Beneficial effect of NNRTI over boosted PI first line cART on CD4 T-cell restoration in older HIV-1 patients

Background: More than 10% of people living with HIV (PLHIV) worldwide are over the age of 50 according to the most recent UNAIDS figures and this percentage is increasing. This, amongst other factors, is due to the success of combination antiretroviral therapy (cART) as well as older people becoming infected with HIV-1. However little is known about the impact of various regimens on immune reconstitution including CD4 T-cell restoration in these patients. We aimed to investigate the effect of NNRTI versus boosted PI first line cART on lymphocyte subset changes in ageing HIV-1-infected subjects.

Methods: HIV-1+ patients managed from 1996-2011, whose first line therapy consisted of either 2NRTI+NNRTI or 2NRTI+boosted PI, were studied to assess the effect of cART regimen and age on lymphocyte restoration. A linear mixed model was generated using MIXED procedure in SAS to derive point estimates by fitting lymphocyte subsets as a dependent variable by age grouped into decades and stratified by first line cART. The differences between restoration slopes for lymphocyte subsets, for both cART regimens, were investigated for PLHIV aged 40 years and older.

Results: 79% of 4,346 HIV-1+ PLHIV started on 2NRTI+NNRTI and the remainder on 2NRTI+boosted PI; 87% were men, 73% Caucasians, and 80% MSM. Since the age of 40, we observed significantly better restoration slopes for NNRTI regimens compared with PI boosted regimens for CD4 T-cell counts (p<0.001), CD4 T-cell percentage (p=0.005) and CD56 NK-cell counts (p=0.005); no differences were observed for CD8 T cells. Significantly better CD4:CD8 T-cell ratios (p=0.049) were observed for PLHIV whose first line cART included NNRTI, although they were consistently below normal values. Moreover, there were no significant differences in plasma HIV-1 RNA levels from the age of 40 years between these two first line treatments (p=0.484).

Conclusion: In our cohort, first line cART that included NNRTI was associated with higher CD4 T-cell count restoration and improved CD4:CD8 T-cell ratios; in addition to the importance of timely initiation of cART, the choice of regimen is also crucial particularly for the ageing PLHIV. Persistence of overall low CD4:CD8 T-cell ratio may be indicative of accelerated immunological ageing and immune senescence. Further studies investigating differences in T-cell activation/exhaustion and viral reservoirs between these two first line cART groups in the context of ageing are warranted.