Switching to DTG/3TC vs. BIC/FTC/TAF and Steatotic Liver Disease: A Sub-study PASODOBLE Trial

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BACKGROUND

Steatotic liver disease (SLD) is a common condition in PLWH, and is linked to overweight and associated metabolic disorders. Both INSTIs and TAF have been associated with weight gain in clinical trials and real-life studies. Likewise, TAF has also been associated with SLD. Conversely, inconsistent associations between INSTIs and SLD have been observed, not even in patients who gain weight. In the PASODOBLE clinical trial reported that, in virologically suppressed PLWH, switching to DTG/3TC is non-inferior to BIC/FTC/TAF and leads to less weight gain (Martínez E, et al. 25th IACS. Munich 2024. Abstr OAB3606LB). Therefore, switching to 3TC/DTG or to BIC/FTC/TAF could have a different impact on SLD. This is the first randomized clinical trial providing data on SLD for these two regimens. Our aim was to compare the effect of switching to DTG/3TC vs. BIC/FTC/TAF on SLD in PLWH.

METHODS

- PLWH from the PASODOBLE clinical trial were included in this sub-study if:
  - They were recruited by centers equipped with a vibration-controlled transient elastography (VCTE) device including CAP.
  - Measurements fulfilling quality criteria were obtained:
    - Success rate: >60%
    - IQR range of liver stiffness (LS) ≦ 30%, provided that LS= 7-30 kPa.
- SLD was defined as a CAP value ≥248 dB/m.
- The FibroScan-AST (FAST) score (Newsome. Lancet Gastroenterol Hepatol 2020), which includes AST, CAP and LSM was calculated.
  - FAST ≥0,67: Likely steatohepatitis with significant fibrosis (F2).
  - FAST ≤0,35: Unlikely steatohepatitis with F2.
- Primary outcome variable: CAP change from baseline to week 48.
- Analyses were planned at weeks 48 and 96.

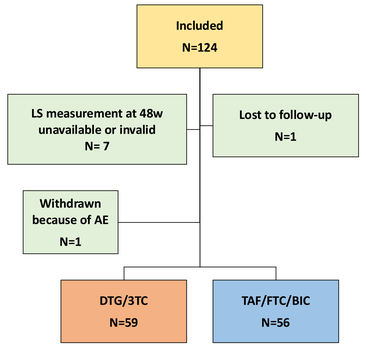
In PLWH who gain weight after switching to DTG/3TC or BIC/FTC/TAF, those treated with BIC/FTC/TAF show a greater increase in the frequency of steatotic liver disease compared to those receiving DTG/3TC.

CONCLUSIONS

- Switching to DTG/3TC or BIC/FTC/TAF is associated with a trend towards an increase in the frequency of SLD. Overall, no difference exists between the increase in CAP value for both regimens after 48 weeks of therapy.
- However, the frequency of SLD among PLWH who gained weight was significantly higher at 48 weeks vs baseline in the BIC/FTC/TAF arm, but not in the DTG/3TC arm. This effect seems to translate into a lower frequency of subjects without MASH with significant fibrosis at 48 weeks vs baseline in those treated with BIC/FTC/TAF.
- The effect on SLD of BIC/FTC/TAF seems to be more obvious in PLWH who were not on TAF before switching.

RESULTS

Participants disposition



Baseline characteristics (n=115)

Parameter n (%)	DTG/3TC n=59	BIC/FTC/TAF n=56	P value
Age*	51 (43-57)	52 (39-58)	0.771
Male sex, n (%)	38 (64)	40 (71)	0.420
Sexual HIV transmission	52 (88)	47 (84)	0.515
Alcohol (units/ day)*	0 (0-1.8)	0.5 (0-1)	0.105
Weight*	73 (64-82)	72 (63-80)	0.679
BMI*	25 (22-28)	25 (22-27)	0.474
Previous AIDS	15 (25)	14 (25)	0.958
CD4 cell counts*	697 (573-845)	607 (458-862)	0.207
ALT (IU/L)	20 (15-33)	25 (20-35)	0.112
AST (IU/L)	24 (19-29)	24 (19-29)	0.860
GGT	29 (19-45)	28 (19-44)	0.889
Liver stiffness (kPa)	4.5 (3.5-5.7)	4.7 (3.7-5.4)	0.646
CAP (dB/m)	232 (205-271)	226 (194-262)	0.417
SLD, n (%)	21 (36)	20 (36)	0.989

*Median (Q1-Q3). BMI: Body mass index; CAP: Controlled attenuation parameter; SLD: Steatotic liver disease

Fig 1. CAP change after 48 weeks

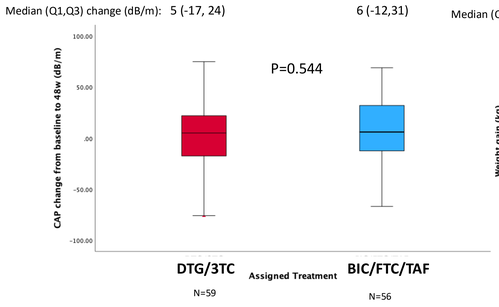


Fig 2. Weight change after 48 weeks

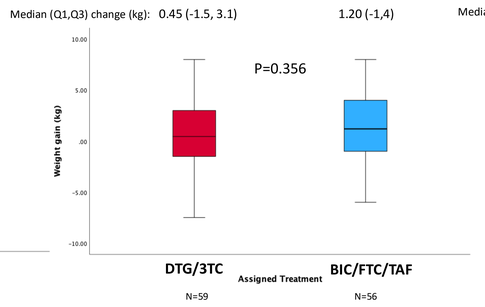


Fig 3. CAP change at week 48: No weight gain vs. any weight gain

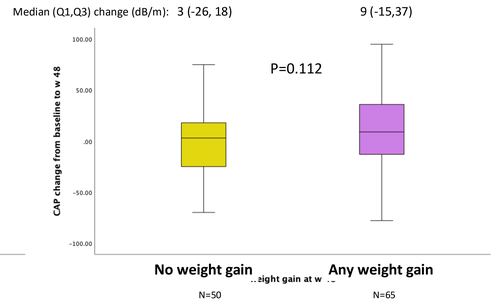


Fig 4. CAP change at week 48: PLWH who gained any weight according to assigned treatment

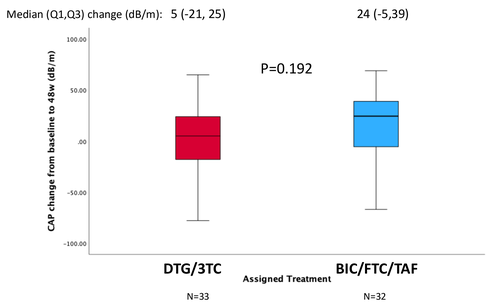


Fig 5. Changes in proportion of PLWH with SLD (≥S1) along the follow-up

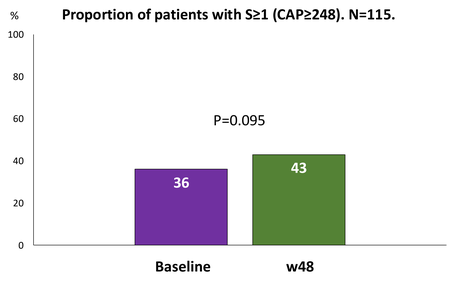


Fig 6. Changes in the proportion of PLWH with SLD according to assigned treatment. PLWH with any weight gain

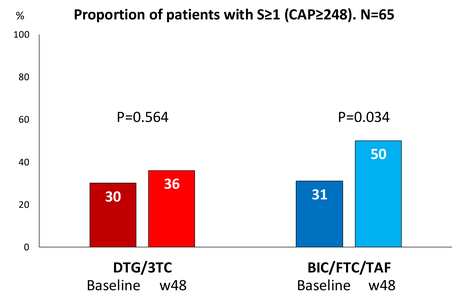


Fig 7. Changes in proportion of PLWH with unlikely steatohepatitis along the follow-up according to assigned treatment

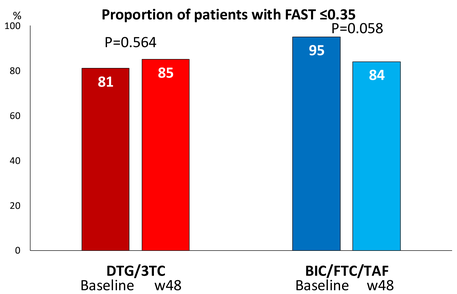
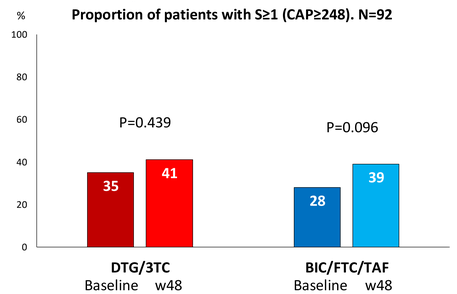


Fig 8. Changes in proportion of PLWH with SLD along the follow-up according to assigned treatment. PLWH without TAF prior to randomization



ADDITIONAL KEY INFORMATION: Funding: ViiV Helathcare. **Contact information:** Prof. J. Macías. Department of Medicine, Hospital Universitario Virgen de Valme, University of Seville. Avda Bellavista s/n. 41014-Seville, Spain. email: jmacias7@us.es