The choice of first-line regimen influences the likelihood of therapy switches and disease progression

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BACKGROUND

❖Highly active antiretroviral therapy (HAART)'s effectiveness has made long-term suppression of HIV-1 RNA plasma viral load possible for both naïve and experienced patients.

❖The new challenges for HAART is to allow long-term sustainability and adherence to the daily requirements of the therapy.

❖Though it is more common to see patients tolerating and preserving their first HAART regimen now, there are still several patients who switch therapies during the course of treatment due to virologic failure, toxicity or tolerability issues.

OBJECTIVES

❖To build explanatory models to identify the most significant variables that explain the number of therapy switches (only due to therapeutic failure) among naïve patients who have started the most common recommended HAART regimens.

METHODS

Study Population

❖Participant eligibility: ≥19 years old,; starting HAART on two nRTIs, or a NtRTI as backbone, plus either a NNRTI, or a PI boosted with a ritonavir dose of <400mg/day.

❖The HAART regimens at baseline: boosted PI-based (booted atazanavir [ATA\r] and boosted lopinavir [LOP\r]) and as NNRTI-based (efavirenz [EFV] and nevirapine [NEV]).

❖HAART start date: between January 1, 2000 and June 30, 2011; and followed until June 30, 2012.

Statisitcal Analysis

❖At 6-month intervals, regimen change was noted based on therapeutic failure, defined by two consecutive viral load measure >50 copies/mL.

❖Allowable therapy switches: NNRTI ↔ unboosted PI, NNRTI ↔ boosted PI, NNRTI ↔ multiple PI (≥2 full PI doses), unboosted PI↔ boosted PI, unboosted PI ↔ multiple PI, and boosted PI ↔ multiple PI.

❖All analyses ran separately by history of injection drug use (IDU) and adjusted our models for sex, age, first HAART, and for time-varying CD4 cell count and viral load.

❖Two multivariable explanatory models using a Quasi-Poisson regression were used to account for overdispersion in our data. The time-varying covariates was summarized using the area under the curve (AUC).

❖The selection of variables for both models was based on two criteria: quasi-Akaike Information Criterion (QAIC) and Type III p-values.

Table 1. Bivariate association stratified by IDU status.

Factors	History of Injection Drug Use		p-value
	No N = 1453	Yes N = 1250	
Therapeutic Switches			
None	932 (57%)	692 (43%)	<0.0001
1	247 (51%)	236 (49%)	
2	165 (53%)	149 (47%)	
3 or more	109 (39%)	173 (61%)	
Sex			
Female	200 (35%)	373 (65%)	<0.0001
Male	1253 (59%)	877 (41%)	
Baseline HAART regimen			
NNRTI	679 (51%)	641 (49%)	0.0186
Boosted PI	774 (56%)	609 (44%)	
Baseline age (years)	43 (36 - 50)	42 (35 - 48)	0.0014
CD4 cell count			
Baseline (cells/mm^3)	210 (110 - 310)	180 (100 - 270)	<0.0001
AUC (cell-years/mm^3)	13575 (7644 - 21945)	10575 (5295 - 17715)	<0.0001
Plasma Viral Load (log_{10} copies/mL)			
Baseline (log_{10} copies/mL)	4.96 (4.51 - 5.00)	4.90 (4.37 - 5.00)	0.0094
AUC (log_{10} copy-years/mL)	51 (32 - 80)	60 (35 - 91)	0.0006
Follow-up from baseline to the interview (years)	4.7 (2.8 - 7.2)	4.7 (2.9 - 7.4)	0.7649

RESULTS

❖A total of 1250 (46%) patients reported having a history of IDU, and were more likely to have switched therapy at least 3 times during follow-up. (Table 1)

❖The number of switches was very skewed with values ranging from zero to greater than nine during the follow-up period. (Figure 1)

❖For patients with a history of IDU, initial HAART did not influence the number of therapeutic switches. (Table 2)

❖For patients without a history of IDU, those starting HAART on a NNRTI-based regimen were 1.34 times more likely to experience a therapeutic switch during follow-up than patients who started on a boosted PI-based HAART. (Table 2)

Figure 1. Number of regimen switches stratified by IDU status.

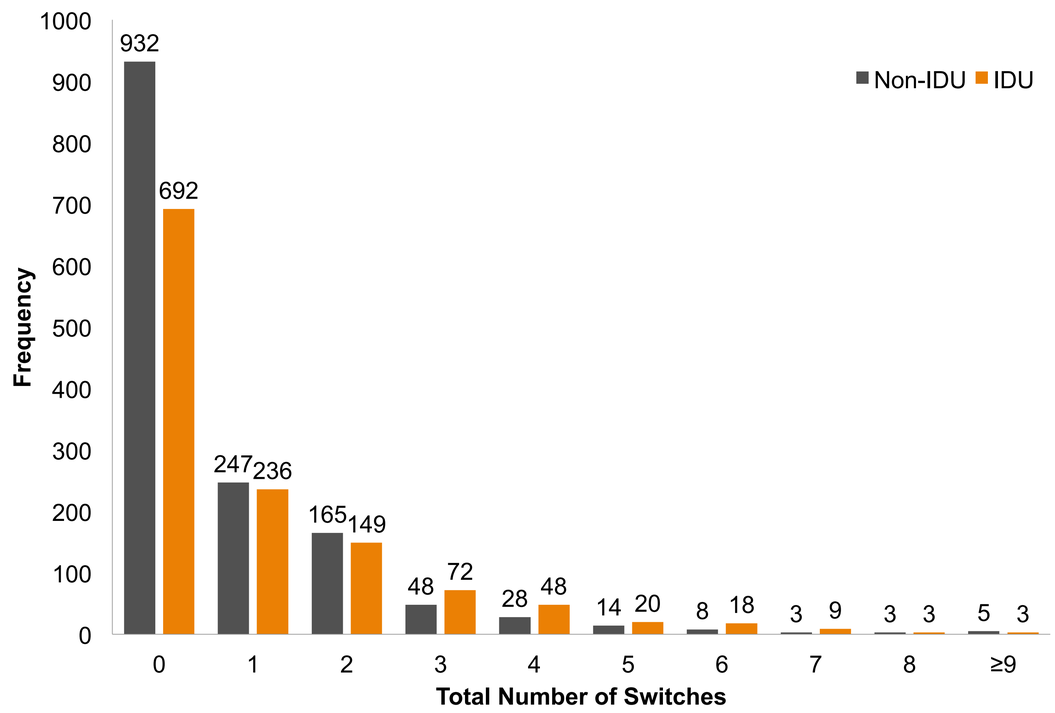

Table 2. Multivariate model stratified by IDU Status.

IDU Model

Variable	Coefficient	Standard Error	95% Confidence Interval	P-value	Rate Ratio
Male vs. Female (ref)	NS				
Age (years)	NS				
Viral Load AUC (log_{10} copy-years/mL)	0.0118	0.0007	0.0105 – 0.0132	<0.0001	1.01
CD4 AUC (per log cell-years/mm^3)	-0.0996	0.0504	-0.1983 – -0.0009	0.0480	0.91
NNRTI vs. Boosted PI (ref)	NS				

Non-IDU Model

Variable	Coefficient	Standard Error	95% Confidence Interval	P-value	Rate Ratio
Male vs. Female (ref)	-0.3225	0.1144	-0.5467 – -0.0984	0.0048	0.72
Age (years)	NS				
Viral Load AUC (log_{10} copy-years/mL)	0.0151	0.0010	0.0130 – 0.0171	<0.0001	1.02
CD4 AUC (per log cell-years/mm^3)	-0.1723	0.0611	-0.2921 – -0.0525	0.0048	0.84
NNRTI vs. Boosted PI (ref)	0.2952	0.0869	0.1249 – 0.4656	0.0007	1.34

DISCUSSION

❖Patients with a history of IDU experienced more therapeutic switches during their treatment, regardless of which antiretroviral class they started HAART on.

❖HAART regimens containing boosted PIs were more resilient than regimens containing NNRTIs when it relates to therapeutic switches related to virologic failure among patients without a history of IDU.

CONCLUSION

❖Close monitoring of the viral of patients on HAART is important in decreasing their risk of virologic failure and to preserve their future therapeutic choices

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