Antiretroviral Therapy Experience of Heavily Treatment-Experienced and Virologically Suppressed Treatment-Experienced People with HIV in the OPERA Cohort

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OPERA® The Longitudinal Cohort

Background

- People with HIV (PWH) routinely experience treatment failure due to viral resistance, drug toxicity, poor adherence, poor tolerability, or drug-drug interactions
- Heavily treatment-experienced (HTE) individuals may require new therapies primarily due to extensive HIV drug resistance
- Some virologically suppressed and treatment-experienced (VSTE) PWH remain on complex regimens due to resistance, intolerance, or other preclusions which can impact adherence, persistence, and quality of life
- VSTE PWH may or may not be on the path toward HTE status

Objective

Characterize the prior, baseline, and next ART regimens of HTE and VSTE individuals in routine clinical care in the OPERA® cohort

Methods

Study population

- OPERA observational cohort: Prospectively captured, routine clinical data from electronic health records (EHR) in the United States (US)
- Inclusion criteria
  - HIV-1 infection
  - ≥18 years old
  - Active in care in OPERA (≥1 visit in previous 24 months)
  - Prescribed ART as of 01DEC2021
  - **HTE** or **VSTE** (defined below)
- Baseline: Start date of ART regimen being taken on 01DEC2021
- Censoring events over follow-up
  - If suppressed (viral load [VL] <200 copies/mL) at baseline, virologic failure:
    - Two consecutive VL ≥200 copies/mL *or*
    - Change in core agent (i.e., antiretroviral of any class except nucleoside reverse transcriptase inhibitor) following a VL ≥200 copies/mL
  - If viremic (VL ≥200 copies/mL) at baseline, virologic suppression (VL <200 copies/mL)
  - Change in ≥1 baseline ART regimen core agent
  - Death
  - Loss to follow-up (12 months after last clinical contact)
  - Study end (30JUN2023)

Definitions

HTE PWH met ≥1 of the following criteria (A or B):

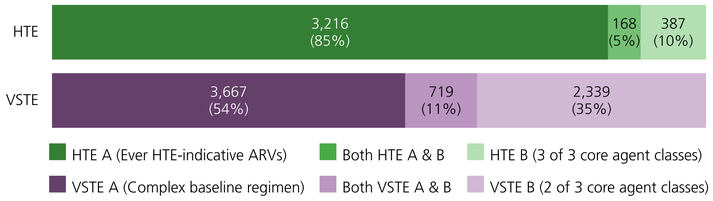
A. Prior or baseline use of HTE-indicative antiretroviral(s): ibalizumab, enfuvirtide, fostemsavir, maraviroc, etravirine, twice daily dolutegravir, or twice daily darunavir
B. Exposure to 3 of 3 core agent classes (INSTI, NNRTI, PI) as of baseline

VSTE PWH were <u>not</u> HTE, were suppressed at baseline, and met ≥1 of the following criteria (A or B):

A. Complex baseline ART regimen, containing either:
   - Boosted PI + ≥1 additional core agent
   - NNRTI + ≥1 additional core agent
   - Darunavir/cobicistat/emtricitabine/tenofovir alafenamide
B. Exposure to 2 of 3 core agent classes (INSTI, NNRTI, PI) as of baseline

Results

Figure 1. People with HIV meeting criteria for HTE (n = 3,771)[a] or VSTE (n = 6,725)[b]



ARV, antiretroviral; HTE, heavily treatment experienced; VSTE, virologically suppressed treatment experienced
[a] The identified HTE individuals represent 5% of adults with HIV in OPERA who are active in care
[b] The identified VSTE individuals represent 9% of adults with HIV in OPERA who are active in care

Table 1. Demographic characteristics

	HTE n = 3,771	VSTE n = 6,725
Age, median years (IQR)	54 (47, 60)	50 (39, 57)
Male sex, n (%)	2,963 (79)	5,287 (79)
Black race, n (%)	1,487 (39)	2,801 (42)
White race, n (%)	2,047 (54)	3,407 (51)
Hispanic ethnicity, n (%)	802 (21)	1,574 (23)

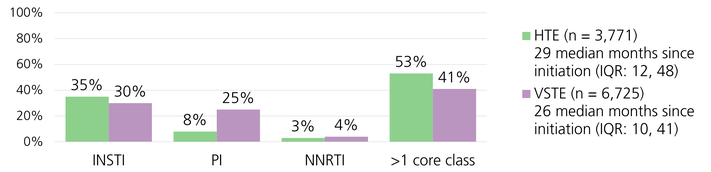
HTE, heavily treatment experienced; IQR, interquartile range; n, number; VSTE, virologically suppressed treatment experienced

Table 2. Summary of prior ART experience

	HTE n = 3,771	VSTE n = 6,725
Months since ART initiation, median (IQR)	90 (48, 143)	66 (32, 113)
Number of prior ART regimens, median (IQR)	4 (2, 7)	3 (2, 5)
Number of prior core agent classes, median (IQR)	3 (2, 3)	2 (1, 2)
Prior use of core agent classes, n (%)[a]		
INSTI	2,701 (76)	3,797 (67)
Protease inhibitor[b]	2,792 (79)	3,027 (53)
NNRTI	2,420 (68)	2,913 (51)
CCR5 antagonist	479 (13)	0
CD4 post-attachment inhibitor	38 (1)	0
gp120 attachment inhibitor	34 (1)	0
Fusion inhibitor	153 (4)	0
Prior use of multiple core agent classes[c], n (%)	2,958 (83)	3,842 (67)

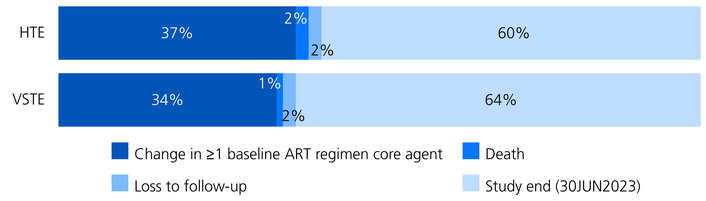
ART, antiretroviral therapy; HTE, heavily treatment experienced; INSTI, integrase strand transfer inhibitors; IQR, interquartile range; n, number; NNRTI, non-nucleoside reverse transcriptase inhibitors; VSTE, virologically suppressed treatment experienced
[a] Categories are not mutually exclusive; a PWH may have previously exposed to multiple core agent classes
[b] Excluding boosting agents cobicistat and ritonavir
[c] In a given ART regimen

Figure 2. Baseline ART regimen core agent classes[a]



ART, antiretroviral therapy; HTE, heavily treatment experienced; INSTI, integrase strand transfer inhibitors; IQR, interquartile range; n, number; NNRTI, non-nucleoside reverse transcriptase inhibitors; PI, protease inhibitor; VSTE, virologically suppressed treatment experienced
[a] Among HTE individuals, 1% used a CCR5 antagonist and <1% used a CD4 post-attachment inhibitor, gp120 attachment inhibitor, or fusion inhibitor as their only core agent

Figure 3. Reasons for censoring for HTE (n = 3,771) or VSTE (n = 6,725)



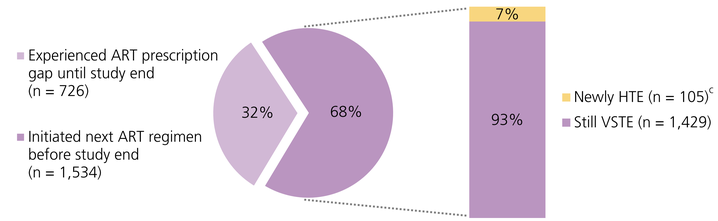
ART, antiretroviral therapy; HTE, heavily treatment experienced; VSTE, virologically suppressed treatment experienced

Table 3. Summary of next ART regimen[a]

	HTE n = 3,771	VSTE n = 6,725
Changed ≥1 baseline core agent before study end, n (%)	1,386 (37)	2,260 (34)
Initiated next ART regimen before study end, n (%)	1,030 (74)	1,534 (68)
Months from baseline to initiation, median (IQR)	31 (12, 56)	28 (13, 47)
VL at initiation, median copies/mL (IQR)[b]	20 (19, 140)	19 (19, 50)
Experienced ART prescription gap until study end, n (%)	356 (26)	726 (32)

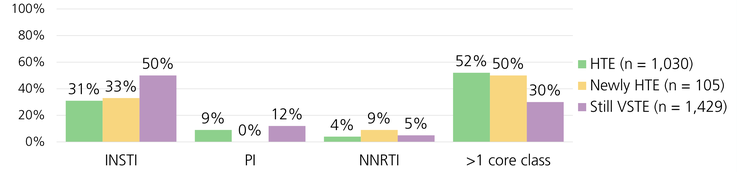
ART, antiretroviral therapy; HTE, heavily treatment experienced; IQR, interquartile range; n, number; VL, viral load; VSTE, virologically suppressed treatment experienced
[a] ART regimen initiated after a change in baseline ART regimen core agent
[b] Viral load at initiation of next ART regimen (±4 weeks); unavailable for 45% of HTE and 40% of VSTE individuals

Figure 4. Status[a] of VSTE PWH who experienced a change in baseline core agent(s)[b]



ART, antiretroviral therapy; HTE, heavily treatment experienced; VSTE, virologically suppressed treatment experienced
[a] VSTE individuals meeting HTE criteria at initiation of next ART regimen were classified as newly HTE; otherwise, they remained VSTE
[b] The most common next ART regimen among both newly HTE and still VSTE PWH was bictegravir/emtricitabine/tenofovir alafenamide
[c] 30 (29%) of the newly HTE individuals were qualified through use of an HTE-indicative antiretroviral; the remaining 75 (71%) newly HTE individuals qualified through exposure to 3 of 3 core agent classes as of initiation of next ART regimen

Figure 5. Next ART regimen[a] core agent classes[b]



ART, antiretroviral therapy; HTE, heavily treatment experienced; INSTI, integrase strand transfer inhibitors; NNRTI, non-nucleoside reverse transcriptase inhibitors; PI, protease inhibitor; VSTE, virologically suppressed treatment experienced
[a] ART regimen initiated after a change in baseline ART regimen core agent
[b] Among HTE individuals, 1% used only a CCR5 antagonist and <1% used a CD4 post-attachment inhibitor. There were no core agents in the next ART regimens of a small proportion of individuals in each group: HTE (3%), newly HTE (<1%), and still VSTE (3%)

Discussion

PWH meeting HTE (5%) or VSTE (9%) criteria

- Most (85%) of 3,771 **HTE** individuals were identified only through prior or baseline use of HTE-indicative antiretroviral(s) [**Figure 1**]
- A majority (65%) of 6,725 **VSTE** individuals were on a complex baseline ART regimen [**Figure 1**]

Characteristics and prior ART experience

- HTE PWH were older than VSTE PWH [**Table 1**]
- A larger proportion of individuals in the HTE group were of White race compared to the VSTE group [**Table 1**]
- HTE PWH had a greater proportion of prior ART regimens containing multiple core agent classes and had longer time since ART initiation than VSTE PWH [**Table 2**]

Baseline and next ART regimens

- Compared to each other, HTE PWH more frequently had >1 core agent class in their baseline ART regimen and VSTE PWH more frequently had only a PI [**Figure 2**]
- The proportion of PWH changing ≥1 baseline ART regimen core agent, time until initiation of next ART regimen, and viral load at initiation were similar across groups [**Figure 3**, **Table 3**]
- Upon initiation of their next ART regimen, 7% of VSTE PWH were newly classified as HTE [**Figure 4**]
- The next ART regimens of HTE and newly HTE PWH more often included >1 core agent class than VSTE PWH [**Figure 5**]
  - VSTE PWH had more INSTI-only next ART regimens

Limitations of EHR data

- Lack of resistance data for identification of HTE and VSTE PWH
- Incomplete documentation on adherence and reasons for ART regimen changes
- Missing data, especially ART regimen history prior to seeing an OPERA provider

Key Findings

- While VSTE PWH may be at risk of progressing to HTE, most of those who initiated a new ART regimen before study end did not newly meet HTE criteria
- A majority of the VSTE PWH who progressed to HTE did so by initiating a new ART regimen containing a new core agent class
- Understanding the use of complex regimens among VSTE PWH and the reasons for progression to HTE may inform novel strategies to simplify treatment

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