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Persistence and Adherence of People With HIV and Mental Health Disorder Diagnosis Who Restart Antiretroviral Therapy

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Conclusions

- Mental health disorders (MHDs) and substance use disorders (SUDs) are prevalent among people with HIV (PWH) with treatment interruptions (TIs) resuming antiretroviral therapy (ART)
- PWH with MHD/SUD restarting bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) were subsequently more persistent compared to those restarting dolutegravir/abacavir/lamivudine (DTG/ABC/3TC), and DTG-based multi-tablet regimens (MTR), and less likely to switch therapy than those on DTG/3TC
- All PWH restarting B/F/TAF were more persistent and less likely to switch therapy compared to those restarting DTG/ABC/3TC and DTG-based MTR
- Adherence among PWH who restart ART was similar by regimen

Plain Language Summary

- Current recommended oral human immunodeficiency virus (HIV) medicines need to be taken once a day to control the virus
- In the US, almost half of people with HIV also have a mental health or a substance use disorder, which can make it harder to always take their HIV medicines every day
- Mental health or substance use disorders may cause people with HIV to sometimes stop and restart their HIV medicine
- When restarting HIV medication after having stopped for some time (at least 90 days), we found that people who restarted the medicine bictegravir/emtricitabine/tenofovir alafenamide then stayed longer on treatment than people who were restarting certain dolutegravir-based regimens

Introduction

- MHDs and SUDs are prevalent among PWH[1]:
  - ~55% of PWH in the US and Canada have been diagnosed with ≥1 MHD, with ~24% experiencing MHD multimorbidity[2]
  - Estimates of SUDs range from 25-48% depending on setting[3,4]
- ART TIs are prevalent among PWH.[5,6] Those who restart usually do so on the same regimen[7]
- Treatment-experienced PWH who face viral rebound after a TI can achieve viral resuppression after restarting ART, but this requires subsequent persistence which may be difficult for PWH with MHD/SUD

Objective

- In this study, we assessed real-world treatment persistence and adherence among PWH who were restarting on the same ART regimen after a TI, with a focus on those with a MHD or SUD comorbidity
- Our goal was to compare PWH restarting B/F/TAF to PWH restarting several other guideline-recommended DTG-based regimens, including DTG/3TC, DTG/ABC/3TC, and DTG-based MTR dolutegravir+emtricitabine/tenofovir disoproxil fumarate (DTG+F/TDF) or dolutegravir+emtricitabine/tenofovir alafenamide (DTG+F/TAF)

Methods

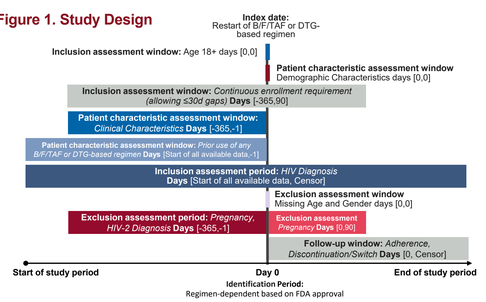
Table 1. Attrition Table

Overall Inclusion Criteria	N
HIV-1 diagnosis in HV dataset from Jan. 1, 2015, to Feb. 29, 2024	958,882
And no diagnosis of HIV-2 from Jan. 1, 2015, to Feb. 29, 2024	942,507
And at least one claim for any ART between Feb. 7, 2018, and Nov. 30, 2023	479,088
And age 18+ at any point during Feb. 7, 2018, through Nov. 30, 2023	476,923
And at least 455 days of continuous enrollment during Feb. 7, 2017, through Feb. 29, 2024	301,027
People indexed on a line of therapy of interest and included in at least one of our cohorts	20,623

Cohort Specific Criteria	B/F/TAF (vs. DTG/3TC)	B/F/TAF (vs. DTG/ABC/3TC)	B/F/TAF (vs. Combined DTG-Based MTR)	DTG/3TC	DTG/ABC/3TC	Combined DTG-Based MTR
Excluding those with ≤ 30 days of persistence	12,945	12,954	12,978	891	4799	2075

- We analyzed pharmacy and medical claims data from HealthVerity Marketplace from January 2015-February 2024
- PWH aged ≥ 18 years restarting one of the following index regimens after a > 90-day gap in therapy were identified: B/F/TAF, DTG/3TC, DTG/ABC/3TC, or DTG-based MTR (DTG+F/TDF or DTG+F/TAF)
- Continuous enrollment was required for ≥ 365 days pre-restart (baseline period) and ≥ 90 days post-restart (**Figure 1**)
- We calculated non-persistence as a discontinuation (medication gap of > 90 days) or regimen switch, from restart date to the earliest of the following events: disenrollment, evidence of pregnancy, or end of data
- Adherence was measured as the proportion of days covered (PDC) while persistent
- We fit inverse probability of treatment weighted (IPTW) Cox models to calculate pair-wise hazard ratios of non-persistence outcomes, with censoring for disenrollment, evidence of pregnancy, or end of data, comparing each other regimen to B/F/TAF

Figure 1. Study Design



Results

- 20,623 unique individuals were indexed restarting the same ART after a TI > 90 days (**Table 1**). Of these, 8953 (43.4%) had any MHD diagnosis,[2] including 5857 (28.4%) with severe MHD (schizophrenias, bipolar disorders, major depression, psychoses, and post-traumatic stress disorder) and 4015 (19.5%) with SUD
- The proportion of PWH insured by Medicaid differed significantly across ARTs, ranging from 71.9% of PWH taking DTG-based MTR and to 54.2% of those on DTG/3TC (**Table 2**). After IPTW for restarters with MHD/SUD, balance (defined as absolute standardized difference [ASD] < 0.1) was achieved on baseline characteristics, except for five characteristics with ASD < 0.28

Upon restarting, compared to individuals on B/F/TAF, the hazard of subsequent non-persistence was higher for DTG/ABC/3TC and DTG-based MTR, but similar for DTG/3TC. Compared to B/F/TAF, the hazard of switching was higher for all regimens, including DTG/3TC (Figure 2)

- Adherence to the index therapy after restart was similar by regimen (weighted PDC range 78.7-80.2%)

Table 2. Baseline characteristics of people with any MHD/SUD diagnosis who restarted B/F/TAF and select DTG-based regimens

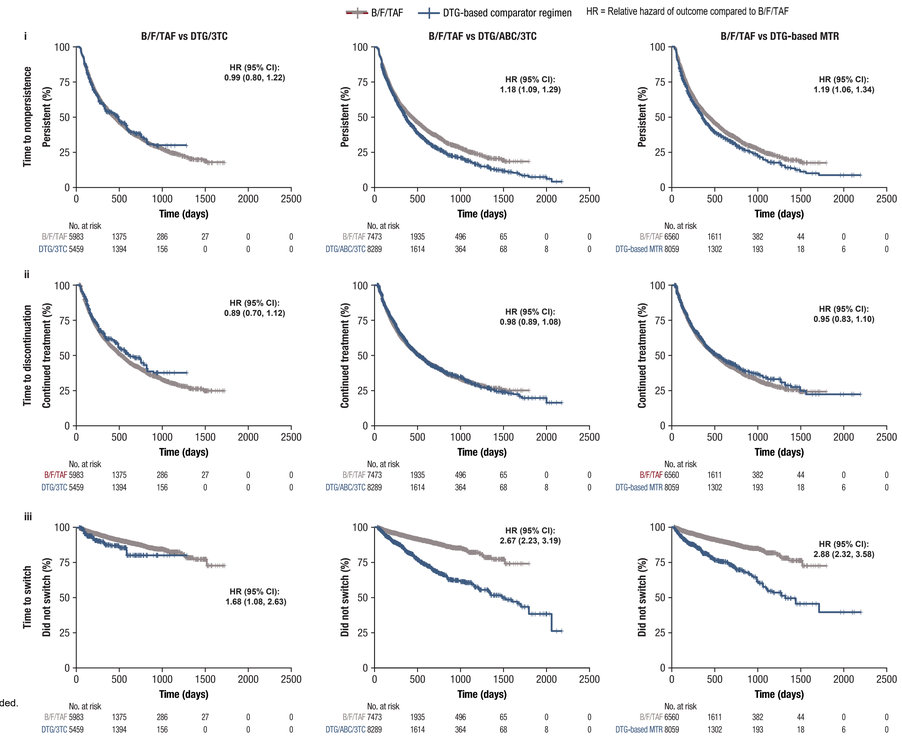
	DTG/3TC vs. B/F/TAF				DTG/ABC/3TC vs. B/F/TAF				Combined DTG-based MTR vs. B/F/TAF			
	B/F/TAF (n = 5627[a])	DTG/3TC (n = 354)	Pre-Weighting ASD[b]	Post-Weighting ASD	B/F/TAF (n = 5632[a])	DTG/ABC/3TC (n = 2014)	Pre-Weighting ASD	Post-Weighting ASD	B/F/TAF (n = 5643[a])	DTG MTR (n = 1008)	Pre-Weighting ASD	Post-Weighting ASD
Mean age, years (SD)	43.1 (12.3)	44.0 (12.3)	0.071	0.009	**43.1 (12.3)**	**45.1 (12.5)**	0.170	0.004	**43.1 (12.3)**	**44.9 (12.1)**	0.14	0.038
Female	1527 (27.1%)	100 (28.2%)	0.025	0.025	1525 (27.1%)	554 (27.5%)	0.010	0.000	**1526 (27.0%)**	**346 (34.3%)**	0.158	0.008
Insurance type												
Commercial	**1297 (23.1%)**	**117 (33.1%)**	0.224	0.021	**1313 (23.3%)**	**551 (27.4%)**	0.093	0.023	**1310 (23.2%)**	**149 (14.8%)**	**0.216**	0.060
Medicaid	**3810 (67.7%)**	**192 (54.2%)**	0.279	0.038	**3798 (67.4%)**	**1227 (60.9%)**	0.136	0.021	**3813 (37.6%)**	**725 (71.9%)**	**0.095**	0.050
Medicare Advantage	**520 (9.2%)**	**45 (12.7%)**	0.111	0.028	**521 (9.3%)**	**236 (11.7%)**	0.081	0.001	**520 (9.2%)**	**134 (13.3%)**	**0.129**	0.003
Mean Charlson Comorbidity Index, excluding HIV	1.1 (1.6)	1.0 (1.7)	0.056	0.078	1.1 (1.6)	1.2 (1.7)	0.050	0.007	**1.1 (1.6)**	**1.4 (1.9)**	0.183	0.012
Any mental health condition	4896 (87.0%)	319 (90.1%)	0.098	0.093	4908 (67.1%)	1771 87.9%)	0.024	0.000	4913 (87.1%)	862 (85.5%)	0.045	0.005
Any severe mental health condition	3637 (64.6%)	212 (59.9%)	0.098	0.044	3646 (64.7%)	1349 (67.0%)	0.047	0.023	**3651 (64.7%)**	**692 (68.7%)**	0.084	0.017
Substance use disorder	**2615 (46.5%)**	**117 (33.1%)**	0.277	0.124	**2600 (46.2%)**	**805 (40.0%)**	0.0125	0.001	**2609 (46.2%)**	**522 (51.8%)**	0.111	0.042
Antidepressant medication	2021 (35.9%)	130 (36.7%)	0.017	0.013	2027 (36.0%)	756 (37.6%)	0.032	0.04	2019 (35.8%)	392 (38.9%)	0.064	0.003
Antipsychotic medication	1365 (24.3%)	89 (25.1%)	0.020	0.022	1369 (24.3%)	456 (22..6%)	0.040	0.009	1368 (24.2%)	268 (26.6%)	0.054	0.025

Bold type = $P < 0.05$ for unweighted differences using Welch's two-sample t-test (continuous variables) or Pearson chi-squared (categorical variables).
[a]As B/F/TAF and comparator cohorts were constructed for pair-wise comparisons, the number indexed on B/F/TAF differed slightly. In rare cases, for example, a person first treated with DTG-based MTR who then switched to B/F/TAF would be indexed on B/F/TAF for the comparison with DTG/3TC, but indexed on DTG-based MTR for the comparison with DTG-based MTR.
[b]ASDs calculated as difference in means divided by pooled unweighted SD. Balance was deemed achieved for ASD < 0.1.

Study Limitations

- Claims data have limitations. Miscoding in claims may lead to misclassification of comorbidities or medications. The presence of a claim only indicates a prescription was filled, not whether the medication was taken consistently and correctly
- Channeling bias is possible, in which PWH with a history of suboptimal treatment patterns may be more likely to be prescribed B/F/TAF
- While IPTW was used to control for confounding, it was not able to control for unobserved characteristics that were not in the database, such as income, education, race, ethnicity, neighborhood, access to transportation and health care facilities, and stigma

Figure 2. Kaplan-Meier Curves for Time to Discontinuation or Switching, B/F/TAF vs. DTG-Based Comparators Among PWH With MHD/SUD



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Disclosures: **TL, UM, MJC** and **NPM** are employees of and hold shares in Gilead Sciences Inc. **AK, JL, DJ, and GA** are employees of Aetion, a Datavant company and may hold options/shares in Datavant. **DY** was an employee of Aetion at the time the study was concluded.

Abbreviations: MHD – mental health disorder. SUD – substance use disorder. PWH – people with HIV. B/F/TAF – bictegravir/emtricitabine/tenofovir alafenamide. DTG/3TC – dolutegravir/lamivudine. DTG/ABC/3TC – dolutegravir/abacavir/lamivudine. DTG-based MTR – dolutegravir based multi-tablet regimen(s), including dolutegravir+emtricitabine/tenofovir disoproxil fumarate and dolutegravir+emtricitabine/tenofovir alafenamide. IPTW – inverse probability of treatment weighting