Increased risk of virologic failure to the first antiretroviral regimen in HIV-infected migrants compared to natives: data from the ICONA cohort

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Abstract

Migrant and Italian HIV-infected patients (n = 5773) enrolled in the ICONA cohort in 2004–2014 were compared for disparities in access to an initial antiretroviral regimen and/or risk of virologic failure (VF), and determinants of failure were evaluated. Variables associated with initiating antiretroviral therapy (ART) were analysed. Primary endpoint was time to failure after at least 6 months of ART and was defined as: VF, first of two consecutive virus loads (VL) >200 copies/mL; treatment discontinuation (TD) for any reason; and treatment failure as confirmed VL >200 copies/mL or TD. A Poisson multivariable analysis was performed to control for confounders. Migrants presented significantly lower CD4 counts and more frequent AIDS events at baseline. When adjusting for baseline confounders, migrants presented a lower likelihood to begin ART (odds ratio 0.80, 95% confidence interval (CI) 0.67–0.95, p 0.012). After initiating ART, the incidence VF rate was 6.4 per 100 person-years (95% CI 4.8–8.5) in migrants and 2.7 in natives (95% CI 2.2–3.3). Multivariable analysis confirmed that migrants had a higher risk of VF (incidence rate ratio 1.90, 95% CI 1.25–2.91, p 0.003) and treatment failure (incidence rate ratio 1.16, 95% CI 1.01–1.33, p 0.031), with no differences for TD. Among migrants, variables associated with VF were age, unemployment and use of a boosted protease inhibitor–based regimen versus nonnucleoside reverse transcriptase inhibitors. Despite the use of more potent and safer drugs in the last 10 years, and even in a universal health care setting, migrants living with HIV still present barriers to initiating ART and an increased risk of VF compared to natives.

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Study group members are listed in the Appendix.

Introduction

Migrant populations in Europe are disproportionately affected by HIV compared to natives; in fact, according to the European Centre for Disease Prevention and Control, in the period 2007–2011, 39% of all new cases of HIV infection were registered in foreign patients [1], who represented only 9.7% of the

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total resident population. In Italy, the proportion of nonnationals among new HIV cases increased up to 24% in the last available 2013 report [2], with a median incidence of HIV infection of 19.1 in migrants compared to 4.9 per 100|000 in Italian-born subjects. This situation reflects the arrival of migrants from countries with generalized HIV epidemics; in addition, HIV sexual transmission after arrival in Europe has also been described in some populations with a high behavioural risk [3].

Reports from various European countries univocally indicate that migrants have higher rates of late presentation compared to natives [1,2,4–6], as was also confirmed in Italy by a recent survey [7], suggesting that barriers still exist which hamper the access to health services, thus delaying HIV testing, linkage to care and antiretroviral therapy (ART) initiation [8,9]. This risk is especially high for nonlegal immigrants [10,11].

Data regarding the probability of response to ART in migrant patients are still scarce and, at least in part, controversial. In fact, while some studies found a reduced virologic and/or immunologic response in nonautochthonous patients compared to natives [12–14], other surveys found no difference in terms of therapy outcome and overall prognosis after adjusting for baseline viroimmunologic parameters [15–19]. Nevertheless, diversities in virus characteristics (HIV-1 subtype, coreceptor tropism, rate of transmitted drug resistance) [20,21], host genetic factors (such as frequency of human leukocyte antigen (HLA) B5701 status) [22], prevalence of other concomitant infections and comorbidities, different tolerability profiles and side effects [23] might influence ART response in the immigrant population.

The aims of this study were to evaluate possible disparities in access and/or risk of failure to first ART regimens in migrants compared to Italian-born patients enrolled in the ICONA cohort and to assess determinants of failure for migrants living with HIV.

Patients and Methods

The ICONA Foundation Study is an observational cohort of HIV-infected individuals who are antiretroviral naïve at the time of enrolment. This cohort was set up in January 1997 and currently consists of more than 13|000 patients from 50 Italian infectious disease units [24]. Demographic and socio-behavioural data, initiation and discontinuation dates of each antiretroviral drug, HIV virus load (VL) and CD4 cell count every 4–6 months and AIDS-defining diseases according to US the Centers for Disease Control and Prevention criteria are recorded for all enrolled patients.

In the present study, all native and migrant naïve patients enrolled in ICONA in the last 10 years, from January 2004 to March 2014, were included. Migrants were defined as those born outside Italy, based on their geographical origin, which was derived from nationality or from country of birth or origin, and classified as follows: Western countries (Europe, North America, Australia, New Zealand), North Africa and the Middle East, sub-Saharan Africa, Latin America and Asia.

Comparison between natives and migrants was performed by the chi-square test for categorical variables and the nonparametric Wilcoxon rank-sum test for continuous variables. Variables associated with ART initiation were evaluated. A multivariable logistic model was performed to assess the adjusted odds ratio (OR) and 95% confidence interval (95% confidence interval (CI)) for beginning ART.

Further analysis was carried out to identify the impact of migration status on response to therapy. The outcome variables were three different measures of response to ART: time to virologic failure (VF) after at least 6 months of therapy, defined as the first of two consecutive VL >200 copies/mL; treatment discontinuation for any reason (TD); and treatment failure (TF), defined as confirmed VL of >200 copies/mL or TD.

Different patient population were considered for analysing the occurrence of the different outcomes: all subjects who initiated ART and had available at least 2 HIV RNA assessments 6 months after start of therapy for time to VF; and all patients initiating ART with at least one HIV RNA assessment during therapy for evaluating TF and TD. Survival analysis was based on the Kaplan-Meier method to estimate the cumulative probability of VF, TF and TD. A multivariable Poisson model was performed to identify factors independently associated with the three different outcomes.

At multivariable analysis, the main covariate of interest (native/migrant) was adjusted for all factors retained from the univariate analysis because of a p value of <0.10. Analyses were performed by Stata 10 (StataCorp, College Station, TX, USA).

Results

Baseline characteristics

A total of 5773 HIV-positive, ART-naïve patients were enrolled in the period 2004–2014, of whom 1175 were migrants (20.4%). Migrants were mostly from sub-Saharan Africa (35.5%) and Latin America (29.1%), followed by Western countries (27.1%, with 10.9% of these from Eastern Europe), Asia (4.3%) and North Africa and the Middle East (4%). Median duration of residency in Italy was 5 years (interquartile range 1–10).

Baseline characteristics significantly differed between the two groups (Table 1); in particular, lower CD4 counts and higher frequency of AIDS events at enrolment were observed in migrants versus natives.

TABLE 1. Characteristics of migrants and natives at study enrolment

Characteristic	Migrants	Natives	p
Number	1175 (20.4%)	4598 (79.6%)	
Male gender, *n* (%)	670 (57.0%)	3914 (85.1%)	<0.001
Age, years, median (IQR)	34 (28–40)	39 (32–47)	<0.001
Nationality, *n* (%)			
Sub-Saharan Africa	416 (35.5%)	—	
Latin America	342 (29.1%)	—	
Western Country	319 (27.1%)	—	
North Africa and Middle East	47 (4.0%)	—	
Asia	51 (4.3%)	—	
Years of residency in Italy, median (IQR)	5 (1–10)	—	
Months from first HIV test and first visit, median (IQR)	1.2 (0.4–8.4)	2.2 (0.5–16.1)	<0.001
Mode of HIV transmission, *n* (%)			
Heterosexual contact	702 (59.7%)	1634 (35.5%)	<0.001
Homosexual contact	310 (26.4%)	2194 (47.7%)	
Intravenous drug use	47 (4.0%)	436 (9.5%)	
Other/unknown	116 (9.9%)	334 (7.3%)	
Recent drug use at enrolment, *n* (%)			
No	900 (76.7%)	3352 (72.9%)	0.005
Yes	21 (1.7%)	149 (3.2%)	
Unknown	254 (21.6%)	1097 (23.9%)	
Smoking habit at enrolment, *n* (%)			
No	791 (67.3%)	2158 (46.9%)	<0.001
Yes	281 (23.9%)	2009 (43.7%)	
Unknown	103 (8.8%)	431 (9.4%)	
Education, *n* (%)			
Elementary school	160 (13.6%)	172 (3.7%)	<0.001
Junior high school	195 (16.6%)	903 (19.6%)	
High school	221 (18.8%)	1414 (30.8%)	
University	87 (7.4%)	566 (12.3%)	
Missing data	512 (43.6%)	1543 (33.6%)	
Occupation, *n* (%)			
Full-time worker	350 (29.9%)	2085 (45.3%)	<0.001
Housewife	47 (4.0%)	109 (2.4%)	
Self-employed	93 (7.9%)	701 (15.2%)	
Temporary employed	99 (8.4%)	78 (1.7%)	
Retired	2 (0.2%)	167 (3.6%)	
Student	24 (2.0%)	183 (4.0%)	
Unemployed	306 (26.0%)	445 (9.7%)	
Other/missing	254 (21.6%)	830 (18.1%)	
HIV subtype, *n* (%)			
B subtype	203 (17.2%)	1344 (29.2%)	<0.001
Non-B subtype	215 (18.3%)	316 (6.9%)	
Unknown	757 (64.5%)	2938 (63.9%)	
Pregnancy status at enrolment, *n* (%)	51 (4.3%)	17 (0.4%)	<0.001
CDC C stage at enrolment, *n* (%)	138 (11.7%)	362 (7.9%)	<0.001
First HIV RNA, log copies/mL, median (IQR)	4.5 (IQR 3.7–5.2)	4.6 (IQR 3.9–5.2)	0.008
First CD4 count, cells/mm^3, median (IQR)	317 (IQR 137–509)	396 (223–577)	<0.001
First CD4 cells/mm^3, *n* (%)			
<200	323 (27.5%)	876 (19.1%)	0.003
200–350	225 (19.1%)	732 (15.9%)	
>350	440 (37.5%)	2197 (47.7%)	
Missing	187 (15.9%)	793 (17.3%)	
HCV coinfection, *n* (%)			
Positive	70 (6.0%)	446 (9.7%)	<0.001
Negative	792 (67.4%)	2882 (62.7%)	
Unknown	313 (26.6%)	1270 (27.6%)	
HBV coinfection, *n* (%)			
Positive	58 (4.9%)	144 (3.1%)	0.008
Negative	782 (66.6%)	3060 (66.6%)	
Unknown	335 (28.5%)	1394 (30.3%)	
CMV coinfection, *n* (%)			
Negative	43 (3.7%)	246 (5.3%)	<0.001
Positive	492 (41.9%)	1579 (34.3%)	
Unknown	640 (54.4%)	2773 (60.4%)	
Sexually transmitted diseases, *n* (%)	97 (8.2%)	425 (9.2%)	0.292
Type of first regimen, *n* (%)			
2 NRTIs + NNRTI	278 (23.7%)	1233 (26.8%)	<0.001
2 NRTIs + PI boosted	502 (42.8%)	1661 (36.2%)	
2 NRTIs + II	12 (1.0%)	94 (2.0%)	
NRTI sparing	20 (1.7%)	97 (2.1%)	
Other	30 (2.5%)	199 (4.3%)	
No ART start	333 (28.3%)	1314 (28.6%)	

ART, antiretroviral therapy; CDC, Centers for Disease Control and Prevention; CMV, cytomegalovirus; HCV, hepatitis C virus; HCV, hepatitis C virus; IQR, interquartile range; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor.

ART initiation

A total of 4126 patients (71.5%) had initiated ART at the time of analysis, including 842 migrants (71.7%) and 3284 (71.4%) Italian-born patients. Migrants were more likely to have received a boosted protease inhibitor (PI)-based regimen when beginning their ART regimen (43% of prescriptions compared to 36% in Italian-born individuals).

At univariable analysis, migration was not associated with a different probability of initiating ART compared to native patients (OR 1.01, 95% CI 0.87–1.17, p 0.912). However, after adjusting for baseline characteristics at multivariable analysis, migrant status resulted associated with a reduced frequency of ART initiation compared to natives (OR 0.80, 95% CI 0.67–0.95, p 0.012); the main confounder of the association between migration and use of ART was the CD4 cell count at enrolment (p at interaction test <0.001). The following variables were also independently associated with a higher probability of initiating ART by multivariable analysis: older age, higher HIV VL at enrolment, pregnancy, occurrence of an AIDS event before enrolment and hepatitis B virus coinfection. Self-employed subjects versus full-time workers, homosexual contacts or intravenous drug users versus heterosexual contacts as route of HIV acquisition and higher CD4 count at enrolment were associated with a lower likelihood of initiating ART (Table 2).

Response to ART

Among the 4126 subjects who initiated ART, 3167 (615 migrants and 2552 natives) were evaluable for TD and TF, and 2321 (422 migrants and 1899 natives) were subjects for VF. After 6 months of the first ART regimen, the incidence rate of VF was 3.3 per 100 person-years of follow-up (PYFU) (95% CI 2.8–3.9); it was higher in migrants (6.4 per 100 PYFU, 95% CI 4.8–8.5) with respect to natives (2.7 per 100 PYFU, 95% CI 2.2–3.3) (p <0.001). The TD incidence rate was 38.4 per 100 person-years (95% CI 34.4–42.8) in migrants and 30.8 in natives (95% CI 29.2–32.6) (p <0.001), while the incidence rate of

TABLE 2. Logistic regression analysis of factors associated with ART initiation

Characteristic	OR	95% CI		p	AOR	95% CI		p
		Upper	Lower			Upper	Lower	
Male gender vs. female	0.87	0.75	1.00	0.057	1.11	0.91	1.36	0.307
Age (per 10-year increase)	1.27	1.20	1.35	<0.001	1.01	1.01	1.02	0.001
Migrants vs. natives	1.01	0.87	1.17	0.912	0.80	0.67	0.95	0.012
Years from first HIV test to enrolment	0.97	0.96	0.99	<0.001	0.98	0.97	1.00	0.071
Education								
Elementary school	1.00				1.00			
Junior high school	0.86	0.64	1.16	0.333	1.06	0.75	1.49	0.750
High school	0.71	0.53	0.94	0.017	0.97	0.70	1.36	0.872
University	0.54	0.40	0.74	<0.001	0.85	0.59	1.23	0.396
Missing data	0.60	0.45	0.79	<0.001	0.89	0.64	1.23	0.470
Occupation								
Full-time worker	1.00				1.00			
Unemployed	1.00	0.83	1.20	0.978	0.90	0.72	1.12	0.341
Self-employed	0.80	0.68	0.96	0.015	0.77	0.63	0.93	0.007
Temporary employed	0.88	0.63	1.24	0.467	0.85	0.57	1.25	0.402
Housewife	1.28	0.87	1.89	0.214	0.92	0.59	1.46	0.732
Retired	1.72	1.14	2.60	0.009	0.85	0.52	1.37	0.503
Student	0.49	0.37	0.66	<0.001	0.76	0.54	1.05	0.096
Other/missing	0.71	0.61	0.82	<0.001	0.72	0.59	0.87	0.001
Mode of HIV transmission								
Heterosexual contacts	1.00				1.00			
Homosexual contacts	0.57	0.50	0.65	<0.001	0.77	0.65	0.91	0.002
Intravenous drug use	0.69	0.55	0.86	0.001	0.67	0.51	0.88	0.004
Other/unknown	0.74	0.59	0.93	0.010	0.78	0.60	1.01	0.058
HIV RNA, log copies/mL at enrolment								
<4	1.00				1.00			
4–4.999	1.49	1.28	1.73	<0.001	1.42	1.20	1.67	<0.001
≥5	4.44	3.67	5.37	<0.001	2.61	2.11	3.23	<0.001
Missing data	1.13	0.96	1.34	0.130	0.85	0.64	1.13	0.260
CD4 cells/mm^3 at enrolment								
<200	1.00				1.00			
200–350	0.48	0.35	0.65	<0.001	0.68	0.49	0.94	0.020
>350	0.09	0.07	0.11	<0.001	0.13	0.10	0.17	<0.001
Missing data	0.12	0.09	0.15	<0.001	0.24	0.17	0.35	<0.001
Smoking habit								
No	1.00				1.00			
Yes	0.81	0.71	0.93	0.002	0.93	0.80	1.08	0.359
Unknown	0.86	0.74	1.00	0.047	0.98	0.83	1.18	0.864
Pregnancy status at enrolment	4.18	1.80	9.67	0.001	6.21	2.58	14.93	<0.001
CDC C stage at enrolment	5.07	3.65	7.04	<0.001	2.36	1.64	3.39	<0.001
HBV-Ag								
Negative	1.00				1.00			
Positive	1.48	1.05	2.08	0.024	1.39	0.95	2.02	0.009
Unknown	1.07	0.94	1.21	0.305	1.36	1.17	1.57	<0.001

AOR, adjusted odds ratio; ART, antiretroviral therapy; CDC, Centers for Disease Control and Prevention; CI, confidence interval; HBV-Ag, hepatitis B virus antigen; OR, odds ratio.

TF was 44.9 per 100 person-years (95% CI 40.4–49.9) in migrants and 33.2 in natives (95% CI 31.5–35.1) (p <0.001).

The multivariable models, fitted for three different outcomes, confirmed that migrants had a significantly higher rate of both VF (incidence rate ratio (IRR) 1.90, 95% CI 1.25–2.91, p 0.003) and TF (IRR 1.16, 95% CI 1.01–1.33, p 0.031), while no difference was observed for the TD rate (IRR 1.09, 95% CI 0.94–1.25, p 0.248). The VF and TF cumulative probability by means of Kaplan-Meier curves is illustrated in Fig. 1. Factors associated with VF and TF are reported in Table 3; in particular, in addition to the migration status, unemployment, lower CD4 count at enrolment and use of a boosted PI–based versus nonnucleoside reverse transcriptase inhibitor (NNRTI)-based regimen were all found to be associated with a higher probability of VF. The multivariable analysis of TF determinants provided similar results; moreover, pregnancy status and a tuberculosis diagnosis before ART initiation were significantly associated with TF.

No association was found at univariate analysis between VF and TF and other comorbidities including coinfections with cytomegalovirus, viral hepatitis and sexually transmitted diseases (STDs) other than HIV.

Determinants of failure in migrant patients

When considering only migrants, the variables associated with a lower VF risk were male gender (OR 0.58, 95% CI 0.32–1.03, p 0.065) and age (for 10-year increase, OR 0.71, 95% CI 0.49–1.04, p 0.081), along with pre treatment CD4 count (per 100 cells/mm^3 more, OR 0.76, 95% CI 0.60–0.96, p 0.023). Unemployment (OR 3.08, 95% CI 1.48–6.43, p 0.003), intravenous drug use as risk factor for HIV acquisition (OR 2.67, 95% CI 0.94–7.55, p 0.064) and use of a boosted PI–based regimen (OR 2.27, 95% CI 1.09–4.74, p 0.03 vs. NNRTI based) were associated with a higher VF risk. None of these variables, however, remained independently associated with outcome by multivariable analysis. Regarding the patient geographical origin,

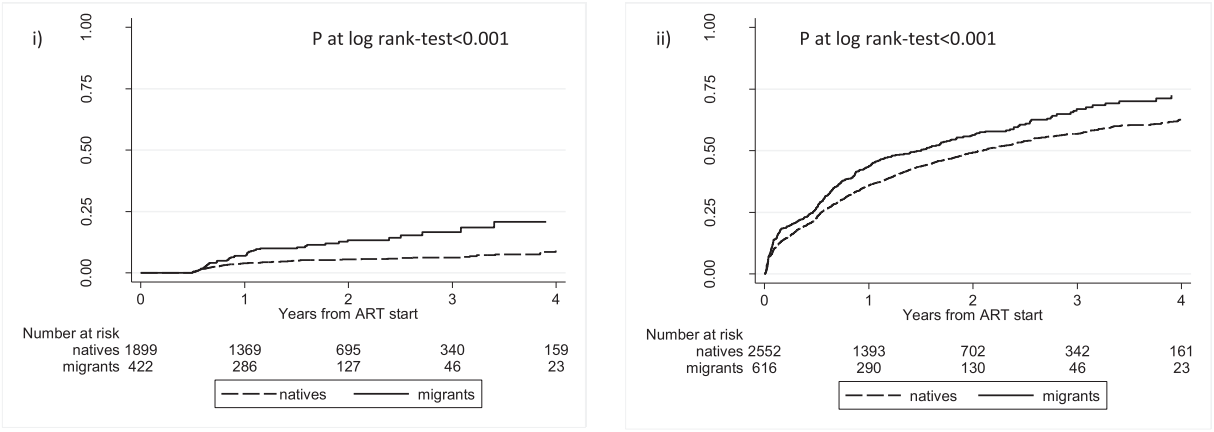

FIG. 1. Kaplan-Meier curves representing cumulative probability of (i) virologic failure (HIV RNA >200 copies/mL) and (ii) treatment failure of first antiretroviral regimen.

TABLE 3. Multivariable Poisson regression models of factors significantly associated with virologic failure (VF) and treatment failure (TF)

	VF				TF			
Characteristic	**ARR**	**95% CI**		**p**	**ARR**	**95% CI**		**p**
Male gender vs. female	0.87	0.54	1.40	0.574	0.80	0.70	0.91	0.001
Migrant vs. native	1.90	1.25	2.91	0.003	1.16	1.01	1.33	0.031
Occupation								
Full-time worker	1.00				1.00			
Unemployed	2.09	1.31	3.32	0.002	1.15	0.99	1.34	0.074
CD4 cells/mm^3 at enrolment								
<200	1.00				1.00			
200–350	0.57	0.37	0.90	0.016	0.83	0.72	0.95	0.008
>350	0.57	0.35	0.93	0.024	0.93	0.81	1.07	0.317
Missing data	0.86	0.35	2.12	0.739	0.93	0.72	1.21	0.597
CDC C stage at enrolment	2.36	1.64	3.39	<0.001	1.14	0.98	1.33	0.084
Tuberculosis before enrolment	—	—	—	—	1.51	1.05	2.15	0.025
Pregnancy status at enrolment	—	—	—	—	2.25	1.57	3.21	0.000
Type of first regimen								
NRTI + NNRTI	1.00				1.00			
NRTI + PI boosted	1.79	1.19	2.69	0.005	1.55	1.39	1.74	0.000
NRTI + II	1.13	0.27	4.74	0.869	0.96	0.63	1.46	0.840
NRTI sparing	2.13	0.82	5.53	0.121	1.44	1.07	1.92	0.015
Other	4.05	1.91	8.59	0.000	3.56	2.92	4.35	0.000

ARR, adjusted risk ratio; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor.

no differences in VF risk were evidenced. Sub-Saharan African migrants presented a higher risk of delaying ART initiation compared to other migrant groups at univariable analysis (OR 1.64, 95% CI 1.18–2.27, p 0.03 vs. NNRTI based); this association, however, was not confirmed by multivariable analysis.

Discussion

The response rate to an initial ART regimen has progressively increased in the last 10 years, approaching 90% with most recent treatment strategies [25]. Despite this high rate of therapy success in randomized clinical trials, in real life, even in developed countries, a certain proportion of patients has been recognized who initiate therapy late and/or have disease that fails to respond to their first ART regimen, thus requiring a targeted approach. In particular, our study demonstrates that migrants still represent a vulnerable subgroup in terms of access to ART and of failure risk, despite the availability in European countries of an universal health care system which assures equal access to highly active ART and health care facilities for all HIV-infected patients and which, in Italy, is also extended to undocumented individuals.

Similar to previous studies, in the present analysis, migrants were diagnosed with HIV infection later compared to natives [1,2,4–7], thereby confirming the need to increase HIV testing in the most vulnerable migrant and ethnic minority populations. This result recalls the debate concerning the necessity to establish a mandatory HIV test when entering Europe, which is not accepted in many countries, including Italy [26], in order to avoid discriminatory practices. In univariate analysis, migrants were found to initiate ART as frequently as natives; however, migrants had lower CD4 cell counts at baseline, and after adjusting for the baseline CD4 level, they showed a lower probability to initiate ART compared to native patients. This finding confirms previous observations [10–27] although it is partially in disagreement with the survey of Jarrin *et al.* [18] regarding a cohort of seroconverted patients in Europe, Canada and Australia (CASCADE) in which no association between geographical origin and ART uptake was found in settings with universal access to healthcare. Differences in the population studied (i.e. seroconverters versus new and prevalent cases) may at least partly explain the disparity between studies. Moreover, Italy is often considered a transit country for undocumented immigrants from across the Mediterranean who generally seek their destination countries later. Therefore, this

high migrant mobility in our country might induce both patients and clinicians to delay initiation of ART in patients with a relatively high CD4 level at presentation.

Migrants experienced ART failure more frequently than natives. This finding was consistent in our analysis independent of the method used to define failure, as higher rates of VF, TD and TF were observed for this patient population. In particular, the risk of VF of >200 copies/mL in migrants was nearly twice that of natives (6.4 vs. 2.7 per 100 person-years). Different rates and predictors of VF according to race and ethnicity have been previously described; however, data regarding response to ART in migrants are controversial in the literature [12–19]. In most studies, similar disease progression and mortality or even better survival has been found for migrants compared to natives, although possible confounders are very difficult to eliminate, such as the health migrant effect (only healthy people embark on a migratory project) and the salmon bias (caused by sick people returning home to die) can lead to erroneous conclusions [28]. A few studies specifically analysed response to therapy, and in particular to the first ART regimen [17,29,30]. Among these, the Spanish study of Pérez Molina *et al.* [17], even if concluding that response to ART among immigrants was similar to that of autochthonous individuals, found a shorter time to TF in the subgroup of Sub-Saharan African and female migrants.

Why migration should determine a higher risk of VF remains unclear. It could be supposed that migrants are less adherent to therapy than natives, even if neither direct measurement of adherence levels was available in this study or evidence of such a difference is proven in the literature. In our study, the reasons underlining failure appeared to be linked more to VF rather than to treatment discontinuation, which was not independently associated with migration by multivariable analysis, thus excluding the notion that different tolerability profiles and side effects might have influenced ART response.

The epidemiology of other concomitant infections and comorbidities was very different in the two groups at baseline but was not associated with VF. Among opportunistic infections, however, tuberculosis was associated with TF with multivariable analysis, as has also been suggested by others [12]; aspects related to drug interactions could play a crucial role in this context. However, the prevalence of other STDs was similar in natives and migrants. In fact, Europe is facing a general epidemic-level increase in all STDs, and public health campaigns would be suitable to address this issue [1].

Other viral characteristics (HIV-1 subtype, tropism, transmitted drug resistance [20,21]) and host genetic factors (HLA B5701 frequency [22]) should also be taken into account; these data, however, were not available for our analysis. Regarding behavioural and socioeconomic issues, younger age and unemployment were found to be associated with VF in the migrant subgroup, thus suggesting that as a result of overwhelming occupational problems HIV care would not be a priority for all migrants. Other sociocultural aspects not directly investigated here (i.e. the role of stigma in some settings or the presence of linguistic barriers) might have determined a lesser willingness to receive treatment or increased risk of failure. Moreover, it should be acknowledged that it is always difficult to group all migrants in an unique category when analysing data (and this also presents a limitation of our study) as a result of the high heterogeneity which characterizes people of different origins.

With respect to treatment strategies, the use of boosted PIs was associated with poorer outcomes. The concept that migrants might require a high-genetic-barrier regimen because of a supposed lack of adherence has probably induced Italian clinicians to prescribe a PI-based regimen more frequently than NNRTIs for migrants compared to natives. Our study suggests a need to promote adherence using a simpler regimen. However, as a consequence of implementing World Health Organization programs regarding introduction of highly active ART in developing countries, based up to now mainly on nevirapine and efavirenz as first-line therapy, the risk of primary resistance to NNRTIs in African patients might increase [21]; this should be evaluated by clinicians before selecting the first regimen.

In conclusion, despite the use of more potent and safer antiretroviral drugs in the last 10 years, and even in a setting of universal access to ART, migrants living with HIV still present barriers to ART initiation and an increased risk of VF compared to natives. Therefore, they require strict and careful management by HIV clinicians.

Transparency Declaration

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Appendix

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