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for including all*

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e da
INMI, Istituto Nazionale per le Malattie Infettive
ISS, Istituto Superiore di Sanità
AMCLI, Associazione Microbiologi Clinici Italiani
SIICA, Società Italiana di Immunologia, Immunologia Clinica e Allergologia
SIMaST, Società Interdisciplinare per lo Studio delle Malattie Sessualmente Trasmissibili
SITA, Società italiana per la Terapia Antinfettiva
SIV-ISV, Società Italiana di Virologia - Italian Society for Virology
ANLAIDS, Associazione Nazionale per la lotta all'AIDS
ARCIGAY, Associazione LGBT Italiana
ASA Onlus, Associazione Solidarietà AIDS Onlus
EpaC Onlus, Associazione EpaC Onlus
LILA, Lega Italiana per la lotta contro l'AIDS
MARIO MIELI, Circolo di Cultura Omosessuale
NADIR, Associazione Nadir Onlus
NPS Italia Onlus, Network Persone Sieropositive
PLUS, Persone LGBT Sieropositive onlus

effetti



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

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BACKGROUND

- F/TAF shows 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 facilitate clinical outcomes and retention in care compared with once-daily multiple-tablet regimens (MTRs) in naive 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 studies⁵

- 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 ART-experienced patients
- To evaluate the association between current dyslipidemia and the risk of F/TAF discontinuation in ART-experienced patients

MATERIAL AND 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)

DEFINITIONS

Dyslipidemia was defined as 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

F/TAF discontinuation: stops of F/TAF independently from the other drugs in the regimen and regardless of the reason

MATERIAL AND METHODS

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

MAIN CHARACTERISTICS OF 4,703 PATIENTS WHO STARTED F/TAF ACCORDING TO ART HISTORY STATUS

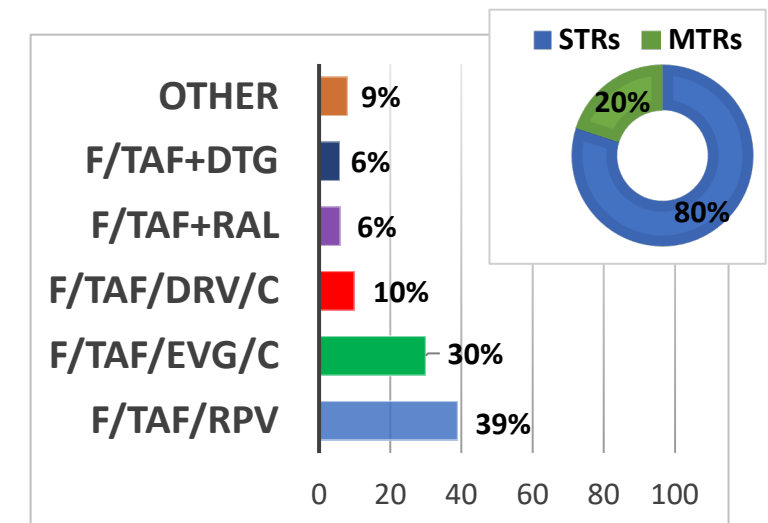
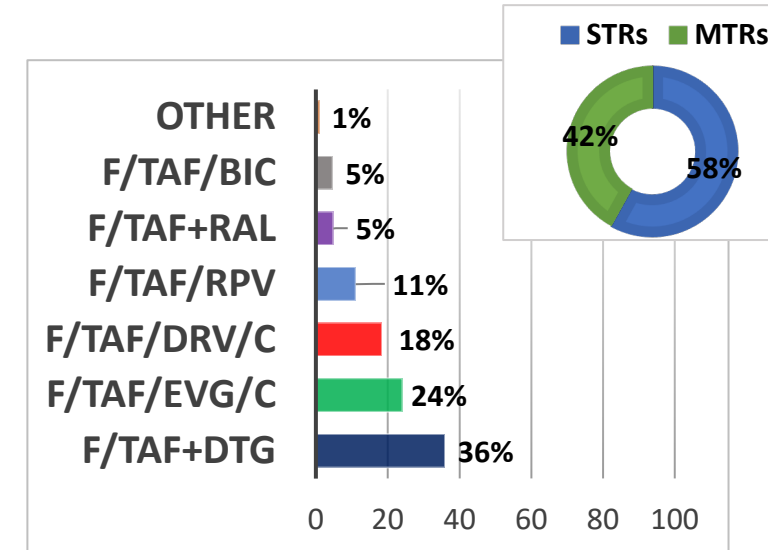


Characteristics	ART History	
	ART-naive N= 1194	ART-Exp VL≤50 copies/mL N= 3509
Gender, n(%)		
Female	194 (16)	679 (19)
Age, years		
Median (IQR)	40 (31, 50)	45 (37, 53)
Mode of HIV Transmission, n(%)		
IDU	60 (5)	314 (9)
Unprotected sexual intercourses	1073 (90)	3003 (85)
AIDS diagnosis, n(%)	109 (9)	427 (12)
CD4 count, cells/mm³		
Median (IQR)	335 (125, 544)	687 (507, 898)
Viral load, log₁₀ copies/mL		
Median (IQR)	4.88 (4.26, 5.48)	-
HCVAb positive, n(%)	43 (4)	402 (11)
Calendar year of baseline		
Median (IQR)	2018 (2017, 2019)	2017 (2017, 2018)
Dyslipidemia, n(%)	403 (25)	3330 (75)

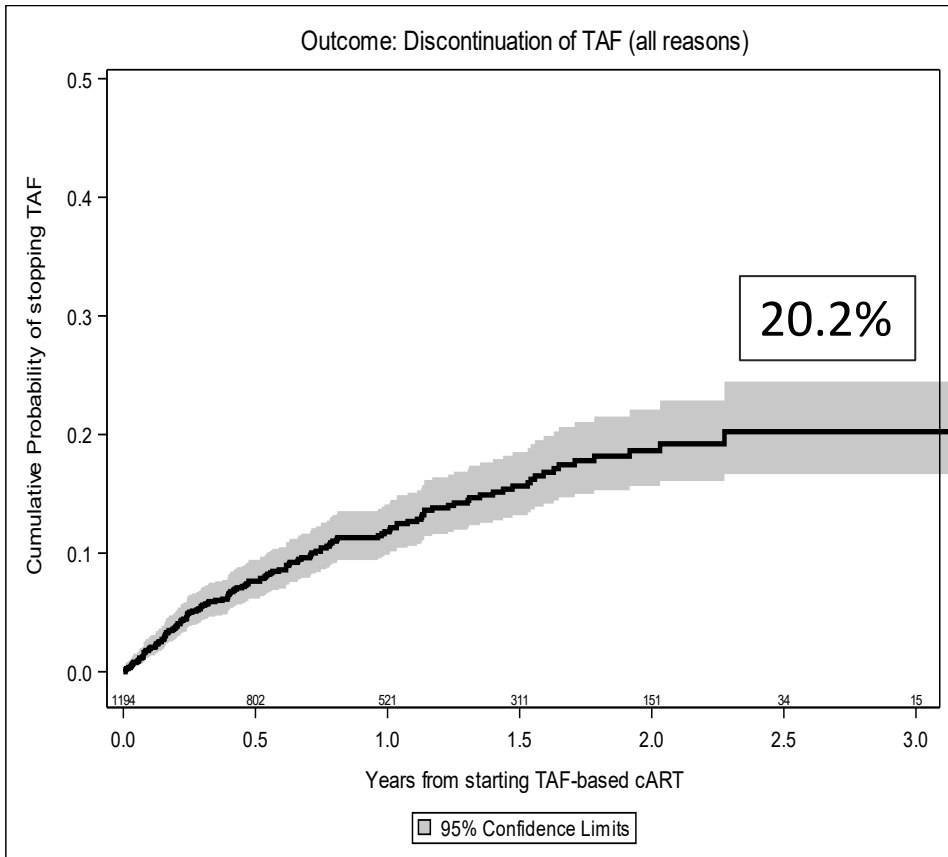
*Chi-square or Kruskal-Wallis test as appropriate

Main regimens in ART-naïve patients (n=1,194)

Main regimens in ART-exp patients (n=3,509)



RISK OF F/TAF DISCONTINUATION REGARDLESS OF THE REASON



No. of stops by 3years	3-year Probability (95% CI)
140	20.2 (16.3, 24.1)

ART-NAÏVE PATIENTS

SUBANALYSIS

- ✓ KM estimates of F/TAF discontinuation after exclusion of switches to ABC/3TC/DTG was 13% by 2 years (95% CI 9.1-16.3)
- ✓ The incidence of switching to ABC/3TC/DTG after F/TAF discontinuation was stable over time

RELATIVE HAZARDS (RH) OF F/TAF DISCONTINUATION[&] FROM FITTING A COX REGRESSION MODEL

Exposure	Unadjusted RH (95% CI)	p-value	Adjusted1* RH (95% CI)	p-value	Adjusted2# RH (95% CI)	p-value
F/TAF formulation						
STR (ref)	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

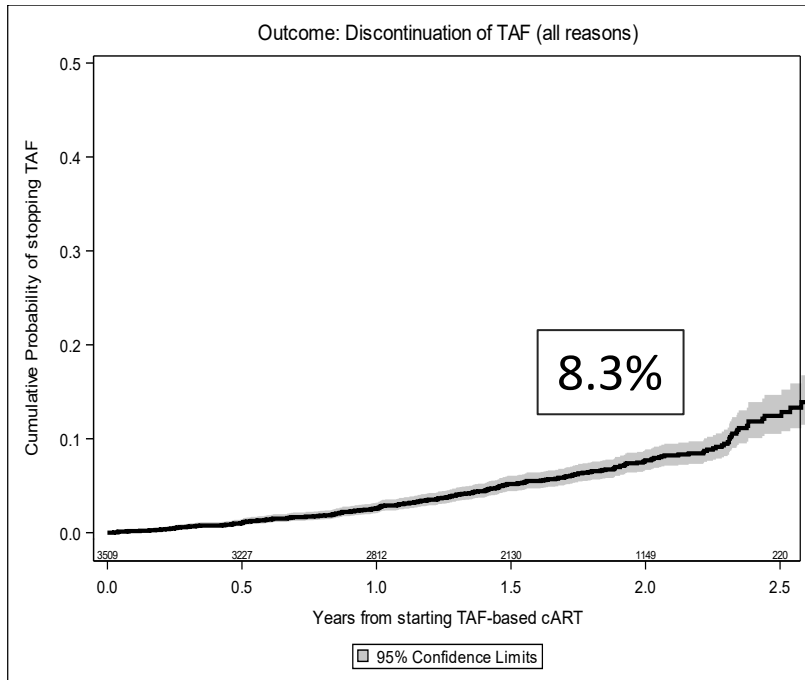
* adjusted for age, year of starting ART and HCV co-infection

adjusted for age, year of starting ART, HCV co-infection, baseline HIV-RNA and AIDS diagnosis
& all stops regardless of the reason; Abbreviation: MTRs, multiple tablet regimens

RISK OF F/TAF DISCONTINUATION REGARDLESS OF THE REASON



ART-EXPERIENCED PATIENTS



RELATIVE HAZARDS (RH) OF F/TAF DISCONTINUATION & FROM FITTING A COX REGRESSION MODEL

Exposure	Unadjusted HR (95% CI)	p-value	Adjusted1*HR (95% CI)	p-value	Adjusted2# HR (95% CI)	p-value
F/TAF formulation						
STR (ref)	1		1		1	
MTR	1.30 (0.98, 1.72)	0.065	1.39 (1.05, 1.85)	0.022	1.42 (1.07, 1.89)	0.016
Current dyslipidemia[§]						
No (ref)	1		1		-	-
Yes	1.44 (0.94, 2.20)	0.098	24.36 (5.63, 105.4)	<.001	-	-

*adjusted for age, year of starting ART and HCV co-infection

#adjusted for age, year of starting ARTHCV co-infection and AIDS

§adjusted for age and time-varying use of statins and censoring using inverse probability of censoring weights (IPW)

&all stops regardless of the reason

No. of stops by 2.5 years	2.5-year Probability (95% CI)
201	8.3 (7.2, 9.5)

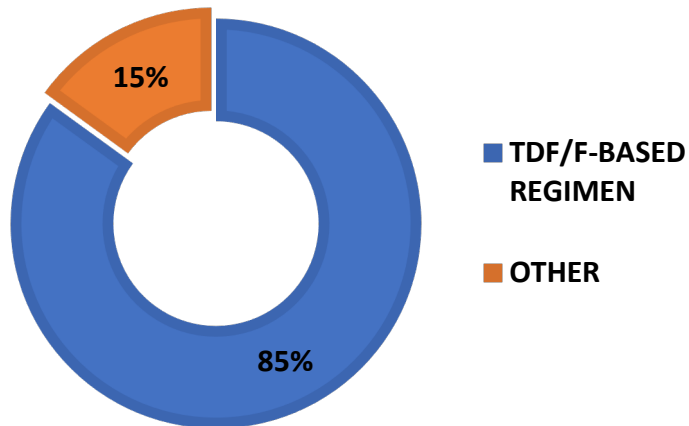
RISK OF F/TAF DISCONTINUATION REGARDLESS OF THE REASON: SUBANALYSIS



ART-EXPERIENCED PATIENTS

RELATIVE HAZARDS (RH) OF DISCONTINUATION FROM FITTING A COX REGRESSION MODEL IN EXPERIENCED PATIENTS RESTRICTED TO THOSE COMING FROM TDF

BACKBONE REGIMEN BEFORE SWITCH TO TAF/F-BASED REGIMEN



	Unadjusted and adjusted marginal relative hazards of discontinuation of TAF&			
	Unadjusted HR (95% CI)	p-value	Adjusted* HR (95% CI)	p-value
Current dyslipidemia				
No	1.00		1.00	
Yes	1.43 (0.91, 2.26)	0.124	35.62 (6.78, 187.1)	<.001

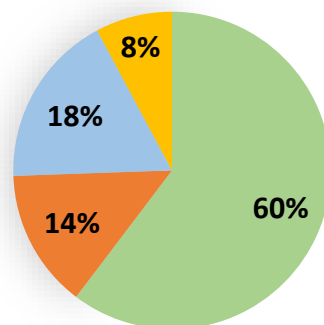
*adjusted for age and time-varying use of statins and censoring using IPW
 &all stops regardless of the reason

RESULTS: REPORTED CAUSES OF TAF DISCONTINUATION

ART-NAÏVE

In the ART-naive group, over a median follow-up of 9 (IQR 4-16) months:

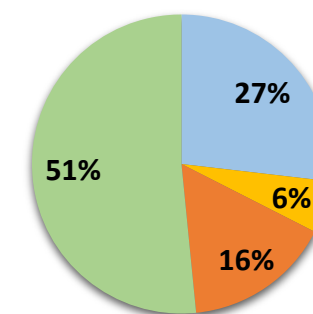
✓ 282/1194 (23.6%) discontinued F/TAF



ART-EXPERIENCED

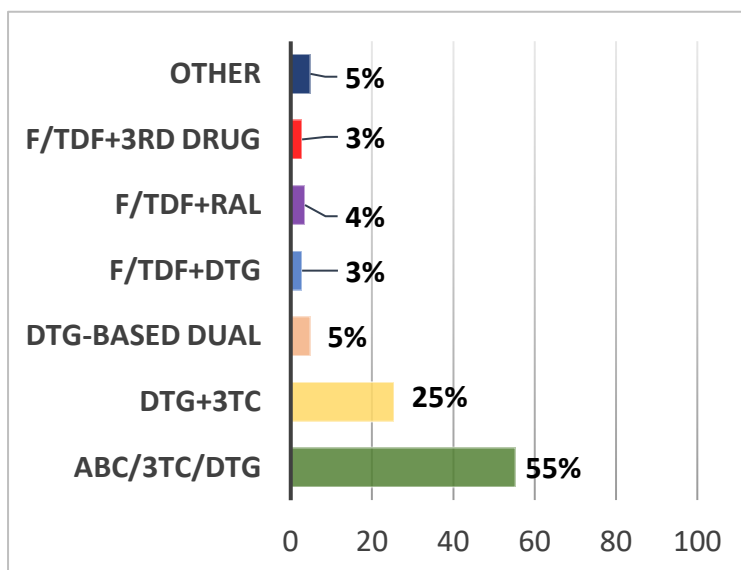
In the ART-exp group, over a median follow-up of 19 (IQR 13-24) months:

✓ 464/3509 (13.2%) discontinued F/TAF

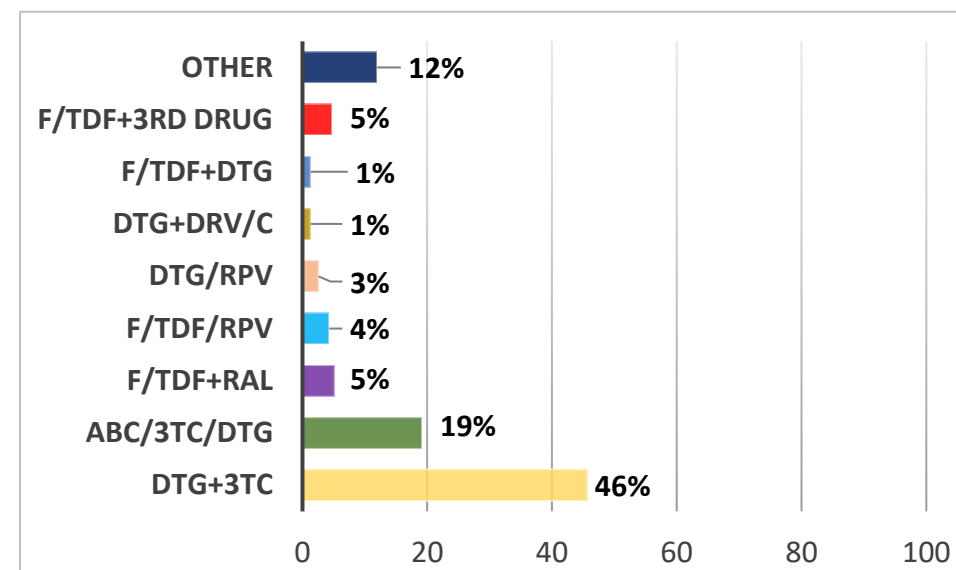


RESULTS: REGIMENS AFTER TAF DISCONTINUATION

ART-naïve: regimens after discontinuation of F/TAF (n.282)



ART-exp: regimens after discontinuation of F/TAF (n.464)



LIMITATIONS

- Observational setting: cannot rule out 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 \leq 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

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