Background

- In order to reduce toxicity and improve adherence for long term efficacy, different antiretroviral (ARV) approaches are currently available in clinical practice.
- Generally, different switching strategies are involved as reducing pill burden up one pill fixed dose combination (single table regimen – STR) or drug burden, in order to reduce regimen toxicity, up to regimens with only two or one drug (less drug regimen, LDR).

Objectives

- The present analysis aims to consider the differences in effectiveness and safety of the two approaches in patients who simplified with suppressed HIV-RNA.

Methods

- From the Italian Icona Cohort, patients who after January 2008 switched to STR or LDR from any triple drug regimen, including two NRTI plus PI or NNCRTI or INI with undetectable HIV-RNA were selected.
- STR included TDF/FTC plus EFV, RPV or EVG fixed dose combinations;
- LDR included dual regimens composed by boosted PI (LPV/r, ATV/r DRV/r) plus any 3TC/FTC, MAR, RAL or ETV, and P/R monotherapy.
- End-point of the analysis was the discontinuation of the regimen and/or the risk of toxicity.
- Poisson regression was used to evaluate statistical associations with the outcome.

Results

- Overall, 842 patients (525 STR, 317 LDR) were included: STR included TDF/FTC/EVF (36.8%), TDF/FTC/RPV (48.4%) and EVG/COB/TDF/FTC (14.9%). LDR included dual regimens: LPV/r, ATV/r, DRV/r plus 3TC/FTC (29.7%), or any MCV, RAL, ETV (15.7%) and P/R monotherapy (54.6%).
- Patients switching to STR more frequently were receiving NNRTI, were on first regimen, had higher hemoglobin, transaminase, and MDRD levels at switching compared to LDR. In contrast, patients switching to LDR were more often on P/R or changed to toxicity, were on older, had longer history of HIV infection, had high number of previous regimens, higher triglycerides and creatinine levels (Table 1).
- Overall, 240 patients (107 STR, 133 LDR) discontinued treatment between 1525 PYFU. The crude IR of DAC was 10.8 ± 100 PYFU (95%CI: 8.9-13.0) in STR and 24.9 (95%CI: 21.0-29.6) in LDR (p<0.001). Among causes of discontinuation, toxicity, as reported by the treating physician, was significantly higher in STR patients (57.0% vs. 28.6%, p<0.001).
- By multivariable Poisson regression [table 2], HCV co-infection, higher creatinine and switching from PI or INI were associated with higher risk of DAC, longer duration of HIV, being at second regimen vs first, STR switch for simplification, as reported by treating physician were found associated with lower risk.
- Switching to STR associated with about a 50% reduction of DAC as compared to switch to LDR. Within STR group, the risk of DAC did not differ among the three STR; while, within LDR group, probability of DAC was higher in mono than dual regimens (IRR: 1.89; 95%CI: 1.33-2.69) with no difference between 3TC/PI or between dual regimens.

Conclusions

- Reducing pill burden (STR) and reducing drug burden (LDR) are strategies that recognize different clinical reasons and settings.
- Switching to STR was associated to greater stability of the regimen and consequently lower treatment discontinuation.
- LDR can be useful in limited settings in order to reduce toxicity. P/R monotherapy predicted higher rates of discontinuation.