Effect of DTG/3TC vs. BIC/FTC/TAF on Steatotic Liver Disease: 96-week Analysis of PASO-DOBLE Trial

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Juan A Pineda[1], Alexis Inciarte[2], Pere Domingo[3], Adrian Curran[4], Juan Tiraboschi[5], Sergio Padilla[6], Pilar Rincón[1], Iván Chivite[2], Paula Prieto[3], Jordi Navarro[4], Luis M Real[1], María Jesús Vázquez[7], Marta De Miguel[8], Esteban Martínez[2,*], Juan Macias[1,*]

[1]Hospital Universitario Virgen de Valme, Seville, [2]Hospital Clínic de Barcelona, Barcelona, [3]Hospital de la Santa Creu i Sant Pau, Barcelona, [4]Hospital Universitari Vall d´Hebrón, Barcelona, [5]Hospital Universitario de Bellvitge, L'Hospitalet de Llobregat, [6]Hospital General Universitario, Elche, [7]ViiV Healthcare, Tres Cantos,[8]Fundación SEIMC-GeSIDA. Spain. *Equal contribution.

BACKGROUND

- Steatotic liver disease (SLD) is common in PLWH and is associated with overweight and its related metabolic disorders. Both INSTIs and TAF have been linked to weight gain in clinical trials and real-life studies. However, conflicting results have been reported regarding their effect on SLD.
- In the PASO-DOBLE clinical trial, switching to DTG/3TC resulted in less weight gain than with BIC/FTC/TAF at 48 and 96 weeks. In the present sub-study, at 48 weeks, the frequency of SLD among PLWH who gained weight significantly increased from baseline in the BIC/FTC/TAF arm, but not in the DTG/3TC arm (Pineda et al. CROI 2025. Abstract 764). However, longer-term data are lacking.
- Here we present the 96 week follow up data of this sub-study, aimed to compare the effect of switching to DTG/3TC vs. BIC/FTC/TAF on SLD.

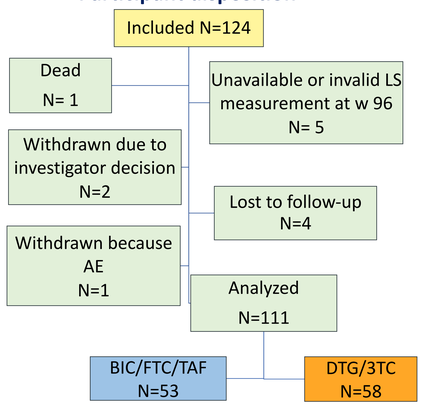
In virologically suppressed PLWH, switching to BIC/FTC/TAF leads to a higher frequency of steatotic liver disease compared to DTG/3TC after 96 weeks of therapy.

METHODS

- PLWH from the open-label, randomized clinical trial PASO-DOBLE were included in this sub-study if:
  - Recruited by centers equipped with a vibration-controlled transient elastography (VCTE) device capable to evaluate Controlled Attenuate Parameter (CAP).
  - VCTE measurements fulfilling the following quality criteria were collected at baseline and week 96 : 1) Success rate: >60%; 2)IQR of liver stiffness (LS)≤30%, if LS=7-30 kPa.
- SLD was defined as a CAP value ≥248 dB/m.
- Main outcome variable: CAP change from baseline to week 96.
- Statistical analysis: Mann-Whitney U test for continuous variables. χ^2/Fisher, Mantel-Haenszel tests for categorical variables. Multiple linear regression with CAP change as dependent variable and parameters associated with SLD in the study or which were different at baseline between two arms (p≤0.1) as covariates.

RESULTS

Participant disposition

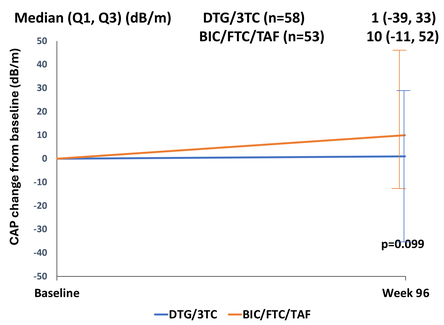


Baseline characteristics (n=111)

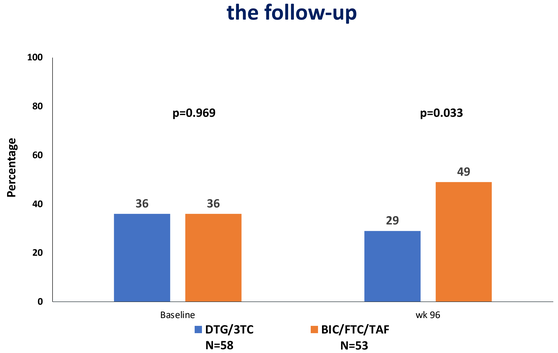
Parameter*	DTG/3TC n=58	BIC/FTC/TAF n=53	*p* value
Age, years	51 (43-57)	51 (39-58)	0.732
Male sex, n (%)	39 (67)	37 (70)	0.771
Caucasian, n (%)	46 (79)	37 (70)	0.250
Weight, kg	74 (66-82)	72 (63-80)	0.431
ALT, IU/L	20 (15-33)	25 (19-34)	0.191
GGT, IU/L	29 (19-44)	32 (19-44)	0.889
Triglycerides, mg/dL	94 (77-131)	120 (93-175)	0.002
HDL cholesterol, mg/dL	54 (45-65)	52 (41-60)	0.349
Fasting glucose, mg/dL	87 (82-98)	86 (79-93)	0.349
Liver stiffness, kPa	4.4 (3.4-5.3)	4.6 (3.9-5.6)	0.360
SLD, n (%)	21 (36)	19 (36)	0.969

*Median (Q1-Q3), unless otherwise specified; SLD: Steatotic liver disease

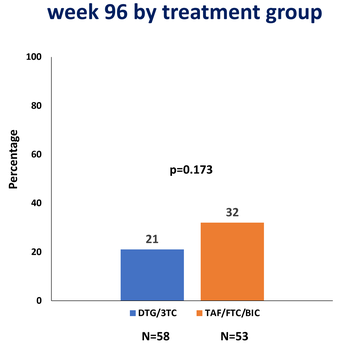
CAP change at week 96 by assigned therapy



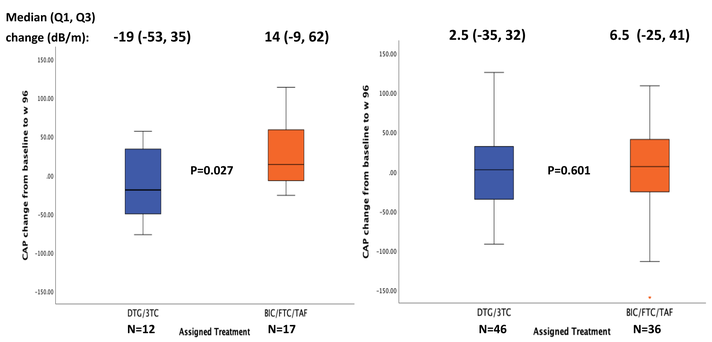
Proportion of participants with S≥1 (CAP≥248) along the follow-up



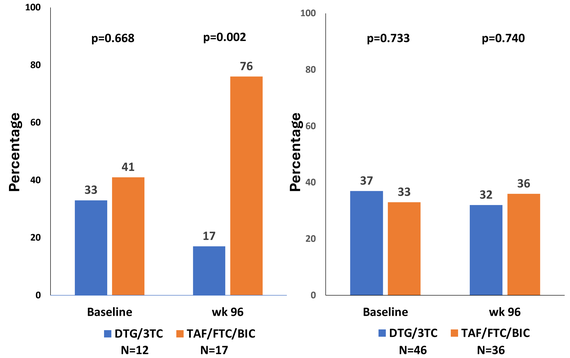
Weight gain ≥5% of baseline at week 96 by treatment group



CAP change at week 96 by weight gain and assigned treatment



Proportion of PLWH with S≥1 (CAP≥248) by weight gain and assigned treatment



Mantel-Haenszel test: Baseline, p=0.899; wk 96, p=0.081

Association between CAP increase and other factors in multivariate analysis

Variable	B (95% CI)	Standard Error	Standardized Beta	*p*
Age	-0.083 (-1.173, 1.006)	.549	-.016	.880
Sex	16.592 (-7.786, 40.969)	12.292	.129	.180
Assigned treatment	23.026 (-0.024, 46.075)	11.622	.192	.050
Baseline plasma triglycerides	-0.181 (-360, -0.002)	.090	-.199	.047
Weight gain	0.940 (-1.297, 3.178)	1.128	.085	.406
First NRTI in prior regimen	-4.908 (-15.866, 6.049)	5.525	-.087	.376
Second NRTI in prior regimen	-9.534 (-27.695, 8.626)	9.157	-.102	.300

CONCLUSIONS

- In virologically suppressed PLWH, switching to BIC/FTC/TAF is associated with a higher frequency of SLD compared to DTG/3TC after 96 weeks of therapy.
- The different impact of these regimens on SLD is more remarkable in PLWH who gain weight after therapy switching.

ADDITIONAL KEY INFORMATION: Funding: ViiV Healthcare. **Contact information:** Prof. J.A. Pineda. Research Unit, Hospital Universitario Virgen de Valme, University of Seville. Avda Bellavista s/n. 41014-Seville, Spain. email: japineda@us.es