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Impact of Tablet Burden and Antiretroviral Therapy (ART) Choice on Virologic Outcomes in Treatment Naive HIV+ Individuals Attending an Inner City Clinic

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Introduction

- Contemporary antiretroviral therapy (ART) regimens for the treatment of HIV-1 infection are available as conventional, multiple-tablet regimens (MTRs) or as new, single-tablet regimens (STRs) that combine ≥3 agents into a single pill
- Half of the currently recommended regimens for patients naive to ART are available as STRs[1]
  - STRs may improve adherence while potentially reducing treatment-emergent drug resistance, healthcare utilization, and costs[2,3]
  - However, studies on clinical and economic outcomes associated with STRs are limited by the relatively short time frame that these agents have been commercially available
- The real-world impact of STRs as an antiretroviral formulation on clinical and economic outcomes in the United States is not known
  - Understanding the durability and effectiveness of STRs in real-world, inner-city settings is a particularly urgent, unmet need
  - An assessment of treatment patterns and outcomes for STRs is needed to provide foundational understanding for conducting future comparative effectiveness studies and pharmacoeconomic modeling

Objectives

- To assess and compare baseline demographics and clinical characteristics and ART utilization patterns by pill burden in patients with HIV-1 infection who are naive to ART

Methods

- The data source for the study was the Henry Ford Health System (HFHS), which provides primary and specialty healthcare for residents of southeastern Michigan
  - Database includes administrative data (medical billing, pharmacy claims) and electronic medical records (eg, laboratory values)
  - Case-selection window was between January 1, 2007 (index date), and September 30, 2015
- Inclusion and exclusion criteria are shown in Table 1

Table 1. Patient Selection Criteria

Inclusion criteria	Exclusion criteria
Confirmed diagnosis of HIV-1 infection and initiated first ART regimen within case-selection window	Prior ART exposure
Age ≥13 years at time of ART initiation	Confirmed diagnosis of HIV-2 infection
≥1 clinic visit, or continuous enrollment in Health Alliance Plan in the year prior to ART initiation	Initiation of ART within a blinded clinical trial
Continuous observation in the year post-index, with ≥3 agents in their first ART regimen and documentation of ≥1 viral load test and ≥1 CD4+ test	Resident in a skilled nursing facility at the time of ART initiation
	Viral load test result <1000 copies/mL within 90 days prior to index

ART, antiretroviral therapy.

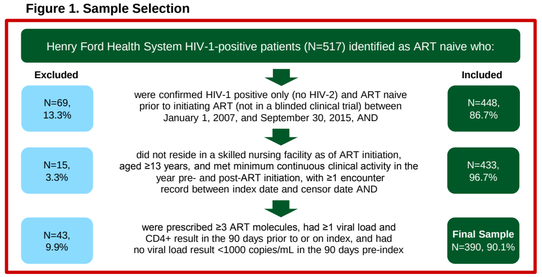
- Planned study outcomes
  - Viral suppression was defined as achievement of plasma HIV-1 RNA <50 copies/mL on the index regimen
  - Viral failure included the following definitions
    - Patients who never achieved suppression post-index
    - Patients with ≥2 consecutive viral load results >200 copies/mL after viral suppression
    - Patients having 1 viral load result >200 copies/mL after viral suppression and having subsequently discontinued the index ART regimen

Results

Baseline Characteristics and Patient Disposition

- Of 517 patients living with HIV-1 infection and identified as ART-naive at the HFHS, 390 were eligible (Figure 1)

Figure 1. Sample Selection



ART, antiretroviral therapy.

- Patients who initiated on an STR (n=254, 65.1%) or MTR (n=136, 34.9%) were significantly different in their demographic and clinical characteristics (Table 2)

Table 2. Baseline Characteristics

	STR (n=254)	MTR (n=136)	*P* value
Mean age, years (SD)	36.2 (11.7)	38.9 (13.9)	0.048
Gender, n (%)			
Male	216 (85.0)	91 (66.9)	<0.0001
Female	34 (13.4)	41 (30.1)	<0.0001
Transgender	4 (1.6)	4 (2.9)	NS
Race, n (%)[a]			
American Indian/Native Alaskan	2 (0.8)	1 (0.7)	NS
Asian/Pacific Islander/Native Hawaiian	4 (1.6)	3 (2.2)	NS
Black	190 (74.8)	100 (73.5)	NS
White	40 (15.7)	23 (16.9)	NS
Other/unknown/declined to respond	18 (7.1)	9 (6.6)	NS
Infection route[b]			
MSM contact only	134 (52.8)	57 (41.9)	0.0412
Heterosexual contact only in women	29 (11.4)	30 (22.1)	0.0052
Other[c]	91 (35.8)	49 (36.0)	NS
Viral load, copies/mL, mean (SD)[d]	161,318 (355,851)	294,050 (831,755)	0.0286
CD4+ counts, cells/μL, mean (SD)[e]	288 (206)	238 (203)	0.0237
Current or historical ADE, n (%)	43 (16.9)	43 (31.6)	0.0009
Any comorbidity, n (%)	88 (34.6)	78 (57.4)	<0.001
≥1 concomitant medication 45 days prior to index, n (%)	176 (69.3)	105 (77.2)	0.0969

ADE, AIDS-defining event; MSM, men who have sex with men; MTR, multiple-tablet regimen; NS, non-significant; SD, standard deviation; STR, single-tablet regimen. [a]Most patients were of non-Hispanic ethnicity (STR, n=221 [87.0%]; MTR, n=116 [85.3%]). [b]Based on a combination of physician reporting and patient self-reporting. [c]Grouping includes the following reported categories, in which statistical comparisons were found to be NS: MSM + intravenous drug use, intravenous drug use only, heterosexual contact in men, multiple modes of infection other than MSM + intravenous drug use, others (blood transfusions, unprotected sex, and not otherwise specified), and unknown. [d]No significant differences between STR and MTR were found in the number of patients with viral loads of <10,000, ≥10,000 to <100,000, or ≥100,000 copies/mL. [e]No significant differences between STR and MTR were found in the numbers of patients with viral loads of ≤350, >350 and ≤500, or >500 cells/μL.

- Significantly more patients who initiated on STRs were taking regimens with non-nucleoside reverse transcriptase inhibitors (NNRTIs) as the third agent (Table 3)

Table 3. ART Regimens

	STR (n=254)	MTR (n=136)	*P* value
ART regimen by third agent class, n (%)			
PI[a]	0	78 (57.4)	<0.0001
NNRTI	174 (68.5)	11 (8.1)	<0.0001
INSTI	80 (31.5)	38 (27.9)	NS
Other	0	6 (4.4)	0.0007
Most common regimens, n (%)			
STRs			
EFV/FTC/TDF	159 (62.6)	—	—
EVG/c/FTC/TDF	60 (23.6)	—	—
DTG/ABC/3TC	20 (7.9)	—	—
RPV/FTC/TDF	15 (5.9)	—	—
MTRs			
DRV/r/FTC/TDF[b]	—	35 (25.7)	—
ATV/r/FTC/TDF[b]	—	27 (19.9)	—
RAL/FTC/TDF[b]	—	21 (15.4)	—
DTG/FTC/TDF[c]	—	8 (5.9)	—
DTG/ABC/3TC[c]	—	7 (5.1)	—

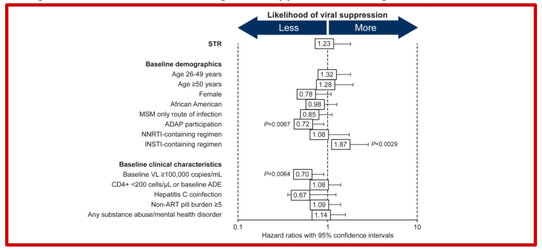
3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; ATV/r, atazanavir with ritonavir; DRV/r, darunavir with ritonavir; DTG, dolutegravir; EFV, efavirenz; EVG/c, elvitegravir with cobicistat; FTC, emtricitabine; INSTI, integrase strand transfer inhibitor; MTR, multiple-tablet regimen; NNRTI, non-nucleoside reverse transcriptase inhibitor; NS, non-significant; PI, protease inhibitor; RAL, raltegravir; RPV, rilpivirine; STR, single-tablet regimen; TDF, tenofovir disoproxil fumarate. [a]STRs are not currently available with protease inhibitors as the third agent. [b]Regimen with ≥3 pills. [c]Regimen with 2 pills.

- Mean (standard deviation [SD]) follow-up time was significantly longer in STR versus MTR initiators (1027 [793] vs 767 days [674]; *P*=0.0013)

Virologic Outcomes

- Viral load suppression occurred in 81% of all patients (STR, n=215 [84.6%]; MTR, n=100 [73.5%]; *P*=0.0079)
- Co-variates associated with statistically significant changes in likelihood of achieving viral suppression included were ART regimens based on INSTIs (hazard ratio [HR] 1.9, *P*=0.0029); baseline viral load ≥100,000 copies/mL (HR 0.7, *P*=0.0064); and participation in the AIDS Drug Assistance Program (HR 0.7, *P*=0.0067; Figure 2)

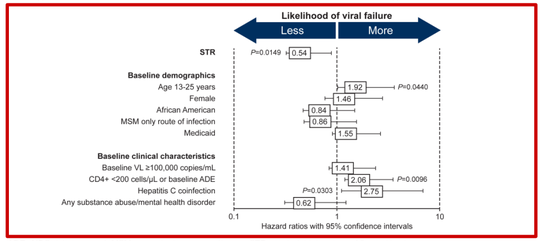
Figure 2. Likelihood of Achieving Viral Suppression Among All Patients



Cox proportional hazard model includes both ART pill burden (STR, MTR) and ART regimen type (INSTI,PI, NNRTI). ADAP, AIDS Drug Assistance Program; ADE, AIDS-defining event; ART, antiretroviral therapy; INSTI, integrase strand transfer inhibitor; MSM, men who have sex with men; MTR, multiple-tablet regimen; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; STR, single-tablet regimen; VL, viral load.

- Among 118 patients initiated on INSTI-based regimens (STR, n=80; MTR, n=38), 107 (90.7%) achieved viral suppression
  - The only co-variate associated with a significantly increased likelihood of achieving viral suppression among patients on INSTI-based therapy was starting therapy in 2014-2015 vs 2007-2013 (HR 1.9, *P*=0.0107)
- Among 185 patients initiated on NNRTI-based regimens (STR, n=174; MTR, n=11), 151 (81.6%) achieved viral suppression
  - High (≥100,000 copies/mL; HR 0.4, *P*=0.0008) or moderate (≥10,000 to <100,000 copies/mL; HR 0.6, *P*=0.0137) baseline viral load and young age (13-25 years; HR 0.6, *P*=0.0129) were associated with a significantly decreased likelihood of achieving viral suppression
- Patients taking STRs were significantly less likely to experience any virologic failure during the study compared with patients taking MTR (STR, n=38 [15%]; MTR, n=34 [25%]; *P*=0.0149; Figure 3)
  - Mean (SD) time to failure was 549 days (433) days in the STR group and 488 (487) days in the MTR group (*P*=0.2041)
  - Virologic failure occurred in 10% of patients on INSTI-based regimens (STR, 9%; MTR, 13%, *P*=0.4590)
  - Factors associated with a significantly increased risk of experiencing viral failure included having a CD4+ count <200 cells/μL or an ADE at baseline (HR 2.1, *P*=0.0096), being co-infected with hepatitis C virus at index (HR 2.7, *P*=0.0303), and age 13 to 25 years (HR 1.9, *P*=0.0440; Figure 3)

Figure 3. Likelihood of Experiencing Virologic Failure Among All Patients



ADE, AIDS-defining event; MSM, men who have sex with men; STR, single-tablet regimen; VL, viral load.

- Resistance occurred in 15% of patients who experienced virologic failure, predominantly in those with NNRTI-resistance mutations
- ≥1 change in initial ART regimen occurred in 22.4% (n=57) of patients taking STRs and 59.6% (n=81) of patients taking MTRs (*P*<0.0001)
  - Mean (SD) time to change in ART was significantly longer in the STR group (925 [875] days) versus the MTR group (485 [468] days; *P*=0.0002)
- Compared with MTR initiators, STR initiators were 59% less likely to experience a change in regimen (*P*<0.0001), 46% less likely to experience virologic failure (*P*<0.05), and 30% more likely to achieve viral suppression (*P*<0.05)

Conclusions

- Patients naive to ART initiating on STRs and MTRs have notable differences in their demographic, clinical, virologic, and immunologic profiles
- Patients who initiated ART with an STR were significantly more likely to achieve viral suppression and less likely to experience a change in ART regimen
  - Higher likelihood of viral suppression and longer duration of initial ART were specifically associated with INSTI-based regimens compared with other regimens
- These results highlight the value of STRs in achieving viral suppression among inner-city patients with HIV-1 infection naive to ART and suggest that STRs are associated with improved tolerability and greater adherence in this population

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