Impact of GLP-1 receptor agonists on body weight in patients with type 2 diabetes and HIV

Amber N Lloyd, PharmD[1]; Marisa B Brizzi, PharmD[1]; Megan M Lyons, PharmD[1]; Leannyn M Rotert, DO[2]; Carl J Fichtenbaum, MD[2]

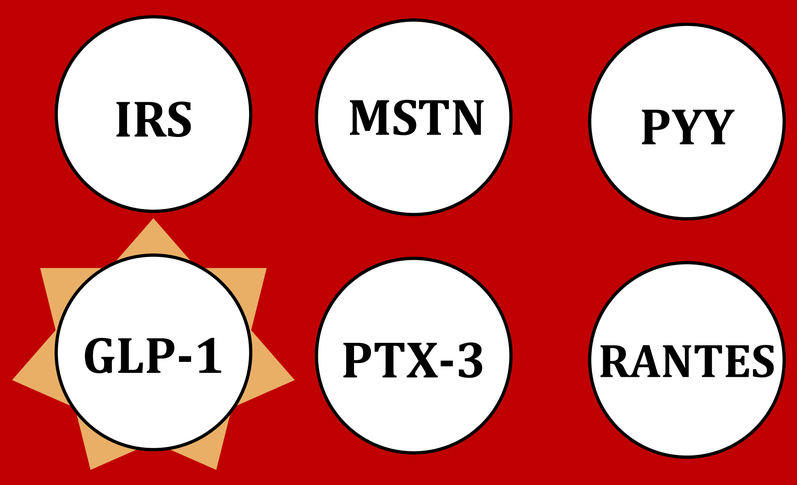
1. UC Health - University of Cincinnati Medical Center, Cincinnati, OH, USA; 2. Division of Infectious Diseases, University of Cincinnati College of Medicine, Cincinnati, Ohio, USA.

BACKGROUND

- People with HIV (PWH) taking antiretroviral therapy (ART) are at greater risk of developing metabolic disorders compared to the general population[1]
- The mechanism behind the development of metabolic syndrome in PWH is poorly understood[1]
- Integrase strand transfer inhibitor- (INSTI-) based regimens have been associated with clinically significant weight gain in PWH[2]
- Glucagon-like peptide-1 (GLP-1) may be depleted during HIV infection and may play a role in weight gain[3]
- The impact of GLP-1 receptor agonists (GLP-1 RAs) on weight in PWH is unknown[3]

Effect of ART on metabolic & inflammatory markers[1]

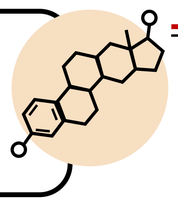
The following parameters are significantly **lower** in men with HIV after starting ART compared to men without HIV:



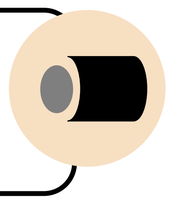
Abbreviations: IRS—irisin; MSTN—myostatin; PYY—peptide YY; GLP-1—glucagon-like peptide-1; PTX3—pentraxin 3; RANTES—normal T cell expressed and secreted

Proposed mechanism of INSTI-mediated weight gain[2]

INSTI interferes with adipocyte differentiation, thermogenesis, and other estrogen-mediated metabolic pathways

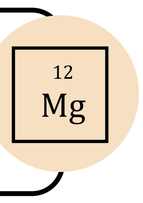


INSTI directly affects adipocytes, adiponectin, or other hormones that regulate glucose and lipid metabolism

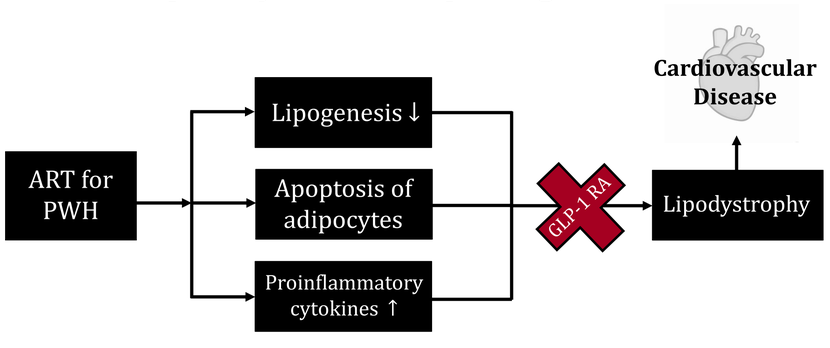


INSTI suppresses melanocortin stimulating system, which increases appetite

INSTI chelates magnesium, which reduces insulin sensitivity



Hypothesis of the pathogenesis of lipodystrophy syndrome and proposed impact of GLP-1 receptor agonists[3]



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OBJECTIVES

Primary Outcome

Change in body weight (kg) before and after initiation of a GLP-1 RA in patients with diabetes mellitus (DM) + HIV compared to patients with DM only

Secondary Outcomes

Percentage change in body weight (kg) before and after the initiation of a GLP-1 RA in patients with DM + HIV compared to patients with DM only

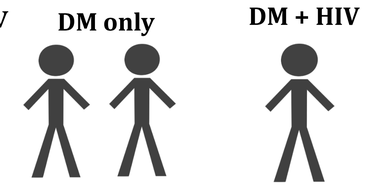
Rates of patients achieving ≥5% weight loss after the initiation of a GLP-1 RA in patients with DM + HIV compared to patients with DM only

Percentage change in HbA1c before and after the initiation of a GLP-1 RA in patients with DM + HIV compared to patients with DM only

METHODS

Study Design

- Retrospective chart review
- Pre- and post-hoc analysis
- Study Period
  - 8/31/17 – 8/31/22
- Matched Population (2:1)
  - Matched by gender, ethnicity & GLP-1 RA dose



Inclusion Criteria	Exclusion Criteria
• Adult patients ≥18 years of age • Type 2 DM diagnosis • Currently being prescribed a GLP-1 RA • Being managed by a UC Health outpatient clinic	• Patients without pre and post weight (kg) • Patients without pre and post HbA1c • Prisoners • Pregnant or breastfeeding women

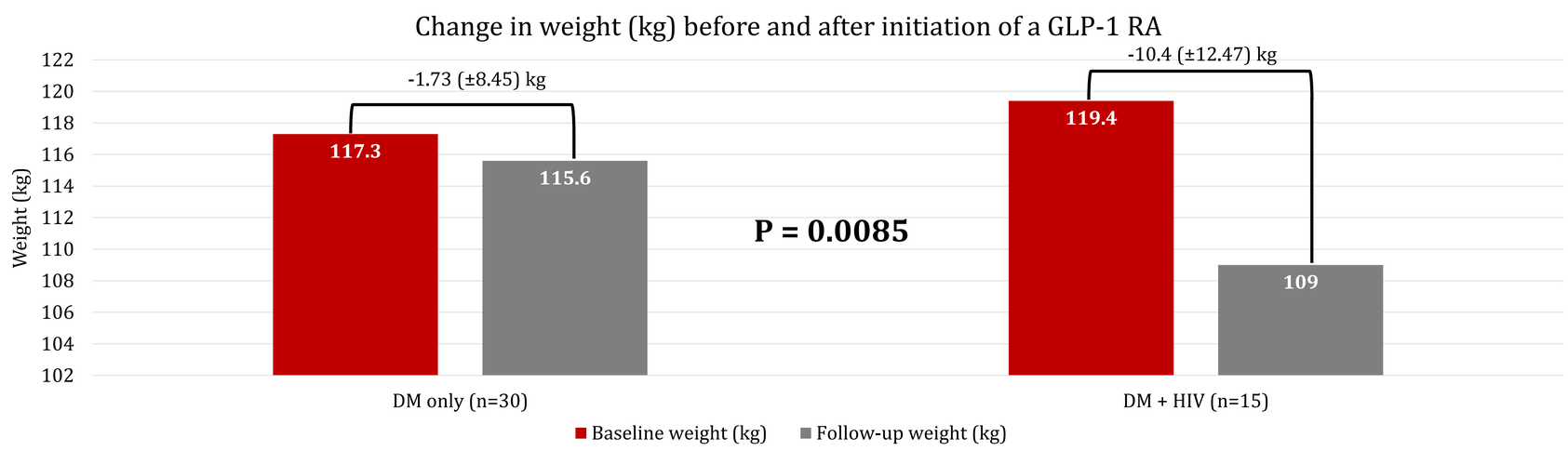
RESULTS

Baseline Characteristics

	DM only (n = 30)	DM + HIV (n=15)	P-value
Age, years	57 (±8.74)	56 (±8.12)	0.7221
Female (%)	4 (13.3%)	2 (13.3%)	>0.999
Race (%) Black/African American White/Caucasian	 16 (53.3%) 14 (46.6%)	 8 (53.3%) 7 (46.6%)	 >0.999 >0.999
Weight, kg	117.3 (±37.7)	119.4 (±34.5)	0.8593
HbA1c, mmol/mol	8.4% (±2.0%)	8.6% (±2.8%)	0.8562
GLP-1 RA (%) dulaglutide semaglutide liraglutide	 22 (73.3%) 4 (13.3%) 4 (13.3%)	 11 (73.3%) 2 (13.3%) 2 (13.3%)	 >0.999 >0.999 >0.999
INSTI-based regimen	-	13 (86.6%)	-

Data presented are n(%) or mean (SD)

Primary Outcome



Secondary Outcomes

	DM only (n = 30)	DM + HIV (n=15)	P-value
% change in weight (%)	-1.47% (±6.8)	-8% (±9.96%)	**0.013**
Patients achieving ≥5% weight loss (%)	10 (33%)	9 (60%)	0.1158
% change in HbA1c, mmol/mol	-0.49% (±2%)	-1.3% (±2.39%)	0.2415

Data presented are n(%) or mean (SD)

CONCLUSION

In this cohort, PWH and DM had significantly greater weight loss compared to people with DM alone. The greater weight loss observed in PWH may be related to differences in the mechanistic pathways leading to weight gain.

REFERENCES

1. Jurkowska K, Szymanska B, Knysz B, Piwowar A. Effect of Combined Antiretroviral Therapy on the Levels of Selected Parameters Reflecting Metabolic and Inflammatory Disturbances in HIV-Infected Patients. J Clin Med. 2022;11(6):1713. doi:10.3390/jcm11061713
2. Wood BR, Huhn GD. Excess weight gain with integrase inhibitors and tenofovir alafenamide: what is the mechanism and does it matter? Open Forum Infect Dis. 2021;8(12):ofab542. doi: 10.1093/ofid/ofab542.
3. Culha MG, Inkaya AC, Yildirim E, Unal S, Serefoglu EC. Glucagon like peptide-1 receptor agonists may ameliorate the metabolic adverse effect associated with antiretroviral therapy. Med Hypotheses. 2016;94:151-153. doi: 10.1016/j.mehy.2016.07.016.

Conflicts of Interest: Marisa B Brizzi discloses ViiV: speaker's bureau and advisory board and Gilead: advisory board. Carl J Fichtenbaum discloses ViiV, Moderna, Gilead, and Merck: researcher. All other authors have no relevant conflicts of interest to declare. The potential effects of relevant financial relationships with ineligible companies have been mitigated.

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