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P055

Perceptions of HIV-infected men who have sex with men as regards functional cure of HIV infection

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Background: While HIV cure and functional cure research are underway, perceptions of HIV patients, the potential primary beneficiary, have yet to be examined. We aimed to understand the awareness and attitude of HIV+ MSM about HIV functional cure by their treatment history.
Methods and materials: Two groups of HIV+ MSM were recruited from respective cohorts of newly diagnosed treatment-naïve and treatment-experienced patients. A self-administered questionnaire was given with brief description on HIV functional cure and questions on: three most important impacts of an HIV cure, knowledge of functional cure, desirability in receiving treatment for functional cure, willingness of joining a functional cure trial and factors associated with the attitude. Differences in proportions between two groups were assessed by z-test.
Results: Totally 217 HIV+ MSM were included in the analysis, of whom 115 have been on treatment for a median of seven years. The most important perceived impacts of HIV cure were "restoration and stabilisation of effective immune function" (66%) and "no longer being infectious" (56%). A higher proportion of newly diagnosed patients chose the former ($p = 0.01$) and "not getting HIV again" ($p = 0.02$). Over half (55%) have never heard of functional cure while the majority (94%) considered this a desirable option by scoring 6 or above in a scale of 0 to 10 and expressed an interest in joining a clinical trial (92%). The most important factors affecting the decision of joining the clinical trial were its safety (97%), advice from healthcare professionals (88%), credibility of the research institution (87%) and the need for interruption of antiretroviral treatment (84%). Major concerns included progression to AIDS or complications (84%), increased viral load (83%) and becoming infectious (73%). The proportions did not differ between two groups.
Conclusions: HIV functional cure is well accepted by HIV+ MSM in Hong Kong, despite a low level of awareness about it. Their perceptions and concerns do not differ much by treatment status. Health and HIV transmissibility statuses were major benefits and concerns. When conducting a clinical trial on functional cure, explanation of its safety issues by healthcare professionals would be important.

P056

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

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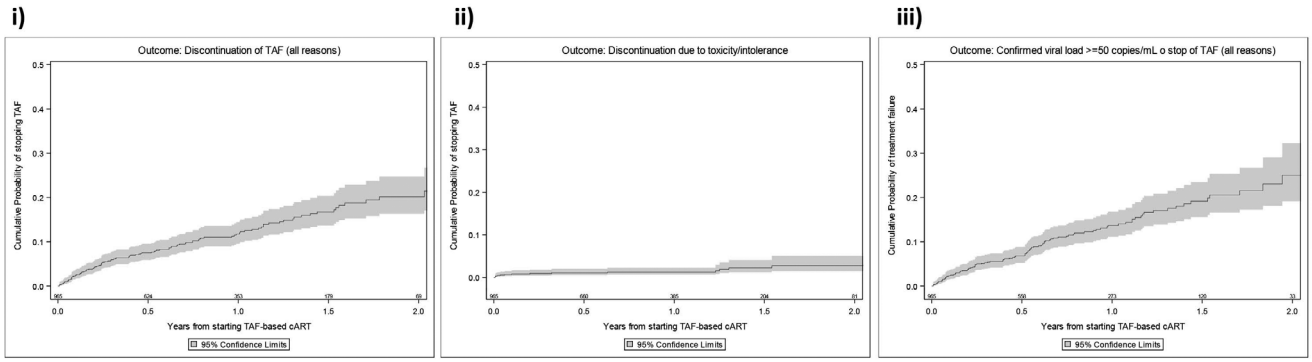
Abstract P056-Table 1. Main characteristics of 4110 patients receiving F/TAF according to ART history

Characteristics	ART-naive (N = 965)	ART-experienced (N = 3145)	*p*-value[a]
Gender, female, n (%)	157 (16.3)	603 (19.2)	0.042
Age, years, median (IQR)	40 (32 to 50)	46 (37 to 53)	<0.001
Mode of HIV transmission, n (%)			<0.001
IDU	50 (5.2)	291 (9.3)	
Homosexual contacts	489 (50.7)	1478 (47.0)	
Heterosexual contacts	368 (38.1)	1197 (38.1)	
Other/unknown	58 (6.0)	1197 (38.1)	
Nationality, not Italian, n (%)	236 (24.5)	514 (16.3)	<0.001
AIDS diagnosis, n (%)	80 (8.3)	397 (12.6)	<0.001
Months HIV diagnosis-cART start, median (IQR)	1 (0 to 2)	69 (34 to 128)	<0.001
Calendar year of baseline, n (%)			<0.001
2015 to 2017	303 (31.4)	1897 (60.3)	
2018	469 (48.6)	1163 (37.0)	
2019	193 (20.0)	85 (2.7)	
CD4 count, cells/mmc, median (IQR)	337 (125 to 543)	685 (498 to 901)	<0.001
CD4 ≤ 200 cells/mmc, n (%)	310 (33.0)	96 (3.1)	<0.001
CD4 count nadir, cells/mmc, median (IQR)	329 (121 to 527)	299 (162 to 435)	0.010
CD8 count, cells/mmc, median (IQR)	848 (565 to 1222)	807 (593 to 1082)	0.037
HIV-RNA, log10 copies/mL, median (IQR)	4.85 (4.22 to 5.45)	0.00 (0.00 to 1.56)	<0.001
Follow-up time, months, median (IQR)	7 (2 to 13)	14 (9 to 18)	<0.001
Type of regimen, n (%)			<0.001
Single-tablet regimen (STR)	434 (45.0)	2231 (70.9)	
Multiple-tablet regimen (MTR)	531 (55.0)	914 (29.1)	
Regimen used, n (%)			<0.001
F/TAF/EVG/cobi	265 (27.4)	999 (31.8)	
F/TAF and DTG	342 (35.4)	202 (6.4)	
F/TAF/RPV	116 (12.0)	1207 (38.4)	
F/TAF/DRV/cobi	173 (17.9)	287 (9.1)	
F/TAF and RAL	50 (5.2)	186 (5.9)	
F/TAF and other third drug	19 (2.0)	264 (8.4)	

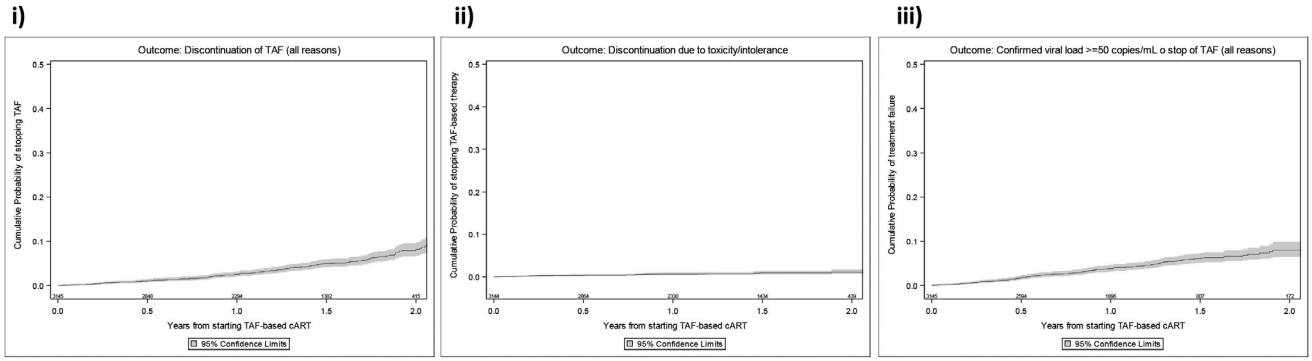
[a]Chi-square or Kruskal-Wallis test as appropriate.

(a) ART-Naive



	No. of stops by 2 years	2-year Probability (95% CI)
i) TAF discontinuation for any reasons	106	19.4 (15.5, 23.4)
ii) TAF discontinuation for toxicity	14	2.7 (1.1, 4.4)
iii) Treatment Failure (TF)	101	21.6 (16.9, 26.3)

(b) ART-experienced



	No. of stops by 2 years	2-year Probability (95% CI)
i) TAF discontinuation for any reasons	121	5.2 (4.3, 6.1)
ii) TAF discontinuation for toxicity	25	1.1 (0.6, 1.6)
iii) Treatment Failure (TF)	135	6.5 (5.3, 7.6)

Abstract P056-Figure 1. KM estimates of discontinuation for i) any reason, ii) toxicity and iii) time to TF in ART-naïve (a) and in ART-experienced patients (b).

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Background: F/TAF showed a comparable efficacy to F/TDF with a better safety profile, nevertheless data from the real-life setting are sparse.
Materials and methods: ART-naïve and virologically suppressed (HIV-RNA ≤ 50 copies/mL before F/TAF start) patients from Icona cohort who started TAF-based triple regimens, in 2015 to 2019 were included. Cumulative probability of TAF discontinuation for any cause, for toxicity and treatment failure (TF; confirmed HIV-RNA > 50 copies/mL, >6 months for ART-naïve, or discontinuation for any cause) were estimated by Kaplan-Meier curves. Factors associated with the risk of the same outcomes were identified using multivariable Cox proportional-hazard model with time-fixed covariates, separately in the two groups.
Results: Four thousand, one hundred and ten patients included: 965 ART-naïve and 3145 ART-experienced. Characteristics are described in Table 1. The main reason of discontinuation was simplification (57% ART-naïve, 52% ART-experienced). In the ART-naïve group, the 2-year risk of discontinuing F/TAF was 19.4% (95% CI 15.5 to 23.4) for any causes and 2.7% (1.1 to 4.4) for toxicity, the 2-year probability of TF was 21.6% (16.9 to 26.3) (Figure 1a). In the ART-experienced group, the 2-year risk was at 5.2% (4.3 to 6.1), 1.1% (0.6 to 1.6) and 6.5% (5.3 to 7.6) for discontinuation for any cause, for toxicity and TF, respectively (Figure 1b). In the subset of people using F/TAF in single-tablet regimen (STR) the 2-year TF rate was even lower: 13.4% (6.6 to 20.3) in the ART-naïve and 5.4% (4.1 to 6.7) in the ART-experienced group. In a multivariable regression model, in the ART-naïve group, using F/TAF as multiple-tablet regimen (MTR) was associated with an increased risk of TF [AHR 2.59 (1.45 to 4.61); $p = 0.001$]. In the ART-experienced group, the risk of discontinuation was higher per more recent time of baseline [per six months AHR 1.47 (1.03 to 2.10); $p = 0.034$], while using F/TAF as MTR was associated with higher risk of both discontinuing TAF [AHR 1.67 (1.19 to 2.35); $p = 0.003$] and of TF [AHR 1.67 (1.18 to 2.36); $p = 0.004$]. A longer

duration of virological suppression before baseline was associated with a reduced risk of TF [AHR 0.95 (0.91 to 0.98); $p = 0.002$].
Conclusions: Approximately 1/5 ART-naive starting TAF-based regimens in the real-life setting discontinue this drug by two years, only 3% for toxicity. As expected, rates were even lower in the ART-experienced group. Our analysis suggests that a low pill burden is a key factor for longer durability of modern TAF-based cART.

P057

Improving methods for patient-reported outcome (PRO) analyses in observational HIV studies

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Background: Patient-reported outcomes (PROs) provide a unique opportunity to tailor clinical care and therapeutic pathways to patients' needs, priorities and experience [1]. Analysing PROs for PLWH is increasingly important for understanding their health-related quality of life (HRQoL). Pharmaceutical industry analyses of PROs often utilise simplistic pairwise comparisons of data obtained at predefined follow-up periods to baseline, yielding limited information on the nature of the change in PRO. Conversely, in cancer research, a range of methods have been proposed [2].
Materials and methods: Pairwise comparison, ANOVAs, linear mixed models (LMMs) and generalised estimating equations (GEEs) were applied to the analysis of the SF-36 mental component score (MCS) and physical component score (PCS) from treatment-naïve patients in TAFNES, a German observational cohort of PLWH at zero, three, six, twelve, eighteen and twenty-four months after initiation of an F/TAF-based treatment regimen. Methods for PRO analysis were assessed against previously identified essential statistical features (Table 1). Changes in MCS and PCS were assessed to compare the benefits of each approach.
Results: Two hundred and eighty-six participants provided an MCS and PCS observation between treatment initiation (M0) and Month 24 (M24). The paired Wilcoxon rank sum test demonstrated statistically significant increases in mean MCS (+3.35, M24) and PCS (+2.12, M24) from baseline to every follow-up visit, assuming, however, that missing data are missing completely at random (MCAR). Use of ANCOVA was limited due to unbalanced data and non-normally distributed residuals. While controlling for covariates including age, sex and comorbidities, LMMs and GEEs (Figure 1) illustrated a statistically significant increase in MCS and PCS, with a steep increase over the first few months followed by a plateau. Statistically significant differences were observed for age (PCS), for participants with comorbidities at baseline, viral load at baseline and late presentation (PCS).
Conclusions: GEEs offer a robust approach to longitudinal modelling, with fewer assumptions than LMMs, facilitating interpretation of results on the original scale of the PRO. However, one limitation is lower certainty of estimates (larger standard errors). Alternative methods to pairwise comparison can better handle missing data, control for confounding factors and thereby produce more informative conclusions.

Abstract P057-Table 1. Evaluation of statistical methods based on important statistical features for patient-reported outcome analyses in HIV studies [2]

	Compare two treatment arms	Adjust for baseline score	Allow for confounding factors	Handle missing data	Handle clustered data	Robust	Allow for time varying covariates	Handle unbalanced designs
Pairwise comparisons ANOVAs	No Yes (ANCOVA)	Yes Yes	No Yes (ANCOVA)	Missing completely at random Missing completely at random	Yes Yes (Repeated measures ANOVA)	Yes Relatively	No No	No No
Linear mixed model	Yes	Yes	Yes	Missing completely at random or Missing at random	Yes	Relatively	Yes	Yes
Generalised estimating equation	Yes	Yes	Yes	Missing completely at random or Missing at random (Weighted GEE)	Yes	Yes	Yes	Yes

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P056

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

A. Vergori[1], A. Cozzi-Lepri[2], N. Gianotti[3], A. Calcagno[4], G. Guaraldi[5], G. Orofino[6], MC. Moioli[7], I. Gentile[8], L. Sarmati[9], S. Cicalini[1]
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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]
- Switching strategies from TDF/F to F/TAF showed a worsening of lipid profile in clinical trials and similar results were found in the real-world setting[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

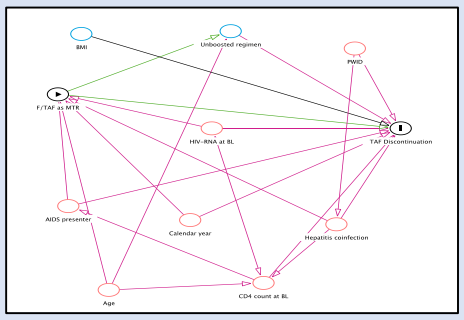
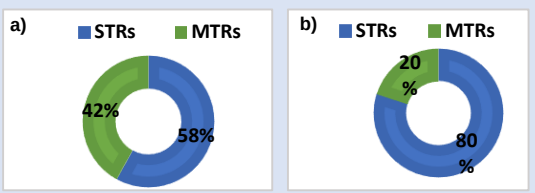


Table 1 – Main characteristics of 4,703 patients who started F/TAF according to ART history

	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).

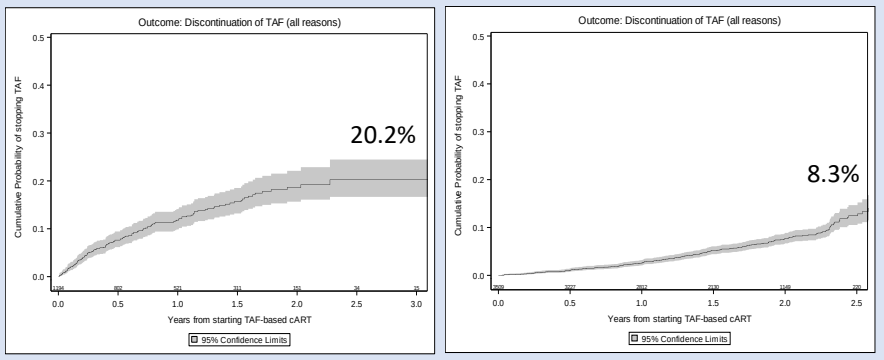


Table 2 –Hazard Ratios of F/TAF discontinuation from fitting a cox regression model in ART-naïve (upper panel) and ART-experienced patients (lower panel)

	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

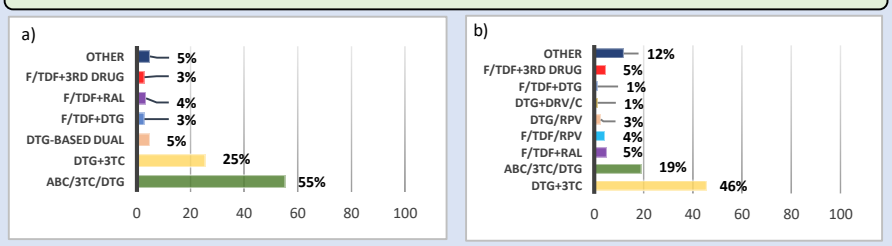
[*]adjusted for age, year of starting ART and hepatitis co-infection
[#]adjusted for age, year of starting ART hepatitis co-infection, baseline HIV-RNA and AIDS
[&]all stops regradless of the reason; Abbreviation: MTR, multiple tablet regimen

	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.

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