Weight Gain Associated with Integrase Inhibitors and Tenofovir Alafenamide (TAF) and Impact on Comorbid Disease States

OKLAHOMA STATE UNIVERSITY
CENTER FOR HEALTH SCIENCES

Oklahoma State University Medical Center, Department of Pharmacy[1] | Oklahoma State University Center for Health Science, Department of Internal Medicine[2], Department of Psychiatry and Behavioral Sciences[3] | Oklahoma State University College of Osteopathic Medicine at Cherokee Nation, Office of Medical Research[4]

Eugene Hernandez III, PharmD, BCIDP(PGY1)[1]*; Micah Hartwell, PhD[3,4]; Jenna Record, PharmD[1]; Michael Hiebert, DO, AAHIVS[2]; Bryan Bozell, PharmD, BCPS, AAHIVP[1,2]*

BACKGROUND

- Today's standard antiretroviral therapy (ART) regimen include an integrase inhibitor and nucleoside reverse transcriptase inhibitor (NRTI), commonly with TAF
- These agents are frequently used due to their lower rates of virologic failure, high barrier to resistance, and in general better tolerability
- There has been a clear correlation established between weight gain associated with the use of TAF and integrase inhibitors
- Previous studies have indicated that this weight gain my correlate with increased cardiovascular risk and increased development of metabolic syndrome

OBJECTIVES

- Evaluate the association between weight gain and an increased risk of cardiovascular events and metabolic syndrome in patients on ART regimens that include (1) integrase inhibitors + TAF, (2) TAF without integrase inhibitors, or (3) integrase inhibitors without TAF

END POINTS

Primary Endpoint:
- Change in BMI over the three visits in each cohort

Secondary Endpoint:
- Changes in A1C and systolic blood pressure over time and by cohort
- Report incidences of new major adverse cardiovascular events (MACE)

METHODS

This study was a single-center retrospective chart review from October 2020 to October 2023 of patients at Oklahoma State University Internal Medicine Specialty Services Clinic (OSU IMSS). An informational technology specialist was instructed to run a report and identify patients in 3 different cohorts based on their ART. 50 patient charts were randomly selected from each cohort. To measure differences between cohorts and over time, we used mixed-effects regression models and controlled for race, sex, age, and whether the patient was taking medications that may influence weight loss. We also reported the incidences of new major adverse cardiovascular events (MACE) during the study timeframe.

RESULTS

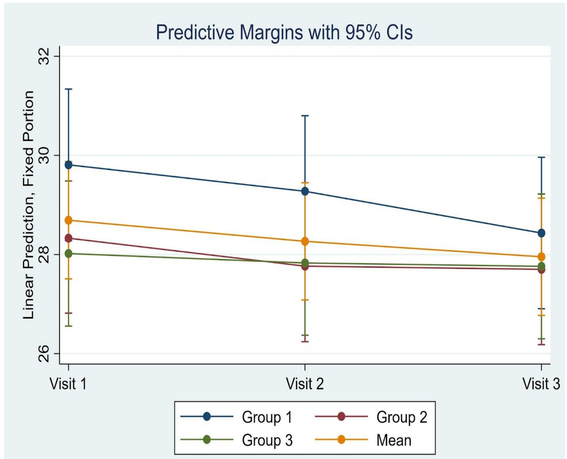

Figure 1. BMI by cohort over time.

The mean baseline BMI by cohort was 29.2 (SE = 0.8) for cohort 1, 28.7 (SE = 1.0) for cohort 2, and 27.6 (SD = 0.8) for cohort 3. The mixed-effects regression model showed that between visits 1 and 3, there was a significant reduction in BMI (b = -1.4, SE = 0.6; t = -2.4, P = .018; Figure 1). For A1C, cohort 2 showed a significant increase between visits 2 and 3 (Figure 2) which was the only significant component of the interaction term. The mixed effects model for systolic BP showed a significant decrease over time (b = -10.2; SE = 2.8, t = -3.64, P <.001, Figure 3). The interaction term for systolic BP was not significant. There were only 2 incidences of MACE—one each in group 1 and group 2

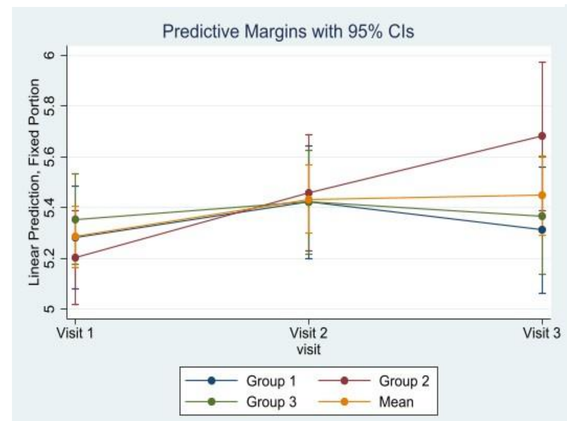

Figure 2. A1C by cohort over time.

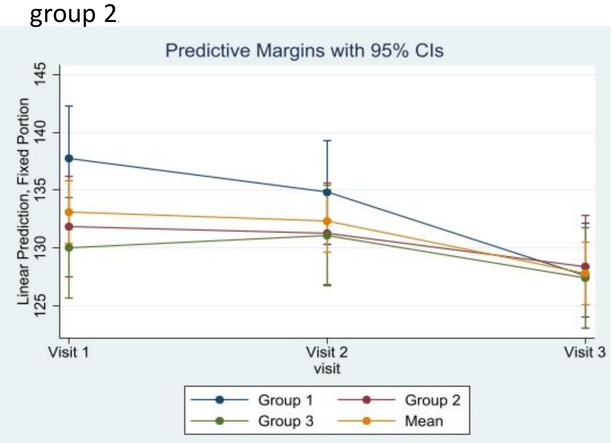

Figure 3. SBP by cohort over time.

CONCLUSIONS

- The decline in BMI over the 3 visits for all 3 cohorts diverges from conventional expectations of weight gain when patients are on these regimens
- A limitation of the study is that the initiation of their current ART regimen was not documented
- The significant rise in A1C in cohort 2, may be due to many of these patients being on protease inhibitors in addition to TAF, which may increase glucose levels
- The decline in SBP over the 3 visits, may indicate better control of patient's blood pressure with antihypertensives
- The 2 incidences of MACE during the study period were not statistically significant

NEXT STEPS

Weight gain at the initiation of these ART regimens has been extensively documented, but the results of this study may indicate that these regimens may have a net neutral effect on weight after some time

DISCLOSURES

Dr. Hartwell receives research funding from the National Institute of Child Health and Human Development (U54HD113173; Shreffler), Human Resources Services Administration (U4AMC44250-01-02, PI: Audra Haney; R41MC45951 PI: Hartwell), and previously from the National Institute of Justice (2020-R2-CX-0014 PI: Beaman). Other authors involved in this project have no competing financial interests to disclose.

REFERENCES

1. Martínez-Sanz J, Serrano-Villar S, Muriel A, et al. Metabolic-Related Outcomes After Switching From Tenofovir Disoproxil Fumarate to Tenofovir Alafenamide in Adults With Human Immunodeficiency Virus (HIV): A Multicenter Prospective Cohort Study. Clin Infect Dis. 2023;76(3):e652-e660.
2. Schafer JJ, Zimmerman M, Walshe C, Cerankowski J, Shimada A, Keith SW. Weight changes in patients with sustained viral suppression switching tenofovir disoproxil fumarate to tenofovir alafenamide. Obesity . 2022;30(6):1197-1204.
3. Sjaarda A, Bernstein A, Sparks A, Saber S, Siegel M. Comparison of weight gain after antiretroviral switch to integrase strand transfer inhibitor or tenofovir alafenamide-based therapy. Infection. 2022;50(2):407-412.
4. Shah S, Hill A. Risks of metabolic syndrome and diabetes with integrase inhibitor-based therapy. Curr Opin Infect Dis. 2021;34(1):16-24.

Scan here to watch video