Poster
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Clinical outcomes of heavily treatment experienced individuals in the OPERA Cohort

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OPERA® The Longitudinal Cohort

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Background

- No single accepted definition of heavily treatment experienced (HTE)
- Prevalence of HTE based on different definitions in the absence of resistance data were previously evaluated in OPERA [1,2]
- Few studies have evaluated clinical outcomes of HTE in people living with HIV (PLWH)

Objective

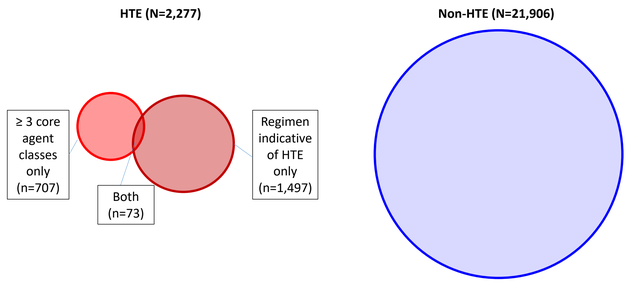
To compare clinical outcomes among heavily treatment-experienced (HTE) people living with HIV (PLWH) and non-HTE, treatment-experienced PLWH in care in the United States.

Methods

Study population

- ART-experienced HIV-1 positive, HIV-2 negative, ≥18 years of age, active in care, prescribed ART as of 31Dec2016
  - HTE:
    - Discontinued core agent from ≥ 3 classes of ART
    or
    - Prescribed a regimen containing (a) dolutegravir (DTG) twice daily, (b) darunavir (DRV) twice daily, (c) etravirine (ETR), (d) integrase strand transfer inhibitor (INSTI) + protease inhibitor (PI), (e) maraviroc (MVC), or (f) enfuvirtide (ENF)
  - Non-HTE:
    - 1 core agent + 2 NRTIs, not meeting the definition of HTE

Figure 1. HTE and Non-HTE Study Populations



Outcomes

- Virologic suppression: Among viremic PLWH, achieve a VL < 50 copies/mL
- Virologic failure: Among PLWH who suppress, failure to maintain VL < 200 copies/mL
- Immunologic preservation: Among PLWH with CD4 count ≥200 cells/µL, maintenance of CD4 count ≥200 cells/µL
- Regimen discontinuation: Any change to the core agents of the regimen
- Morbidity & mortality: A new AIDS defining illness or death

Statistical analyses

- Baseline pairwise comparison: Pearson Chi-Square test (categorical variables), Fisher's exact test (few events), Wilcoxon Rank Sum test (continuous variables)
- Time to event, comparison of survival distributions: Kaplan-Meier, log-rank tests

Results

Table 1. Baseline characteristics of HTE and non-HTE PLWH

	HTE Population N=2,277	Non-HTE Population N=21,906	p-value[c]
Age, median (IQR)	50 (42, 56)	44 (33, 52)	<.0001
Female, n (%)	431 (19%)	3615 (17%)	0.0068
Black Race, n (%)	906 (40%)	8612 (39%)	0.0610
Hispanic Ethnicity, n (%)	572 (25%)	5626 (26%)	0.2142
MSM, n (%)	1190 (52%)	12798 (58%)	<.0001
Years since HIV Diagnosis, median (IQR)	15.3 (7.0, 21.8)	7.1 (2.5, 14.5)	<.0001
Viral Load $\log_{10}$ copies/mL, median (IQR)	2.0 (1.3, 4.2)	1.3 (1.3, 2.0)	<.0001
CD4 Count cells/uL, median (IQR)	412 (209, 636)	587 (396, 801)	<.0001
AIDS defining events (ADE), n (%)	1221 (54%)	6294 (29%)	<.0001
Any comorbid condition,[a] n (%)	1823 (80%)	15132 (69%)	<.0001
Any concomitant medications,[b] n (%)	1477 (65%)	11071 (51%)	<.0001

[a] Autoimmune disease, cardiovascular disease, invasive cancers, endocrine disorders, mental health disorders, liver diseases, bone disorders, peripheral neuropathy, renal disease, hypertension
[b] DAA, antidepressants, NSAIDS, immune modulators, antibiotics, anxiolytics, hypnotics, sedatives, lipid lowering agents, anti-diabetics
[c] Caution: Due to large sample size, clinically insignificant differences could be statistically significant for some baseline variables

Figure 2. Cumulative probability of virologic suppression to VL < 50 copies/mL
(Among viremic PLWH at baseline)

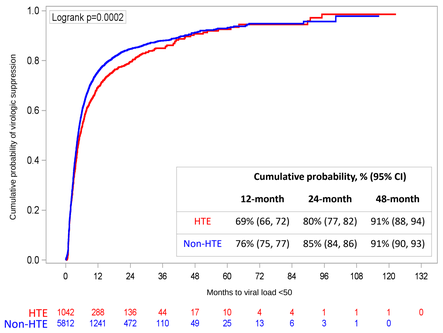


Figure 3. Cumulative probability of remaining virologically suppressed to VL < 200 copies/mL
(Among PLWH who achieved suppression)

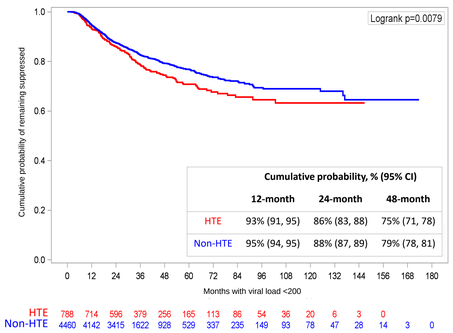


Figure 4. Cumulative probability of maintaining CD4 cell count ≥200 cells/µL
(Among PLWH with baseline CD4 ≥200)

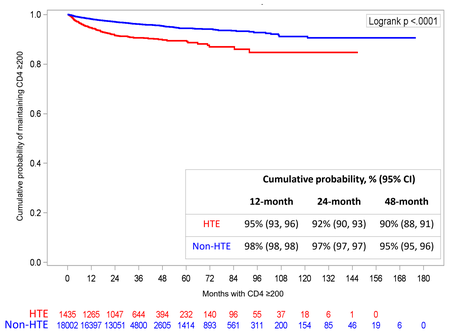
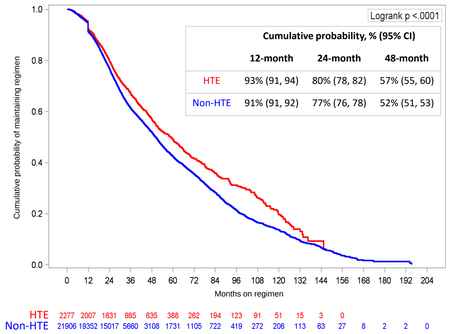


Figure 5. Cumulative probability of remaining on the regimen of interest
(Among all PLWH)



* HTE = heavily treatment experienced; MSM = men who have sex with men; VL = viral load

- Out of 1,527 HTE PLWH with follow-up VL (viremic: baseline VL ≥50 copies/mL: n=807, suppressed: <50 copies/mL: n=720): 238 (15.6%) had VL ≥200 copies/mL at 12 months
- Out of 15,199 non-HTE PLWH with follow-up VL (viremic: baseline VL ≥50 copies/mL: n=4,297, suppressed: <50 copies/mL: n=10,902): 1,248 (8.2%) had VL ≥200 copies/mL at 12 months; p<0.0001

Table 2. Clinical outcomes in HTE and non-HTE PLWH

	HTE Population N=2,277	Non-HTE Population N=21,906	p-value
New ADEs	108 (5%)	506 (2%)	<.0001
New non-ADE comorbid conditions	1,026 (45%)	7,608 (35%)	<.0001
Deaths	36 (2%)	163 (1%)	<.0001

Discussion

- The HTE population was older, with higher viral loads and lower CD4 counts at baseline than the non-HTE population; the HTE population had also been diagnosed with HIV a significantly longer time before baseline
- While the non-HTE PLWH fared slightly better, HTE PLWH had 80% cumulative probability of suppressing to viral loads < 50 copies/mL and of maintaining their regimen at 24 months
- The HTE population experienced a high burden of AIDS-defining conditions, concomitant medications, and comorbid conditions at baseline; they were also more likely to develop new comorbid conditions and die over follow up than the non-HTE population
- Non-HTE PLWH were more likely to remain virologically suppressed and maintain their CD4 count above 200 cells/µL

Key Findings

HTE PLWH were less likely to maintain their CD4 count above 200 cells/µL or to remain virologically stable, and at greater risk of death than non-HTE PLWH, suggesting additional therapeutic options are needed for this vulnerable population.

References

1. Henegar C, Fusco J, Vannappagari V, FuscoG. Evaluation of the Prevalence, Treatment, and Demographic Characteristics of the Heavily Treatment-Experienced (HTE) HIV-Positive Patient Population in the OPERA® Cohort Study Report. January 15, 2018 (updated April 5, 2018).
2. Hsu R, Henegar C, Fusco J, Vannappagari V, Llamoso C, Lackey P, Pierone G, Fusco G. Identifying heavily treatment experienced patients in the OPERA cohort. 22nd International AIDS Conference (AIDS). Abstract A-899-0141-05163. Amsterdam, Netherlands; July 23-27, 2018.

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