PE 7.9/9

Late starting of HAART remains frequent among HIV-infected patients in Spain and is related to a higher rate of virological failure. Results from a subanalysis of the GESIDA 5808 study

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INTRODUCTION

- Delayed initiation of HAART can have deleterious effects, such as incomplete immunovirological response, higher rate of virological failure, and disease progression.
- At community level, the higher incidence of AIDS-defining conditions, hospitalizations, and HAART-related adverse events in HIV-infected patients increases health costs.
- Today, 11.3% of the Spanish population is foreign-born, and a third of newly diagnosed HIV-infected patients are immigrants. The risk of starting HAART late could be more frequent among this population because of communication difficulties, social exclusion, and cultural factors that could act as barriers to health care.

METHODS

Study population

- Subanalysis of a historical cohort study of HIV-infected individuals attending the HIV clinics of 33 Spanish hospitals (GESIDA 5808. See poster PE 7.9/2).
- Patients: antiretroviral-naïve adults who started HAART between January 2005 and December 2006, and who had al least one follow-up visit in the following six months.

Objectives and endpoints

- The primary objective was to compare the **time to treatment failure** between patients who started HAART late and those who did not in order to know whether late starting is associated with a different prognosis of HIV infection, and whether being an immigrant is associated with late starting. The analysis was performed on an intention-to-treat (ITT) basis and failure was defined as virological failure, loss to follow-up, new HIV-related opportunistic infection not due to immune reconstitution, death, and switch or discontinuation of therapy because of toxicity/intolerance.
- Secondary endpoints: **time to treatment failure expressed as observed data** (same endpoints as time to treatment failure, but missing patients were censored) and **time to virological failure** (same endpoints as time to treatment failure, but missing patients and treatment discontinuations not due to virological failure were censored).
- Late starters were considered to have a CD4 lymphocyte count <200 μL at the start of therapy, a prior or concomitant diagnosis of AIDS at the start of therapy, or both.

Statistical analyses

- Survival was calculated using Kaplan-Meier plots and differences were evaluated using the log-rank test.
- A Cox regression model was used to control for confounders. For primary and secondary endpoints, an "explicative" strategy was followed, including, in all models, the variable "Late starter: Yes vs. No".

RESULTS

Demographics

- We identified a total of 1080 naive patients: 606 (56.1%) were late starters and 474 (43.9%) were not (Table 1).
- Late starters accounted for 56% of the study population.
- Being a late starter was associated with older age, male gender, lower educational and socioeconomic level, intravenous drug use, and poorer occupational status.
- There were no differences within immigrant late starters according to geographical origin (Table 2).

Laboratory parameters

- The average CD4 lymphocyte gain during the study period was equivalent in both late starters and non–late starters (202 vs. 199; difference, 3; 95% CI, −20.9 to 28.2) while the average decrease in HIV-1 Log_{10} viral load was slightly higher (−3.07 vs. −2.80; difference, -0.27; 95% CI, −0.35 to −0.02).

Effectiveness

- The proportion of virological failure, death, and AIDS-defining illness not due to immune restoration was higher among late starters (Table 3).
- In the univariate analysis, time to treatment failure was similar in both groups (median time 157 weeks for late starters vs. 171 weeks for non–late starters; log-rank P=0.77), as was the time to treatment failure expressed as observed data (log-rank P=0.27) (Figures 1 and 2).
- However, time to virological failure in the univariate analysis was significantly shorter for late starters than for non–late starters (log-rank P=0.008) (Figure 3).
- Cox regression models included the following as covariates: late starter (Yes vs. No), age, weeks of known HIV infection before starting HAART, gender, risk behaviour for HIV infection, co-infection with HBV or HCV, occupational status, and viral load.
- After adjusting for these variables, the time to treatment failure was not different between late starters and non–late starters (hazard ratio [HR]=0.97; 95% confidence interval [CI], 0.78-1.20). Similarly, there were no differences in time to treatment failure expressed as observed data (HR 1.18; 95% CI, 0.88-1.58). Nevertheless, the time to virological failure was also significantly shorter for late starters than for non–late starters (HR 1.97; 95% CI, 1.18-3.29).

RESULTS (CONT.)

TABLE 1. Baseline Characteristics: late starters vs. non–late starters.

	Non–late starters (n=606)	Late starters (n=474)	p value
Age years, median (IQR)	36 (31-42)	39 (33-44)	<0.001
Gender, female, %	33.8	25.4	0.003
Immigrants	35.2	35.6	0.88
Risk behaviour, %			0.01
Heterosexual relations	42.8	32.7	
MSM	32.9	30.4	
Injection drug users	17.5	25.9	
Other	6.8	6.6	
Current drug user, %	4.2	5.0	0.84
Active alcohol consumption, %	10.3	11.2	0.89
Educational level, %			0.017 linear trend
No school	10.5	11.0	
Primary	16.5	20.0	
Other	25.8	33.1	
Secondary	30.3	24.2	
University	16.8	11.7	
Occupation, %			0.030 linear trend
Unemployed	24.7	32.7	
Working 25-50% of the time	2.7	2.5	
Working more than >50% of the time	68.1	58.4	
Other	4.5	6.4	
Co-infection with HCV and/or HBV, %			0.23
HCV	20.5	24.6	
HBV	4.9	3.6	
HCV+HBV	0.8	1.5	
Not co-infected	63.9	55.8	
Not available	9.9	14.5	
CD4+T-cell count cells/mm^3 median (IQR)	284 (244-342)	91 (36-166)	<0.001
HIV-1 RNA log_{10} copies/mL median (IQR)	4.73 (4.2-5.2)	5.01 (4.6-5.6)	<0.001
Time elapsed to start HAART* (weeks), median (IQR)	20 (3-36)	12 (1-47)	0.019
Antiretroviral therapy, %			0.013
2 NUCs+ATV/r	5.1	3.6	
2 NUCs+EFV	56.4	57.9	
2 NUCs+FPV/r	1.5	4.0	
2 NUCS+LPV/r	18.6	20.7	
2 NUCs+NVP	9.1	4.3	
2 NUCs+SQV/r	3.6	3.8	
3-4 NUCs	2.1	2.6	
Other**	3.6	3.0	

* Time from diagnosis of HIV infection to start of treatment. **Generally quadruple regimens with 3NUCs plus either a non-nucleoside reverse transcriptase inhibitor or a boosted protease inhibitor or both. ATV, atazanavir; EFV, efavirenz; FPV, fosamprenavir; IQR, interquartile range; LPV, lopinavir; MSM, men who have sex with men; NUCs, nucleos(t)ides; NVP, nevirapine; SQV, saquinavir.

TABLE 2. Comparison between immigrants according to geographical origin.

Region	Non–late starters (n=606)	Late starters (n=474)
Sub-Saharan Africa	32.6%	33.1%
North Africa-Middle East	18.1%	14.4%
South and Central America	34.7%	35.9%
Estern Europe	6.9%	7.2%
ASIA	7.6%	9.4%

χ^2=1.01; P=0.91

TABLE 3. Reasons for discontinuation of antiretroviral therapy.

	Non–late starters (n=606)	Late starters (n=474)
End of study period	326 (68.8)	410 (67.7)
Loss to follow-up	75 (15.8)	78 (12.9)
Change of therapy due to toxicity	53 (11.2)	63 (10.4)
Virological failure	18 (3.8)	45 (7.4)
Death	2 (0.4)	8 (1.3)
AIDS-defining illness not secondary to immune restoration	0 (0.0)	2 (0.3)

χ^2=11.72; P=0.039. Values are expressed as number of patients (%).

FIGURE 1. Time to treatment failure. Curves represent Kaplan-Meier time-to-event analyses.

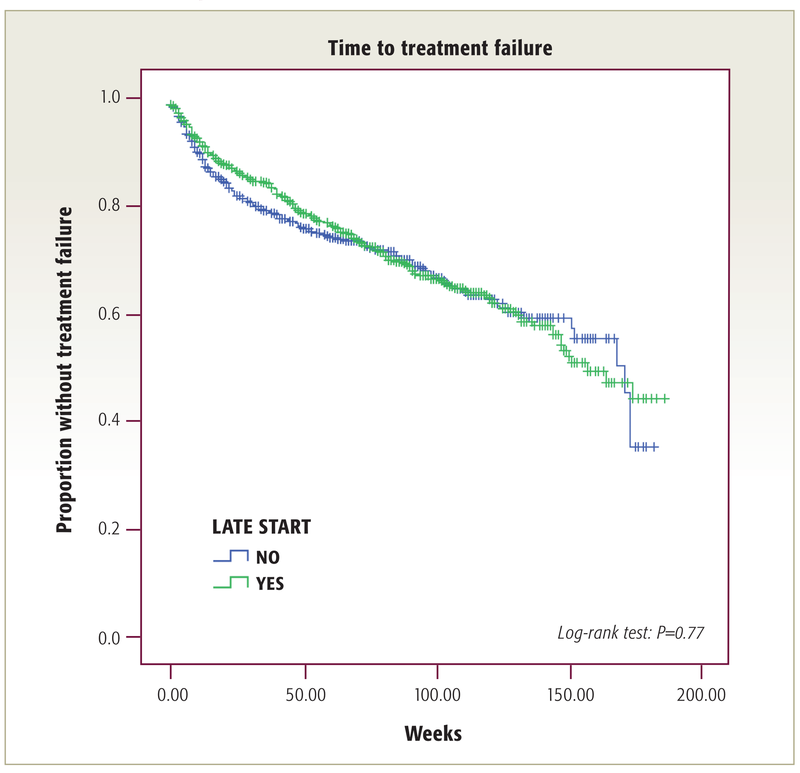


FIGURE 2. Time to treatment failure (observed data). Curves represent Kaplan-Meier time-to-event analyses.

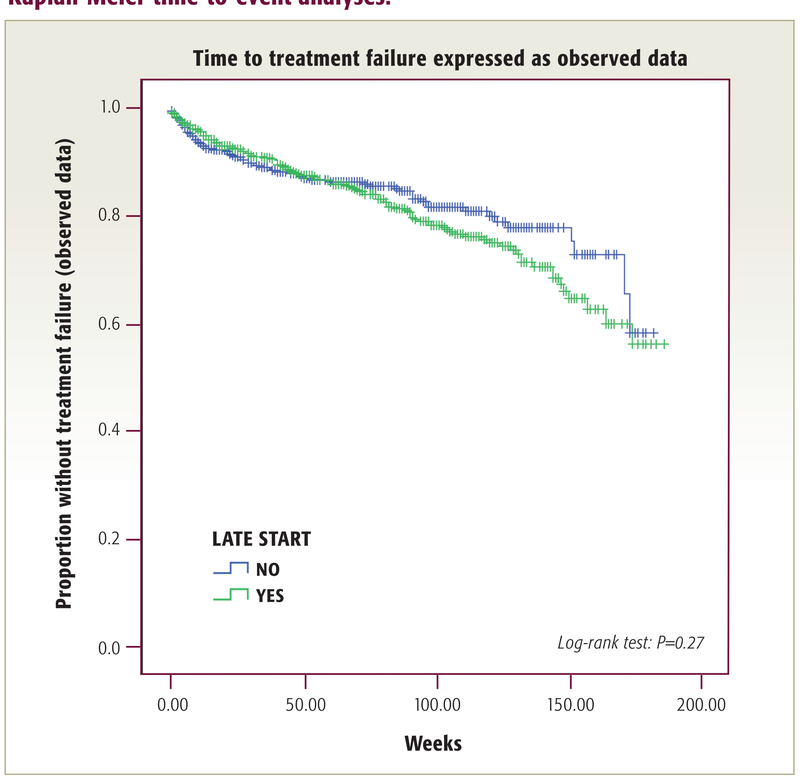
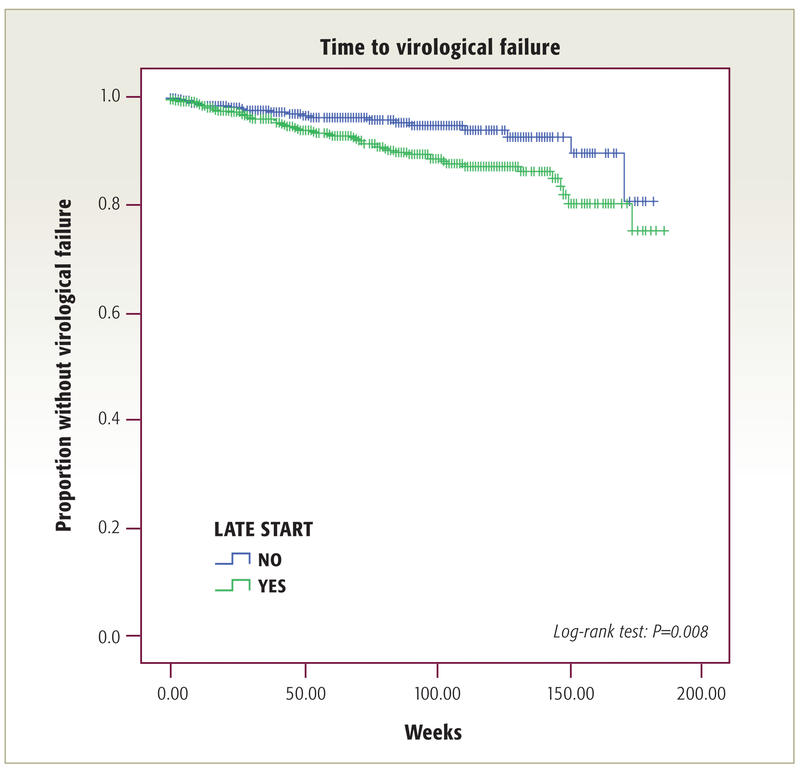


FIGURE 3. Time to virological failure. Curves represent Kaplan-Meier time-to-event analyses.



CONCLUSIONS

- In our cohort, being an immigrant was not related to late starting of HAART, whereas older age, male gender, lower educational and socioeconomic level, intravenous drug use, and poorer occupational status were.
- Late starting of HAART resulted in an increased rate of virological failure, opportunistic infections, and death.
- Despite universal and free access to HAART in Spain, measures to ensure early diagnosis and treatment of HIV infection are necessary.

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