Do HIV-Infected Immigrants Initiating HAART have Poorer Treatment-Related Outcomes than Autochthonous Patients in Spain? Results of the GESIDA 5808 Study[§]

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Abstract: *Objective*: Currently, 12% of the Spanish population is foreign-born, and a third of newly diagnosed HIV-infected patients are immigrants. We determined whether being an immigrant was associated with a poorer response to antiretroviral treatment.

Methods: Historical multicenter cohort study of naïve patients starting HAART. The primary endpoint was time to treatment failure (TTF) defined as virological failure (VF), death, opportunistic disease, treatment discontinuation (D/C), or missing patient. Secondary endpoints were TTF expressed as observed data (TFO; censoring missing patients) and time to virological failure (TVF; censoring missing patients and D/C not due to VF). A multivariate analysis was performed to control for confounders.

Results: A total of 1090 treatment-naïve HIV-infected patients (387 immigrants and 703 autochthonous) from 33 hospitals were included. Most immigrants were from Sub-Saharan Africa (28.3%) or South-Central America/Caribbean (31%). Immigrants were significantly younger (34 y *vs* 39 y), more frequently female (37.5% *vs* 24.6%), with less HCV coinfection than autochthonous patients (7% *vs* 31.3%). There were no differences in baseline viral load (4.95 Log_{10} *vs* 4.98 Log_{10}), CD4 lymphocyte count (193.5/µL *vs* 201.5/µL), late initiation of HAART (56.4% *vs* 56.0%), or antiretrovirals used. Cox-regression analysis (HR; 95%CI) did not show differences in TTF (0.89; 0.66-1.20), TFO (0.95; 0.66-1.36), or TVF (1.00; 0.57-1.78) between immigrants and autochthonous patients. Losses to follow-up were more frequent among immigrants (17.8% *vs* 12.1; p=0.009). Sub-Saharan African patients and immigrant females had a significantly shorter TTF.

Conclusions: The response to HAART among immigrant patients was similar to that of autochthonous patients, although they had a higher rate of losses to follow-up. Sub-Saharan Africans and immigrant females may need particular measures to avoid barriers hindering antiviral efficacy.

Keywords: Immigrants, antiretroviral therapy, HAART, Sub-Saharan Africans, Latin Americans, cohort studies, ethnic groups,

INTRODUCTION

Migration is a growing social phenomenon with a well-recognized impact on the epidemiology of infectious diseases. In 2004, it was estimated that approximately 2% of the world's population were migrants (>200 million) [1]. The health characteristics of migrants after arrival are influenced by their health status in their country of origin, exposure during migration, and health risks in the host country [1, 2]. Immigrants and refugees from areas where infections such as tuberculosis, HIV, or HBV persist provide a challenge to physicians in developed countries in terms of disease control and elimination strategies.

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In Spain, immigration is a relatively recent phenomenon, and, in 2009, immigrants represented 12% of the Spanish population [3]. Most come from Sub-Saharan and North Africa, South-Central America/Caribbean, and Eastern Europe, where the prevalence of chronic viral illnesses is higher than in Spain [4-7]. Taking the immigrant population as a whole, the prevalence of HIV infection is in the range of 0.6% to 5.2% [8-13], and is higher in Sub-Saharan Africans than in patients from South-Central America/Caribbean. Nevertheless, most data come from populations with high-risk behaviours, a factor that may lead us to overestimate the figures. In 1997, immigrants accounted for 3% of all AIDS cases in Spain; in 2007, this proportion had increased to 20.7% (77.5% were from South-Central America/Caribbean and Africa) [14]. In terms of diagnosis, immigrants constitute nearly 30% of the total HIV-infected population cared for at hospitals [15,16]. Furthermore, the proportion of immigrants among newly diagnosed cases of HIV infection rose from 29% in 2003 to 37% in 2007, and there has been an increase in the number of immigrants among HIV-infected patients cared for in Spanish hospitals, from 15.4% in 2001 to 33.3% in 2008 [17]. This trend has also been observed in other European countries since the late 1990s [18, 19]. Some of Europe's migrant and ethnic minority populations are especially vulnerable to the deleterious impact of HIV/AIDS. Lack of knowledge of the local language, social exclusion, and cultural and socio-economic factors can act as barriers to prompt medical attention and early diagnosis [20-23]. Moreover, HIV infection in immigrants may present origin-related characteristics that should be borne in mind by health care professionals. These include the higher prevalence of non-B subtypes [9, 24], different reference ranges for laboratory tests [25], the presence of imported infections [26], different AIDS-defining illnesses [27], different patterns of HBV/HCV infection [5-7], slower disease progression [28], and different abilities to tolerate the adverse effects of antiretroviral drugs and HIV-associated symptoms [29, 30].

Although several studies have addressed the diverse health care–related issues of the HIV-infected immigrant population in Spain, there have been none on treatment and outcome. We performed a historical cohort study to describe the clinico-epidemiological characteristics, treatment, and outcome of immigrants in Spain, and to determine whether being an immigrant is associated with a poorer response to antiretroviral therapy, as compared with the autochthonous population.

METHODS

Study Population

We performed a historical cohort study on HIV-infected individuals attending the HIV clinics of 33 Spanish hospitals. We selected previously antiretroviral-naïve patients who started HAART between January 2005 and December 2006, and who had at least one follow-up visit in the following six months. We classified them into one of two groups: autochthonous or immigrants. We considered a patient as an immigrant if he or she was born outside Spain. Follow-up was censored on September 30th 2008. Patients were identified using medical records, electronic databases, pharmacy registries, and discharge or follow-up reports. To avoid selection bias, all patients identified during the study period were included. Follow-up was managed according to routine clinical care at each hospital. Demographic and clinical data were recorded on standardized electronic case report forms.

Objectives and Endpoints

The primary objective was to compare the time to treatment failure between autochthonous and immigrant patients in order to know whether being an immigrant is associated with a poorer response to antiretroviral therapy, as compared with the autochthonous population. The analysis was performed on an intention-to-treat (ITT) basis and failure was defined as any of the following: (a) an increase in HIV-1 RNA levels above the limit of quantitation (LOQ) in two consecutive determinations during follow-up after an initial response (only one determination was required if the physician changed therapy after the first viral load above the LOQ, or when this determination corresponded to the last visit available); (b) not reaching an HIV-1 RNA level <50 copies/mL during the first 24 weeks; (c) no decrease in HIV-1 RNA level $\geq$2 $\log_{10}$ at week 12-16, if no other visit was available; (d) loss to follow-up; (e) new HIV-related opportunistic infection not due to immune reconstitution; (f) death; and (g) therapy change or discontinuation. Time to treatment failure was counted from baseline to failure (when two viral loads above the LOQ were available, time to treatment failure was considered the time to the first viral load), and was considered as "0" for those patients with no virological response (HIV-1 RNA levels never reached <50 copies/mL).

Secondary endpoints included the time to treatment failure as observed data (same endpoints as time to treatment failure but censoring missing patients) and time to virological failure (same endpoints as time to treatment failure but censoring missing patients and treatment discontinuations not due to virological failure). Late initiation of HAART was defined as either 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. The average change in CD4 lymphocyte count, HIV-1 RNA, and liver enzyme and lipid levels was compared between groups at pre-specified timepoints using a last observation carried forward approach.

Statistical Analyses

Baseline characteristics were analyzed using descriptive statistics. Qualitative variables were expressed as absolute frequencies and percentages, and quantitative variables as the median and interquartile range (IQR). Categorical variables were compared using the χ^2 or Fisher exact test, and continuous variables by the *t* test or Mann-Whitney U test. A p value <0.05 was considered significant.

Survival curves were calculated using the Kaplan-Meier method and differences were evaluated using the log-rank test. Three multivariate Cox regression models were developed to estimate the association between belonging to

the immigrant or autochthonous cohort and failure of treatment (primary and secondary endpoints, respectively), after adjusting for other possible confounders. The requirements of the Cox analysis were checked by graphic methods and Schoenfeld residuals. Variables were included in the model according to their significance in the univariate analysis and to the importance given to each variable, regardless of whether or not it was clearly significant in this analysis. The variable "cohort" (Immigrant or autochthonous) was forced into a non-automatic backward elimination strategy aimed at providing a valid estimate, so that the variable with the highest p value that was not a confounder was excluded at every step [31]. Variables were considered to be confounders if the estimate of the coefficient of the variable "cohort" changed by more than 10% when that variable was removed from the maximal model.

RESULTS

Population Description

Between January 2005 and December 2006, we identified a total of 1105 naïve patients who started HAART (397 immigrants and 708 autochthonous) from 33 Spanish hospitals. Fifteen were excluded because they did not have at least one follow up visit (10 immigrants *vs* 5 autochthonous) Table **1** summarizes the baseline characteristics of both

Table 1. Baseline Characteristics: Immigrant Patients *vs* Autochthonous Patients

	Immigrants (n=387)	Autochthonous (n=703)	p Value
Age, years (Median [IQR])	34 (29-40)	39 (34-45)	<0.001
Gender, female (%)	37.5	24.6	<0.001
Risk behaviour (%)			<0.001
Heterosexual relations	56.3	32.7	
MSM	29.2	30.4	
Injection drug users	5.9	31.0	
Other	8.5	5.8	
Current drug user (%)	1.8	6.1	<0.001
Active alcohol consumption (%)	8.3	12.2	0.044
Educational level (%)			0.15
No school	13.8	9.0	
Primary	19.8	17.6	
Other	25.7	32.0	
Secondary	26.1	27.6	
University	14.6	13.8	
Occupation (%)			0.002
Unemployed	29.0	28.9	
25-50%	4.3	1.8	
>50%	64.7	61.9	
Other	2.0	7.4	
Coinfection with HCV and/or HBV (%)			<0.001
HCV	7.0	31.3	
HBV	5.4	3.7	
HCV+HBV	1.3	1.1	
Not co-infected	74.4	50.9	
Not available	11.9	12.9	
Previous AIDS (%)	25.9	27.1	0.69
CD4+ T-cell count cells/mm^3 (Median [IQR])	193.5 (77-280)	201.5 (78-289)	0.51
HIV-1 RNA log$_{10}$ copies/mL (Median [IQR])	4.95 (4.29-5.44)	4.98 (4.50-5.35)	0.22
Time elapsed to start HAART* (Weeks, Median [IQR])	8.0 (2-27)	21 (3-71)	<0.001
Late initiation of HAART** (%)	216 (56.4)	390 (56.0)	0.88
Antiretroviral therapy (%)			0.78
2 NUCs+ATV/r	3.6	4.6	
2 NUCs+EFV	60.6	55.0	
2 NUCs+FPV/r	2.6	3.0	
2 NUCS+LPV/r	17.9	20.8	
2 NUCs+NVP	6.5	6.4	
2 NUCs+SQV/r	3.1	3.9	
3-4 NUCs	2.1	2.7	
Other**	3.6	3.6	

*Time from diagnosis of HIV infection to start of treatment. **Generally corresponded to quadruple regimens with 3 NUCs 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.

groups. The immigrant population differed from the autochthonous population in that it was younger, with a higher proportion of women, more frequent heterosexual relations as possible route of infection, and a shorter period between diagnosis of HIV infection and initiation of treatment. The proportion of intravenous drug users (possible route of infection) was greater among the autochthonous population, and this also meant a higher percentage of patients coinfected by HCV. However, no differences were observed in variables related to the status of HIV infection at the initiation of HAART, namely, CD4 lymphocyte count, viral load, or previous AIDS diagnosis. Neither were there significant differences in baseline therapy regimens. More than half of the patients started treatment late, although this was no more the case in immigrants than in the autochthonous population.

There were 89 and 143 cases of AIDS-defining conditions in immigrants and autochthonous patients, respectively (Table **2**). Tuberculosis, either disseminated or pulmonary, and wasting syndrome were more frequent among immigrants, whereas *Pneumocystis jiroveci* pneumonia, Kaposi sarcoma, oesophageal candidiasis, and progressive multifocal leukoencephalopathy were more common among autochthonous patients.

The immigrants were from South-Central America/Caribbean (31%), Sub-Saharan Africa (28.3%), Western Europe and the United States (12.2%), North Africa (7.7%), Asia (7.4%), Eastern Europe (6.3%), the Middle East (6.1%), and other regions (4.4%). For the sake of the comparison between the different regions of origin, immigrants from Western Europe and the United States were excluded (their characteristics were very similar to those of the autochthonous population, as reported elsewhere [16]), as was the group of immigrants from other regions (there were few cases and the origins were very diverse), whereas those from North Africa and the Middle East were grouped together. Significant differences were detected between the five different regions of origin (Table **3**). Sub-Saharan Africans had a higher proportion of heterosexual transmission, virological failure, and loss to follow-up, as well as a lower educational level and occupational status. Immigrants from South-Central America/Caribbean had a greater proportion of men who had sex with men, a better occupational status, and more switches of HAART. Immigrants from North Africa-Middle East had a higher proportion of women and a good occupational status. Immigrants from Eastern Europe had a greater history of intravenous drug use, active drug consumption, and a better educational level. Finally, immigrants from Asia had a higher proportion of men and fewer treatment failures. The proportion of patients who initiated HAART late was similar in all regions. There were no significant differences in viral load, CD4 lymphocyte count, or in AIDS-defining diseases at baseline (data not shown).

Effectiveness Outcomes

The proportion of virological failure was similar between the cohorts, although losses to follow-up and switches in treatment due to intolerance or toxicity were more frequent in the immigrant cohort (Table **4**). Kaplan-Meier plots showed that time to treatment failure was significantly shorter for immigrant patients than for autochthonous patients (median time 147 weeks *vs* 168 weeks; log-rank, p=0.014) (Fig. **1**). However, additional sensitivity analyses according to the different reasons for censoring showed that

Table 2. AIDS-Defining Conditions Prior to or at the Moment of Starting HAART

Diagnosis (%)	Immigrants (n=89)	Autochthonous (n=143)	Total
***P. jiroveci* pneumonia**	14.6	25.2	21.1
Pulmonary tuberculosis	19.1	11.9	14.7
Extrapulmonary tuberculosis	20.2	10.5	14.2
Kaposi sarcoma	7.9	10.5	9.5
Oesophageal candidiasis	5.6	11.2	9.1
Cerebral toxoplasmosis	5.6	5.6	5.6
CMV disease	5.6	5.6	5.6
Wasting syndrome	7.9	2.8	4.7
Non-Hodgkin lymphoma	4.5	3.5	3.9
***Cryptosporidium* species diarrhoea**	3.4	2.1	2.6
Progressive multifocal leukoencephalopathy	0.0	4.2	2.6
Recurrent pneumonia	0.0	2.8	1.7
Extrapulmonary cryptococcosis	1.1	1.4	1.3
HIV-related encephalopathy	0.0	2.1	1.3
Chronic intestinal isosporiasis	3.4	0.0	1.3
Recurrent *Salmonella* species bacteraemia	0.0	0.7	0.4
Disseminated histoplasmosis	1.1	0.0	0.4

χ^2=29.41; p=0.021.

Table 3. Baseline Characteristics: Immigrant Cohort by Region of Origin

	South-Central America/Caribbean (n=117)	Sub-Saharan Africa (n=107)	North Africa-Middle East (n=52)	Asia (n=28)	Eastern Europe (n=24)	p Value
Age, years (Median [IQR])	33 (28-39)	35 (29-42)	31 (28-36)	36 (28-40)	32 (29-35)	0.052
Gender, female (%)	30.8	45.8	57.7	21.4	37.5	0.002
Risk behaviour (%)						<0.001
Heterosexual relations	47.9	77.6	75.0	39.3	33.3	
MSM	45.3	13.1	13.5	42.9	37.5	
Injection drug users	2.6	1.9	3.8	0.0	12.6	
Other	4.3	7.5	7.7	17.9	16.7	
Current drug user (%)	1.7	0.9	0.0	0.0	8.3	0.041
Educational level (%)						<0.001
No school	4.8	26.0	20.9	12.0	6.7	
Primary	40.3	27.4	7.0	0.0	6.7	
Other	11.3	19.2	46.5	32.0	13.3	
Secondary	27.4	16.4	20.9	40.0	33.3	
University	16.1	11.0	4.7	16.0	40.0	
Occupation (%)						0.001
Unemployed	14.9	44.7	34.8	22.2	25.0	
25-50%	4.1	7.1	0.0	0.0	12.5	
>50%	78.4	48.2	58.7	77.8	62.5	
Other	2.7	0.0	6.5	0.0	0.0	
Coinfection with HCV and/or HBV (%)						0.51
Yes	10.3	13.5	10.9	3.7	19.0	
Previous AIDS (%)	25.0	21.0	25.5	23.1	39.1	0.51
Late initiation of HAART (%)	56.5	56.1	50.0	60.7	56.5	0.90
Reasons for discontinuation of antiretroviral therapy						0.001
End of study period	63.2	45.8	73.1	85.7	75.0	
Loss to follow-up	8.5	29.9	17.3	7.1	12.5	
Change of therapy due to toxicity	21.4	14.0	5.8	0.0	4.2	
Virological failure	4.3	9.3	3.8	7.1	8.3	
Death	1.7	0.0	0.0	0.0	0.0	
AIDS-defining illness not secondary to immune restoration	0.9	0.9	0.0	0.0	0.0	

the time to treatment failure as observed data (p=0.33) and time to virological failure did not differ between the cohorts (p=0.77). In both cases, median survival time could not be calculated because survival was greater than 50%.

When compared by gender, the median time to treatment failure was significantly shorter for women than for men (147 weeks *vs* 171; p<0.001). Nevertheless, when stratified by cohort, the difference was significantly shorter for immigrant women (124 weeks *vs* 171; p<0.001), but not for autochthonous women (151 weeks *vs* 173; p=0.14).

A multivariate analysis was performed using Cox regression models, including the following as possible confounders: age, weeks of known HIV infection previous to initiation of HAART, gender, risk behaviour for HIV infection, coinfection with HBV or HCV, occupational status, and the interaction between occupational status and cohort. After adjusting for these variables, the time to treatment failure was no different between immigrant patients and autochthonous patients (hazard ratio [HR]=0.88; 95% confidence interval [CI], 0.66-1.20). Similarly, there were no differences in time to treatment failure as observed data (HR 0.95; 95% CI, 0.66-1.36) or time to virological failure (HR 1.005, 95% CI, 0.57-1.78).

Immigrant patients from Sub-Saharan Africa showed a significantly greater proportion of treatment failure for any reason than immigrant patients from the other areas (Table **3**). The failures were mainly secondary to a greater proportion of virological failure and a greater proportion of losses to follow-up. Time to treatment failure was significantly shorter for Sub-Saharan African patients than for the other groups (log-rank, p=0.003) (Fig. **2**). The univariate HRs for the other regions compared to Sub-Saharan African immigrants were significantly lower: North-Africa Middle East, 0.53 (95% CI, 0.30-0.96); South-Central

Table 4. Reasons for Discontinuation of Antiretroviral Therapy

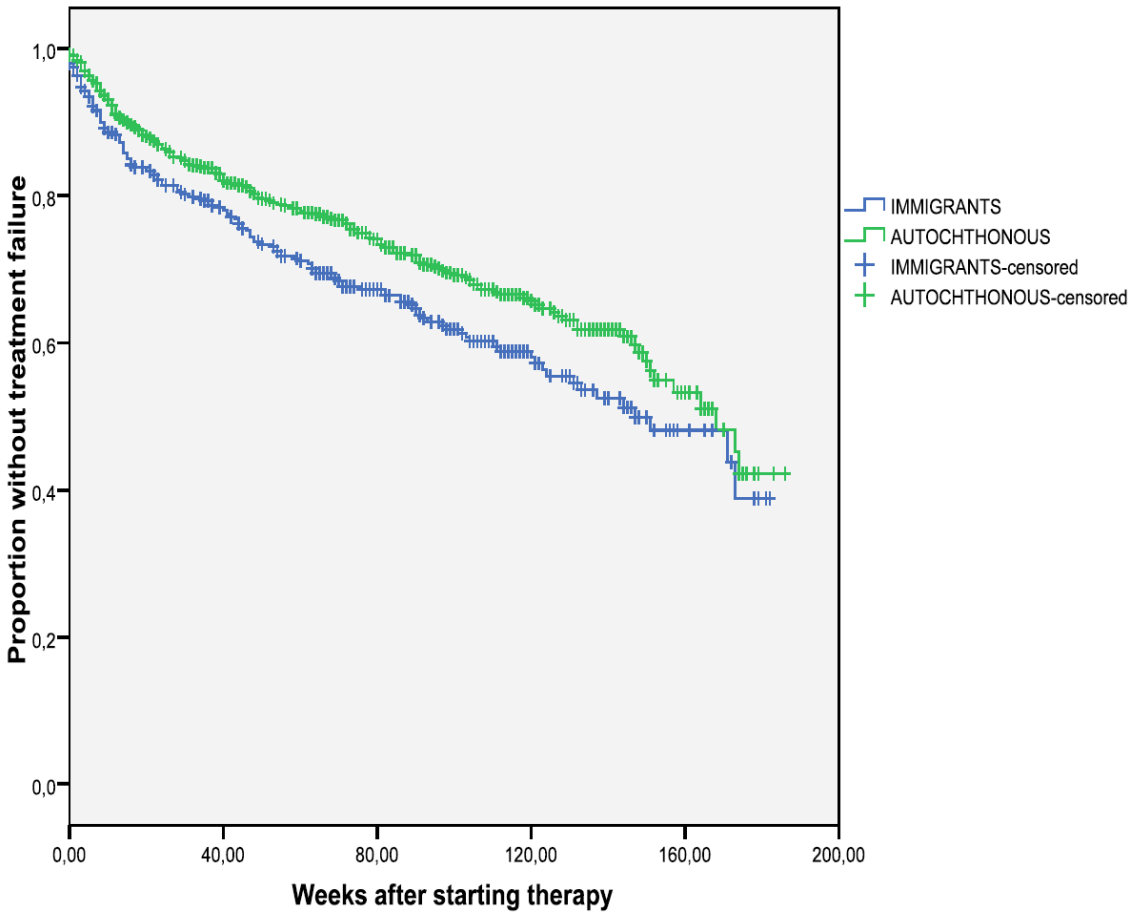
	Immigrants (n=387)	Autochthonous (n=703)	Total
End of study period	245 (63.3)	500 (71.1)	745 (68.3)
Lost to follow-up	69 (17.8)	85 (12.1)	154 (14.1)
Change of therapy due to toxicity	48 (12.4)	68 (9.7)	116 (10.6)
Virological failure	21 (5.4)	42 (6.0)	63 (5.8)
Death	2 (0.5)	8 (1.1)	10 (0.9)
AIDS-defining illness not secondary to immune restoration	2 (0.5)	0 (0.0)	2 (0.2)

χ^2=14.61; p=0.012. Values are expressed as number of patients (%).

America/Caribbean, 0.62 (95% CI, 0.42-0.93); Eastern Europe, 0.41 (95% CI, 0.19-1.0); and Asia, 0.23 (95% CI, 0.08-0.65).

Laboratory Parameters

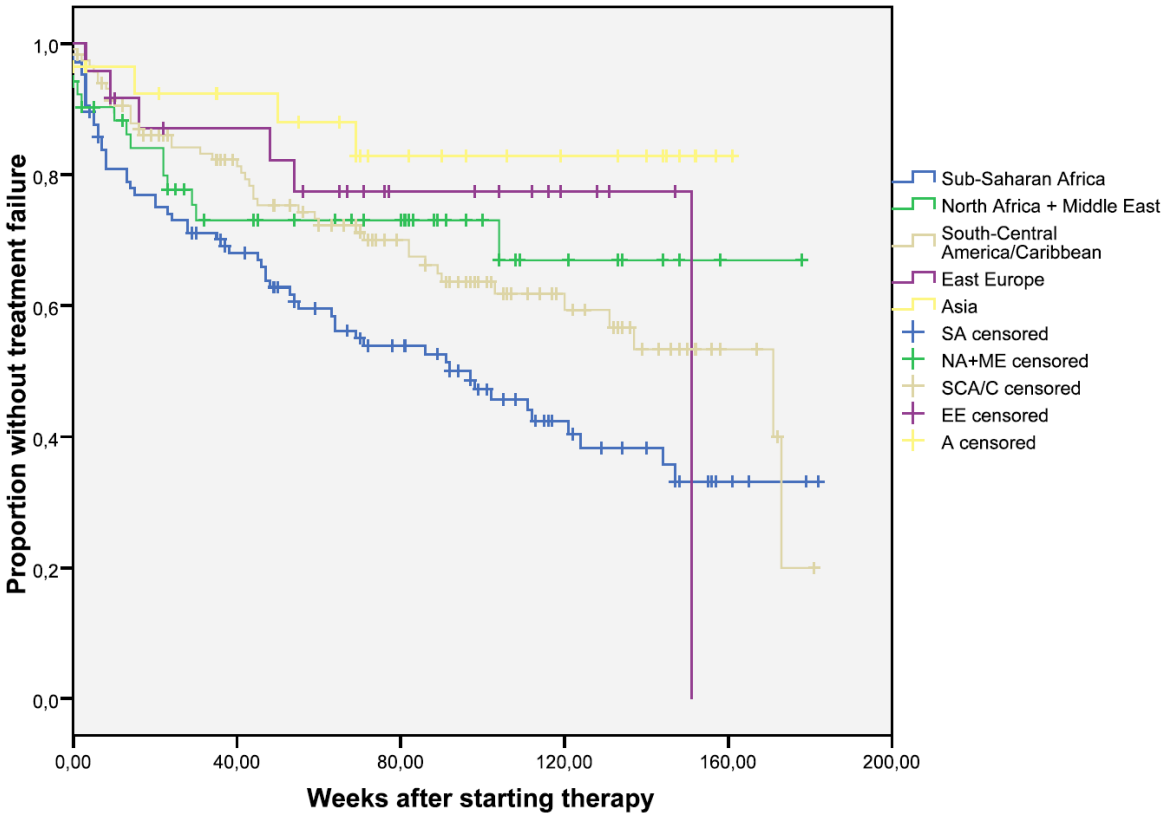
At baseline there were no significant differences between immigrant and autochthonous patients in (median) CD4 cells/μL (193.5 *vs* 201.5), HIV-1 Log_{10} viral load (4.95 *vs* 4.98), total cholesterol (154 mg/dL *vs* 156 mg/dL), low-density lipoprotein cholesterol (92 mg/dL *vs* 96 mg/dL), aspartate aminotransferase (28 IU/mL *vs* 30 IU/mL), or bilirubin (0.5 mg/dL *vs* 0.5 mg/dL). Significant differences were detected in (median) triglycerides (106 mg/dL *vs* 119 mg/dL), high-density lipoprotein cholesterol (41 mg/dL *vs* 36 mg/dL), alanine aminotransferase (26 IU/mL *vs* 31



No. at risk						
Immigrants	387	255	166	72	15	0
Autochthonous	703	480	325	139	27	0

Log-rank test: 6.06 (p=0.014)

Fig. (1). Time to treatment failure by cohort group. Curves represent Kaplan-Meier time-to-event analyses.



No. at risk						
Sub-Saharan Africa	107	66	44	21	8	0
North Africa-Middle East	52	30	22	8	1	0
South-Central America/Caribbean	117	78	55	25	5	0
Eastern Europe	24	18	9	4	0	0
Asia	28	21	13	8	1	0

Log-rank test: 16.1 (p=0.003)

Fig. (2). Time to treatment failure for immigrants by region of origin. Curves represent Kaplan-Meier time-to-event analyses.

IU/mL), and gammaglutamyl transpeptidase (27 IU/mL *vs* 37 IU/mL). CD4 lymphocyte gain during the study period was similar in both immigrant patients and autochthonous patients (162 *vs* 168; difference –6.0; 95% CI, –39 to 20), while HIV-1 Log_{10} viral load decrease was slightly lower in immigrants patients (–2.63 *vs* –3.01; difference 0.38; 95% CI, 0.20 to 0.55). For the remaining parameters, there were no statistically significant differences in the median change during the study period.

In the cohort of immigrants, there were no significant differences between regions at baseline with regard to laboratory parameters or with regard to median change during the study period (data not shown).

DISCUSSION

Our results show that, in Spain, the response to antiretroviral therapy among treatment-naïve HIV-infected patients is similar, irrespective of whether the patients are immigrants or autochthonous.

Although treatment failure during the study was more frequent and time to treatment failure (interruption for any reason) was shorter for immigrant patients in the univariate analysis, this was not verified in the multivariate analysis when it was controlled for potential confounders. Similarly, when losses were censored or only virological failure, death, and opportunistic infections not caused by immune restoration were considered as an event, no differences were detected between the cohorts. This divergence in the primary endpoint seems to be a consequence of the high rate of losses to follow-up in the Sub-Saharan Africa group (29.9%) and the North Africa-Middle East group (17.3%), which could also have negatively affected the difference in viral load as a result of carrying the last observation forward in its calculation.

The recovery of the CD4 lymphocyte count was the same in both cohorts, and the decrease in viral load, while a little more pronounced in the autochthonous patients, was not clinically relevant.

Both the present study and results from other Spanish cohorts [15, 16, 32] show that immigrants are generally younger, the proportion of women is greater, and the main route of contagion is heterosexual relations. However, it is noteworthy that the frequency of transmission by sexual relations has been increasing in Spain over the last few years. The rate of coinfection by hepatotropic viruses was significantly lower in immigrant patients, given their less common history of addiction to intravenous drugs, with the exception of those from Eastern Europe. Other European studies have revealed an increase in the number of immigrants among HIV-infected patients, with heterosexual relations as the predominant risk practice, a greater rate of perinatal transmission, lower age, and a greater proportion of women among immigrants [19, 33-36].

We did not find differences between the cohorts regarding the proportion of late starters, previous AIDS, or antiretroviral regimens used. These results contrast with those of reports from other European and American series, in which immigrants show greater immunological impairment or greater prevalence of AIDS before starting HAART [19, 35-40], although they are consistent with the findings of other Spanish reports [15, 16, 41]. Most HIV-infected immigrants in Spain are from South-Central America/Caribbean and their ability to speak Spanish and cultural proximity to Spain may mean that health care is more readily accessible. Furthermore, voluntary HIV testing is more frequent among immigrant patients than in autochthonous patients [42]. However, in the West, Sub-Saharan Africans are the predominant population, and cultural and socioeconomic factors and functional illiteracy may prevent them from receiving prompt medical attention and an early diagnosis [20-23, 43]. In Spain, access to treatment for HIV infection is universal and free through the national health system. Irrespective of their financial situation, all patients with a medical card receive health care from the national health system or through collaboration with different NGOs. The fact that access to medical care and antiretroviral treatment is not a differentiating factor between immigrant and autochthonous patients in Spain might explain why we found no differences in this area.

Our results also show that the immigrant population is not homogeneous and that the particular characteristics of some groups could make a difference in the outcome of HIV infection. Time to treatment failure was shorter due to the greater rate of loss to follow-up and changes in treatment in the immigrant cohort, mainly among those from Sub-Saharan Africa. This particular group is often at greater risk, as they arrive in precarious conditions and without identification, which hinders their access to the health service. These data are consistent with those of other studies comparing the response to HAART in treatment-naïve immigrants compared with the autochthonous population. Sub-Saharan Africans have been shown to have specific characteristics, such us a greater risk of abandonment, more frequent virological failure, or greater mortality [44-46]. Nevertheless, not all authors show this poorer outcome [19].

Although access to health care is equal for immigrants, follow-up and adherence may be negatively affected by several factors. The Sub-Saharan Africans in our study had a lower educational level and occupational status, which, combined with their high geographic mobility looking for work, may have negatively affected follow-up [47]. The association between poverty, unemployment, and HIV has been reported to be frequent among HIV-infected Sub-Saharan Africans in Europe [48]. Furthermore, HIV infection itself contributes to job insecurity and, as with other chronic illnesses, can have negative effects on the social and personal identity of patients [21]. Additional factors that may affect response to therapy among black patients are an increased rate of adverse events after initiating antiretroviral therapy [30], cultural reluctance to undergo blood testing [49], racial differences in laboratory parameters [50,51] and drug metabolism [52], or a differential pattern in resistance mutations of HIV-1 non-B subtypes [53]. However, race itself does not seem to predict HAART failure [54], and some results indicate that the immune response could be better in Sub-Saharan Africans than in native Europeans [28].

The time to treatment failure was significantly shorter for women. When data were stratified by cohort, this difference was only observed to be significant among immigrant women, although this does not to seem to be explained by reduced access to HIV testing (all women have access to screening during antenatal care), but twice as many immigrant women as autochthonous women underwent voluntary testing [42], even among women with high-risk behaviour [42]. The reasons for this greater rate of failure with HAART could include the higher number of sex workers among HIV-infected immigrant women [8,9], the greater difficulty in attending scheduled check-ups due to work responsibilities, a low educational level [43], or the stigma associated with HIV infection, which often affects women more intensely.

GES-5808 provides a fairly representative sample of patients starting antiretroviral therapy in Spain today. This representativeness is strengthened by the high number of patients and participating centres, their wide geographic distribution, and the similarity between the number of immigrants infected and the number of new cases of HIV infection detected. As cohort composition is based on routine care practice, thus making it possible to include almost all patients who were prescribed HAART in the participating hospitals, the study gives a fairly reliable picture of the day-to-day care of patients with this disease. However, a potential weakness of the study could be the inclusion of patients who had at least one follow-up visit, excluding those that never came back for follow-up. If the dropout rate had been greater in immigrants, this could have skewed the efficiency of antiretroviral treatment in their favour. However, this seems unlikely, as very few patients were excluded from the study for this reason and the study itself detected a higher rate of loss to follow-up among immigrants. Another characteristic of GES-5808 is that baseline data correspond to the start of treatment and not to when the patient is first diagnosed with HIV infection. Although the median time from diagnosis is not very long (8 weeks for immigrants *vs* 21 weeks for autochthonous patients), this must be taken into account when making comparisons with other series, given that factors related to late HIV testing or delayed presentation to HIV care may differ [55].

To conclude, response to antiretroviral therapy is similar in treatment-naïve HIV-infected immigrants living in Spain and treatment-naïve HIV-infected autochthonous patients. Differences in some seemingly more vulnerable groups, such as Sub-Saharan Africans or immigrant women, are probably related to sociocultural and occupational factors that hinder access to health care. We must develop measures to correct the factors that prevent some HIV-infected immigrant groups from taking advantage of HAART.

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APPENDIX

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