#1499

TESAMORELIN REDUCES VISCERAL ADIPOSE TISSUE AND LIVER FAT IN INSTI-TREATED PERSONS WITH HIV

T. McLAUGHLIN[1], T.L. STANLEY[2], L.T. FOURMAN[2], S. GRINSPOON[2]

[1]Medical Affairs Theratechnologies Inc, Montréal, Canada; [2]Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA.

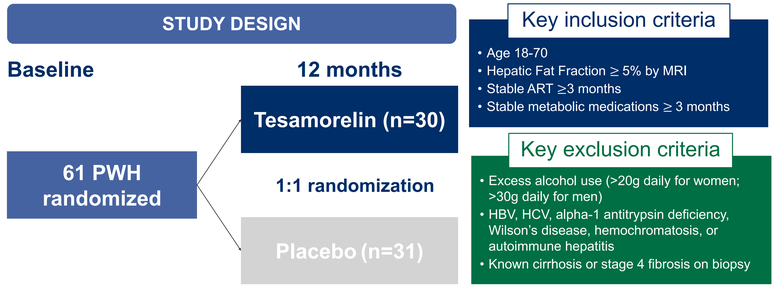
Background

- Recent studies have shown an association of treatment-emergent weight gain with use of integrase inhibitors (INSTIs), including dolutegravir (DTG), in people with HIV (PWH).
- Although few studies have examined the fat composition of this weight gain, the accumulation of visceral adipose tissue (VAT) has been shown to be a component of antiretroviral (ARV)-associated weight gain.[1]
- Excess VAT has been associated with downstream comorbidities, including metabolic-associated steatotic liver disease (MASLD).[2] Therefore, the clinical implications of ARV-associated weight gain are a growing concern.
- Tesamorelin, a growth hormone releasing hormone analogue, has previously been shown to reduce visceral adipose tissue (VAT) by over 15% in 26 weeks in PWH with excess visceral abdominal fat. However, with this study conducted in 2008, few PWH were on INSTI-containing regimens.
- Here, we investigated if tesamorelin could reduce VAT and liver fat in PWH on INSTI-containing regimens.

Can treatment with tesamorelin reduce visceral and hepatic fat in PWH on current INSTI-containing regimens?

Methods

STUDY DESIGN



Key inclusion criteria

- Age 18-70
- Hepatic Fat Fraction ≥ 5% by MRI
- Stable ART ≥3 months
- Stable metabolic medications ≥ 3 months

Key exclusion criteria

- Excess alcohol use (>20g daily for women; >30g daily for men)
- HBV, HCV, alpha-1 antitrypsin deficiency, Wilson's disease, hemochromatosis, or autoimmune hepatitis
- Known cirrhosis or stage 4 fibrosis on biopsy

- Data from a Phase II study of tesamorelin among PWH with NAFLD were leveraged, in which participants were randomized to tesamorelin (2mg) vs placebo daily for 52 weeks.[4]
- All participants received nutritional counseling from clinical research nutritionists at baseline and every 6 months.
- Measurements of body composition and hepatic fat fraction (HFF), as assessed by magnetic resonance imaging/spectroscopy (MRI/MRS), were taken at baseline & after 12 months of treatment.
- Post-hoc analyses were performed to evaluate changes in body composition amongst individuals receiving INSTIs.

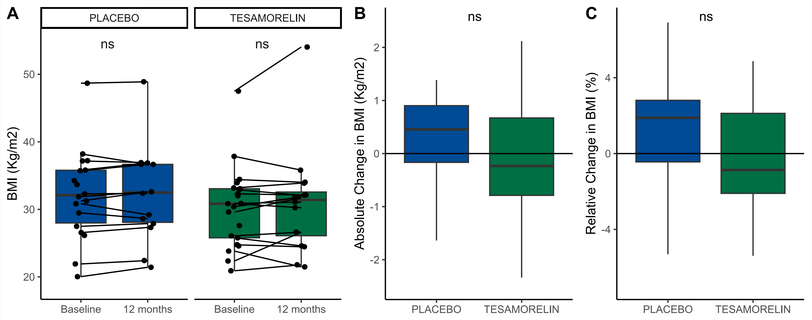
Results

Table 1: Baseline characteristics of participants on INSTI-containing and non-INSTI-containing regimens

	INSTI (n=39)	Non-INSTI (n=22)	Unadjusted p-value
Demographic			
Age (years)	54 ± 7	51 ± 8	ns
Sex – Male†	29 (74.4)	19 (86.4)	ns
Race†			ns
White	23 (59.0)	17 (77.3)	
Black or African American	14 (35.9)	4 (18.2)	
Other/Unknown	2 (5.2)	1 (4.5)	
HIV Related Parameters			
HIV Duration (years)	17 ± 10	16 ± 7	ns
HIV Viral Load (copies/mL)	12 ± 29.2	5 ± 12.8	ns
CD4 Count (cells/mm^3)	754 ± 269.4	785 ± 291.5	ns
Use of ART medications			
NRTI	34 (87.2)	22 (100.0)	ns
NNRTI	8 (20.5)	15 (68.2)	0.001
PI	7 (17.9)	8 (36.4)	ns
Other	2 (5.2)	0 (0.0)	ns
Body Composition			
Weight (kg)	92.4 ± 15.9	96.5 ± 19.57	ns
BMI mean (kg/m^2)	31.1 ± 6.27	32.1 ± 6.16	ns
Waist circumference (cm)	110 ± 12.1	111 ± 16.9	ns
Hip circumference (cm)	108 ± 11.2	110 ±12.2	ns
Visceral adipose tissue (cm^2)	235 ± 102.3	251 ± 88.8	ns
Subcutaneous adipose tissue (cm^2)	314 ± 164.1	305 ± 156.6	ns
Total fat (kg)	32.2 ± 11.7	32.7 ± 11.0	ns
Lean mass (kg)	59.1 ± 10.1	62.7 ± 12.0	ns
Hepatic fat fraction (%)	13.5 ± 8.73	14.4 ± 7.83	ns

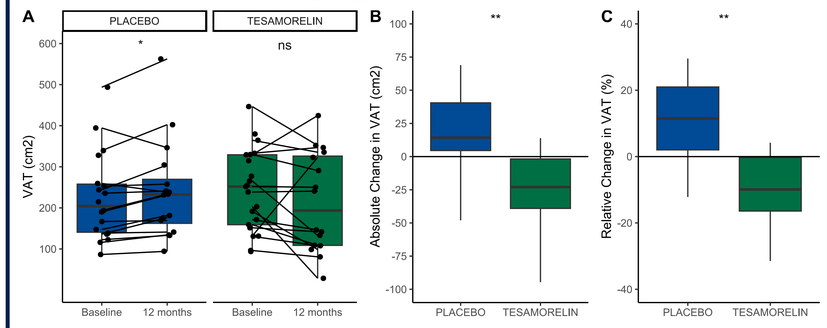
Continuous variables are reported as mean ± SD and categorical values reported as n (%). Ns denotes not significant (*P*>0.05). The use of metabolic medications did not differ between groups at baseline.

Figure 1: BMI was stable over one year in PWH on INSTI-containing regimens, irrespective of treatment assignment



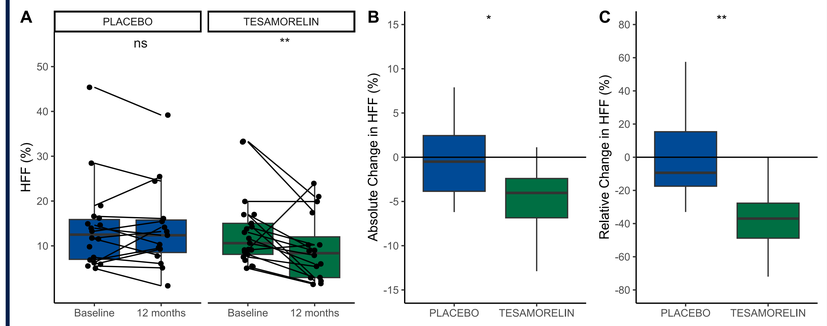
There was no baseline difference in BMI by treatment assignment among participants on INSTI-containing regimens (p=0.58). There also was no change in BMI over 12 months A) within treatment arms (placebo p=0.39, tesamorelin p=0.63) or B-C) between treatment arms (absolute change p=0.8; relative change p=0.8). Box and whiskers represent the median and IQR with dots representing individual participant values. Paired Wilcoxon signed rank test was performed to evaluate differences between baseline and 12 months. Mann-Whitney tests were used to evaluate between-group differences.

Figure 2: Tesamorelin reduced visceral adipose tissue (VAT) among PWH on INSTI-containing regimens



(A) Participants on INSTI-containing regimens who received placebo over 12 months experienced a gain in VAT (+10.8%, p= 0.01), whereas VAT in tesamorelin-treated participants tended to decline (-8.3%, p= 0.09). After 12 months of treatment, there was a significant difference in (B) absolute (p=0.003) and (C) relative (p=0.001) change in VAT between placebo and tesamorelin-treated participants on INSTI-containing regimens. Box and whiskers represent the median and IQR with dots representing individual participant values. Paired Wilcoxon signed rank test was performed to evaluate differences between baseline and 12 months. Mann-Whitney tests were used to evaluate between-group differences.

Figure 3: Tesamorelin reduced hepatic fat fraction (HFF) in PWH on INSTI-containing regimens



(A) Participants on INSTI-containing regimens who received placebo over 12 months had no change in HFF, (-0.1%, p=0.76), whereas HFF in tesamorelin-treated participants declined (-4.9%, p=0.006). After 12 months of treatment, there was a significant difference in (B) absolute (p=0.02) and (C) relative (p=0.006) change in HFF between placebo and tesamorelin-treated participants on INSTI-containing regimens. Box and whiskers represent the median and IQR with dots representing individual participant values. Paired Wilcoxon signed rank test was performed to evaluate differences between baseline and 12 months. Mann-Whitney tests were used to evaluate between-group differences.

Conclusions

- PWH on INSTI-containing regimens experienced a gain in VAT after 12 months in the placebo-treated arm, despite a stable BMI
- Tesamorelin reduced both visceral and hepatic fat in PWH on INSTI-containing regimens, which supports its use among individuals with INSTI-associated changes in body composition

Author Contact: **LFourman@mgb.org**

[1]Hill et al, CROI 2020. Oral Abstract 81. [2]Yu SJ et al. Medicine 2015; [3]Falutz et al. AIDS 2008; [4]Stanley et al, Lancet HIV 2019 [5]Falutz et al. JAcquirImmuneDeficSyndr. 2010; [6]Falutz et al. JClinEndocrinolMetab. 2010