BACKGROUND

- F/TAF showed a comparable efficacy to that of F/tenofovir disoproxil fumarate (TDF) with a better kidney and bone safety.
- Single-tablet regimens (STRs) may improve clinical outcomes and retention in care compared with once-daily multiple-tablet regimens (MTRs) in ART-naive and experienced patients.
- An increase in both LDL and HDL (but no change in the ratio) was seen after a switch to F/TAF in clinical trials and observational studies.

AIMS

- To provide estimates of the risk discontinuation of F/TAF by up to 3 years of use in the clinics.
- To evaluate whether the use of different F/TAF formulations (MTRs vs. STR) was associated with the risk of TAF discontinuation in ART-naive and experienced patients.
- To evaluate the association between current dyslipidemia and the risk of F/TAF discontination in ART-experienced patients.

METHODS

Study Design: retrospective, observational, multicentric study

Study population: All HBSAg negative patients included in the Icona Foundation Study cohort who started F/TAF-based triple regimens for the first time over January 2015-July 2020 (ART-naive and ART-experienced with HIV RNA ≤50 copies/mL).

Definition of dyslipidemia: fasting total cholesterol ≥200 mg/dL, LDL ≥100 mg/dL, HDL <40 mg/dL for females or <50 mg/dL for males, triglycerides ≥150 mg/dL.

Outcome: TAF discontinuation, stops of TAF independent of the remaining antiretrovirals.

Statistical Analysis: Cumulative probability of TAF discontinuation for any cause was estimated by Kaplan-Meier curves and (unweighted) and weighted Cox regression models were used to estimate the effect of the exposures of interest on the risk of F/TAF discontinuation, separately in ART-naive and experienced. Multivariable models were constructed by including all potential confounders for the exposures of interest, under our assumptions regarding the causal structure of the data (see example in Figure 1).

RESULTS

Main characteristics of the study population are shown in Table 1. The main baseline characteristics were F/TAF-DTG (36%) in ART-naive and F/TAF-RPV (39%) ART-experienced patients.

Figure 1 - ART-naive patients

Exposure: F/TAF used in MTR
Outcome: Discontinuation of F/TAF regardless of the reason
Minimal sufficient adjustment sets to estimate the total effect of exposure on outcome: AIDS diagnosis, age, calendar year of starting F/TAF, HIV RNA at F/TAF initiation, HIV control

Table 1 – Main characteristics of 4,703 patients who started F/TAF according to ART history

Table 2 – Hazard Ratios of F/TAF discontinuation from fitting a cox regression model

Unadjusted and adjusted marginal relative hazards of discontinuation for TAF

Table 3 – KM estimates of the risk of F/TAF discontinuation for any causes in ART-naive (left panel) and ART experienced patients (right panel).

Figure 2 - Coformulation at baseline in a) ART-naive, b) ART-ex groups

In ART-naive the 3-year risk of discontinuing F/TAF was 20.2% (95% CI 16.3, 24.1) for any causes (Figure 3a); this estimate, after the exclusion of switches to ABC/3TC/DTG, was 13% by 2 years (95% CI 9.1-16.3), if an early switch was defined as early as soon as HIV RNA ≤50 copies/mL. In the ART-ex, the 2.5-year risk was estimated at 8.3 (7.2, 9.5). (Figure 3b)

In a multivariable regression model, in the ART-naive, using F/TAF as MTR was associated with an increased risk of F/TAF discontinuation [AHR=2.85 (1.92, 4.23, p<0.001)]. In the ART-ex, the risk of discontinuation was higher for patients who discontinued dyslipidemia [AHR=2.46 (1.53, 305, 424) (95% CI p<0.001) (Table 2)].

LIMITATIONS

Observational setting: unmeasured and residual confounding bias; estimates rely on models correct specification.

- In the ICONA cohort, approximately 20% of ART-naive patients and 8% of those starting TAF-based regimens with HIV-RNA≤50 copies/mL in the real-life setting discontinue this drug by 2.5 years, regardless of the reason.
- A low pill burden is a key factor for achieving longer durability of modern F/TAF-based cART.
- In our cohort of ART-experienced population, onset of dyslipidemia under treatment was associated with an increased risk of discontinuation of F/TAF.

References