Treatment Patterns in Virologically Suppressed, Treatment-Experienced People With HIV: a US Real-World Database Study

P067

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Conclusions

- Treatment changes were common among people with HIV who are virologically suppressed with treatment experience (PWH-VSTE), with 1451 (41.4%) individuals experiencing ≥3 treatment regimens across all available follow-up
  - There were 1546 (36.6%) PWH-VSTE that eventually discontinued treatment, and the mean percent of days covered (PDC) was only 73% for all follow-up
- While the mean duration of a line of therapy (LOT) decreased over each subsequent LOT in the 6-month and all available follow-up periods, some patterns were different between the near- and long-term follow-up
  - Experiencing multiple LOTs in the first 6 months was accompanied by an increased mean pill burden with short gaps between ending one LOT and starting the next LOT
  - During all available follow-up, the mean pill burden did not change through LOTs 1–5 and the mean time between LOTs was much longer
- These differences in treatment patterns may indicate specific treatment strategies for PWH who change treatment regimens relatively quickly early in their VSTE journey versus those who persist longer on their first LOT
  - The increase in pill burden for those switching early may reflect a need to split up single-tablet regimens into multi-tablet regimens in order to manage early-presenting side effects or toxicities
  - Treatment switches that occur after longer durations could be related to addressing treatment-emergent resistance and the pill burden of the next prescribed LOT may remain lower to encourage adherence
- Optimised treatment options could help improve persistence and LOT duration challenges observed in this population and positively impact health-related quality of life by avoiding the physical and psychological impacts of new regimens[1,2]

Plain Language Summary

- While many people with HIV get treatment with a single pill, others have to take treatments where many pills are taken at the same time, or they have to take them many times in the day to help treat their HIV[3–7]
  - Some people have to change their medications many times to find a treatment that works for them
  - It is important to know how to find these individuals because their HIV is difficult to treat and may lead to more medical problems and a poorer quality of life[1,2]
- This study used three ways to find people with HIV that are taking many pills to treat their HIV, and looked at what medications they were being prescribed and how their medications changed over time
- Knowing how these people are being treated for their HIV will help doctors find better ways to treat these people by getting the best treatment available for them
  - This may help people to take their medicine in the correct way
  - This will also help lower side effects and the chance for drug interactions, and also help improve quality of life

Background

- Most PWH can use single-tablet HIV treatments to successfully maintain virologic suppression (VS), while others require multiple changes to their treatment regimens due to a variety of reasons, including intolerance, safety, or HIV resistance, and may eventually require increasingly complex treatment regimens to achieve and maintain VS[1,2]
- While virologically suppressed people on complex regimens have been the subject of some clinical trials,[3–7] this population is not widely recognised, treatment guidelines have not been specifically developed for this population, and the definition of a complex regimen varies between studies
- We previously identified and characterised a population of PWH-VSTE using the Veradigm Network Electronic Health Record (VNEHR) database linked with administrative claims using three pre-determined treatment experience criteria, which all included evidence of sustained VS during treatment (HIV-1 RNA ≤200 copies/mL)[8]
- Understanding how this subset of PWH are being treated in real-world settings may help optimise treatment strategies

Objective

- To report treatment patterns for PWH-VSTE using the VNEHR database linked with claims

Methods

Study Design

- We conducted a retrospective, observational analysis of the VNEHR database linked with administrative claims
  - This dataset integrates data from US primary care EHR platforms (i.e., the VNEHR dataset, which includes the Allscripts, Practice Fusion, and NextGen EHR components) with pharmacy and medical claims data
  - A subset of the individuals represented in the VNEHR also had data available in the claims dataset. The linkage between EHR and claims was achieved via individual-level de-identified tokens
  - The final linked data set was created by merging the patient-level de-identified tokens in each individual dataset and contained no protected health information
  - EHR and claims data were extracted from the database during the study period: January 1, 2015–December 31, 2022

VSTE-Defining Criteria

- HIV treatment-experienced individuals were identified based on claims for ≥2 antiretroviral (ARV) LOTs
- A set of criteria were developed to identify PWH-VSTE from this initial population of treatment-experienced individuals (**Table 1**)
- PWH-VSTE were first identified as those who met ≥1 of three VSTE-defining treatment criteria while having evidence of VS (HIV-1 RNA ≤200 copies/mL) during the index LOT
- A subset of the PWH-VSTE population was then further refined by a requirement to show sustained VS, defined as evidence of VS within 90 days of initiating the index LOT and showing no evidence of viral rebound (HIV-1 RNA >200 copies/mL) during the index LOT
- Eligible PWH-VSTE were: aged ≥18 years on index date; had a record of HIV diagnosis at any time prior to/on the index date; had continuous enrollment in medical and pharmacy claims, and with activity in the EHR ≥6 months before and after the index date

Table 1. VSTE-Defining Criteria

	Evidence of VS[a] and Meeting ≥1 of the Following VSTE-Defining LOT Criteria	Medications/Medication Classes	
1	On a complex ARV regimen meeting ≥1 of the following definitions: 1. Has a LOT containing ≥2 ARV medication classes 2. Has a LOT consisting of the four medications listed 3. Has a LOT requiring dosing that is more frequent than once daily 4. Has a multi-tablet regimen (has a LOT with ≥2 pills/day)[b]	ARV Classes: • NNRTI • INSTI • PI	Medications: • Darunavir • Cobicistat • Emtricitabine • Tenofovir alafenamide
2	Resistance to exactly two ARV classes at any time in all available data from the EHR	• NNRTI • INSTI • NRTI • PI	
3	Prior exposure to exactly two ARV classes at any time in all available data from the EHR and claims data	• NNRTI • INSTI • PI	

[a]Evidence of sustained VS (HIV-1 RNA ≤200 copies/mL) must be present within 90 days of the PWH-VSTE-defining LOT, and there must be no evidence of virologic rebound during that LOT.
[b]Excluding regimens generally representative of available single-tablet regimens, specifically: INSTI or an NNRTI plus 1–2 NRTIs (dolutegravir or raltegravir or efavirenz or rilpivirine or doravirine) plus (emtricitabine/tenofovir or emtricitabine/tenofovir alafenamide or lamivudine+/-abacavir).
ARV, antiretroviral; EHR, electronic health records; INSTI, integrase strand transfer inhibitor; LOT, line of therapy; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PWH-VSTE, people with HIV who are virologically suppressed with treatment experience; VS, virologic suppression; VSTE, virologically suppressed with treatment experience.

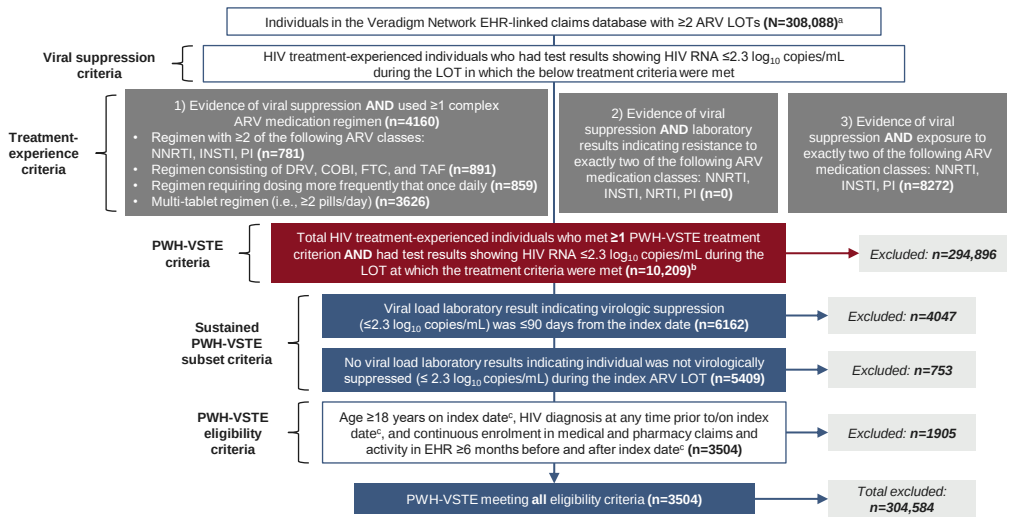
Treatment Patterns Analysis

- Index date was defined as the most recent date on which one of the VSTE-defining criteria was met
- The follow-up period was the variable period (minimum 6 months) after (and including) the index date, allowing for assessment of the change in PWH-VSTE clinical characteristics shortly after meeting VSTE criteria
- A LOT was defined as the continuous period during which an individual had a supply of a treatment regimen
  - LOTs were constructed using claims only
  - ARV combinations were identified by a minimum overlap of 45 days in prescription fills for each ARV
- The time between LOTs was defined as the amount of time between the last day of supply of medications in the prior LOT and the first day of supply of medications in the current LOT
- The PDC was measured for all data in a given period and for individual LOTs
  - PDC was calculated as the total number of days with a medication prescription in a time period divided by the total days in the time period

Results

- Of 308,088 treatment-experienced PWH, 5409 (1.8%) people met ≥1 VSTE-defining criteria with sustained VS, and 3504 people were eligible for analysis (**Figure 1**)

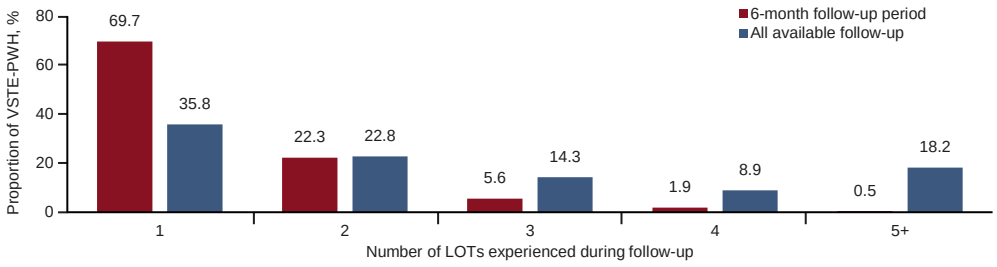
Figure 1. PWH-VSTE Study Attrition Diagram



[a]Identified within the study period of January 1, 2015–December 31, 2022. [b]2223 PWH met ≥2 treatment experience criteria. [c]Index date was defined as the most recent date on which one of the VSTE-defining treatment criteria was met.
ARV, antiretroviral; COBI, cobicistat; DRV, darunavir; EHR, electronic health records; FTC, emtricitabine; INSTI, integrase strand transfer inhibitor; LOT, line of therapy; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PWH-VSTE, people with HIV who are virologically supressed with treatment experience; TAF, tenofovir alafenamide.

- The mean (SD) duration of follow-up was 1150.4 (727.8) days, or approximately 38 (24) months
- Mean PDC (SD) over the initial 6 months of follow-up was 84% (22%) and over all available follow-up, PDC dropped to 73% (26%)
- During the initial 6 months of follow-up, 783 (22.3%) PWH-VSTE experienced two LOTs, 195 (5.6%) experienced three LOTs, and 84 (2.4%) experienced ≥4 LOTs (**Figure 2**)
  - During all available follow-up, 798 (22.8%) experienced two LOTs, 500 (14.3%) experienced three LOTs, and 951 (27.1%) experienced ≥4 LOTs

Figure 2. Proportion of PWH-VSTE Experiencing LOT Changes (N=3504)



LOT, line of therapy; PWH-VSTE, people with HIV who are virologically suppressed with treatment experience.

- Across all available follow-up, 2865 (81.8%) participants did not persist with their index LOT (LOT1); 1546 (44.1%) eventually discontinued treatment (**Table 2**)
  - Median (interquartile range) treatment duration was 257 (89–619) days during LOT1, decreasing to a median of 90–128 days for LOT2–5
  - Mean (SD) PDC was 93.2% (11.1%) during LOT1, and 90–92% in LOT2–5
  - Mean time from the end of one LOT to the start of the next was 0–11.9 days in the initial 6 months; during all follow-up, these treatment gaps increased to a mean of 40–46 days
  - The mean (SD) pills/day were 1.7 (1.0) during LOT1
    - Pill burden increased over subsequent LOTS to a mean (SD) of 2.6 (1.0) by LOT5 during the initial 6-month follow-up period
    - After all available follow-up, mean pill burden was consistent across LOTs 2–5, at 1.7–1.8 pills/day

Table 2. Treatment Patterns in PWH-VSTE

Variable	6-Month Follow-Up Period					All Available Follow-Up				
	LOT1 (n=3504)	LOT2 (n=1062)	LOT3 (n=279)	LOT4 (n=84)	LOT5 (n=19)	LOT1 (n=3504)	LOT2 (n=2249)	LOT3 (n=1451)	LOT4 (n=951)	LOT5 (n=639)
Mean duration of LOT (SD), days	474.7 (536.9)	418.1 (556.8)	244.6 (383.9)	229.5 (354.9)	213.8 (349.1)	438.9 (479.8)	324.7 (441.6)	270.7 (381.7)	234.8 (348.8)	227.9 (332.7)
Mean time to LOT (SD), days	0.1 (1.6)	11.9 (28.4)	4.5 (16.9)	3.6 (13.1)	0.0 (0.0)	0.1 (1.6)	43.0 (115.6)	40.5 (109.4)	39.5 (92.5)	45.9 (116.8)
Mean PDC during LOT (SD), %	93.2 (11.1)	90.7 (16.4)	89.9 (16.4)	87.8 (19.3)	91.8 (14.0)	93.2 (11.1)	91.7 (15.2)	91.4 (14.9)	90.1 (17.2)	91.9 (14.0)
Mean number of pills/day in LOT (SD)	1.7 (1.0)	1.7 (1.0)	2.0 (1.1)	2.0 (1.1)	2.6 (1.0)	1.7 (1.0)	1.7 (1.0)	1.7 (0.9)	1.7 (0.9)	1.8 (0.9)
Number of pills/day in LOT, n (%)										
1	1845 (52.7)	587 (55.3)	104 (37.3)	34 (40.5)	2 (10.5)	1845 (52.7)	1310 (58.2)	777 (53.5)	518 (54.5)	316 (49.5)
2	984 (28.1)	252 (23.7)	100 (35.8)	21 (25.0)	8 (42.1)	984 (28.1)	533 (23.7)	406 (28.0)	257 (27.0)	194 (30.4)
3	463 (13.2)	160 (15.1)	43 (15.4)	21 (25.0)	5 (26.3)	463 (13.2)	272 (12.1)	189 (13.0)	127 (13.4)	99 (15.5)
4	170 (4.9)	53 (5.0)	25 (9.0)	7 (8.3)	4 (21.1)	170 (4.9)	106 (4.7)	60 (4.1)	43 (4.5)	28 (4.4)
5+	42 (1.2)	10 (0.9)	7 (2.5)	1 (1.2)	0 (0.0)	42 (1.2)	28 (1.2)	19 (1.3)	6 (0.6)	2 (0.3)
Reason for end of LOT, n (%)										
Persistent	2189 (62.5)	737 (69.4)	188 (67.4)	65 (77.4)	15 (78.9)	639 (18.2)	409 (18.2)	242 (16.7)	150 (15.8)	96 (15.0)
Not persistent[a]	1315 (37.5)	325 (30.6)	91 (32.6)	19 (22.6)	4 (21.1)	2865 (81.8)	1840 (81.8)	1209 (83.3)	801 (84.2)	543 (85.0)
Switch without gap	143 (4.1)	35 (3.3)	13 (4.7)	1 (1.2)	0 (0.0)	343 (9.8)	154 (6.8)	111 (7.6)	63 (6.6)	41 (6.4)
Switch with gap	38 (1.1)	11 (1.0)	2 (0.7)	0 (0.0)	0 (0.0)	139 (4.0)	112 (5.0)	79 (5.4)	52 (5.5)	44 (6.9)
Discontinuation	253 (7.2)	46 (4.3)	7 (2.5)	0 (0.0)	1 (5.3)	616 (17.6)	389 (17.3)	258 (17.8)	162 (17.0)	121 (18.9)
Discontinuation with restart	131 (3.7)	6 (0.6)	2 (0.7)	0 (0.0)	0 (0.0)	514 (14.7)	315 (14.0)	209 (14.4)	152 (16.0)	93 (14.6)
Augmentation	159 (4.5)	107 (10.1)	27 (9.7)	10 (11.9)	1 (5.3)	387 (11.0)	353 (15.7)	203 (14.0)	161 (16.9)	99 (15.5)
Subtraction	521 (14.9)	111 (10.5)	36 (12.9)	6 (7.1)	2 (10.5)	740 (21.1)	488 (21.7)	315 (21.7)	185 (19.5)	132 (20.7)
Augmentation/subtraction	70 (2.0)	9 (0.8)	4 (1.4)	2 (2.4)	2 (0.1)	126 (3.6)	29 (1.3)	34 (2.3)	26 (2.7)	13 (2.0)

[a]A switch in treatment was defined as the presence of a new ARV class not in the current LOT while discontinuing use of all ARV medication classes in the current LOT. A gap in treatment was defined as not having a supply of medication for >45 days. Discontinuation was defined as the presence of a gap of >45 days in all of the current medication class(es) with no subsequent use of any ARVs before the end of the follow-up period. Treatment discontinuation followed by restart was defined as gaps >45 days in length in all of the current medication class(es) followed by use of all the medication classes in the previous LOT without the intermediate use of any other ARV classes. Augmentation of a LOT was defined as the presence of a new ARV class while continuing to use all of the prior ARV class(es). Subtraction was defined as discontinuation of one or more ARV classes while continuing one or more ARV classes in the prior LOT.
ARV, antiretroviral; LOT, line of therapy; PDC, percent of days covered; PWH-VSTE, people with HIV who are virologically suppressed with treatment experience.

- **Table 3** shows the most common ARV combinations (>3% in LOT1) for LOT1–5
  - The most common regimen during the first six months of follow-up was a single-tablet regimen consisting of two NRTIs and one INSTI

Table 3. Most Common Medication Regimens (>3% in LOT1) for the 6-month Follow-Up Period

Medication Classes in LOT[1]	6-Month Follow-Up Period				
	LOT1 (n=3504)	LOT2 (n=1062)	LOT3 (n=279)	LOT4 (n=84)	LOT5 (n=19)
NRTI-NRTI-INSTI	947 (27)	250 (24)	36 (13)	7 (8)	1 (5)
NRTI-NRTI-INSTI-COBI	555 (16)	130 (12)	15 (5)	5 (6)	0 (0)
INSTI,NRTI-NRTI	292 (8)	88 (8)	26 (9)	9 (11)	2 (11)
NRTI-NRTI-NNRTI	161 (5)	50 (5)	7 (3)	2 (2)	0 (0)
NRTI-NRTI,PI	154 (4)	49 (5)	17 (6)	9 (11)	2 (11)
NRTI-NRTI-INSTI	947 (27)	250 (24)	36 (13)	7 (8)	1 (5)

[1]Hyphenated terms represent a single-tablet regimen. Terms separated by commas represent a multi-tablet regimen.
COBI, cobicistat; INSTI, integrase strand transfer inhibitor; LOT, line of therapy; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor.

Limitations

- Individuals who may have been identified as VSTE by their use of a complex regimen may have switched back to a non-complex regimen, and were not excluded from follow-up
  - Limited resistance and VS data may have led to missed identification and under reporting of the PWH-VSTE population size
  - Minimal impact from missing resistance data is estimated as most individuals with resistance likely met and were identified through the other study criteria

References **1**. Altice F, et al. *Patient Prefer Adherence.* 2019;13:475–490. **2**. Cutrell J, et al. *Ther Adv Infect Dis*. 2020;7:1–15. **3**. ClinicalTrials.gov. Available at: https://clinicaltrials.gov/study/NCT05502341. (Accessed October 2024). **4**. Fagard C, et al. *JAIDS*. 2012;59(5):489–493. **5**. Hsu RK, et al. *BMC Infect Dis*. 2023;23(1):91. **6**. Rolle C-P, et al. *J Virus Erad*. 2020;6:100021. **7**. Mounzer K, et al. Presented at AIDS 2024. July 22-26. Munich, Germany. Presentation OAB2602. **8**. Gupta S, et al. Presented at IDWeek 2024. October 16–19, 2024. Los Angeles, CA, USA. Presentación P-481.

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