Adherence and Persistency with Modern Single vs Multi-Tablet Antiretroviral (ARV) Regimens in 1st treatment of HIV in Clinical Practice

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1. BACKGROUND AND AIMS

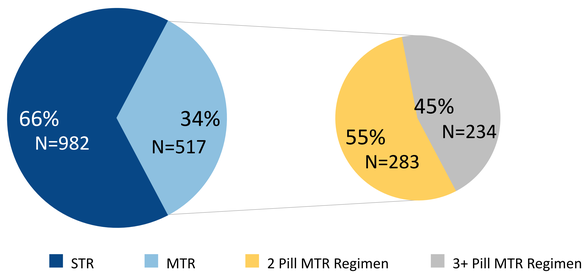
Prior studies have reported improved adherence, persistency, virologic outcomes and lower risk of hospitalizations with single tablet (STR) vs multi tablet regimens (MTR) in HIV treatment. However, most studies were conducted using prescription and medical claims data limited to efavirenz (EFV)-based therapies. In this study, we utilized electronic medical records, prescription, and specialty pharmacy dispensing data to assess STR and MTR adherence and persistency as observed in a network of clinical practices with more contemporary regimens.

2. METHODS

Data were collected for 1499 HIV-infected patients in care at 6 US-based HIV treatment centers. Patients eligible for the study initiated their 1st ARV between Jan 2015 and Dec 2016. First ARV regimen was defined based on absence of prior ARV prescriptions and a 30-day pre-treatment period with no ARV dispensed or for rapid starts, a high baseline viral load (>= 10,000 copies/ml). Adherence was assessed using Medication Possession Ratio (MPR) and Proportion of Days Covered (PDC). (See PLoS One 2012:7:e31591) Follow up was ≥365 days with duration capped at 365 days for adherence comparisons. Limitations include inability to determine true treatment naïve status, first regimens may have reflected subsequent regimens after an undetermined hiatus. Additional confounders could include inaccurate date of therapy stop or initiation due to unmonitored, payer-dictated switches in pharmacies, and other inaccuracies inherent to clinical practice EMR and specialty pharmacy dispense data. Comparisons were conducted using chi-squared (categorical variables) or Student t (continuous variables) testing.

3. REGIMEN USE

The majority of patients were on STR at time of ARV initiation (66%, 982/1499). 2 regimens accounted for 53% of STR use: EVG/c/TDF/FTC (27%, 265/982) and EVG/c/TAF/FTC (26%, 250/982). MTR were used in 34% (517/1499) of patients, with 55% (283/517) receiving 2 pill regimens and 45% (234/517) 3 pill regimens. Top 2 pill regimens were DTG+TDF/FTC (24%, 69/283) and DRV/c + TDF/FTC (14%, 40/283). Top 3+ pill regimens were DRV+RTV+TDF/FTC (26%, 60/234) and ATV+RTV +TDF/FTC (15%, 34/234).



Top 5 regimens			
STR	**MTR (all)**	**MTR 2 tablet**	**MTR 3+ tablets**
EVG/c/TDF/FTC, 27% (265)	DTG + TDF/FTC, 13% (69)	DTG + TDF/FTC, 24% (69)	DRV + RTV + TDF/FTC, 26% (60)
EVG/c/TAF/FTC, 26% (250)	DRV + RTV + TDF/FTC, 12% (60)	DRV/c + TDF/FTC, 14% (40)	ATV + RTV + TDF/FTC, 15% (34)
DTG/ABC/3TC, 17% (171)	DRV/c + TDF/FTC, 8% (40)	RAL + TDF/FTC, 8% (22)	ABC/3TC + DRV + RTV, 5% (12)
EFV/TDF/FTC, 15% (151)	ATV + RTV + TDF/FTC, 7% (34)	DTG + TAF/FTC, 6% (17)	DRV + DTG + RTV + TDF/FTC, 4% (9)
RPV/TDF/FTC, 12% (119)	RAL + TDF/FTC, 4% (22)	DRV/c + TAF/FTC, 4% (12)	DRV + RAL + RTV + TDF/FTC, 3% (6)

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4. BASELINE POPULATION DEMOGRAPHICS BY 1ST REGIMEN TYPE

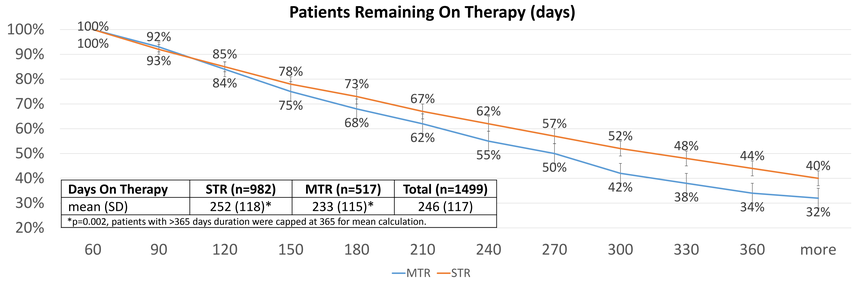
Lower mean age, higher mean CD4 counts, male, Hispanic, non-black, and higher mean eGFR were associated with STR. Baseline ALT and AST were not significantly different between STR and MTR groups.

no. (%) unless indicated	STR (n=982)	MTR 2 tablet (n=283)	MTR 3+ tablet (n=234)	All MTR (n=517)	TOTAL (n= 1,499)
Age - mean (SD)	44 (12)*	49 (12)	51 (10)	50 (11)*	46 (12)
Male	862 (88%)*	222 (79%)	202 (86%)	424 (82%)*	1,286 (86%)
Race					
Black	268 (27%)*	95 (34%)	90 (39%)	185 (36%)*	453 (30%)
White	510 (52%)	139 (49%)	110 (47%)	249 (48%)	759 (51%)
Other	154 (16%)	35 (12%)	31 (13%)	66 (13%)	220 (15%)
Unknown	50 (5%)	14(5%)	3 (1%)	17 (3%)	67 (5%)
Hispanic Ethnicity	264 (27%)*	55 (19%)	47 (20%)	102 (20%)*	366 (24%)
ALT u/L - mean (SD)	32 (30) n=731	33 (26) n=211	31 (31) n=166	32 (28) n=377	32 (29) n=1,108
AST u/L - mean (SD)	29 (21) n=729	29 (18) n=210	31 (26) n=165	30 (22) n= 375	29 (21) n=1,104
CD4 cells/mm^3 - mean (SD)	640 (300) n=724*	532 (312) n=209	472 (277) n=166	506 (298) n= 375*	594 (306) n=1,099
eGFR ml/min - mean (SD)	90 (22) n=730*	85 (23) n=210	84 (24) n=163	85 (24) n=373*	88 (23) n=1,103

* Indicates p<0.05. Age (p<0.001), Male (p=0.002), Black (p=0.001), Hispanic (p=0.008), CD4 (p<0.001), eGFR (p<0.001).

5. PERSISTENCY BY 1ST REGIMEN TYPE (PATIENTS REMAINING ON THERAPY – DAYS)

Patients receiving STR had a higher mean duration (252 days) compared to MTR (233 days). Difference between groups appear most evident when duration is greater than 270 days.

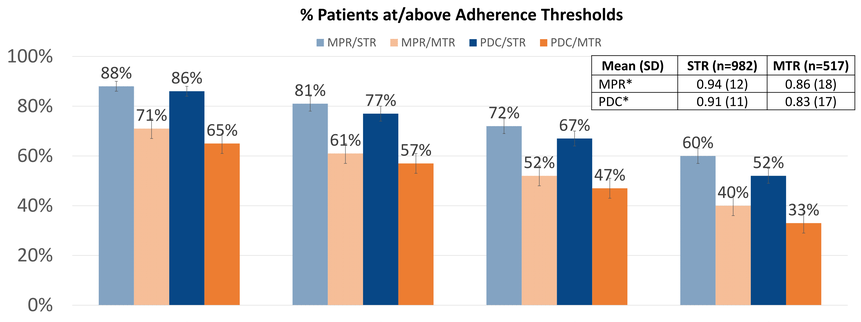


Days On Therapy	STR (n=982)	MTR (n=517)	Total (n=1499)
mean (SD)	252 (118)*	233 (115)*	246 (117)

*p=0.002, patients with >365 days duration were capped at 365 for mean calculation.

6. PROPORTION OF PATIENTS ACHIEVING ADHERENCE THRESHOLDS

The percentage of patients achieving adherence with STR by either MPR or PDC was significantly higher than with MTR across different threshold measures.



Mean (SD)	STR (n=982)	MTR (n=517)
MPR*	0.94 (12)	0.86 (18)
PDC*	0.91 (11)	0.83 (17)

MPR = Medication Possession Ratio; PDC = Proportion of Days Covered; STR = Single Tablet Regimen; MTR = Multi Tablet Regimen ,*p<0.001 for all comparisons

7. BASELINE POPULATION DEMOGRAPHICS WITHIN ADHERENCE GROUPS

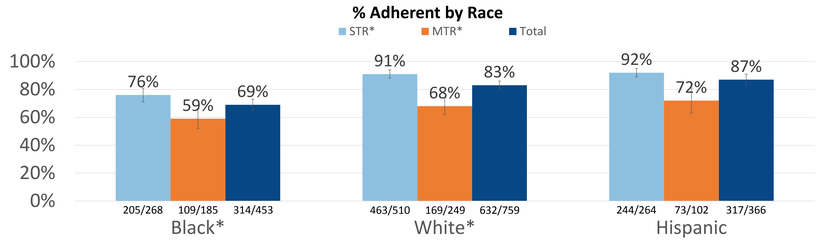
Adherence was categorized utilizing 80%+ PDC adherence. Within the STR group, adherence was associated with older age and white race and non-adherence was associated with black race. Within the MTR group, there were no demographic factors associated with adherence, and non-adherence was associated with black race.

no. (%) unless indicated	STR (n=982)		MTR (n=517)		Total (n=1499)	
	Adherent n=841	Non-Adherent n=141	Adherent n=337	Non-Adherent n=180	Adherent n=1,178	Non-Adherent n=321
Age – mean	*45	*42	50	49	46	46
Male	740 (88%)	122 (87%)	272 (81%)	152 (84%)	1,012 (86%)	274 (85%)
Race						
Black	*205 (24%)	*63 (45%)	*109 (32%)	*76 (42%)	*314 (27%)	*139 (43%)
White	*463 (55%)	*47 (33%)	169 (50%)	80 (44%)	*632 (54%)	*127 (40%)
Other	125 (15%)	29 (21%)	44 (13%)	22 (12%)	169 (14%)	51 (16%)
Unknown	48 (6%)	2 (2%)	15 (4%)	2 (1%)	63 (5%)	4 (2%)
Hispanic Ethnicity	244 (35%)	20 (24%)	73 (26%)	29 (25%)	*317 (32%)	*49 (25%)
ALT u/L - mean (SD)	33 (31) n= 641	28 (19) n= 90	31 (25) n= 256	35 (34) n= 121	32 (29) n= 897	32 (29) n= 211
AST u/L - mean (SD)	29 (22) n= 641	26 (12) n= 88	29 (21) n= 256	33 (23) n= 119	29 (22) n= 897	30 (19) n=207
CD4 cells/mm^3 - mean (SD)	644 (298) n= 637	611 (317) n= 87	526 (303) n= 255	463 (283) n= 120	610 (304) n= 892	525 (306) n= 207
eGFR ml/min - mean (SD)	90 (21) n= 642	93 (25) n= 88	84 (23) n= 255	86 (24) n= 118	88 (22) n= 897	89 (25) n= 206

*Comparisons within 1st Regimen Groups. STR: Age (p=0.010), Black (p<0.001), White (p<0.001). MTR: Black (p=0.026).

8. PERCENT POPULATION WITH 80%+ ADHERENCE, BY RACE/ETHNICITY

Within the STR group, percentage of black patients that achieved 80%+ PDC adherence was significantly lower than white patients. Percentage adherence was not significantly different for MTR between white and black groups. Within black, white or Hispanic groups, adherence was significantly higher for STR regimens.



*STR: Black v White (p<0.001). Comparisons between STR and MTR were p<0.001 for each race/ethnicity.

9. SUMMARY

In this study, we utilized EMR, prescription, and pharmacy dispensing data to assess STR and MTR adherence and persistency with contemporary regimens as observed in a network of clinical practices. Data were obtained for patients who initiated their 1st ARV between Jan 2015 and Dec 2016. Key summary points are:

- Of 1499 patients, 66% (982) received STR and 34% (517) MTR
- Higher CD4 counts, male, Hispanic, non-black race, and/or higher mean eGFR were associated with STR use.
- Mean duration of therapy was significantly longer for STR users (252 days) compared to MTR (233 days)
- Adherence was greater with STR compared to MTR as determined by both MPR (STR mean = 0.94, MTR mean = 0.86), and PDC (STR mean = 0.91, MTR mean = 0.83). There were differences in adherence for black compared to white patients that were also significant (p<0.001).

This study of adherence with STR vs MTR HIV therapy is novel, as it includes current DHHS recommended regimens and was conducted utilizing EMR, prescription, and dispensing data. Dispensing data may give a more accurate picture of medication usage by patients compared to prescription data. The results of better adherence and persistency with STR ART underscores the ongoing importance of simpler treatment for HIV.

Dr. Mills advises and receives research funding from Gilead, ViiV Healthcare, and Merck. He is on the speaker's bureau for Gilead. J. Priest, A. Oglesby and Dr. Mrus are employees of ViiV Healthcare and own company stock as part of their employment. N. Wick is employed by Trio Health and received grants from Gilead, AbbVie, and Merck. Dr. Althoff previously served on a Medical Advisory Board for Gilead. Dr. Eron consults for Merck, ViiV Healthcare, Gilead and Janssen. The University of North Carolina receives research funding from ViiV Healthcare, Gilead and Janssen from which he receives support as an investigator. Dr. Huhn advises for and received grants from Gilead, ViiV Healthcare and Janssen. He advises for Theratechnologies, and received grants from Proteus. Dr. Jayaweera has received research grant support from Gilead, ViiV Healthcare and Janssen. Dr. Mounzer advises for Gilead, ViiV Healthcare and Janssen. He is on the speakers' bureau for Merck, Gilead and Janssen. Mounzer has received grants from Merck, Gilead, ViiV Healthcare and Janssen. Dr. Moyle serves as a speaker and advisor to Merck, Gilead Sciences and Janssen and TheraTechnologies. Dr. Ramgopal is a speaker for Gilead, AbbVie, Janssen and Allergan. He is a consultant for ViiV Healthcare, Merck and Gilead. Dr. Santiago serves on the Medical Advisory Board for Gilead and is a Speaker for Gilead and Janssen. Dr. Sax consults for Gilead, ViiV Healthcare, Merck and Janssen. He has received grants from BMS, Gilead, Merck and ViiV Healthcare. Dr. Voskuhl has received grants from Gilead, ViiV Healthcare, Merck, Janssen and advises for Gilead. Dr. Elion receives grants from Gilead and Proteus, serves on the Advisory boards for Gilead and ViiV, and is a speaker for Gilead and Janssen. Drs. Althoff, Elion, Eron, Huhn, Jayaweera, Mills, Mounzer, Moyle, and Sax serve on Trio Health's Scientific Advisory Board.