SURVIVAL AND DISEASE PROGRESSION IN ART-NAÏVE LTNP WITH UNDETECTABLE HIV-REPLICATION

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BACKGROUND

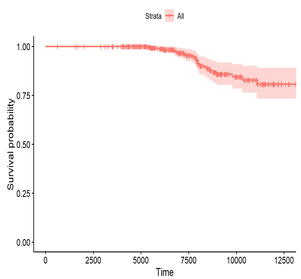
A multicenter, prospective study in retrospect including clinical and epidemiological data collected from 313 long-term non progressors (LTNP), in 21 hospitals, was carried out.

METHODS

Patients: LTNP were ART-naïve HIV-positive individuals who maintained CD4+ T cell counts over 500 cells/µl for at least 10 years. In addition, elite controllers LTNP (EC-LTNP) were able to maintain undetectable levels of viral replication, while viremic LTNP (vLTNP) have detectable but under 10,000 copies/mL viral loads.

Statistics: A Kaplan-Meier method and multivariate Cox proportional hazards regression model were used to estimate the probability of survival and progression-free survival for the individuals included in the cohort.

A



B

Time	Survival probability	95% Confidence interval
5 years	100%	100%-100%
10 years	100%	100%-100%
15 years	99.6%	98.8%-100%
20 years	96.1%	93.4%-98.8%
25 years	85.8%	80.2%-91.6%
30 years	82.8%	76.3%-79.9%

C

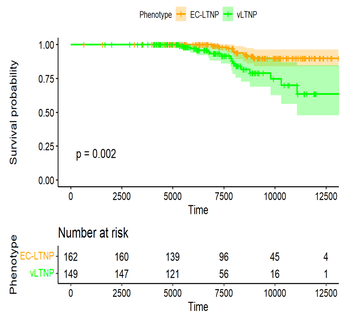


Figure 1. Probability to survive in LTNP-RIS cohort and hazard ratios. Kaplan-Meier estimates for the entire cohort (A) and associated survival probabilities (B). Kaplan-Meier estimates comparing EC-LTNP and vLTNP populations.(C). Time is expressed in Kaplan-Meir curves as days from HIV+ diagnosis.

- EC-LTNP showed lower CD4+ T cell count loss, higher CD4/CD8 ratios, and lesser increases in viral load, compared with other LTNPs with detectable viral replication.

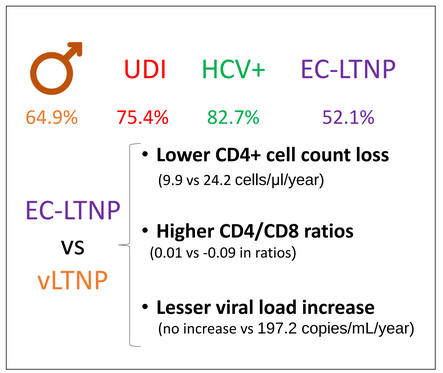
- EC-LTNP exhibited lower hazard of exitus and higher probabilities to preserve LTNP status with time.

- EC-LTNP represent one of the most favorable phenotypes of immune activation against HIV-1 found in nature.

- EC-LTNP are strong candidates to be considered as a model of functional cure of HIV-1 infection.

RESULTS

Survival probabilities for all-cause mortality at 30 years from HIV+ diagnosis were 0.90 for EC-LTNP and 0.70 for vLTNP ($p=1.9x10^{-3}$). The hazard of exitus was associated with the initial vLTNP phenotype, whereas EC-LTNP was related to improved survival (HR=0.28; 95% CI: 0.12-0.65; p=0.02) (Figure 1).



A total of 172 (55.0%) and 42 (13.4%) out of the 313 participants maintained LTNP status for at least 20 and 30 years, respectively. The probability to preserve LTNP status at 20 years was 0.88 for EC-LTNP and 0.57 for vLTNP, whereas at 30 years, these probabilities dropped to 0.51 for EC-LTNP and 0.18 for vLTNP ($p<10^{-15}$).

Risk factors associated to the loss of LTNP status were: higher age at diagnosis and the increase of viral load, whereas the increase of CD4+ T cell counts and CD4/CD8 ratio, the EC-LTNP phenotype, and HCV coinfection, were considered protective factors (Figure 2).

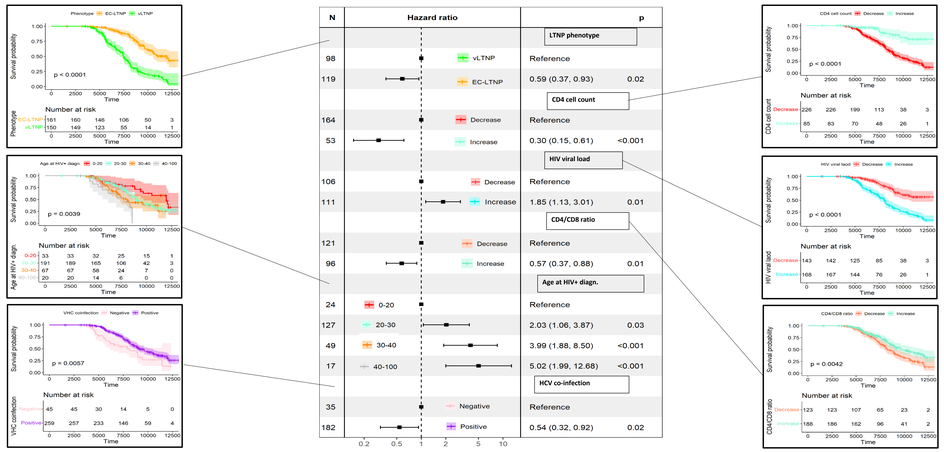


Figure 2. Probability of retaining LTNP phenotype in the LTNP-RIS cohort participants and hazard ratios of significant variables. Kaplan-Meier estimates of the probability of retaining LTNP phenotype of the statistically significant covariates in univariate analyses (LTNP phenotype, age at HIV+ diagnosis, HCV coinfection and variations in CD4 cell count, HIV viral load and CD4/CD8 ratio). Determinants associated with loss of LTNP phenotype in a multivariate Cox proportional hazards model are showed in the middle. Time is expressed in days from HIV+ diagnosis.

CONCLUSIONS

We have identified epidemiological and clinical characteristics differentiating EC-LTNP status from other LTNP with detectable viral load, denoting an even better survival and slower disease progression in EC-LTNP. These individuals represent one of the most favorable phenotypes of immune activation against the virus found in nature and, are strong candidates to be considered as a model of functional cure of HIV-1 infection.

Acknowledgments

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