An exploratory analysis to assess the potential effect of ART in modifying the Framingham risk score in HIV-infected patients enrolled in the Icona Foundation Study

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Background: The aim of this analysis was to quantify the potential effect of ART and other HIV-related factors in modifying the Framingham risk score (FRS) in HIV-positive patients living in Italy.

Methods: Baseline for the analysis was defined as the date of enrolment (for person years of follow-up (PYFU) while patients were still off-ART) and the date of starting ART (for the PYFU post-ART). We studied patients for whom data on smoking, blood pressure (BP), cholesterol (total, HDL) was available at baseline and their gender-specific FRS was calculated at each subsequent clinical visit. The progression to a FRS ≥5% was analysed using KM curves and Cox regression; PYFU pre-ART were censored at the time of initiation of ART. Predictors studied included the FS has been found to be consistent with that of the observed data although the model lacked calibration. The lack of calibration means that in HIV-infected population the risk of CVD for a given set of parameters in a fitted proportional hazards Cox regression model is shown in the Table.

Results: Of a total of 903 patients eligible for this analysis, 492 (54%) were excluded because they had a FRS of 1-4% at baseline. Of the 411 included, 151 contributed PYFU pre-ART (49% female, 30% smokers) and 260 post-ART (60% female, 30% smokers), none of the patients contributed to both. Median baseline parameters at enrolment and at ART initiation were: 31 vs. 34 years of age, 152 vs. 154 mg/dl of total cholesterol, 120 vs. 120 mmHg of BP, 48 vs. 45 mg/dl of HDL, 568 vs. 289 CD4 cells/µl and 4.17 vs. 4.32 VL log copies/mL. Overall, 40 patients experienced a FRS ≥5% over a median of 0.7 PYFU pre-ART and 2.9 PYFU post-ART. By 3 years from baseline FRS increased to a value ≥5% in 9% (95% CI:1-17) of patients over PYFU in which they were ART-naive and in 12% (95% CI:8-16) over PYFU in which they were ART-exposed (log-rank test p=0.62). Crude and adjusted relative hazards of a FRS ≥5% from fitting a proportional hazards Cox regression model are shown in the Table.

Conclusions: There was little evidence supporting that ART is implicated in a dramatic modification of parameters currently included in the FRS, although the power of our analysis was low. Besides the FRS parameters, a lower baseline CD4 count was the only factor associated with a higher risk of experiencing a FRS ≥5%.

Comment: It is well known that the Framingham risk equation or Framingham score (FS) may under- or over-estimate the absolute risk of cardiovascular disease (CVD) in populations other than that used to derive this particular equation. When the FS was applied to the data of a large collaborative observational cohort study including HIV-infected patients enrolled throughout Europe, USA and Australia (the D.A.D. collaboration) the ordering of individuals' risks according to the FS has been found to be consistent with that of the observed data although the model lacked calibration. The lack of calibration may be due to the fact that in HIV-infected population the risk of CVD for a given set of parameters in the FS is exacerbated by HIV itself, drug toxicities which act via a mechanism different from the worsening of lipid profiles or a combination of these factors. This analysis represents an attempt to investigate whether patients’ FS is
likely to be modified by the use of ART in HIV-infected patients rather than by HIV-infection alone (i.e. in the absence of treatment). Because patients in Icona are enrolled when they are ART-naïve and subsequently followed to study their response to ART, the cohort represents an ideal setting where to address this question. The results of the analysis are consistent with the view that antiretroviral treatment does not seem to worsen the pattern of FS modification over time over and above what is caused by HIV alone and that therefore, if there is an effect of ART on the risk of cardiovascular disease, it seems to act via altering parameters that are currently not included in the FS. Indeed, it has been hypothesised that inflammatory mechanisms induced by HIV and/or ART may explain the excess of risk seen in HIV-positive treated patients.