

How do different types of treatment regimens affect short-term response to HAART in lower income countries?

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Background

Non-nucleoside reverse transcriptase inhibitors (NNRTI), in combination with various nucleoside reverse transcriptase inhibitors (NRTI), are commonly used in low-income settings.

Debate continues as to the equivalent potency of NNRTI-based regimens compared to protease inhibitor (PI) based regimens.

Objective

To describe the effect of PI-based vs. NNRTI-based regimens on CD4 and plasma viral load response to treatment in previously antiretroviral therapy naïve individuals initiating HAART in lower income countries.

Methods

Study Population:

The ART-LINC Collaboration

The Antiretroviral Therapy in Lower Income Countries (ART-LINC) Collaboration is a multinational collaborative observational operational cohort. For this study, 18 centres in 16 countries in Africa, Brazil, India, and Thailand contributed data.

Included in the analysis were all previously ART naïve individuals who initiated treatment with a NNRTI- or PI-based combination, who were aged at least 16 years, with known gender, with known baseline CD4 and viral load, and a follow-up CD4 and viral load at 6 months (defined as plus/minus 2 months), and known date of antiretroviral initiation.

Outcome Measures:

- CD4 increase at 6 months (continuous)
- Undetectable plasma viral load (pVL) at 6 months (defined as < 500 copies/ml).

Statistics:

- > CD4 outcome: Multi-level mixed effects linear regression
 - random effect on cohort
 - random intercept model on cohort and patient ID
- > pVL outcome: GEE random effects model
 - random effect on cohort
- > Explanatory variables considered: type of regimen (NVP-based vs. PI-based), age, gender, baseline CD4 and pVL, time, and cohort.

Results

The current dataset includes 8,631 patients on HAART. Analyses presented here are based on the 4810 (56%) ART-naïve patients with complete baseline data and a least one follow up visit. Among these:

- 4291 (89%) started with a PI-based or NNRTI-based combination
- 2215 (46%) used nevirapine; 1139 (24%) used efavirenz
- 2383 (50%) had a baseline and 6-month CD4 count
- 1081 (22%) had a baseline and 6-month viral load

The median number (IQR) of CD4 cells gained in the first 6 months was 106 cells/μL (43-180) and 846 (78%) had undetectable viral load (<500 copies/ml) at 6 months. Several variables were associated with the number of CD4 cells gained, and the probability of reaching undetectable viral load (Tables 2 and 3).

Table 1. Characteristics at baseline of individuals initiating HAART with PI-based vs. NNRTI-based combinations

	Protease Inhibitor Based Regimens n=900	NNRTI Based Regimens n=3,354
Women	369 (41%)	1811 (54%)
Age, years (median, IQR)	36 (31 – 43)	35 (30 – 40)
Baseline CD4 (cells/μL) (median, IQR)	130 (44 – 253)	95 (31 – 189)
Baseline HIV RNA (copies/ml) (median, IQR)	138,400 (36,500 – 403,799)	141,000 (43,100 – 432,000)

Table 2. Adjusted change over 6 months in CD4 cell counts. Results from multi-level mixed effects linear regression model. (n=1136)

Co-variables	Change (+/-) in CD4 compared to reference	P value
Intercept	66.9 cells	0.022
Sex (women vs. men)	+26 cells	0.004
Age (per 10 year increase)	-15.0 cells	0.004
Baseline HIV RNA >=100,000 copies/ml vs. < 100,000 copies	+9.1 cells	0.311
PI-based vs. NNRTI-based regimen	-0.10 cells	0.996
Absolute CD4 at baseline (per cell increase)	+0.92 cells	<0.001

Table 3. Odds ratios of having an undetectable viral load (<500 copies/ml) at 6 months post-treatment initiation

	Unadjusted Odds ratio (95% CI)	Adjusted Odds ratio (95% CI)
Age (per 10 year increase)	1.01 (0.87-1.18)	1.08 (0.91-1.27)
Male sex (vs. female)	1.15 (0.88-1.49)	1.14 (0.86-1.50)
Baseline CD4 (cells/μL) (per 100 cell increase)	1.14 (1.02-1.26)	1.09 (0.97-1.21)
Baseline HIV RNA (copies/ml) (per log increase)	0.68 (0.57-0.81)	0.68 (0.56-0.82)
Type of regimen (PI-based vs. NNRTI-based)	0.49 (0.35-0.69)	0.46 (0.32-0.64)

Conclusions

Only a small proportion of patients starting HAART in this multi-national cohort collaboration from lower income countries had CD4 and viral load testing at baseline and 6 month.

The potential for selection bias is considerable, and the results presented here should therefore be interpreted with caution.

The type of regimen was not associated with CD4 increase, but patients starting PI-based regimens were half as likely to have an undetectable viral load at six months. PIs were more commonly used in earlier years and PI-based HAART may have been interrupted more frequently than NNRTI-based regimens.

Further analyses are required to fully elucidate these findings.

Women and younger individuals gained more CD4 cells than men and older patients, which may be related to differences in adherence (better in women than in men) and less complete immune restoration in older patients. Adherence is not currently measured in ART-LINC.

The associations observed for baseline CD4 count and baseline viral load are similar to those observed in cohorts from industrialised countries.

The Antiretroviral Therapy in Lower Income Countries (ART-LINC) Collaboration

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Funders: National Institutes of Health Office of AIDS Research (Paolo Miotti) and the Agence Nationale de Recherche sur le Sida (Brigitte Bezin)

Special thanks also to the Canadian Institutes for Health Research for their support of Dr. Paula Braitstein through a Post-Doctoral Fellowship.

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