Viral load (VL) was found to be associated with a worse prognosis in a previous multi-cohort study [1] on HIV-infected subjects who started antiretroviral triple therapy (ART) before 1998 [the median calendar month of ART start was December 1997 (IQR: June 1997 – July 1998)]. In a population-based analysis [2], pre-ART HIV RNA >100,000 copies/mL showed a markedly significant risk of death. Thus, the aim of this study was to evaluate whether, in recent years, pre-ART VL is still predictive of all-cause mortality, AIDS- or non-AIDS-related mortality, in a large population of HIV-infected treatment-naïve patients who started ART.

METHODS
We included HIV-infected treatment-naïve patients, from San Raffaele Fate and ICONA Cohort, who started ART (≥3 drugs) ≥1998 and with available pre-ART VL and CD4+ cell count [the nearest values before ART start].

Pre-ART VL values (cross-sectional, single time-point) were categorized as ≤100, ≥100-500, ≥500-1000, >1000 copies/mL.
Kaplan-Meier curves and Cox regression analyses were used to evaluate the association between pre-ART VL and the risk of all-cause, AIDS- or non-AIDS-related mortality.

RESULTS
Overall, 11877 patients included: 7313, 3334, 652, 578 patients with pre-ART VL ≤100, >100-500, >500-1000, >1000 copies/mL, respectively.
The median (IQR) calendar year of ART initiation was 2011 (2005-2014); other patients’ characteristics are shown in Table 1. Among a median follow-up of 3.8 years (IQR: 1.6-7.2) after ART start, a total of 494 patients died, including 171 AIDS-related deaths (35%), 272 non-AIDS-related deaths (55%) and 51 of unknown cause (10%). Incidence rates of death according to pre-ART VL are shown in Table 2.
Pre-ART VL predicted all-cause, AIDS- or non-AIDS-related mortality in a single-factor analysis (Figure 1, Figure 2) and remained strongly predictive of all-cause mortality after adjusting for the other factors (Table 3); people with pre-ART VL in the >500-1000 range >1000 range had adjusted HRs (AHR) of 1.48, and 2.23, respectively, relative to those with ≤100.
Separating out causes of death, the associations with AIDS-related mortality were confirmed in the >500-1000 range (AHR=1.98) and in the >1000 range (AHR=2.16); pre-ART VL was also associated with non-AIDS-related mortality; a significant higher risk was evident for subjects with a pre-ART VL (≥2.60).

CONCLUSIONS
In recent years, pre-ART VL predicted all-cause and AIDS-related mortality. The decision of whether to prioritize patients at risk for ascending pre-ART VL ranges and was more than double for subjects with pre-ART VL=1000 as compared to those with pre-ART VL<1000. The effect of pre-ART VL on the risk of non-AIDS-related death seems to be less potent and needs further investigations. These findings suggest that viral-induced damage does not completely regress even with modern antiretroviral therapies; therefore, patients with high pre-ART VL may have a worse prognosis regardless the efficacy of ART.

REFERENCES