A total of 2,249 persons in Icona Foundation Cohort were enrolled: 985 started 2NRTI+ATV/r, 1023 2NRTI+DRV/r and 241 2NRTI+RAL when ART-naive were included.

Primary endpoint: treatment failure (TF) defined by the composite endpoint of virological failure (VF) (confirmed HIV-RNA >200 copies/mL after 6 months of therapy) or discontinuation of the regimen for any cause

Secondary endpoints:
- confirmed HIV-RNA>50 copies/mL after 6 months of therapy (VF50)
- discontinuation of DRV/r or ATV/r or RAL for any reasons
- discontinuation of DRV/r or ATV/r or RAL because of intolerance/toxicity

Methods

For the comparison of characteristics at time of treatment initiation among the three groups, Chi-square or Kruskal-Wallis tests were used as appropriate.

Survival analysis with Kaplan-Meier curves and Cox regression model with time fixed covariates at TF initiation stratified by clinical site was used. Participants' follow-up accrued from the date of TF initiation to the date of event or to the date of last available visit/viral load.

Results

Over a median follow-up of 2.9 years (IQR: 1.5-4.3), the 2-year probability of treatment failure was 45.9% (95%CI: 42.7-49.2) for persons receiving TFV/r, 43.7% (95%CI: 40.4-47.0) for persons receiving DRV/r and 49.6% (95%CI: 41.3-58.4) for those receiving RAL (p=0.089).

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Figure 1: Kaplan Meier estimates of reaching the different end-points stratified by third drug

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Figure 2: Distribution of reasons for discontinuation stratified by third drug

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Table 2. Causes of discontinuation for toxicity

After controlling for a number of confounders (footnote of Table 3) subjects treated with TFV/r showed a higher rate of treatment failure and of risk of discontinuation (for any reasons and due to toxicity) than the DRV/r group. In contrast, still compared to TFV/r, patients who started a RAL-based regimen showed a lower rate of discontinuation due to toxicity and a lower rate of virological failure (VF50) (Table 3).

Table 3. Relative hazards from fitting 4 separate Cox regression models

Our data were somewhat different from those observed in the ACTG2537 randomized comparison: - when the composite endpoint treatment failure was considered, TFV/r-based regimens showed a 19% higher risk than DRV/r
- when considering virological failure, with a threshold of 50 copies/mL, data are suggesting a lower rate of virological failure for RAL than DRV/r.

In contrast, regarding the discontinuation end-point, our results seem to be consistent with those of the ACTG 2527, indicating a higher propensity to discontinue TFV/r for reasons due to toxicity vs. DRV/r group.

We found also a lower rate of discontinuation for toxicity in RAL-based regimens compared to DRV/r. TFV/r showed also a higher risk of discontinuation regardless the reason as compared to DRV/r.

The comparison between analyses conducted in the observational settings and those coming from RCT is always a difficult one to do and we cannot rule out possible bias due to unmeasured confoundings or other introduced by the subjective nature of the data reported (e.g. the reason for stopping a drug).

Conclusions

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