P069

Effectiveness, persistence and safety of E/C/F/TAF, F/TAF+3rd agent or R/F/TAF use in treatment-experienced HIV-1 infected patients – 12-month results from the German TAFNES cohort study

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Background

Successful ART has converted HIV-infection into chronic disease. Minimizing side effects, optimizing long-term tolerability of ART and durable virologic suppression are essential requirements for achieving durable healthy ageing. In clinical trials, tenofovir alafenamide (TAF) showed comparable effectiveness and less off-target effects on renal and bone markers than tenofovir disoproxil fumarate (TDF). The 24-month prospective TAFNES cohort study was initiated to provide real world data and evaluate the effectiveness and safety of F/TAF-based regimens when used in treatment-naïve and treatment-experienced patients in routine clinical care.

Methods

- Evaluation of month 12 (M12) outcomes of using F/TAF-based regimens, i.e. E/C/F/TAF (elvitegravir/cobicistat/emtricitabine/TAF), F/TAF+3rd agent or R/F/TAF (rilpivirine/F/TAF), in treatment-experienced (TE) adults.
- The analysis population consisted of TE patients starting treatment at least 9 months prior to data-cut (May 2018) and with either a documented visit within the predefined M12 visit window (between months 9 and 15 after TAF initiation) or a documented premature study/treatment discontinuation.
- Outcome measures included ART persistence (using Kaplan-Meier analyses), virologic effectiveness (HIV-RNA<50 cp/mL, modified ITT-analyses (mITT), discontinuation=failure, loss-to-follow-up and missing=excluded), incident serious/non-serious adverse drug reactions (SADRs/ADRs; i.e. events considered at least possibly related to study drug by the investigator) and health-related quality of life (HRQL) using validated questionnaires, namely the SF-36 (norm based scoring, higher scores indicate higher HRQL), the HIV Symptom Index (HIV-SI; range 0-80, higher scores indicate more bothersome symptoms), and treatment satisfaction (TS, range 0-60, higher scores indicate greater satisfaction).

Results

Study population

- N=434 TE patients were eligible for analysis, 154 patients were switched to E/C/F/TAF, 146 to F/TAF+3rd agent (30% dolutegravir, 16% nevirapine, 13% raltegravir, 11% darunavir/ritonavir) and 134 to R/F/TAF. 93% were switched from TDF-based ART.
- Reasons for switch (multiple responses allowed) to F/TAF-based ART were simplification (n=127, 29%), patient wish (n=138, 32%), side effects on previous ART (n=185, 43%), and other (n=77, 18%; including aiming to minimize long-term toxicity (n=55, 13%)).

Table 1. Baseline characteristics*		Overall	E/C/F/TAF	F/TAF + 3rd agent**	R/F/TAF
N (%)		434 (100)	154 (35)	146 (34)	134 (31)
Male gender, n (%)		393 (91)	137 (89)	137 (94)	119 (89)
Age, years, median (IQR)		51 (40-57)	45 (36-54)	56 (53-61)	44 (35-52)
Age ≥50 years, n (%)		251 (58)	58 (38)	146 (100)**	47 (35)
HIV-related characteristics					
CD4 count, cells/µL, median (IQR)		629 (472-831)	633 (487-882)	577 (431-800)	678 (521-816)
CDC stage C (AIDS), n (%)		90 (21)	34 (22)	38 (26)	18 (13)
HIV-1 RNA (cp/mL)	<50, n (%)	405 (95)	140 (93)	140 (97)	125 (96)
	50 - <200, n (%)	13 (3)	7 (5)	3 (2)	3 (2)
	200 - 100,000, n (%)	6 (1)	3 (2)	1 (1)	2 (2)
	>100,000, n (%)	1 (<1)	1 (1)	0 (0)	0 (0)
Previous antiretroviral regimen, n (%)					
	INI-based	153 (35)	96 (62)	53 (36)	4 (3)
	NNRTI-based	164 (38)	26 (17)	25 (17)	113 (84)
	PI-based	75 (17)	25 (16)	39 (27)	11 (8)
	Other	42 (10)	7 (5)	29 (20)	6 (5)

*Calculations are based on observed data; IQR, interquartile range; **inclusion criteria for this group age ≥50 years

Persistence on F/TAF and reasons for discontinuation until month 12

ART persistence was high with >90% after 12 months in all groups (Figure 1).

Overall, 8% (n=35/434) discontinued study and/or study drug before M12 visit, after a median time of 26 weeks. Reasons for discontinuation are shown in Table 2.

Figure 1. Time on drug by treatment groups - Kaplan-Meier analyses (loss to follow-up censored)

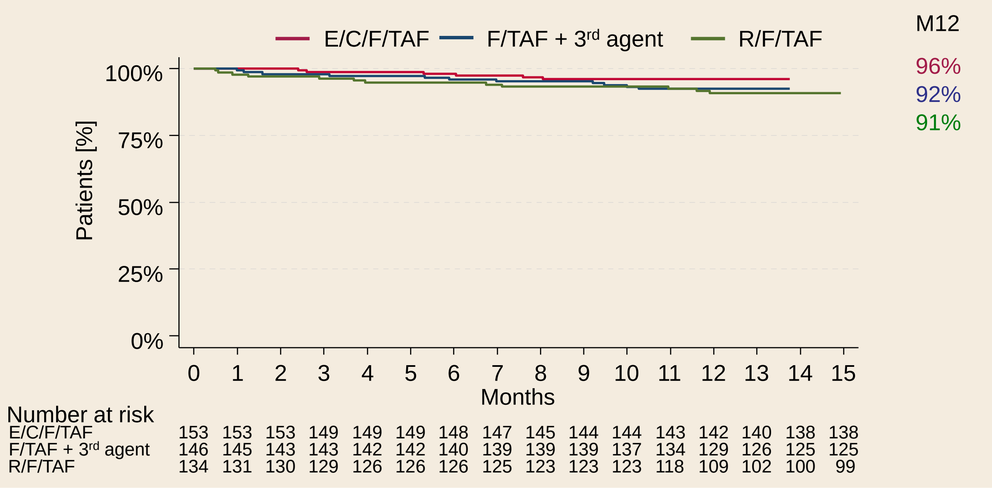


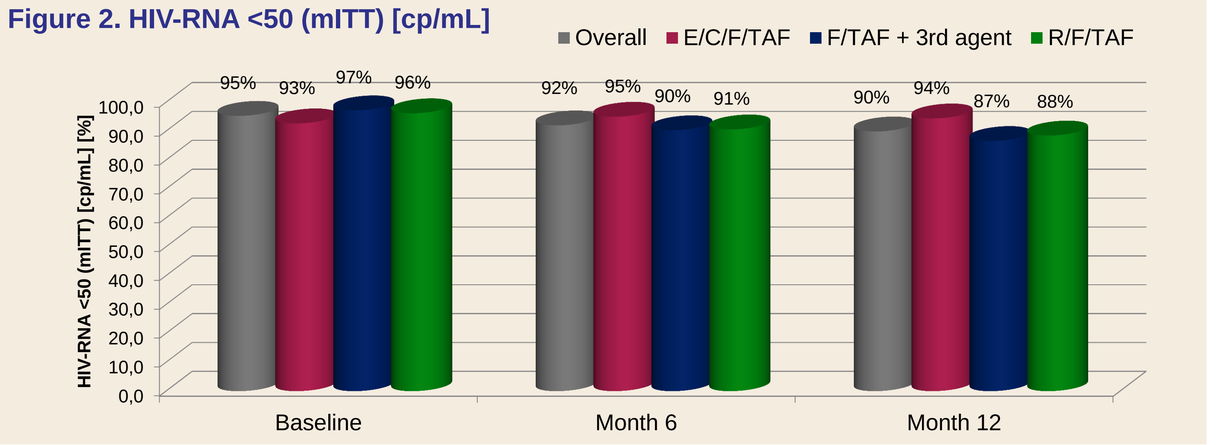
Table 2. Reasons for study and/or study drug discontinuation, n (%)	Overall	E/C/F/TAF	F/TAF + 3rd agent	R/F/TAF
ADRs	9 (2)	3 (2)	1 (1)	5 (4)
Patient decision	6 (1)	1 (1)	3 (2)	2 (1)
Virologic failure (VF)	3° (1)	1* (1)	0 (0)	2** (1)
Death	2^ (<1)	0 (0)	1 (1)	1 (1)
Other	9 (2)	1 (1)	6 (4)	2 (1)
Loss to follow-up	6 (1)	4 (3)	0 (0)	2 (1)

°all with <50 cp/mL at baseline; *1 pat. without baseline (BL) resistance test, but with multiple resistance associated mutations (RAMs) at VF incl. NNRTI mutations and thymidine analogue mutations (TAMs) indication historic failure (previous ART: DTG+F/TDF); **1 pat. without BL resistance test and no resistance mutations at VF (previous ART R/F/TDF); 1 pat. without BL RAMs but RAMs at VF incl. TAMs (previous ART: DRV/r+F/TDF); ^causes of death: 1x esophageal variceal bleeding, 1x unknown;

Effectiveness

At M12 visit, 90% (n=372/414) had HIV-RNA levels <50 cp/mL (mITT), i.e. 94% of patients treated with E/C/F/TAF (n=134/142), 87% of patients on F/TAF+3rd agent (n=123/142) and 88% of patients on R/F/TAF (n=115/130) (see Figure 2).

Figure 2. HIV-RNA <50 (mITT) [cp/mL]



Incident ADRs/SADRs (coded with MedDRA preferred terms)

- By M12, overall 19 ADR reports were documented in 3% of patients (15/434) leading to study discontinuation in 2% of patients (9/434).
- 7 SADRs were documented in 1% of patients (4/434) (see Table 3).

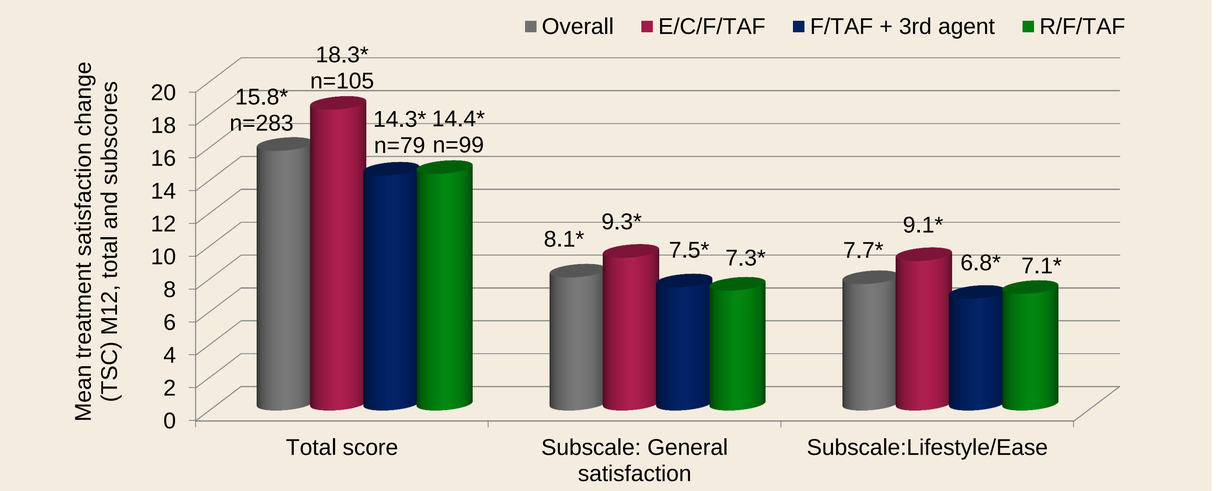
Table 3.	ADRs per patient	Disc.°	SADRs per patient	Disc.°
E/C/F/TAF	- Pathological fracture	No	- Palpitations, headache	Yes
	- Weight increased	No		
	- Headache, vertigo and hyperhidrosis	Yes		
	- Dermatological ADR	Yes		
F/TAF + 3rd agent	- Sleep disorder	No	- Oesophageal dysplasia, gastric dysplasia, oesophageal carcinoma stage 0	No
	- Myalgia, periostitis, cutaneous symptoms	No		
	- Lipodystrophy acquired	No		
	- Arthropathy	No	- Intra-abdominal fluid collection	No
	- Neuropsychiatric ADR	Yes		
R/F/TAF	- Libido decreased	No	- Fatigue	No
	- Depression	Yes		
	- Depression	Yes		
	- Nightmare	Yes		
	- Abdominal pain upper	Yes		
	- Weight increased	Yes		

°Disc.: study drug discontinuation;

Health-related quality of life (HRQL): SF-36, HIV-SI and TS

- At baseline, SF-36 mean mental component scores (+/- standard deviation, SD) were 45.0 (12.5) for E/C/F/TAF, 45.8 (13.3) for F/TAF + 3rd agent, and 47.2 (13.4) for R/F/TAF
- SF-36 mean physical component scores were 53.8 (10.1) for E/C/F/TAF, 48.9 (11.9) for F/TAF + 3rd agent, and 54.3 (9.8) for R/F/TAF.
- Mean HIV SI scores (SD) were 15.0 (14.2) for E/C/F/TAF, 15.8 (15.3) for F/TAF + 3rd agent, and 13.1 (12.7) for R/F/TAF.
- At month 12, changes in SF-36 and HIV-SI were not statistically significant for the total study population nor within the groups.
- At baseline, mean HIV TS scores (SD) were 52.6 (8.8) for the total study population, 50.8 (9.7) for E/C/F/TAF, 54.2 (7.2) for F/TAF + 3rd agent, and 53.1 (9.0) for R/F/TAF.
- By month 12, treatment satisfaction (TS) significantly increased in treatment-experienced patients for all treatment groups (Figure 3).

Figure 3. Treatment satisfaction (TS) change score at month 12



Higher total scores indicate greater treatment satisfaction, range -30 - +30,
*p<0.05 (sign. difference from zero in TS change score)

Conclusions

- F/TAF-based regimens showed good persistence of more than 90% after 12 months in this observational cohort of adult treatment-experienced patients and low discontinuation rates due to ADRs (2%) or virologic failure (<1%).
- Significant improvements in treatment satisfaction demonstrate a high degree of patient acceptability of using F/TAF as part of single-or multi-tablet regimens.

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