BACKGROUND

A low CD4/CD8 ratio during antiretroviral therapy (ART) identifies subjects with heightened immunovirological and immunosenescence, and have been shown to predict morbidity and mortality (Serrano-Villar, PLoS Patho 2014).

It is unknown whether the different first-line ART regimens have different impact on the rates of CD4/CD8 ratio normalization.

We aimed to assess the effects of the INSTI, PI or NNRTI-based first-line ART on long-term CD4/CD8 ratio recovery in a large prospective cohort.

METHODS

Prospective cohort study in 13,026 HIV-infected individuals registered in the Spanish HIV Research Network (CoRIS) cohort.

We included subjects who started triple ART and achieved HIV RNA suppression at 48 weeks.

We used multilevel mixed models with linear splines to compare longitudinal changes in the CD4/CD8 ratio and Cox proportional-hazard models to compare the times to CD4/CD8 normalization by treatment groups (NNRTI, PI, INSTI) at 0.5, 1 and 1.5 cut-offs.

Analyses were adjusted for sex, country of origin, mode of transmission, calendar year, educational level, baseline HIV RNA, presence of AIDS, pre-ART nadir CD4, acme CD8 cell count and backbone NRTI.

RESULTS

A total of 6,804 individuals contributing to 37,149 persons/years and 37,680 observations met the inclusion criteria. The median follow-up was 49 months (IQR 22-89).

The study sample was representative of a medium-aged population (median age 36 [IQR 30-44] years) with higher representation of men (85.3%), median nadir CD4+ T-cell count of 304 (IQR 178-438) cells/µL, and median baseline CD4/CD8 ratio 0.33 (IQR 0.19-0.52).

The median time from ART initiation to virologic suppression was 18 (IQR 10-29) months, and first-line regimens included 2,820 subjects starting ART with 2 NRTI+NNRTI (41.5%), 1,574 (23.1%) with 2 NRTI+PI and 2,410 (35.4%) with 2 NRTI+INSTI.

Sub-analyses by piecewise indicated that these differences were driven by changes during the first year of ART (Table 1) without significant differences in the adjusted CD4/CD8 ratio trajectories after the second year of ART. Hence, a stronger effect of INSTI during the first year of ART determined greater difference in CD4/CD8 ratio values after a similar follow-up.

Table 1 shows the incidence rates of ratio normalization by treatment group for each cut-off point. Table 3 shows the incidence rates of ratio normalization by treatment group for each cut-off point.

Subanalyses adjusted for backbone NRTIs did not show differences in the rates of CD4/CD8 ratio normalization between raltegravir, dolutegravir and elvitegravir (Table 4).

Table 2 shows the Kaplan-Meier failure estimates for CD4/CD8 ratio normalization at cut-off ≥1.5 compared to INSTI (Table 2).

CONCLUSIONS

This study with prospective design, large sample size, and long follow-up shows that first line ART is associated with a greater CD4/CD8 ratio gain compared to NNRTI and PI-based ART.

Our findings were independent of the immunovirological covariates analyzed (i.e., CD4 nadir, maximum HIV RNA, and development of virological failure during ART).

This study in real life indicates that ART initiation with INSTI improves immune recovery with respect to other ART classes, which could affect long-term mortality.

Subanalyses adjusted for backbone NRTIs did not show differences in the rates of CD4/CD8 ratio normalization between raltegravir, dolutegravir and elvitegravir (Table 4).