P2/3

17th EUROPEAN AIDS CONFERENCE

Effectiveness, persistence and safety of elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF), F/TAF+3rd agent or rilpivirine/F/TAF (R/F/TAF) in treatment-naïve HIV-1 infected patients – 24-month results from the German TAFNES cohort study

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Background

The prospective TAFNES cohort study was initiated to evaluate the effectiveness and safety of F/TAF-based single-tablet (STR) or multi-tablet regimens (MTR) in people living with HIV (PLHIV) in a real-life setting.

Methods

Inclusion criteria for month 24 (M24) evaluation

- Treatment-naïve (TN) adults initiated on E/C/F/TAF, R/F/TAF or F/TAF + another 3rd agent according to the specific SmPCs (summaries of product characteristics)
- Treatment start at least 21 months prior to data-cut (03/31/2019) and with either a documented visit within the predefined M24 visit window (between 21 and 27 months after F/TAF initiation) or a documented premature study/treatment discontinuation

Outcomes of interest

- ART persistence (Kaplan-Meier estimates; withdrawal of consent/loss to follow-up censored)
- Virologic effectiveness (HIV-RNA<50 cp/mL; discontinuation=failure, loss to follow-up/ withdrawal of consent/missing=excluded)
- Incident serious/non-serious adverse drug reactions (SADRs/ADRs)
- Change in health-related quality of life (HRQL) using validated questionnaires (SF-36, HIV Symptom Index (HIV-SI)) (using Wilcoxon signed-rank test for testing statistical significance of within-group changes)

Results

Study population

- N=247 TN patients were included in the analysis population, 150 patients received E/C/F/TAF, 69 patients F/TAF+3rd agent (86% dolutegravir [DTG], 7% darunavir/ritonavir, 4% raltegravir, 3% other), and 28 patients R/F/TAF.
- Late presentation (CD4 cell count <350 cells/µL and/or CDC stage C) was particularly common in patients receiving E/C/F/TAF or F/TAF+3rd agent (Table 1).

Table 1. Baseline characteristics*

	Overall	E/C/F/TAF***	F/TAF + 3rd agent**,***	R/F/TAF***
N (%)	247 (100)	150 (61)	69 (28)	28 (11)
Male gender, n (%)	234 (95)	143 (95)	65 (94)	26 (93)
Age, years, median (IQR)	36 (30-46)	36 (30-46)	39 (30-48)	35 (30-43)
CD4 count, cells/µL, median (IQR)	450 (253-623)	505 (317-648)	293 (153-539)	482 (382-642)
CDC stage C (AIDS), n (%)	18 (7)	8 (5)	10 (14)	0 (0)
Late presentation, n (%)****	83 (34)	43 (29)	36 (53)	4 (15)
HIV-RNA, log_{10} cp/mL, median (IQR)	4.4 (4.0-5.1)	4.3 (3.9-4.9)	5.1 (4.3-5.6)	4.0 (3.7-4.5)
HIV-RNA >100,000 cp/mL, n (%)	71 (29)	32 (21)	39 (57)	0 (0)

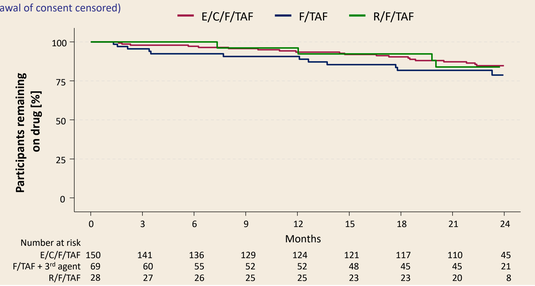
IQR, interquartile range; *Calculations are based on observed data; **3rd agent was in 86% DTG; ****groups not comparable, e.g. due to different inclusion criteria based on SmPCs (summaries of product characteristics), such as: HIV-RNA level ≤100,000 cp/mL for the R/F/TAF group;* ****defined as CD4 cell count <350 cells/µL and/or CDC stage C (AIDS)

Persistence on F/TAF, reasons for discontinuation to M24

- Estimated overall persistence on F/TAF was 83% at M24; persistence in the subgroups is shown in Fig. 1.
- In total, 32% (n=78/247) of patients discontinued study medication and/or the study before M24 (including patients lost to follow-up and withdrawals of consent).
- Reasons for study and/or study drug (E/C/F/TAF or F/TAF or R/F/TAF) disc. are shown in Table 2.

Figure 1. Drug persistence to M24 by treatment group - Kaplan-Meier analyses

(loss to follow-up/withdrawal of consent censored)



M24
85%
79%
84%

Groups not comparable, e.g. due to different inclusion criteria

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

	Overall	E/C/F/TAF	F/TAF + 3rd agent	R/F/TAF
Total discontinuations by M24; n/N (%)	78/247 (32)	43/150 (29)	27/69 (39)	8/28 (29)
ADR	9 (3.6)	5 (3.3)	3 (4.3)	1 (3.6)
Drug-drug-interaction	6 (2.4)	5 (3.3)	0 (0.0)	1 (3.6)
Therapy simplification	6 (2.4)	0 (0.0)	6 (8.7)	0 (0.0)
Investigator decision	5 (2.0)	2 (1.3)	2 (2.9)	1 (3.6)
Withdrew consent	5 (2.0)	3 (2.0)	2 (2.9)	0 (0.0)
*Virologic failure**	3 (1.2)	3 (2.0)	0 (0.0)	0 (0.0)
Other/unknown	9 (3.6)	5 (3.3)	3 (4.3)	1 (3.6)
Loss to follow-up	35 (14.2)	20 (13.3)	11 (15.9)	4 (14.3)

*Baseline resistance testing available for 1 of 3 patients (no RAMs, resistance ass. mutations); no resistance data at virologic failure; in 1 case, an HIV-RNA level of 46 cp/mL between month 6 and 12 was classified as virologic failure leading to ART change.

Safety

By M24, 25 ADRs were documented in 18 patients (7.3%). Incident ADRs are shown in Table 3.

One patient (0.4%) on F/TAF + DTG experienced virologic failure which was classified as SADR with documented relationship to both F/TAF and DTG.

Table 3. ADRs and SADRs (per patient)

		Disc.*			Disc.*
E/C/F/TAF	- Dizziness and concentration disorder	Yes	**E/C/F/TAF** cont.	- Loss of libido	No
	- Headache	No		- Myalgia	No
	- Headache	Yes			
	- Diarrhea and acne	No	**F/TAF + 3rd agent** (ADRs related to F/TAF	- Nephropathy toxic**	Yes
	- Diarrhea (formerly gastrointestinal ADR)	Yes		- Flatulence, vertigo and abnormal dreams	No
	- Migraine and sleep disorder	Yes		- Gastrointestinal ADR	Yes
	- Pruritus	Yes		- Headache and general feeling of illness	Yes
	- Pruritus (2x)	No		- Virologic failure (SADR)	No
	- Flatulence	No			
	- Fatigue	No	**R/F/TAF**	- Weight decreased, panic attack and sleep disorder	Yes
	- Erectile dysfunction	No			

*Disc.: study drug discontinuation due to documented ADR; ** macroalbuminuria and proteinuria

Virologic effectiveness

At M24, HIV-RNA level was <50 cp/mL in 80% of patients in the effectiveness analysis set (E/C/F/TAF 83%; F/TAF+3rd agent 72%; R/F/TAF 79%; Figure 2, Table 4).

Stratification acc. to BL characteristics: HIV-RNA ≤ vs. >5 log_{10}: 81% (115/142) vs. 76% (45/59), CD4 cells ≥ vs. <200/µL: 80% (134/168) vs. 77% (24/31); late presentation yes vs. no: 79% (55/70) vs. 80% (103/129); CDC A/B vs. C: 81% (151/187) vs. 67% (10/15)

Figure 2. HIV-RNA <50 cp/mL

(discontinuation=failure, loss to follow-up/withdrawal of consent/missing=excluded)

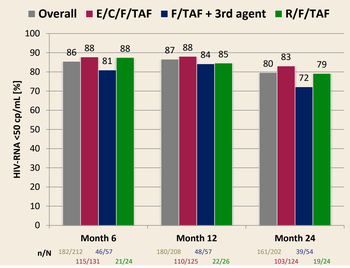


Table 4. Patient disposition and virologic outcomes at M24

	Overall	E/C/F/TAF	F/TAF + 3rd agent	R/F/TAF
Total, N	247	150	69	28
Loss to follow-up, n	35	20	11	4
Withdrawal of consent, n	5	3	2	0
Missing values, n	5	3	2	0
Effectiveness set, n (%)	202 (100)	124 (100)	54 (100)	24 (100)
HIV-RNA<50, n (%)	161 (80)	103 (83)	39 (72)	19 (79)
HIV-RNA<200, n (%)	2 (1)	1 (1)	1 (2)	0 (0)
HIV-RNA≥200, n (%)	1 (0)	0 (0)	0 (0)	1 (4)
Disc. due to VF, n (%)	3 (1)	3 (2)	0 (0)	0 (0)
Disc. for other reasons*, n (%)	35 (17)	17 (14)	14 (26)	4 (17)

*see table 3 for details; Disc.: study and/or study drug discontinuation; VF: virologic failure
Groups not comparable, e.g. due to different inclusion criteria

Health-related quality of life (HRQL)

Overall HRQL outcomes indicated improvements in symptom distress (HIV-SI) and in the mental and physical components of the SF-36 questionnaire (Figure 3, Table 5).

Figure 3. HIV-SI: Change in symptom distress

Groups not comparable, e.g. due to different inclusion criteria

HIV-SI (20 items), range 0-80, higher summary scores indicate more bothering symptoms, a decrease from BL in HIV-SI indicates an improvement. For total scores at baseline see Table 5.

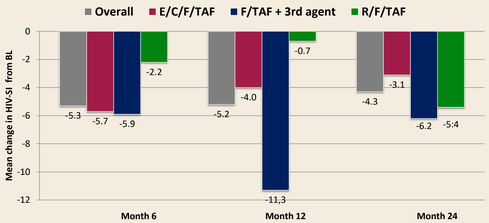


Table 5. SF-36 scores and HIV-SI at baseline (BL) and changes from BL to month 12

			Overall	E/C/F/TAF	F/TAF + 3rd agent	R/F/TAF
SF-36[1]	Mental Component	BL, mean (+/-SD) [n]^	40.4 (13.8) [111]	40.6 (13.0) [70]	38.7 (15.5) [31]	44.7 (14.5) [10]
		BL, mean (+/-SD) [n]^^	45.9 (11.5) [114]	47.2 (11.2) [68]	42.6 (12.4) [30]	46.5 (10.0) [16]
		Change from BL, mean (+/-SD)	+3.7 (12.7)*	+3.5 (11.3)*	+3.7 (16.2)	+5.0 (11.5)*
	Physical Component	BL, mean (+/-SD) [n]^	51.5 (10.5) [111]	52.2 (9.9) [70]	48.8 (12.3) [31]	54.6 (7.1) [10]
		BL, mean (+/-SD) [n]^^	55.0 (7.9) [114]	55.1 (7.9) [68]	55.2 (7.1) [30]	54.0 (9.2) [16]
		Change from BL, mean (+/-SD)	+2.1 (9.1)*	+2.9 (8.1)*	+0.1 (10.1)	+2.4 (11.3)
HIV-SI[2]		BL, mean (+/-SD) [n]^	18.6 (15.2) [113]	17.3 (13.4) [71]	25.6 (18.4) [30]	8.5 (8.3) [12]
		BL, mean (+/-SD) [n]^^	12.9 (11.8) [111]	11.3 (10.6) [64]	17.3 (13.7) [33]	9.6 (9.8) [14]
		Change from BL, mean (+/-SD)	-4.3 (9.9)*	-3.1 (8.8)*	-6.2 (10.8)*	-5.4 (12.0)

^Black font color: patients with completed questionnaires only at BL; ^^blue font color: patients with completed questionnaires at BL and M24; 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; *Annotations: i) groups not comparable, e.g. due to different inclusion criteria; ii) potential for possible positive selection bias due to high rate of non-completers at BL and/or M24;*

Conclusions

- Persistence was high with F/TAF-based regimens in treatment-naïve PLHIV in the TAFNES cohort, 83% during 24 months of observation.
- Overall virologic effectiveness was >80% two years after ART initiation with only 2% virologic failures and low discontinuation rates (<4%) due to ADRs.
- Improvements in self-reported HRQL and symptoms after 24 months of treatment support the safety and effectiveness of F/TAF-based regimens in routine clinical care.

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