			
Median (Q1, Q3)	8.60 (5.05, 14.1)	8.85 (4.00, 17.1)	8.61 (4.30, 16.5)
Years Undetectable			
Median (Q1, Q3)	5.53 (2.96, 8.52)	5.17 (2.80, 9.37)	5.21 (2.88, 9.22)
Years on Current ART			
Median (Q1, Q3)	1.73 (1.16, 2.36)	1.46 (1.23, 1.94)	1.57 (1.17, 2.12)
eGFR (ml/min/m^2)			
Median (Q1, Q3)	88.7 (78.8, 96.3)	90.0 (79.8, 93.2)	90.0 (79.0, 96.1)
Total Cholesterol (mg/dL)			
Median (Q1, Q3)	190 (165, 213)	191 (161, 211)	191 (163, 211)
HDL (mg/dL)			
Median (Q1, Q3)	48.0 (39.0, 57.0)	44.0 (39.0, 57.5)	45.0 (39.0, 57.0)
LDL (mg/dL)			
Median (Q1, Q3)	121 (102, 140)	114 (92.0, 131)	115 (95.0, 134)
Triglycerides (mg/dL)			
Median (Q1, Q3)	95.5 (76.8, 129)	114 (80.0, 159)	108 (80.0, 139)



After 48 weeks from switching DTG/3TC to BIC/FTC/TAF we found no significant impact on plasma IL-6 levels.

RESULTS

- A total of 117 participants completed the 48-week follow-up; 17% women, mean age 44 ± 11 years, 79% white, 62% MSM, 9% with past AIDS diagnosis, median nadir CD4 338 cells/uL, baseline CD4 counts 776/uL, median duration of HIV suppression 5.2 years.
- Median IL6 levels in all study participants 0.96 pg/mL, IQR 0.53-1.44 (within normal ranges) (**Table 1**).
- No differences were observed in the general characteristics between groups.
- No significant differences in IL-6 changes were observed between groups from week 0 to 48.
- Median fold change for DTG/3TC, 1.1 [0.7-1.7]; for BIC/FTC/TAF, 1.2 [0.8-1.8], Mann Whitney, P value = 0.688 (**Figure 1**); group effect in linear regression analysis: Coef -0.07, P = 0.931 (**Figure 2**).

Figure 1

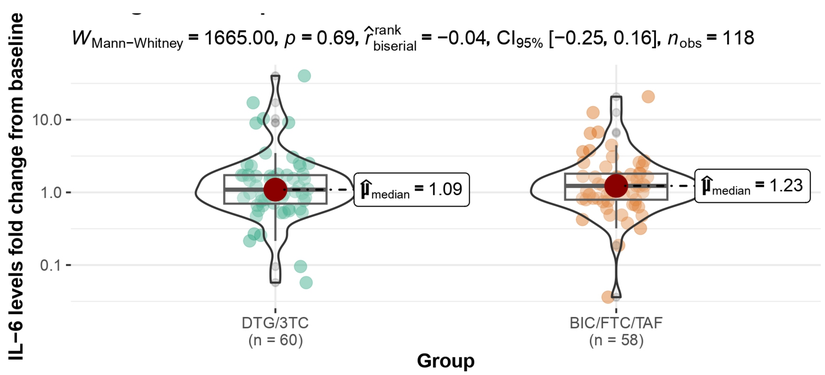
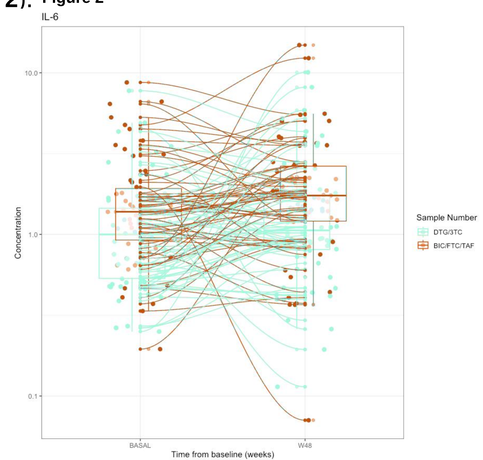


Figure 2



CONCLUSIONS

This analysis revealed no significant impact on IL-6 levels when switching from DTG/3TC to BIC/FTC/TAF in the first 48 weeks. These preliminary findings suggest a neutral inflammatory effect for the ART switch, warranting further study to elucidate the longer-term influence on inflammation.

ADDITIONAL KEY INFORMATION

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Author Contact Information: lauramp627@gmail.com