P052

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

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Background

Based on controlled clinical trials, emtricitabine/tenofovir alafenamide (F/TAF) - based regimens are among recommended regimens for first- and further-line antiretroviral treatment of HIV-infection in Germany. To evaluate the effectiveness and safety of TAF-based single-tablet (STR) or multi-tablet regimens (MTR) when used in treatment-naïve (TN) or treatment-experienced adult HIV-infected patients in a real-life setting, the non-interventional 24-month prospective TAFNES cohort study was initiated.

Methods

- Evaluation of month 12 (M12) outcomes of using F/TAF-based regimens, i.e. E/C/F/TAF, (elvitegravir/cobicistat/F/TAF), F/TAF+3rd agent or R/F/TAF (rilpivirine/F/TAF), in treatment-naïve (TN) adults.
- The analysis population consisted of TN 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 F/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) and health-related quality of life (HRQL) using validated questionnaires, namely the SF-36 and the HIV Symptom Index (HIV-SI).

Results

Study population

- N=239 TN patients were included in the analysis population, 143 patients were initiated on E/C/F/TAF, 65 patients on F/TAF+3rd agent (85% dolutegravir, 5% raltegravir, 10% other), and 31 patients on R/F/TAF.
- Late presentation was particularly common in patients receiving E/C/F/TAF or F/TAF+3rd agent. Baseline characteristics are shown in Table 1.

Table 1. Baseline (BL) characteristics

	Overall	E/C/F/TAF	F/TAF + 3rd agent*	R/F/TAF
N (%)	239 (100)	143 (60)	65 (27)	31 (13)
Male gender, n (%)	225 (94)	136 (95)	61 (94)	28 (90)
Age, years, median (IQR)	36 (30-46)	36 (31-46)	39 (30-47)	36 (30-43)
HIV-related characteristics				
CD4 count, cells/µL, median (IQR)	462 (282-629)	494 (310-629)	353 (161-582)	506 (428-642)
CD4 <200 cells/µL, n (%)	36 (15)	18 (13)	18 (29)	0 (0)
CDC stage C (AIDS), n (%)	20 (8)	10 (7)	9 (14)	1 (3)
Late presentation, n (%)**	80 (34)	45 (32)	31 (49)	4 (13)
HIV-RNA, log cp./mL, median (IQR)	4.4 (3.9-5.1)	4.3 (3.8-4.9)	5.1 (4.3-5.6)	4.2 (3.7-4.5)
HIV-1 RNA >100,000 cp/mL, n (%)	67 (28)	31 (22)	36 (55)	0 (0)

*3rd agent was in 85% dolutegravir; **defined as CD4 cell count <350 cells/µL and/or CDC stage C (AIDS); IQR, interquartile range;

Persistence on F/TAF, reasons for discontinuation and safety

- ART persistence was high with ≥90% after 12 months in all groups (Figure 1).
- Overall, 13% (n=32/239) of patients discontinued study medication and/or the study before M12 visit, after a median treatment time of 21 weeks. Reasons for study and/or study drug discontinuation are shown in Table 2.
- Incident ADRs and SADRS are shown in Table 3. By M12, overall, 19 ADRs were documented in 5% of patients (n=11/239; 2 SADRs were documented in 1% (n=2/239) of patients.

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

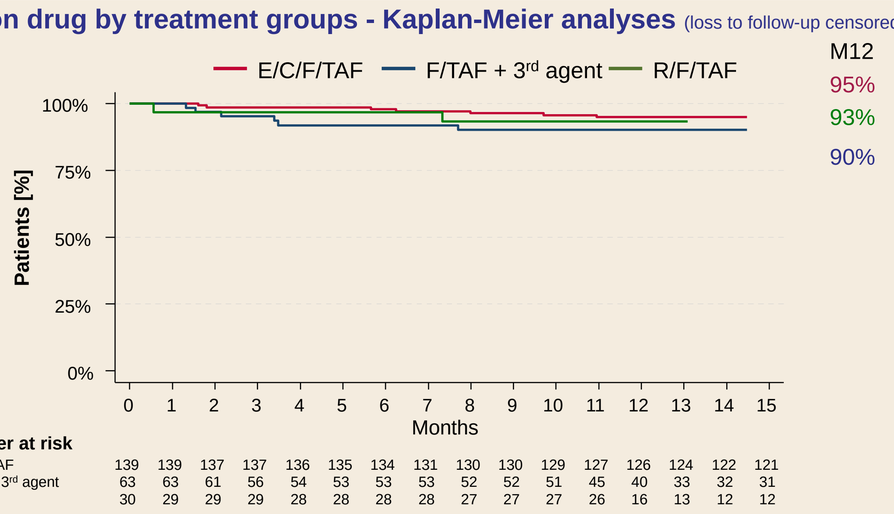


Table 2. Reasons for study and/or study drug discontinuation, n (%)

	Overall	E/C/F/TAF	F/TAF + 3rd agent	R/F/TAF
ADRs	4 (2)	2 (1)	2 (3)	0 (0)
Drug-drug-interaction	4 (2)	3 (2)	0 (0)	1 (3)
Virologic failure (VF)	2* (1)	1 (1)	0 (0)	1 (3)
Patient decision	2 (1)	0 (0)	2 (3)	0 (0)
Other	3 (1)	1 (1)	2 (3)	0 (0)
Loss to follow-up	17 (7)	8 (6)	7 (11)	2 (6)

*baseline resistance testing available for 1/2 patients (no RAMs, resistance ass. mutations); no resistance data at VF

Table 3. ADRs/SADRs (coded with MedDRA preferred terms)

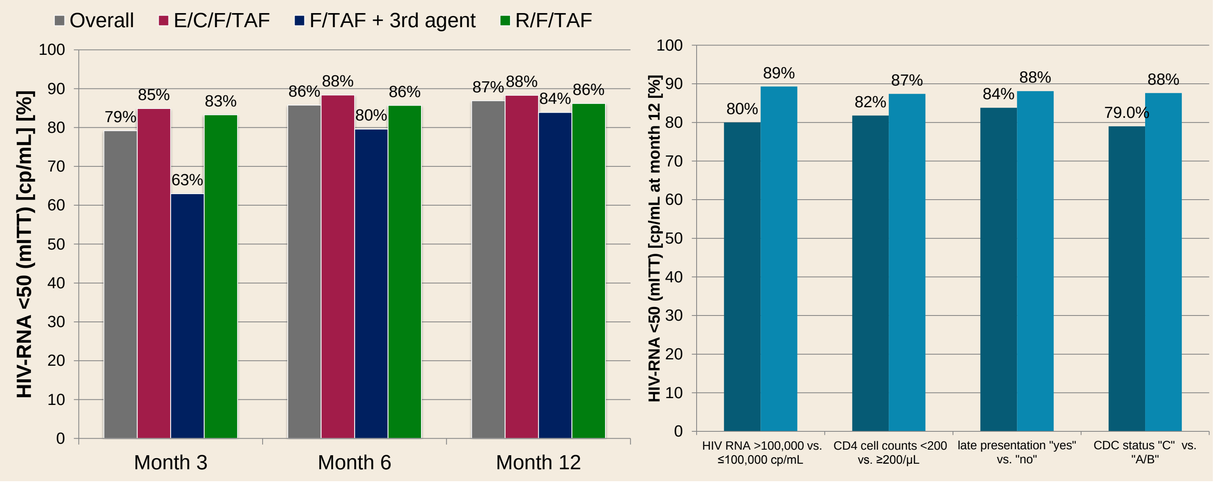
Regimen	ADRs per patient	Disc.*	SADRs p. pat.	Disc.*
E/C/F/TAF	- Dyspepsia and malaise	No		
	- Headache	No		
	- Diarrhea and acne	No		
	- Migraine and sleep disorder	Yes		
	- Pruritus (2x)	No		
	- Flatulence	No		
	- Gastrointestinal adverse drug reaction^	Yes		
F/TAF + 3rd agent	- Nephropathy toxic	Yes	- Diarrhea	No
	- Flatulence, vertigo and abnormal dreams	No	- Diarrhea	No
	- Sleep disorder	No		
	- Headache, general feeling of illness	Yes		
R/F/TAF	– Weight decreased, panic attack and sleep disorder	No		

*Disc.: study drug discontinuation;

Virologic effectiveness

- At M12 visit, 87% (n=185/213) of patients had HIV-RNA levels <50 cp/mL (mITT); 88% of patients treated with E/C/F/TAF (n=113/128), 84% of patients treated with F/TAF+3rd agent (n=47/56) and 86% of patients treated with R/F/TAF (n=25/29).

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



Health-related quality of life (HRQL): SF-36 and HIV Symptom Index (HIV-SI)

- Overall HRQL outcomes indicated significant improvements in symptom distress and in the mental and physical components of the SF-36 (Figure 3, Table 4).

Figure 3. HIV-SI: Decrease in symptom distress

HIV-SI (20 items), range 0-80, higher summary scores indicate more bothering symptoms, a decrease in HIV-SI indicates an improvement. For total scores at baseline and month 12, see Table 4.

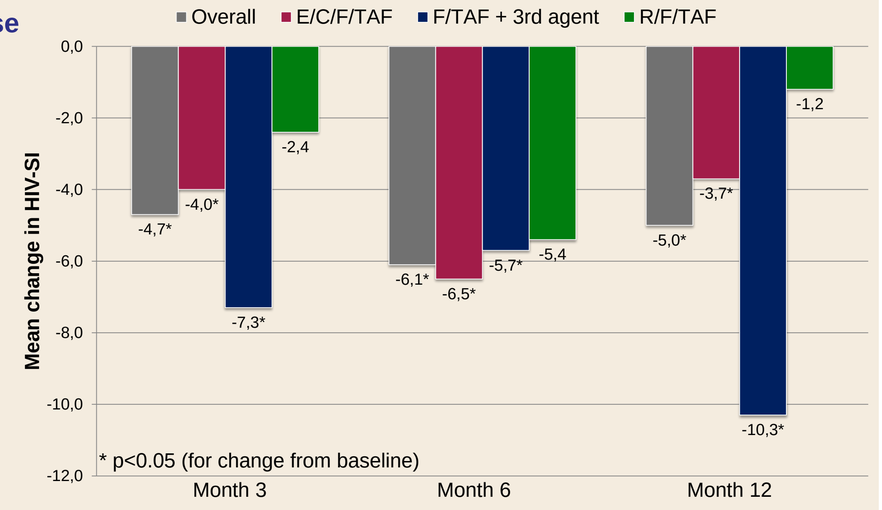


Table 4. HRQL: Baseline (BL) and month 12 (M12) outcomes, changes from BL*

	Overall	E/C/F/TAF	F/TAF + 3rd agent	R/F/TAF
N (%)	239 (100)	143 (60)	65 (27)	31 (13)
BL SF-36 score, mental component[1], mean (+/-SD)	43.6 (12.9)	43.7 (12.4)	41.0 (14.0)	48.2 (11.4)
M12 SF-36 score, mental component[1], mean (+/-SD)	49.1 (11.0)	49.9 (10.3)	47.0 (12.1)	49.9 (12.3)
Change in SF-36 score, mental component[1], mean (+/-SD)	4.9 (11.7)*	5.1 (11.4)*	5.2 (13.9)*	3.7 (9.6)
BL SF-36 score, physical component[1], mean (+/-SD)	53.4 (9.6)	53.3 (9.4)	53.2 (10.3)	54.7 (8.9)
M12 SF-36 score, physical component[1], mean (+/-SD)	56.2 (7.9)	56.7 (6.9)	54.7 (8.7)	56.6 (10.1)
Change in SF-36 score, physical component[1], mean (+/-SD)	2.1 (8.5)*	2.9 (8.7)*	1.1 (8.8)	1.1 (7.4)
BL HIV SI[2], mean (+/-SD)	15.4 (13.8)	14.4 (12.6)	19.9 (16.3)	10.3 (10.9)
M12 HIV SI[2], mean (+/-SD)	10.4 (11.1)	10.3 (10.8)	11.9 (13.6)	8.2 (6.5)
Change in HIV SI[2], mean (+/-SD)	-5.0 (12.7)*	-3.7 (10.7)*	-10.3 (16.7)*	-1.2 (10.8)

*Annotations: Calculations are based on observed data; SD, standard deviation; [1]norm based scoring, higher scores indicate higher HRQL, [2]range 0-80, higher scores indicate more bothering symptoms; *p<0.05 (for change from baseline)

Conclusions

- F/TAF-based regimens for initial ART showed good persistence with >90% after 12 months in this prospective cohort of treatment-naïve adults.
- Low discontinuation rates due to ADRs (<2%) and significant improvements in HRQL confirm the safety of using F/TAF in clinical routine care.
- Evaluation of SF-36 and HIV-SI indicated significant improvements in mental and physical HRQL, as well as in symptom distress.

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