The risk and determinants of malignancies in HIV-infected patients enrolled in the Icona Foundation Study

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Introduction
It has been shown that the risk of death from non-AIDS defining severe events is higher in people with lower CD4 counts, even when the CD4 count is greater than 350 cells/cmm. There is less evidence that this is true for severe events non leading to death. We aimed to estimate the incidence of both AIDS (ADM) and non-AIDS defining (NADM) malignancies and to identify their predictors.

Methods
We studied patients of the Icona Foundation Study, with at least 1 CD4 count measurement, followed from enrolment to the minimum time between the last follow up date and the date of occurrence of a malignancy. Malignancies were divided into ADM and NADM, using the CDC93 definition and excluding in-situ cervicae carcinoma. Incidence rates of ADM and NADM were estimated as numbers of non-recurring malignancies per 1,000 person years follow up (PYFU) overall and by current CD4 strata (in a cause specific analysis). Multivariable Cox proportional hazard models were used to identify predictors of ADM/NADM malignancies in separate analyses. All covariates were fit as time fixed, using the value at enrolment, with the exception of current CD4 count, HIV-RNA load, and initiation of antiretroviral treatment (ART).

Results
6691 patients were included in the study (71% male, 94% of European or North Americans, 37 years old on average, 41% HCV Ab positive, 7% HBV co-infected, 56% smokers, 40% alcohol users, 36% intravenous drug users, 1.1% with malignancies before enrolment). Overall, we observed 169/33517 ADM, corresponding to an incidence rate of 5.0 per 1000 PYFU (95% CI: 4.3-5.8). For NADM, we observed 83/33517 events, corresponding to an incidence rate of 2.5/1000 (95% CI: 2.0-3.1). Incidence rates of ADM were 2.2/1,000 (95% CI: 1.3-3.5) in patients with a current CD4 of 350-500 cells/cmm and 2.0/1,000 in those with a CD4>500 cells/cmm (95% CI: 1.4-2.8) (p=0.96), whilst for NADM the corresponding rates were 2.5/1,000 (95% CI: 1.6-3.9) and 1.5/1000 (95% CI: 1.1-2.2) (p=0.081). Adjusted relative hazards of ADM and NADM fitted from the Cox models are shown in Figure 1 (only RH for variables associated at 0.05 level with the risk of malignancies are shown). Models were adjusted also for HIV-RNA log10 cp/ml, nationality, sex, HCVAb positivity, HBV co-infection, smoking status, malignancies at anamnesis, and year of enrolment.

Figure 1:
Conclusions

The incidence of NADM in our study population was relatively low compared to that of ADM. There was a tendency for the risk of both ADM and NADM to continue to increase even at CD4 count >350 cells/cmm, though not significant when comparing to CD4 count >500. Apart from the higher risk of both ADM and NADM produced by lower CD4 counts and age, there was a clearer increased risk of ADM for homosexual/bisexual mode of HIV transmission group, presumably due to the correlation with Kaposi’s Sarcoma.