

Effect of Tesamorelin in Patient with HIV with Integrase Inhibitor Associated Weight Gain

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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, studies have demonstrated the accumulation of visceral adipose tissue (VAT) as a component of antiretroviral therapy (ART)-associated weight gain.¹

Lipohypertrophy is characterized by localized abnormal fat accumulation, most commonly seen as excess VAT in the intra-abdominal compartment. Lipohypertrophy can present as a mixed lipodystrophy, which includes both lipoatrophy – characterized by the presence of peripheral wasting – and lipohypertrophy.²

In PWH, multiple factors contribute to lipohypertrophy, including:

- Patient characteristics (i.e female sex and older age)
- HIV viral load and nadir CD4 count
- Duration or type of ART³
- Impaired fatty acid metabolism and endocrine alterations, such as impaired growth hormone secretion⁴

Tesamorelin, a growth hormone-releasing hormone (GHRH) analog, is the only FDA-approved agent indicated for the reduction of excess abdominal fat in HIV-infected adult patients with lipodystrophy.⁵ However, it remains unclear if treatment with tesamorelin would impact the accumulation of VAT seen with ART-associated weight gain.

CASE PRESENTATION

The patient is a 64-year-old Hispanic male living with HIV since 2002 and prior history of lipodystrophy, manifested by facial and limb lipoatrophy and abdominal and dorsocervical lipohypertrophy - attributed to prior NRTI and PI based regimens. **He presents with weight gain and worsening abdominal and dorsocervical fat while on a DTG-based regimen.**

CASE PRESENTATION (CONT.)

- **February 2016:** Patient established care with the clinic. He had been on tenofovir/abacavir/nevirapine (TDF/ABC/NVP) for over 5 years and weighed 167 lbs. Previous ART regimens included zidovudine, indinavir, ritonavir, stavudine, nelfinavir and efavirenz.
 - Viral load: below the limits of detection (<50 copies/mL)
 - Nadir CD4 count: 334 cells/mm³
 - Past medical history includes asthma, former smoker (quit in 1995), peripheral neuropathy, HCV previously treated with sofosbuvir/velpatasvir with sustained virologic response
 - Past surgical history includes surgical fusion of C1-C2 in 2014 and liposuction from shoulder and neck in 2004
- **May 2016:** Patient was switched to an INSTI-based regimen, abacavir/lamivudine/dolutegravir (ABC/3TC/DTG), for regimen simplification.
- Ongoing weight gain noted in subsequent visits after ART switch.
 - No other medication changes or significant lifestyle changes were noted to contribute to the weight gain.
- **February 2018:** Patient reached a peak weight of 213 lbs (total weight gain of 28% in slightly under 2 years).
 - Patient's waist-to-hip ratio (WHR) was 1.07, with no fat accumulation in areas of prior residual lipoatrophy. His shirt neck size increased from 16 to 18.5 in.
 - Patient expressed that he could no longer button his shirt or bend down to tie his shoes and switched to loafers for work.
 - Patient was counseled on lifestyle changes and referred to nutrition. He consistently attended appointments and implemented dietary changes. He was able to lose small amounts of weight, but there was no change to areas of fat accumulation.
- **October 2018:** After much discussion, the patient desired to stay on his DTG-based regimen, given his history of lipodystrophy and other intolerances on prior regimens, and tesamorelin was initiated.
- Close monitoring occurred following tesamorelin initiation and anthropometric measurements were collected (Table 1).
 - Along with improvements in weight, BMI, waist circumference (WC), and WHR, triglyceride levels were reduced by 47 mg/dL and HDL levels increased by 9 mg/dL (Nov 2018 → Aug 2019).

Table 1. Body Composition Measurements on Tesamorelin

	Date	ART	Weight (lb)	BMI (kg/m ²)	Waist Circumference (cm)*	Hip Circumference (cm)	Waist to Hip Ratio*
Prior to ART change	2/25/2016	TDF/ABC/NVP	167	27.80	-	-	-
After ART change	2/6/2018	ABC/3TC/DTG	213	35.00	114.30	106.70	1.07
Tesamorelin initiation 10/04/2018							
Visit 1: Week 6	11/29/2018	ABC/3TC/DTG	199	32.70	111.50	106.70	1.04
Visit 2: Week 15	1/17/2019	ABC/3TC/DTG	196	32.50	110.00	107.50	1.02
Visit 3: Week 22	3/7/2019	ABC/3TC/DTG	180	30.00	109.00	104.00	1.04
Visit 4: Week 35	6/13/2019	ABC/3TC/DTG	176	29.00	101.50	99.00	1.03
Visit 5: Week 44	8/22/2019	ABC/3TC/DTG	173	28.80	100.00	98.50	1.02

*WC and WHR are the most commonly used surrogate indexes of visceral adiposity.⁶ World Health Organization indicates substantially increased risk of metabolic complications with a WC >102 cm (men), >88 cm (women) or WHR ≥0.90 (men), ≥0.85 (women).⁷

OUTCOMES AND DISCUSSION

- Patient had a progressive weight loss of 40 lbs, accompanied by decreases in WC (~14 cm, or 5.5 in) and WHR at subsequent visits while on tesamorelin treatment. BMI category improved and returned to near baseline BMI prior to ART switch.
- Patient stated that his shirt collar size had decreased to 17 ¾ in since starting the medication.
- Improvement in patient-related outcomes with body image and quality of life were also reported.
- Notably, abdominal and dorsocervical fat deposition and overall body composition measurements improved.

CLINICAL RELEVANCE

- INSTI-derived weight gain has been associated with increases in visceral abdominal fat in people with HIV.
- Tesamorelin, a synthetic form of growth hormone-releasing hormone, was chosen to reverse VAT increases in a patient experiencing weight gain while on a DTG-based regimen.
- Importantly, this case demonstrates that treatment with tesamorelin was effective at reducing ART-associated weight gain and excess visceral adiposity. Tesamorelin may be a beneficial treatment option for patients with a similar clinical presentation.⁸

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