P056

Durability of F/TAF-based regimens in a large cohort of PLWH seen for care in Italy

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BACKGROUND

- F/TAF showed a a comparable efficacy to that of F/tenofovir disoproxil fumarate (TDF) with a better kidney and bone safety [1,2]
- 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[3,4]
- 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[5]

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 discontinuation 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 antiretroviral drugs.

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 exprienced. 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 regimen at baseline were F/TAF+DTG (36%) in ART-naive and F/TAF/RPV (39%) ART-exp patients.

Figure 1. ART-naive patients

Exposure: F/TAF used in MTRs

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, HCV coinfection

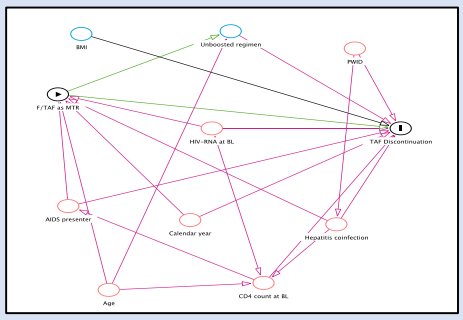
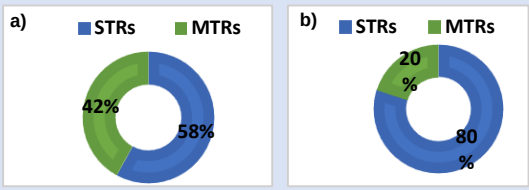


Table 1 – Main characteristics of 4,703 patients who started F/TAF according to ART history

	ART history	
Characteristics	**ART-naive**	**ART-exp**
	N= 1194	N= 3509
Gender, n(%)		
Female	194 (16)	679 (19)
Age, years		
Median (IQR)	40 (31, 50)	45 (37, 53)
Mode of HIV Transmission, n(%)		
IDU	60 (5)	314 (9)
Unprotected sexual intercourses	1073 (90)	3003 (85)
AIDS diagnosis, n(%)	109 (9)	427 (12)
HCVAb +, n (%)	43 (4)	402 (11)
CD4 count, cells/mmc		
Median (IQR)	335 (125, 544)	687 (507, 898)
Viral load, log_{10} copies/mL		
Median (IQR)	4.8 (4.3, 5.5)	0.0 (0.0, 1.5)
Dyslipidenmia, n(%)	403 (25)	3330 (75)
Use of statins, n(%)	17 (1.4)	387 (11.0)

Distribution of the type of coformulation at baseline are shown in figure 2 a,b.

Figure 2 - Coformulation at baseline in a) ART-naïve, b) ART-exp groups



In ART-naïve, the 3-year risk of discontinuing F/TAF was 20.2% (95%CI 16.3, 24.1) for any causes (Figure 3 a); this estimate, after the exclusion of switches to ABC/3TC/DTG, was 13% by 2 years (95% CI 9.1-16.3), if speculating that an early switch occured as soon as HLA-B*5701 is available.

In the ART-exp, the 2.5-year risk was estimated at 8.3 (7.2, 9.5), (Figure3b).

In a multivariable regression model, in the ART-naïve, using F/TAF as MTR was associated with an increased risk of F/TAF discontinuation [AHR=2.85 (1.92, 4.23),p<.001)]. In the ART-exp, the risk of discontinuation was higher for patients who developed dyslipidemia [AHR=24.36 (5.63, 105.4),p<.001] (Table 2).

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

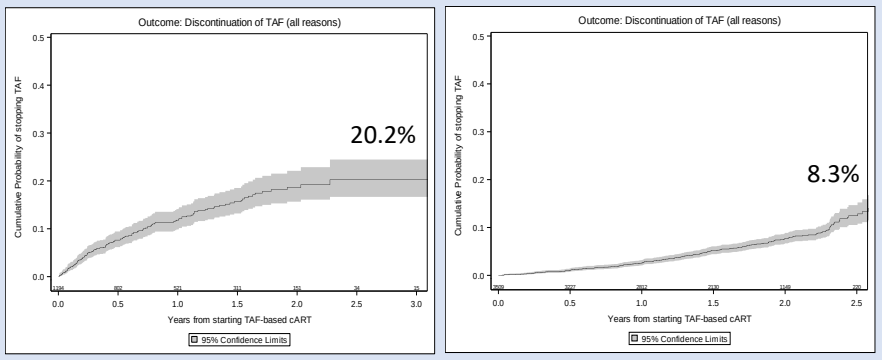


Table 2 –Hazard Ratios of F/TAF discontinuation from fitting a cox regression model in ART-naïve (upper panel) and ART-experienced patients (lower panel)

	Unadjusted and adjusted marginal relative hazards of discontinuation of F/TAF[&]					
Exposure	**Unadjusted RH (95% CI)**	**p-value**	**Adjusted1[*] RH (95% CI)**	**p-value**	**Adjusted2[#] RH (95% CI)**	**p-value**
F/TAF formulation						
STRs	1		1		1	
MTRs	2.77 (1.91, 4.04)	<.001	2.96 (2.02, 4.34)	<.001	2.85 (1.92, 4.23)	<.001

[*]adjusted for age, year of starting ART and hepatitis co-infection

[#]adjusted for age, year of starting ART hepatitis co-infection, baseline HIV-RNA and AIDS

[&]all stops regradless of the reason; Abbreviation: MTR, multiple tablet regimen

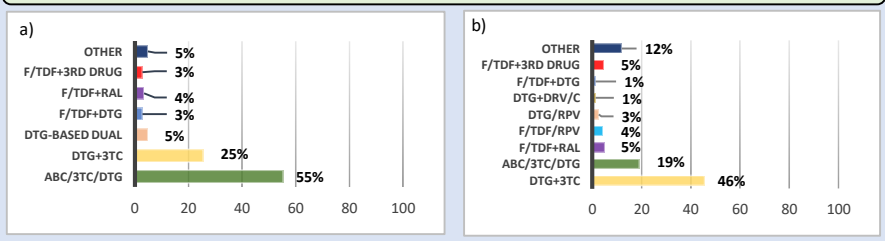
	Unadjusted and adjusted marginal relative hazards of discontinuation of TAF[&]			
Exposure	**Unadjusted HR (95% CI)**	**p-value**	**Adjusted[*] HR (95% CI)**	**p-value**
Current dyslipidemia				
No	1		1	
Yes	1.44 (0.94, 2.20)	0.098	24.36 (5.63, 105.4)	<.001

[*]adjusted for age and time-varying use of statins and censoring using IPW

[&]all stops regardless of the reason

In the ART-naive group, over a median follow-up of 9 (IQR 4-16) months, 282/1194 (23.6%) discontinued F/TAF and in ART exp, over a median follow up of 19 (IQR 13-24) months, 464/3509 (13.2%) discontinued F/TAF. The main reported cause of TAF discontinuation was simplification (60% in ART-naive and 56% in ART-exp). The main regimens choosen after F/TAF stop are shown in figure 4 a,b.

Figure 4. Regimens after F/TAF discontinuation in a) ART-naïve, b)ART-exp



LIMITATIONS

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

CONCLUSIONS

- ✓ 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: 1.Gupta SK, et al. AIDS. 2019;33(9):1455-1465; 2.Tao X, et al. Int J Infect Dis. 2019;87:43-53; 3.Hemmige V, et al. AIDS Care. 2018;30(8):1017-1024; 4. Altice F, et al. Patient Prefer Adherence. 2019;13:475-490; 5. Kauppinen KJ, et al. AIDS Patient Care STDS. 2019 Dec;33(12):500-506.

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