Trends in HIV Antiretroviral Tablet Burden in Treatment Naïve Patients in the United States

Phil Lackey[1], Kathy L. Schulman[2], Cassidy Henegar[3], Ronald D'Amico[4], Susan Zelt[4], and Jennifer Fusco[3]

[1]Carolinas Healthcare System, Charlotte, NC; [2]Outcomes Research Solutions, Waltham, MA; [3]Epividian, Inc., Durham, NC; [4]ViiV Healthcare, Inc., Research Triangle Park, NC

Contact Information:
4819 Emperor Blvd., Suite 400 Durham, NC 27703
P: 919-825-3457 F: 919-313-4505
Email: jennifer.fusco@epividian.com

OPERA® The Longitudinal Cohort

BACKGROUND

The standard of care for antiretroviral therapy (ART) in ART naïve, HIV + patients requires a regimen which contains at least three active drugs from two or more classes.

- Regimen selection is based on virologic efficacy, the potential for adverse effects and drug-drug interaction, pill burden, cost, comorbid conditions and social determinants. These factors are of increasing importance as the focus of therapy shifts from the preservation of life to the lifelong treatment of a chronic condition.
- Typically, initial therapy consists of two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) combined with a third agent such as an integrase strand transfer inhibitor (INSTI), a non-nucleoside reverse transcriptase inhibitor (NNRTI), or a pharmacologically boosted protease inhibitor (PI). The recommended regimen may be prescribed as a single (STR) or multiple tablet (MTR) regimen, the latter either as a 2 pill, once a day, regimen (2-pill MTR) or as a 3+ pill per day regimen (3+ Pill MTR).
- Meta-analyses have suggested that patients initiating on an STR are more adherent, more likely to achieve viral suppression and less likely to be hospitalized.[1-3] While the number of STR's available to clinicians has increased notably since 2011, annual trends in tablet burden and quality metrics have not been well studied.

OBJECTIVE:

To evaluate trends in ART pill burden and quality metrics in a national sample of ART naïve patients.

METHODS

- The Observational Pharmaco-Epidemiology Research & Analysis (OPERA) database comprises electronic health records from 79 US community-based outpatient HIV or multispecialty clinics in 15 states. The data represent ~ 70,000 HIV positive patients, or ~7% of all HIV-positive patients linked to care in the U.S. It is the largest continually operating HIV cohort in the US refreshed daily.
- HIV+ patients initiating ART between 1/1/2007 and 12/31/2014 were identified in the OPERA database. Patients were followed from treatment start to regimen change, death, loss to follow-up, or study end.
- ART tablet burden was classified into STR, two-pill MTR regimens and 3+ pill MTR regimens.
- The rate of new AIDS defining events (ADE) post ART initiation was measured as was the frequency of, and time to, first viral suppression (HIV-1 RNA viral load <50 copies/mm3).
- Simple linear regression assessed only the impact of time on the frequency of STR use, the likelihood of experiencing an AIDS defining event (ADE) and achieving viral suppression as well as the time to viral suppression.

RESULTS

A total of 8,397 patients met study eligibility criteria

- By year, the sample ranged from a low of 418 patients who initiated in 2007 to a high of 1,878 patients who initiated in 2014.
- Across all years, 59.3% of patients initiated on an STR; 5.8% on a 2-pill MTR and 34.9% on a 3+ pill MTR.
- Median (IQR) follow-up was significantly (p<0.0001) lower among 2-Pill and 3+ Pill MTR initiators at 12.2 (5.8, 17.3) and 14.9 (7.0, 29.7) respectively as compared to STR initiators at 17.3 (10.3, 30.3) months.
- Table 1 details select demographic and clinical characteristics of the population. There were significant differences in age, ethnicity, route of infection, payer type, and baseline viral load/ CD4 count as well as the proportion of patients with AIDS and HCV co-infection as of the date of the first ART initiation.
- The percentage of patients initiating on an STR or 2-Pill MTR increased from 57% and 2% in 2007 to 69% and 15% in 2014 (p=0.02. 0.04 respectively) while those initiating on a 3+ Pill MTR decreased from 41% to 16% (p=0.01) during the same period. Figure 1 depicts the change in ART tablet burden over time.
- While the overall trend towards STR, and away from 3+ Pill MTR, was consistent across payers, the magnitude of the change varied. A total of 72% of patients with ADAP/Ryan White coverage initiated on an STR in 2014 as compared to only 51% of patients with Medicare. Figures 2a, 2b depict STR and 3+MTR pill utilization by payer and year.

Table 1: Selected Patient Characteristics at Baseline

	Initiated ART with…..			
Baseline Characteristic	STR N= 5542	2-Pill MTR N= 561	3+ Pill MTR N= 3087	P-value
Age, Median (IQR)	32.7 (26.1, 42.7)	34.8 (27.4, 44.9)	38.9 (30.0, 46.9)	<0.0001
Male	4875 (88.0%)	497 (88.8%)	2501 (81.0%)	<0.0001
Risk of Infection, MSM	3376 (60.9%)	308 (54.9%)	1620 (52.5%)	<0.0001
Race, African American	2168 (39.1%)	219 (39.0%)	1183 (38.3%)	0.763
Ethnicity, Hispanic	1461 (26.4%)	100 (17.8%)	701 (22.7%)	<0.0001
Log10 Viral Load, Median (IQR)	4.7 (4.2, 5.0)	4.7 (4.3, 5.1)	4.9 (4.3, 5.3)	<0.0001
CD4 Count, Median (IQR)	365.0 (239.0, 506.0)	340.0 (192.0, 496.0)	244.0 (100.0, 384.0)	<0.0001
AIDS	226 (4.1%)	36 (6.4%)	345 (11.2%)	<0.0001
HCV	255 (4.6%)	40 (7.1%)	257 (8.3%)	<0.0001
Payer Type				
ADAP/Ryan White	2825 (51.0%)	239 (42.6%)	1397 (45.3%)	<0.0001
Commercial	1600 (28.9%)	227 (40.5%)	852 (27.6%)	<0.0001
Medicaid	644 (11.6%)	74 (13.2%)	557 (18.0%)	<0.0001
Medicare	453 (8.2%)	26 (4.6%)	263 (8.5%)	<0.0001
None	746 (13.5%)	62 (11.1%)	426 (13.8%)	<0.0001

IQR=interquartile range; MSM=men who have sex with men; MTR-multi-tablet regimen

Figure 1. ART Tablet Burden Among ART Naive Patients Initiating ART in a Community Setting between 2007 and 2014

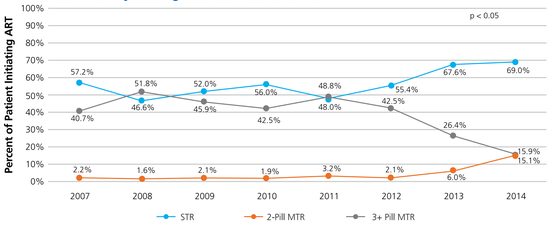
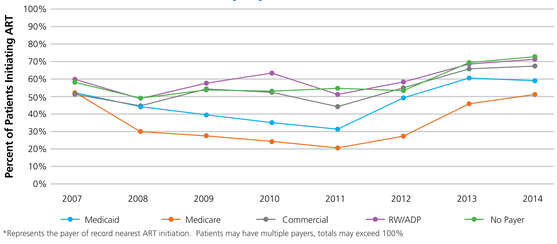
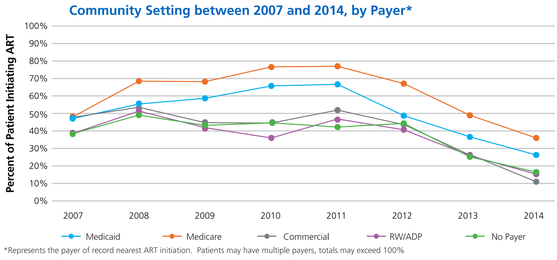


Figure 2a. Percent of ART Naive Patients Initiating an STR in a Community Setting between 2007 and 2014, by Payer*



*Represents the payer of record nearest ART initiation. Patients may have multiple payers, totals may exceed 100%

Figure 2b. Percent of ART Naive Patients Initiating an 3+ Pill MTR Regimen in a Community Setting between 2007 and 2014, by Payer*



*Represents the payer of record nearest ART initiation. Patients may have multiple payers, totals may exceed 100%

- Time trends in ADE reduction were significant for naïve patients initiating on an STR (4.2% to 1.8%, p=0.003) but not for 3+ MTR (8.8% to 5.8%, p=0.16). Cell size for 2-pill regimens was not sufficient in all years to support trend evaluation (Figure 3).
- Regardless of pill burden, the percentage of patients achieving viral suppression after ART initiation rose from 58% to 70% (p=0.06) while those experiencing an ADE dropped from 6.0% to 2.2% (p<0.001) (Data not shown).
- Viral suppression rates increased in STR initiators from 67% to 75% (p=0.15) and from 44% to 47% (p=0.40) among 3+ pill MTR regimens initiators.
- Median time to suppression dropped from 4.3 to 3.0 months (p=0.06) driven primarily by the change in time to suppression in STR initiators (4.1 to 3.2 months, p=0.051). Time to suppression did not change significantly among 3+ pill MTR initiators during the same time frame (4.6 to 3.9, p=0.7) (Table 2).

Figure 3. New AIDS Defining Events by Year of ART Initiation

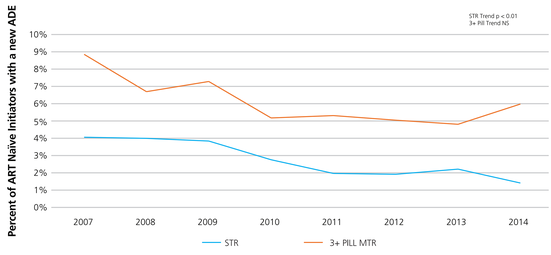


Table 2. Median (IQR) Time (Months) to First Viral Suppression by ART Pill Burden and Year of Initiation

	Initiated ART with…..		
	STR N= 5542	2-Pill MTR N= 561	3+ Pill MTR N= 3087
Initiating ART in CY	Median (IQR) Time to First Viral Suppression		
2007	4.1 (2.6, 6.6)	3.0 (2.5, 7.0)	4.6 (2.7, 7.2)
2008	4.4 (2.7, 6.4)	21.8 (7.4, 36.2)	4.6 (2.8, 6.2)
2009	4.6 (3.1, 6.6)	7.5 (5.2, 8.6)	3.8 (2.1, 7.4)
2010	4.6 (3.0, 7.1)	3.9 (1.4, 4.9)	4.5 (2.3, 7.2)
2011	4.6 (3.2, 6.4)	3.5 (2.3, 4.1)	4.5 (2.3, 8.1)
2012	4.3 (2.8, 7.1)	3.0 (2.6, 8.1)	5.0 (2.8, 8.4)
2013	4.1 (2.0, 6.4)	2.5 (1.1, 4.7)	5.0 (3.2, 7.4)
2014	3.2 (1.6, 5.2)	2.5 (1.2, 4.2)	4.0 (2.1, 7.1)
2015	3.2 (1.5, 5.0)	1.8 (1.0, 3.6)	3.9 (2.4, 7.5)

DISCUSSION

- There has been a significant trend towards prescribing ART with a lower pill burden in the last decade. More than two-thirds of naïve patients initiated on an STR in 2014.
- Trends are consistent across payers although adoption of STR is highest among patients with Ryan White/ADAP or a commercial payer and lowest among those with Medicare or Medicaid.
- Changes in clinician prescribing preference since 2011, after the introduction of alternate STR formulations, comprised of either NNRTI or INSTI based regimens, has resulted in a shift away from PI based regimens which are available as MTRs.
- Notwithstanding differences in efficacy, adherence and tolerability of the various antiretrovirals during the timeframe analyzed, significant trends were also noted in achieving viral suppression and reducing disease progression.

ACKNOWLEDGMENTS

This research would not be possible without the generosity of the OPERA HIV caregivers and their patients sharing their experiences. Additionally, we are grateful for the following individuals: Gregory Fusco MD MPH (Advisory Board coordination), Robin Beckerman (SAS programming), Ted Ising (Database Arch & Mgmt), Bernie Stooks (Database Mgmt), Judy Johnson (Med Terminology Classification), Rodney Mood (Site Support & Data Analyst), Elizabeth Yancy (Data Analyst).

REFERENCES

1. Sutton SS et al. Single- versus multiple-tablet HIV regimens: adherence and hospitalization risks. Am J Manag Care. 2016 Apr;22(4):242-8. PubMed PMID: 27143289.
2. Nachega JB et al. Lower pill burden and once-daily antiretroviral treatment regimens for HIV infection: A meta-analysis of randomized controlled trials. Clin Infect Dis. 2014;58(9):1297-307.
3. Astuti N, Maggiolo F. Single-tablet regimens in HIV therapy. Infect Dis Ther. 2014;3(1):1-17.

SPONSORSHIP

This research was funded by ViiV Healthcare

ViiV Healthcare | Epividian®