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

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## 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**

## 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

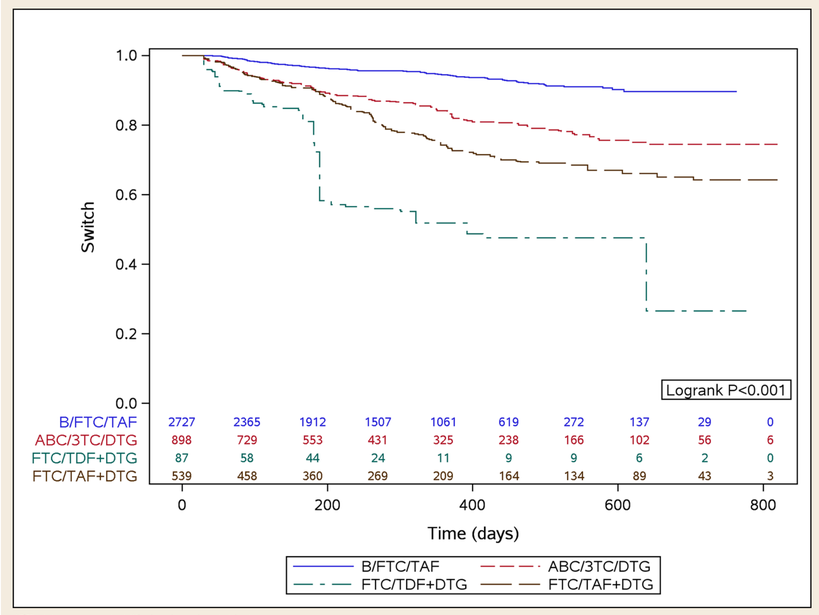
| | Total (n = 4,251) | Regimen | | | |
|---|---|---|---|---|---|
| | | B/FTC/TAF (n = 2,727) | ABC/3TC/DTG (n = 898) | FTC/TDF+ DTG (n = 87) | FTC/TAF+DTG (n = 539) |
| Total follow-up time, days, mean (SD) | 370.6 (203.0) | 333.1 (178.5) | **428.0 (223.6)*** | **453.7 (217.0)*** | **450.6 (230.3)*** |
| 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 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

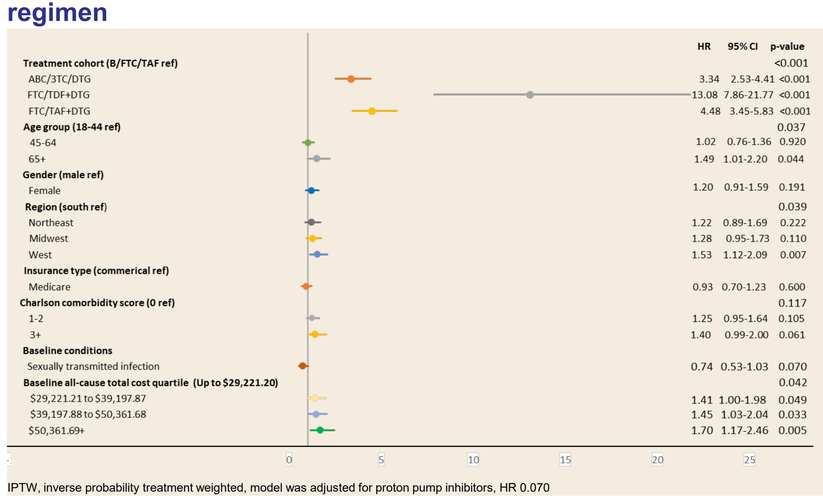



IPTW, inverse probability treatment weighted

### 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

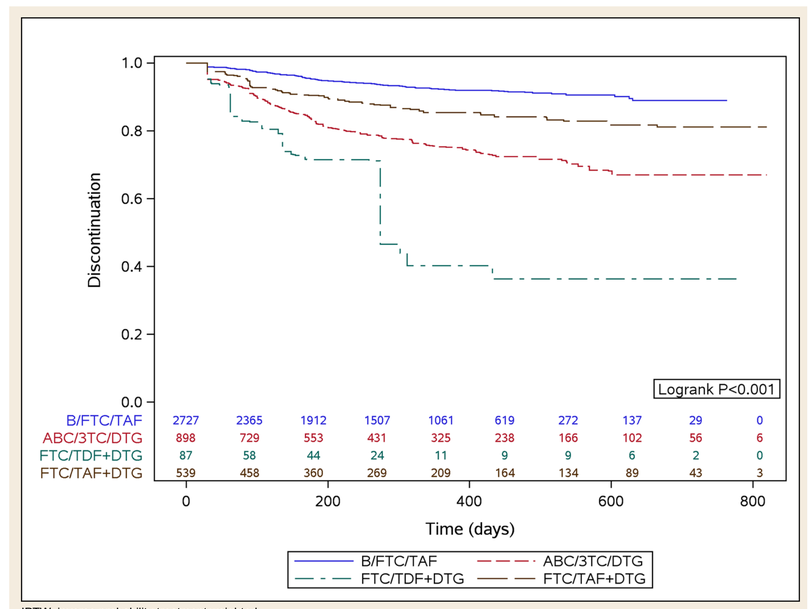



IPTW, inverse probability treatment weighted, model was adjusted for proton pump inhibitors, HR 0.070

### 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

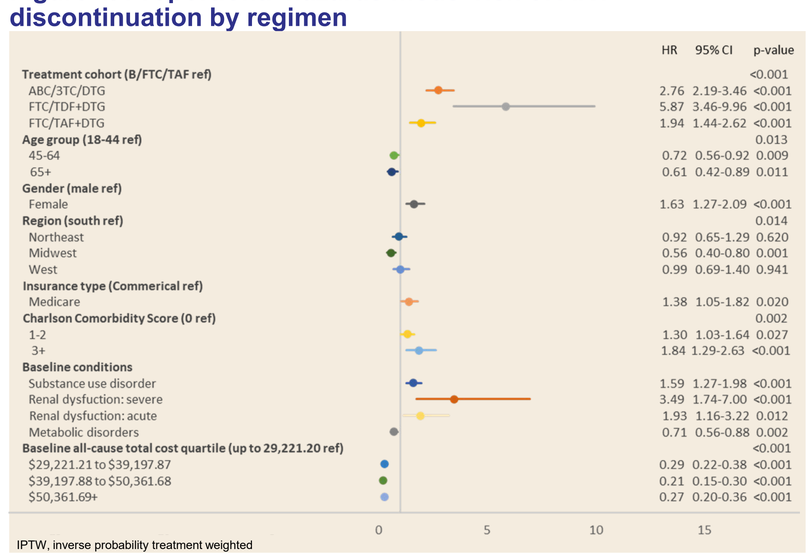



IPTW, inverse probability treatment weighted

### 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

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