ART Regimen Persistence Among Treatment-Experienced Patients With HIV Switching to a MTR or STR Since 2018

Benjamin Chastek[1], Amy Anderson[1], Noah Webb[1], Marvin Rock[2], Joshua Gruber[2], Sunil Majethia[2], Woodie Zachry[2], Joshua Cohen[3], Amy Colson[4]

[1]Optum, Eden Prairie, MN, USA; [2]Gilead Sciences, Foster City, CA, USA; [3]Independent Healthcare Analyst; [4]AccessHealth MA, Boston, MA, USA

Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404
Tel: (650) 522-6009
Fax: (650) 522-5260

Background

- There are approximately 38 million people living with HIV (PLWH) worldwide and approximately 1.7 million people are newly infected each year[1]
- Lack of adherence to antiretroviral treatment (ART) may result in both disease progression and HIV transmission due to uncontrolled viremia[2,3]
- Current guidelines indicate that integrase strand transfer inhibitors (INSTIs) are the preferred anchor drugs in antiretroviral drug regimens and are often combined with one or two nucleoside reverse transcriptase inhibitors (NRTIs)[4]
- This study investigates differences in treatment persistence among the different DHHS recommended INSTI-based triple-drug single tablet regimens (STRs) and multi-tablet regimens (MTRs)

Objective

- Determine the rates of regimen switching and of antiretroviral treatment discontinuation for three-drug INSTI-based STRs and MTRs among treatment experienced PLWH

Methods

- A retrospective study using claims data from Optum Research Database (01/01/2010-03/31/2020)
- Inclusion criteria:
  - ≥1 non-diagnostic medical claim with a diagnosis code for HIV during the baseline or follow-up periods
  - ≥1 pharmacy claim for guideline-recommended INSTI-based triple therapy from 01/01/2018 – 12/31/2019 (identification period)
    - Lines after the first eligible line were excluded
  - Continuously enrolled in the health plan for ≥12 months prior to (baseline period) and ≥3 months following (follow-up period) the first claim for an INSTI-based regimen
  - Treatment experienced (≥1 line of ART prior to the start of eligible INSTI-based triple therapy)
  - ≥18 years of age as of the first ART claim
  - No medical claims for HIV-2 or pharmacy claims for pre- or post-exposure prophylactic therapy
- Measures
  - Baseline patient demographics and clinical characteristics
  - Comorbid conditions were defined using the Clinical Classifications Software[5,6]
    - This measure generated indicator variables for specific disease conditions based on ICD-9-CM and ICD-10-CM diagnoses[5,6]
  - LOT duration and reason for LOT cessation
    - ART discontinuation – a gap in ART therapy ≥ 60 days
    - ART switch – change in any core antiretroviral component
    - End of available data – LOTs were censored at the end of the study period, 03/31/2020
- Analyses
  - Inverse probability treatment weighting (IPTW) was conducted to control for differences in baseline patient demographic and clinical characteristics
  - Standardized mean differences were calculated for patient characteristics to check for balance between cohorts after IPTW. A standardized mean difference ≥ 10 compared to B/F/TAF indicated an imbalance
  - Comparisons were made for the following LOT types
    - INSTI-based triple MTR vs STR
    - Specific INSTI-based triple drug regimens vs B/FTC/TAF
  - Kaplan-Meier analysis were conducted
  - Hazard ratios (HR) from Cox proportional hazards models was utilized to control for differences that remaining after IPTW

Results

Table 1. Baseline demographic and clinical characteristics

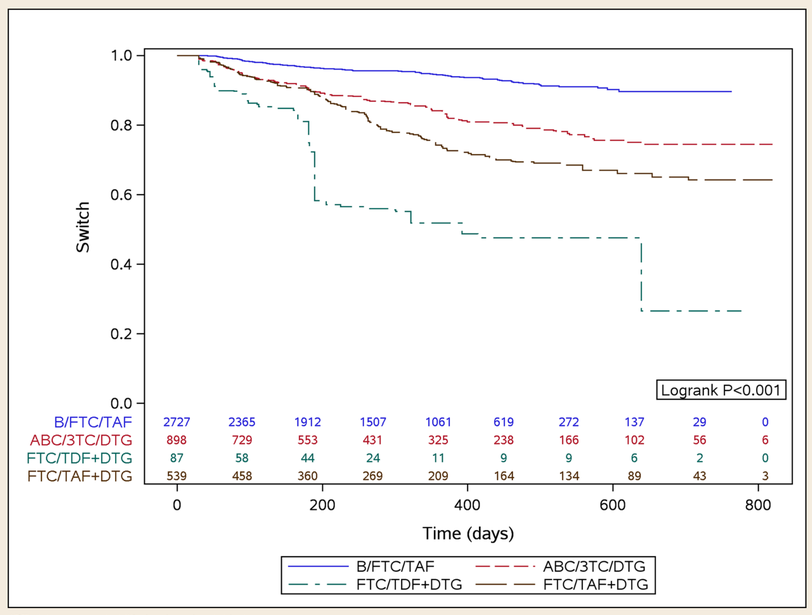
	Total (n = 4,251)	Regimen			
		B/FTC/TAF (n = 2,727)	ABC/3TC/DTG (n = 898)	FTC/TDF+ DTG (n = 87)	FTC/TAF+DTG (n = 539)
Age, mean (SD)	52.3 (12.8)	52.4 (12.6)	52.0 (13.1)	**49.6 (14.5)**	52.7 (12.4)
Male, n (%)	3,575 (84.1)	2,288 (83.9)	757 (84.4)	76 (87.3)	454 (84.2)
Female, n (%)	676 (15.9)	439 (16.1)	141 (15.7)	11 (12.7)	85 (15.8)
Region, n (%)					
Northeast	574 (13.5)	362 (13.3)	130 (14.5)	**8 (9.8)**	73 (13.6)
Midwest	594 (14.0)	381 (14.0)	130 (14.4)	12 (13.6)	72 (13.3)
South	2,481 (58.4)	1,605 (58.9)	515 (57.3)	**44 (51.0)**	316 (58.7)
West	602 (14.2)	379 (13.9)	123 (13.7)	**22 (25.7)**	78 (14.4)
Commercial insurance, n (%)	2,800 (65.9)	1,797 (65.9)	598 (66.6)	**57 (65.9)**	348 (64.7)
Medicare, n (%)	1,451 (34.1)	930 (34.1)	300 (33.4)	30 (34.1)	191 (35.4)
Charlson comorbidity score, mean (SD)	0.9 (1.6)	0.9 (1.6)	0.9 (1.6)	**0.7 (1.4)**	1.0 (1.7)
Baseline conditions, n (%)					
Substance use disorder	959 (22.6)	615 (22.6)	204 (22.7)	21 (23.6)	119 (22.1)
End-stage renal disease	44 (1.0)	26 (1.0)	11 (1.2)	**0 (0.0)**	7 (1.3)
Severe renal dysfunction	22 (0.5)	12 (0.4)	9 (1.0)	**0 (0.0)**	1 (0.2)
Metabolic disorders	2,117 (49.8)	1,347 (49.4)	445 (49.5)	45 (51.9)	280 (51.9)
Sexually transmitted infections	682 (16.0)	431 (15.8)	148 (16.5)	11 (12.5)	92 (17.1)
Baseline medications, n (%)					
Immunosuppressive therapy	1,121 (26.4)	734 (26.9)	232 (25.9)	**15 (17.4)**	140 (25.9)

*†Modified comorbidity score was calculated based on the presence of diagnosis codes on medical claims after excluding HIV/AIDS in the calculation.
IPTW, inverse probability treatment weighted
Standardized mean difference ≥ ± 10 compared to B/FTC/TAF

Time to ART switch by regimen: Kaplan-Meier analysis

- Figure 1 displays the Kaplan-Meier analysis for time to ART switch
- Rates of switching were lowest for B/FTC/TAF vs other INSTI-based regimens

Figure 1. Kaplan-Meier Analysis: Time to ART switch

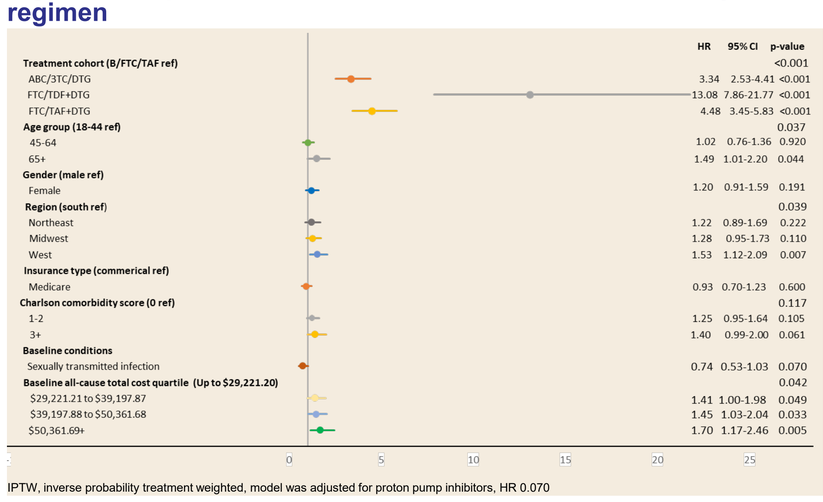


IPTW, inverse probability treatment weighted

Risk of ART switch by regimen

- Compared to B/FTC/TAF, the risk of switching was higher for all other regimens, p <0.001 (Figure 2)
- The risk of switching was higher for patients with: age ≥ 65 year old, residence in the Western US, and higher baseline all-cause healthcare costs

Figure 2. Proportional hazards model risk of ART switch by regimen



IPTW, inverse probability treatment weighted, model was adjusted for proton pump inhibitors, HR 0.070

Results (cont'd)

- The final study sample included 4,251 treatment-experienced PLWH on the following regimens at entrance into the study:
  - B/FTC/TAF: n = 2,727 (64.2%)
  - ABC/3TC/DTG: n = 898 (21.1%)
  - FTC/TDF+DTG: n = 87 (2.1%)
  - FTC/TAF+DTG: n = 539 (12.7%)
- After weighting, characteristics for ABC/3TC/DTG and FTC/TAF+DTG were similar to B/FTC/TAF. Differences remained with FTC/TDF+DTG vs. B/FTC/TAF (Figure 1)

Persistence and reasons for end of LOT – STRs vs MTRs

- MTRs were more likely than STRs to be discontinued (15% v 11%, p=0.003) or switched (25% v. 7%, p < 0.001)

Table 2. Persistence and reason for end of LOT by STRs vs MTRs

	Total (n = 4,251)	Regimen	
		STRs (n = 3,625)	MTRs (n = 626)
Total follow-up time in days, mean (SD)	371.6 (203.5)	357.8 (195.6)	**451.5 (228.8)***
Length of line in days, mean (SD)	307.4 (197.2)	305.5 (190.7)	318.2 (231.4)
LOT duration as a percent of follow-up days, %		85.4	70.5
Reason for end of line, n (%)			
ART discontinuation	495 (11.6)	399 (11.0)	**96 (15.3)***
ART switch	413 (9.7)	257 (7.1)	**156 (24.9)***
Disenrollment or end of study period	3,343 (78.6)	2,969 (81.9)	**375 (59.8)***

*p-value <0.05
IPTW, inverse probability treatment weighted

Persistence and reasons for end of LOT by regimen

- B/FTC/TAF was less likely than other regimens to be discontinued or switched
  - Discontinuation rates were lower for B/FTC/TAF LOTs compared with other regimens (6.4% versus 13%-37.4%)
  - Switching rates were lower for B/FTC/TAF LOTs compared with other regimens (5.1% versus 14.4%-36.7%)

Table 3. Persistence and reason for end of LOT by regimen

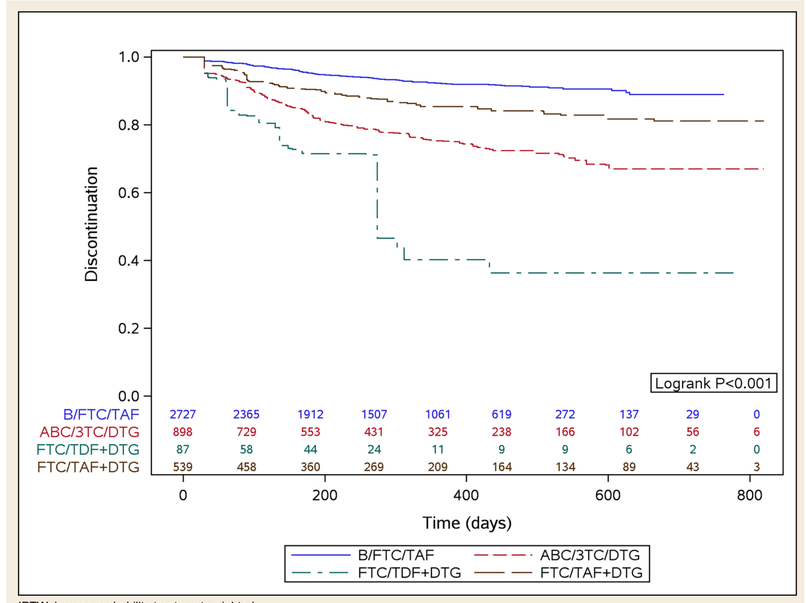
	Total (n = 4,251)	Regimen			
		B/FTC/TAF (n = 2,727)	ABC/3TC/DTG (n = 898)	FTC/TDF+ DTG (n = 87)	FTC/TAF+DTG (n = 539)
Total follow-up time, days, mean (SD)	370.6 (203.0)	333.1 (178.5)	**428.0 (223.6)***	**453.7 (217.0)***	**450.6 (230.3)***
Length of line, days, mean (SD)	307.7 (197.0)	307.0 (178.6)	303.2 (222.8)	**205.5 (177.5)***	335.2 (233.4)
LOT duration as a percent of follow-up days, %		92.2	70.8	45.3	74.4
Reason for end of LOT, n (%)					
ART discontinuation	479 (11.3)	175 (6.4)	**201 (22.4)***	**33 (37.4)***	**70 (13.0)***
ART switch	422 (9.9)	139 (5.1)	**129 (14.4)***	**32 (36.7)***	**122 (22.7)***
Disenrollment or end of study period	3,350 (78.8)	2,413 (88.5)	**568 (63.2)***	**23 (26.0)***	**346 (64.3)***

*p-value <0.05 versus B/FTC/TAF
IPTW, inverse probability treatment weighted

Time to discontinuation by regimen: Kaplan-Meier analysis

- Figure 3 displays the Kaplan-Meier analysis for time to end of LOT for regimens that ended in ART discontinuation
- Cumulative risk of discontinuation was lowest for the B/FTC/TAF regimen vs other INSTI-based regimens

Figure 3. Kaplan-Meier Analysis: Time to discontinuation of ART

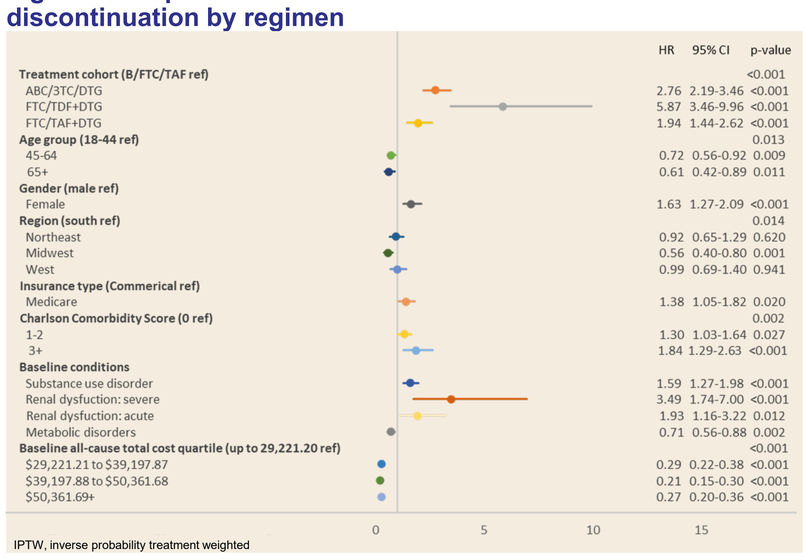


IPTW, inverse probability treatment weighted

Risk of ART discontinuation by regimen

- The risk of discontinuation was lower for B/FTC/TAF compared to all other regimens, p< 0.001 (Figure 4)
- The risk of discontinuation was higher for patient with: female gender, Medicare coverage, higher Charlson comorbidity score, substance use disorder, acute renal dysfunction and severe renal dysfunction

Figure 4. Proportional hazards model risk of ART discontinuation by regimen



IPTW, inverse probability treatment weighted

Limitations

- PLWH were primarily covered by commercial insurance, and results might not be generalizable to a broader population
- This study was conducted only in the United States and the geographic distribution was skewed to the US South

Conclusions

- Treatment experienced patients with HIV who are treated with STRs are less likely to switch or discontinue treatment compared to patients on MTRs
- Patients treated with B/FTC/TAF are less likely to switch or discontinue ART compared to patients on other INSTI-based regimens

References:
1.Dybul M, Attoye T, Baptiste S, et al. The case for an HIV cure and how to get there. Lancet HIV 2021;8(1):e51-e58. DOI: 10.1016/S2352-3018(20)30232-0.
2.Bae JW, Guyer W, Grimm K, Altice FL. Medication persistence in the treatment of HIV infection: a review of the literature and implications for future clinical care and research. AIDS 2011;25(3):279-90. DOI: 10.1097/QAD.0b013e328340feb0.
3.Deeks SG, Overbaugh J, Phillips A, Buchbinder S. HIV infection. Nat Rev Dis Primers 2015;1:15035. DOI: 10.1038/nrdp.2015.35.
4.Gunthard HF, Aberg JA, Eron JJ, et al. Antiretroviral treatment of adult HIV infection: 2014 recommendations of the International Antiviral Society-USA Panel. JAMA 2014;312(4):410-25. DOI: 10.1001/jama.2014.8722.
5. Bayliss EA, Ellis JL, Shoup JA, Zeng C, McQuillan DB, Steiner JF. Association of patient-centered outcomes with patient-reported and ICD-9-based morbidity measures. Ann Fam Med 2012;10(2):126-33. (In eng). DOI: 10.1370/afm.1364.
6. Quan H, Li B, Couris CM, et al. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. Am J Epidemiol 2011;173(6):676-82. (In eng). DOI: 10.1093/aje/kwq433.

Disclosures:
Chastek B, Anderson A, and Webb N are employees of Optum; Rock M, Gruber J, Majethia S, and Zachry W are employees of Gilead; Cohen J is a principal investigator sponsored by Gilead Sciences; Colson A is an employee of AccessHealth MA