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Long-term survivors in a cohort of HIV+ patients diagnosed between 1985 and 1992: predictive factors associated with more than 25 years of survival

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Introduction

HIV, in the last three decades, has radically changed the history of millions of women and men and has dramatically reduced their expectancy and quality of life. Although generations of patients, diagnosed during the pre-HAART era, has been deprived of any chances to survive, a considerable number of them is still alive.

Some authors classified these subjects in **pre and post HAART long term survivors** to highlight the value that the opportunity of access to care has represented for most of them.

Crucially a considerable number of this patients aged next to the their doctors and they, together, represent the witnesses of one of the more painful, but at the same time, exciting social and scientific period of recent history.

Aim

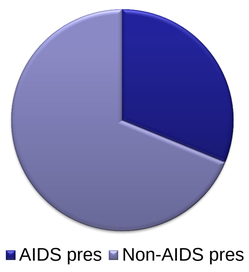
Aim of this study was to evaluate the percentage of HIV long term survivors (LTS) (more than 25 years) in a cohort of **HIV+ subjects diagnosed between 1985 and 1992** in an infectious diseases unit in southern Italy speculating on potential predictive factors associated to a so long survival.

Patients and methods

Single-center retrospective study. Data were collected from clinical files or historical databases. In accord with the protocol were considered epidemiological and clinical data collected at the time of HIV diagnosis. Longitudinal observation was stopped on 31 Dec 2017. Were considered LTS or NLTS all the subjects with more or below than 300 months of survival during the assigned interval time

Globally 186 subjects were enrolled; 148 (79.5%) males, all but one Caucasian, 100 (53.8%) IVDUs, 38 (20.4%) MSMs, 33 (17.7%) heterosexuals. Median age 28 (IQR 24.6-34.5) years, median CD4+ 239 (IQR 56-477) cells/µl; 141 (76%) were late presenters, 58 (31.2%) AIDS presenters, 53% anti HCV+. Epidemiological and clinical data registered at diagnosis are resumed below

Fig 1 and 2 AIDS presentation and HCV co-.infection prevalence at diagnosis



Route of infection	N (%)
IVDUs	**100 (54%)**
MSMs	**38 (20%)**
Heterosex	**33 (18%)**
Multitransf	**11 (6%)**
unknown	**4 (2%)**

Statistical analysis

The comparison between the groups was performed using the chi-square with the Yates correction or the exact Fischer test. For the analysis of quantitative data distributed normally the comparison between two groups was made using the Student's T test. The Mann Whitney U test was used to compare the two groups of undistributed values. The Kaplan-Meier curves were used for survival analyzes. Statistical comparisons were made using the log-rank test and the Holm-Sidak method for multiple comparison. Identified variables in the univariate analysis with a p value <0.05 were included in the logistic regression model

Results

Ten (5.4%) untraceable subjects were considered lost to the follow up and excluded from survival analysis. Finally data related to 176 subjects were analyzed. 72 subjects of them (38.7%) were LTS (fig 3); all but 2 alive at the end of follow up. Data on median survival are shown in the table below

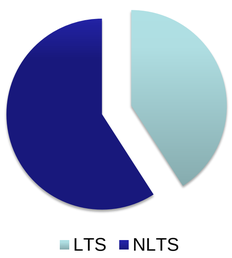


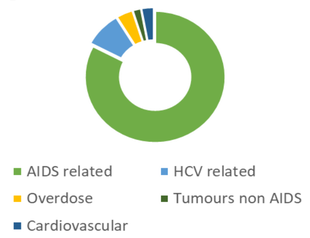
Fig 3 long term survival prevalence

	LTS	NLTS
Survival (months)	350 (318-378)	37 (14-121)

104 (55.9%) subjects died before 25 years (NLTS) with a median survival of 37 (14-121) months

Globally during the follow up 102 (54.8%) subjects were diagnosed with an AIDS defining illness (ADI). 101 (57.4%) were treated with any antiretroviral treatment, all but 4 (55.1%) with any HAART regimen. The main cause of dead (81.1%) was an HIV associated event. All the causes of death are reported in the picture below (fig 4)

Fig 4. causes of death



	LTS	NLTS	p-value
Age at diagnosis	26 (22-29)	29 (26-36)	<0,00001

	LTS	NLTS	p-value
AIDS presenter	1 (1%)	57 (55%)	<0,00001
AIDS	16 (22%)	86 (83%)	<0,00001

At univariate analysis to be LTS vs NLTS was associated with some of the conditions registered at the time of diagnosis: female sex (29.1% vs 14.4%, p=0.022), median younger age [26 (22-29) vs 29 (26-36) p<0,0001], HCV coinfection (65,5% vs 44% p < 0,01), AIDS presentation (1,4% vs 98.6% p < 0,0001). while 22,2% vs 82.7% developed an ADI.

	LTS	NLTS	p-value
CD4/µl	397 (235-613)	78 (31-280)	<0.00001

CD4 at diagnosis	Survival (media±sd)		p-value
<200	100 (±16)	<200 vs 200-500	<0,00001
200-500	294 (±17)	<200 vs >500	<0,00001
>500	324 (±31)	200-500 vs >500	0,183

Fig 5. CD4 at diagnosis and probability of survival (Kaplan Meyer analysis)

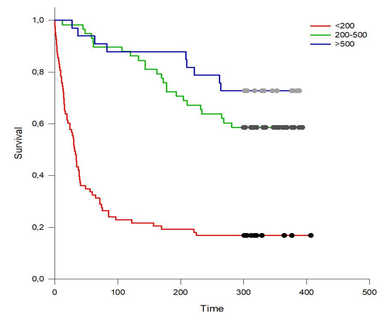
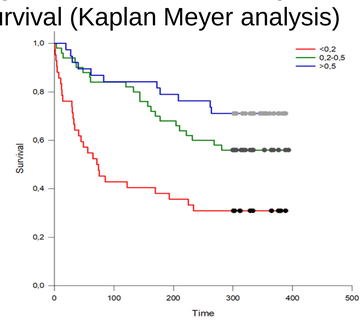


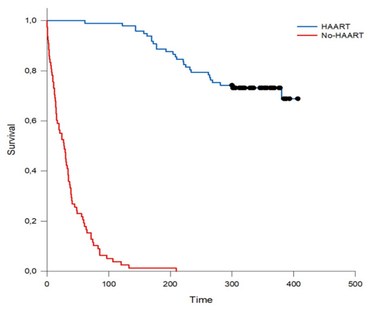
Fig 6 CD4/CD8 ratio at diagnosis and probability of survival (Kaplan Meyer analysis)



Also immunological data registered at diagnosis, specifically median CD4 cell number [397 (236-613) vs 78 (31-280) p<0,0001] and CD4/CD8 ratio [0,4 (0,27-0,73) vs 0,24 (0,06-0,41) p=0,024] were associated at LTS condition.

Finally during the follow up respectively 75% and 100% of LTS were exposed to suboptimal ARV treatment or HAART vs 45% and 24% of NLTS (p<0,0001)

Fig 7.HAART treatment and survival probability (Kaplan Meyer analysis)



Median survival for HAART exposed subjects was 351 (±10) months vs 35 (±4) months for unexposed (Log-Rank p<0,00001).
At multivariate analysis younger age, lack of ADI during the follow up and to be treated with HAART remain significally associated with the conditon of long term survivor

Multivariate analysis of factors associated to LTS

	OR (IC 95%)	p-value	OR correct (IC 95%)	p-value
M/F	0,37 (0,17-0,80)	0,0224	0,297 (0,066-1,329)	0,1122
age		<0,00001	1,146 (1,047-1,255)	**0,0031**
CD4 cell count		<0,00001	1 (0,998-1,003)	0,7307
Anti HCV+	0,42 (0,22-0,79)	0,0088	6,063 (1,218-30,18)	**0,0277**
AIDS presentation	86,5 (11,6-65,5)	<0,00001	2,573 (0,15-44,232)	0,5148
ADI	21,4 (9,5-48,1)	<0,00001	8,273 (2,56-26,733)	**0,0004**
TARV	0,28 (0,14-0,53)	<0,0001	1,038 (0,229-4,705)	0,9615
HAART	0,005 (0,0006-0,06)	<0,00001	0,002 (0,000134-0,045)	**<0,00001**

Conclusions

Surprisingly more than one third of patient of our cohort survived more than 25 years from diagnosis with a median of 350 months. At univariate analysis conditions traditionally associated with late presentation as male sex, older age, low CD4 and AIDS presentation were associated to bad prognosis, but, in accord with multivariate analysis, only young age and lacking of clinical progression towards AIDS could be considered the main favorable condition driving to ARV treatment that has to be considered the stronger predictor and the main actor of the so long term survival.

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