POSTER #1512

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The Impact of Antiretroviral Tablet Burden and Polypharmacy on Viral Suppression in Treatment-Naïve Patients

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BACKGROUND

Studies have suggested that the tablet burden associated with antiretroviral therapy (ART), as well as non-ART polypharmacy, may negatively influence adherence to treatment and subsequently virologic outcomes.[1,2] This study assessed the effect of single- and multiple-tablet ART regimens (STR and MTR) and of non-HIV pill burden on initial virologic suppression and rebound in treatment-naïve patients.

OBJECTIVE:

To assess the effects of STR and MTR, as well as non-ART pill burden, on virologic outcomes.

METHODS

- The study population was selected from the Observational Pharmaco-Epidemiology Research and Analysis (OPERA) cohort, which includes prospectively-captured, routine clinical data from patients at 79 outpatient clinics in the United States.
- Study population included treatment-naïve HIV+ patients initiating ART between 1/1/2007 and 3/31/2015. Patients were followed from treatment start date until regimen change, death, loss to follow-up, or study end (March 31, 2016).
- Outcomes included:
  - Virologic suppression: A single HIV-1 RNA (VL) of <50 copies/mL
  - Virologic rebound: = 1 VL >200 after suppression followed by regimen discontinuation OR 2 VL>200 copies/mL
- Pill burden from all chronic (>90 days use) non-ART medications was measured at baseline, totaled, and categorized as 0-4, 5-9, or 10+ non-ART pills per day.
- Multivariable Cox proportional hazards regression modeled the association between HIV pill burden and the outcomes of virologic suppression and virologic rebound.

Table 1. Baseline Characteristics of Patients Initiating ART According to HIV Pill Burden

Characteristic		Initiated with STR N= 5542	Initiated with MTR N= 3648	P-value
Age	13-25 years old	1368 (24.7%)	509 (14.0%)	**<0.0001**
	26-49 years old	3607 (65.1%)	2532 (69.4%)	
	50+ years old	567 (10.2%)	607 (16.6%)	
Gender	Male	4875 (88.0%)	2998 (82.2%)	**<0.0001**
Race	African American	2168 (39.1%)	1402 (38.4%)	0.51
Ethnicity	Hispanic	1461 (26.4%)	801 (22.0%)	**<0.0001**
Log10 Viral Load	Median (IQR)	4.7 (4.2, 5.0)	4.8 (4.3, 5.3)	**<0.0001**
CD4 Count	Median (IQR)	365.0 (239.0, 506.0)	263.0 (112.0, 406.0)	**<0.0001**
AIDS at Baseline	Yes	239 (4.3%)	399 (10.9%)	**<0.0001**
Non-HIV Pill Count	0-4	5089 (91.8%)	3070 (84.2%)	**<0.0001**
	5-9	378 (6.8%)	453 (12.4%)	
	10+	75 (1.4%)	125 (3.4%)	
HCV		251 (4.5%)	294 (8.1%)	**<0.0001**
Syphilis		1448 (26.1%)	901 (24.7%)	0.12
Substance Abuse		738 (13.3%)	560 (5.4%)	**0.006**
Co-morbidity Count	0	3598 (64.9%)	1959 (53.7%)	**<0.0001**
	1	1377 (24.9%)	1049 (28.8%)	
	2+	567 (10.2%)	640 (17.5%)	

IQR=interquartile range; MTR=multi-tablet regimen

RESULTS

- A total of 9,190 eligible treatment-naïve HIV+ patients initiating ART were included in the analysis, including 5,542 (60.3%) taking STR ART and 3,648 (39.7%) taking MTR ART.

Figure 1. Baseline Viral Load

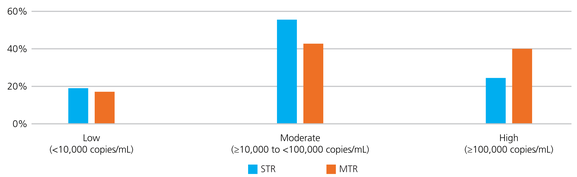
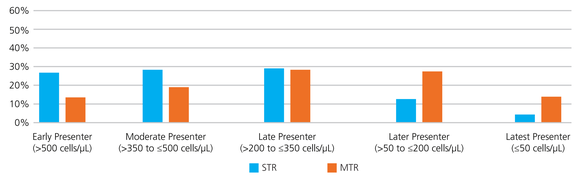
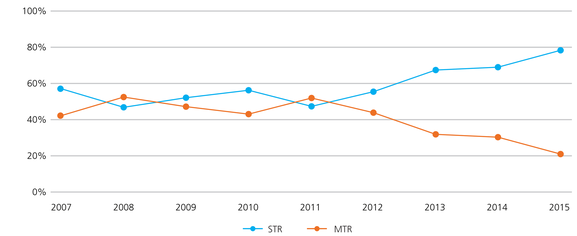


Figure 2. Baseline CD4 Count



- Patients initiating on an STR vs. MTR were younger and healthier, with a lower median baseline VL and higher median baseline CD4 (cells/mm3). STR patients were also less likely to have experienced an AIDS defining event prior to baseline, have a history of hepatitis C infection or substance abuse, and had fewer comorbidities and lower non-HIV pill burden.

Figure 3. ART Tablet Burden in HIV+ Naive Patients Initiating ART in a Real-World Clinic Setting Between 2007 and 2015



- STR use became more common over the study period as more regimen options became available in STR form. By the first quarter of 2015, 78% of patients were being started on an STR.

Table 2: Virologic Outcomes Of Patients Initiating ART By ART Pill Burden

	Initiated with STR N= 5542	Initiated with MTR N= 3648	p-value
Achieved virologic suppression (<50 copies/mL) during initial ART regimen	3896 (70.3%)	1985 (54.4%)	**<0.0001**
Time to first VL < 50 copies/mL (months) Median (IQR)	4.0 (2.2, 6.2)	4.2 (2.3, 7.1)	**0.003**
Had at least one VL after baseline	4891 (88.3%)	3035 (83.2%)	**<0.0001**
Of those with at least one VL, Never achieved suppression	995 (20.3%)	1050 (34.6%)	**<0.0001**
Rebound 1 X (VL >200 copies/mL) after suppression (<50 copies/mL) plus discontinuation of initial ART regimen	206 (3.7%)	174 (4.8%)	**0.01**
Rebound 2 x (VL>200 copies/mL) after suppression (<50 copies/mL)	264 (4.8%)	223 (6.1%)	**0.005**
Of those with at least one VL, Rebound by either definition[1]	470 (12.1%)	397 (20.0%)	**<0.0001**

[1] Among patients who first achieved suppression; rebound defined as 1 VL >200 copies/mL followed by discontinuation or 2 VL's >200 copies/mL

- Patients taking an STR were both more likely to achieve suppression (70.3% STR vs. 54.4% MTR) and less likely to rebound after suppression (12.1% STR vs. 20.0% MTR). (Table 2)
- Multivariable Cox regression comparing STR initiators to MTR initiators indicate increased likelihood of suppression and decreased risk of rebound. (Table 3)

Figure 4: Anchor Agents of Initial ART

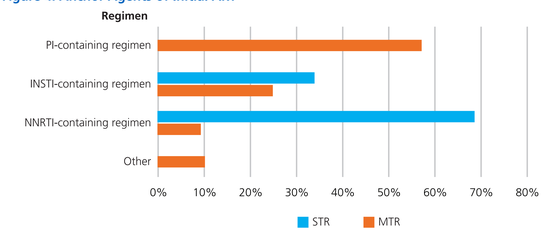


Table 3: Virologic Outcomes During Initial ART Regimen Stratified by Anchor Agent Class

	All Patients		PI Regimen		NNRTI Regimen		INSTI Regimen	
	STR	MTR	STR	MTR	STR	MTR	STR	MTR
Achieved virologic suppression[1]	70.3%	54.4%	....	49.8%	66.9%	49.9%	77.4%	77.4%
Adjusted HR (95% CI)[2,3]	1.38 (1.30, 1.46)		....		1.23 (1.04, 1.44)		1.01 (0.92, 1.12)	
Experienced rebound[4]	12.1%	20.0%	....	24.3%	15.0%	17.4%	6.7%	14.0%
Adjusted HR (95% CI)[4,5]	0.54 (0.47, 0.62)		....		0.75 (0.50, 1.10)		0.42 (0.31, 0.57)	

1 Suppression Defined as VL<50 copies/mL; 2 Referent= MTR; HR > 1.0 indicates increased likelihood of suppression; 3 Cox regression adjusted for age at baseline, sex, African American race, Hispanic ethnicity, baseline VL, baseline CD4, AIDS, non-ART pill burden, history of HCV, syphilis and substance abuse, and total comorbid conditions at baseline; 4 Only among patients who first achieved suppression; rebound defined as 1 VL >200 copies/mL followed by discontinuation or 2 VL's >200 copies/mL; 5 Referent =MTR; HR <1.0 indicates decreased risk of rebound after suppression

- Patients taking integrase strand transfer inhibitor (INSTI)-based regimens were the most likely to suppress and the least likely to experience virologic rebound after suppression compared to other drug classes, regardless of whether they were taking an INSTI-based STR or MTR.
- Among just patients taking INSTI-based ART, patients taking an STR were equally as likely to suppress as patients taking an MTR, but had a reduced risk of virologic rebound after suppression.
- Patients taking an NNRTI-based STR were more likely to achieve suppression than those taking an NNRTI MTR. In a multivariable model, STR did not appear protective against rebound compared to MTR among patients taking an NNRTI, however a small number of patients (n=161) and events (n=28) in the MTR group created less precise hazard ratio estimates.
- Predictive models identifying independent factors associated with suppression and rebound after suppression failed to show an association between non-HIV pill burden and either virologic outcomes.

DISCUSSION

- Treatment-naïve patients initiating on an STR were more likely to achieve viral suppression and less likely to experience virologic rebound than patients initiating on a MTR.
- For initial suppression among treatment-naïve patients, the potency of INSTIs appears to overcome the benefit of regimen simplification (i.e., STRs). However, for long-term treatment benefit (reduced risk of virologic rebound), patients do appear to benefit from a simplified INSTI-based STR regimen.
- Chronic non-ART pill burden at initiation did not have a significant impact in either suppression or rebound models. More research is needed into the optimal description of this variable and the contribution of medications given for less than 90 days.

KEY FINDING

Overall, treatment-naïve patients were more likely to achieve viral suppression and less likely to experience virologic rebound on an STR. However, INSTIs were an exception where suppression was achieved regardless of the pill count. Longterm virologic control, however, was favored in INSTI-based STR with viral rebound less likely to occur in patients receiving this formulation of ART.

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SPONSORSHIP

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