Longitudinal analysis of antiretroviral therapy switch in HIV patients

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Background

Antiretroviral therapy (ART) has evolved across the last years, remaining difficult to decide whether change or not a regimen. Even though some international studies had described factors associated with therapy switching, the conclusions are not consensual. Besides, the majority of studies conducted have only investigated factors associated to first switch.[1] So, factors associated with further changes remain largely unknown.

Objectives

This study aims to examine factors associated with ART switching, using survival models adequate to study characteristics.

Methods

A retrospective cohort study was conducted with HIV-1 patients followed at Hospital de Santa Maria (Lisbon, Portugal).

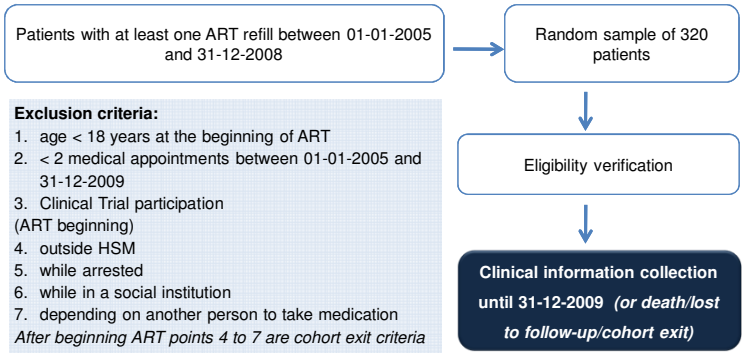

Figure 1. Sampling and eligibility evaluation

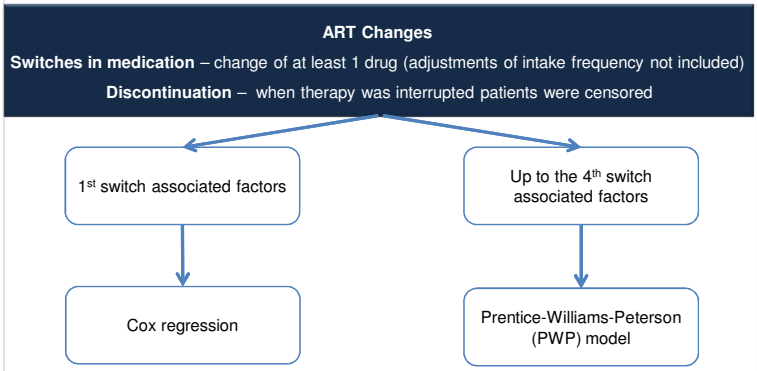

Figure 2. Changes definition and statistical analysis.

To fit multivariate models, covariates where selected using stepwise method considering an inclusion p-value of 0.20 and an exclusion p-value of 0.25. All models included a variable adjusting for year of ART beginning (before 2000, between 2000 and 2004 and after 2004). R software (version 2.15.2) was used.

References:
1. Leite A. Análise longitudinal da mudança terapêutica nos doentes seropositivos para o VIH. Master thesis, Sciences Faculty, University of Lisbon, 2012.

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Results

Study sample

From 320 initial sample, 194 (60.6%) were included, with a mean age of 36.1±10.0 years at ART beginning, 36.1% were female. 29.4% of the subjects started ART before 2000, 40.2% between 2000 and 2004 and 30.4% after 2004. Subjects had a median time of follow-up of 23.1 months.

Factors associated with first switch

Time of beginning, initial regimen and beginning of therapy before or after HAART were retained in the final model. Hazard ratios are presented in Table 1.

Table 1. Hazard ratio estimates and confidence intervals for the final model.

Variables	Hazard Ratio (95%CI)
Timming of ART beginning (Ref = Before 2000)	
2000-2004	0.58 (0.30 – 1.13)
After 2005	0.89 (0.36 – 2.22)
Initial regimen (Ref = 2NRTI + NNRTI)	
2NRTI + PI	**1.78 (1.12 – 2.82)**
Other	**2.59 (1.06 – 6.23)**
Before HAART (Ref = No)	
Yes	1.52 (0.88 – 2.61)

Legend: ART – antiretroviral therapy; NNRTI – nonnucleoside reverse transcriptase inhibitors; NRTI – nucleoside reverse transcriptase inhibitors; PI – protease inhibitors; Ref – reference class..

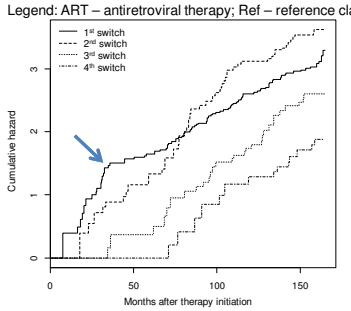
Factors associated with switches up to the fourth

Only CD4+ cells count was associated with switches until the fourth (Table 2).

Table 2. Hazard ratio estimates and confidence intervals for the final model.

Variables	Hazard Ratio (95%CI)
Timming of ART beginning (Ref = Before 2000)	
2000-2004	0.72 (0.47 – 1.10)
After 2005	0.82 (0.42 – 1.53)
CD4+ cells count (/mm^3)	**0.9990* (0.9984 – 0.9997)**

Legend: ART – antiretroviral therapy; Ref – reference class.



Cumulative hazards for each of studied switches are present in figure 2. We verify that 2nd, 3rd and 4th switch have a similar pattern but for the 1st a desaceleration can be observed after month 35 (**arrow**).

Figure 3. Cumulative hazards for each of the studied switches.

Discussion and Conclusions

- Factors associated with first therapy switch differ from the ones associated with the switches until the fourth.
- Lower CD4+ counts are associated with therapy switching. No other factor seems to have an effect on therapy switching decision.
- Cumulative risk of first change differs from the remaining which suggests different decisions according to different regimens.
- With PWP model we were able to study factors associated with switches after the 1st.