Real-world effects of treatment with emtricitabine/tenofovir alafenamide versus emtricitabine/tenofovir disoproxil fumarate-based regimens in people living with HIV in a clinical cohort in Germany

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Background

- Treatment with tenofovir disoproxil fumarate (TDF) has been associated with impairment of renal function in HIV-1 infected patients and may cause proximal renal tubular abnormalities and/or decrease of estimated glomerular filtration rate (eGFR)[1].
- The TAFNES study was initiated in 2016 to evaluate the real world effectiveness and safety of emtricitabine/tenofovir alafenamide (F/TAF) based regimens in people living with HIV (PLHIV).

Objective

- The objective of this analysis was to evaluate the effects of elvitegravir/cobicistat/F/TAF (E/C/F/TAF) on renal function among the PLHIV switching from elvitegravir/cobicistat/emtricitabine/TDF (E/C/F/TDF).

Materials and Methods

- TAFNES is an ongoing prospective observational clinical cohort of PLHIV initiating or switching to F/TAF based regimens in routine care in Germany.
- PLHIV switching from E/C/F/TDF (with a minimum usage of 30 days) to E/C/F/TAF, with eGFR data at the time of switch, in an interim data cut dated 1 August 2018 were included in the present analysis.
- Selection of E/C/F/TAF was based on clinician discretion and was in accordance with SMPC in Germany. eGFR was calculated using the CKD-EPI equation[2].
- Univariate analyses were performed in the subset of patients that had eGFR data at all visits from time of switch to month 12 (time of switch, months 3, 6 and 12), whereas all patients switching from E/C/F/TDF to E/C/F/TAF were included in multivariate analyses.
- Change within subject over time in eGFR was evaluated univariately by Wilcoxon signed-rank test.
- Multivariate mixed linear models were used to evaluate change over time in eGFR with adjustment of age, gender, HIV-RNA level at time of switch, CD4 T lymphocyte count at time of switch and duration of previous E/C/F/TDF use.
- Analyses were performed for all patients and for subgroups of patients with eGFR at time of switch < 90 and ≥90 ml/min/1.73m².

Results

DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

- A total of 84 PLHIV were included in the present analyses, and 66 out of them had eGFR data at all visits from time of switch to month 12.
- 92.9% of all patients switched were male and median (interquartile range) age at the time of switch was 40 (34 – 52) years (**Table 1**).
- 94.0% had HIV RNA <50 copies/mm³ at the time of switch and 70.2% of the PLHIV had CD4 T-lymphocyte count >500 cells/mm³ (**Table 1**).
- Median (IQR) time on E/C/F/TDF prior to switch was 24 (12-36) months (**Table 1**).
- Patients with baseline eGFR≥ 90 mL/min/1.73m² were younger and had been significantly less time on E/C/F/TDF than patients with baseline eGFR <90 mL/min/1.73m² (**Table 1**).

Table 1. Demographics and medical characteristics of the patients

	All switched (n=84)	eGFR at the time of switch subgroups		P values*
		≥ 90 mL/min/1.73m² (n=41)	<90 mL/min/1.73m² (n=43)	
Gender; male, n (%)	78 (92.9)	37 (90.2%)	41 (95.3%)	0.374
at time of switch				
Age (year); median (IQR)	40 (34 – 52)	38 (33 – 45)	44 (36 – 54)	0.014
Age >50 years, n (%)	23 (27.4)	7 (17.1%)	16 (37.2%)	
CD4 T-lymphocyte count, cells/mm³; median (IQR)	641 (476 – 888)	565 (472 – 851)	667 (480 – 920)	0.437
CD4 T-lymphocyte >500 cells/mm³; n (%)	59 (70.2)	27 (65.9%)	32 (74.4%)	
HIV RNA <50 copies/mm³; n (%)	79 (94.0)	38 (92.7%)	41 (95.4%)	
Previous E/C/F/TDF usage duration; month, median (IQR)	24 (12 – 36)	24 (12 – 36)	36 (24 – 48)	0.034
At the time of diagnosis				
CD4 T-lymphocyte > 500 cells/mm³; n (%)	24 (28.6)	14 (34.1)	10 (23.3)	
CD4 T-lymphocyte <200 cells/mm³; n (%)	20 (23.8)	6 (14.6)	14 (32.6)	

IQR: interquartile range
* P values from univariate comparison; an additional logistic regression model using backward selection of gender, age, log(CD4 T-lymphocyte count), log(HIV RNA) and previous E/C/F/TDF usage duration revealed that patients with baseline eGFR≥ 90 mL/min/1.73m² were younger (odds ratio [95%CI]: 0.95 [0.90 - 0.99], P=0.018) and had been significantly less time on TDF (odds ratio [95%CI]: 0.98 [0.95 - 0.99], P=0.034) than patients with baseline eGFR <90 mL/min/1.73m²

ESTIMATED GLOMERULAR FILTRATION RATES

Change over time (univariate analysis)

- Median eGFR increased significantly from time of switch to month 12 (from 86.2 to 94.7 ml/min/1.73m², p=0.004) (**Table 2**).
- Significant increases were observed at each visit for the patients with eGFR at the time of switch < 90 mL/min/1.73m² whereas no significant change was observed for those with eGFR≥ 90 mL/min/1.73m² at the time of switch (**Table 2**).

Table 2. Unadjusted estimated glomerular filtration rates over time in patients with data from the time of switch to month 12

	median (IQR)	P*
All switched (n=66)		
At the time of the switch	86.2 (75.3 – 98.9)	
Month 3	91.1 (81.9 -100.7)	0.148
Month 6	88.1 (77.7 - 100.4)	0.518
Month 12	94.7 (81.7 - 103.7)	*0.004*
eGFR at the time of switch ≥ 90 mL/min/1.73m² (n=28)		
At the time of the switch	103.4 (97.2 - 111.0)	
Month 3	101.1 (97.6 - 111.6)	0.806
Month 6	100.1 (92.9 - 110.1)	0.399
Month 12	102.1 (97.2 - 116.9)	0.857
eGFR at the time of switch < 90 mL/min/1.73m² (n=38)		
At the time of the switch	77.0 (67.9 - 83.3)	
Month 3	84.4 (74.5 - 90.8)	*0.002*
Month 6	81.7 (73.0 - 88.7)	*0.021*
Month 12	84.3 (74.07 - 95.0)	*0.001*

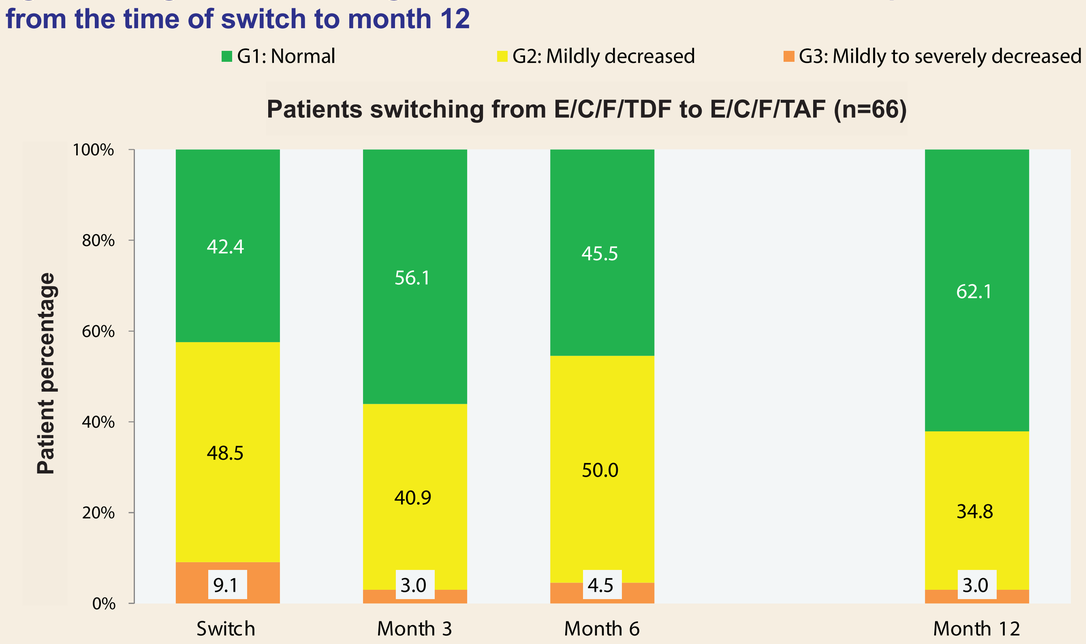
eGFR: estimated glomerular filtration rates, IQR: interquartile range
* P values are for the comparison between each time point and the time of switch by using univariate Wilcoxon signed-rank test

Results (cont'd)

eGFR stages

- The percentage of patients with normal eGFR increased from 42.4% at the time of switch to 62.1% at month 12 with an increase of 19.7% (**Figure 1**).
- The percentage of patients with moderately to severely decreased eGFR declined from 9.1% at the time of switch to 3.0% at month 12 with a decrease of 6.1% (**Figure 1**).

Figure 1. Stages of estimated glomerular filtration rates over time in patients with data from the time of switch to month 12

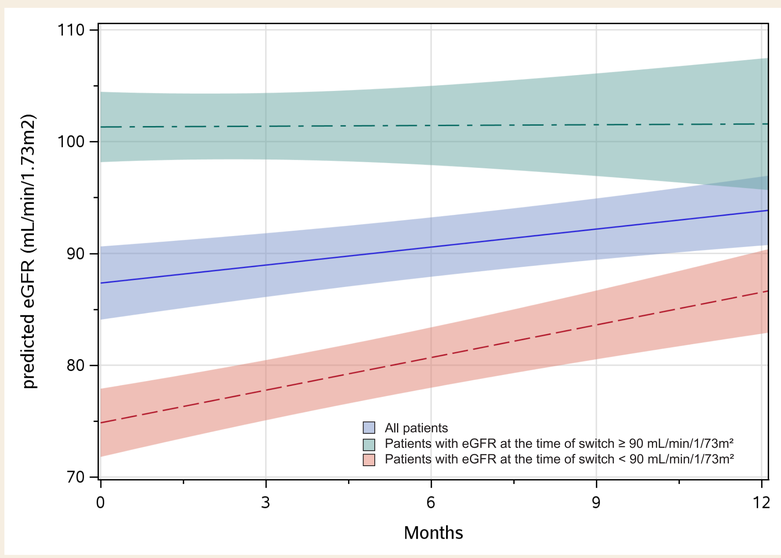


eGFR: estimated glomerular filtration rate
G1: Normal, eGFR ≥ 90 mL/min/1.73m², G2: Mildly decreased, 60 mL/min/1.73m² ≤ eGFR < 90 mL/min/1.73m²,
G3: Mildly to moderately or moderately to severely decreased, 30 mL/min/1.73m² ≤ eGFR < 60 mL/min/1.73m²

Change over time (adjusted for characteristics at the time of switch)

- Overall, the multivariate mixed model showed a significant positive effect for duration on TAF, and significant negative effects on increasing age and increasing duration of previous TDF usage;
  - Looking at all patients, eGFR increased significantly from 88.0 mL/min/1.73m² at the time of switch to 94.4 mL/min/1.73m² at month 12 (**Figure 2**).
  - In the subgroup of patients with eGFR at the time of switch < 90 mL/min/1.73m², eGFR increased significantly from 75.4 mL/min/1.73m² at the time of switch to 87.1 mL/min/1.73m² at month 12 (**Figure 2**).
  - In the subgroup of patients with eGFR at the time of switch ≥ 90 mL/min/1.73m², no significant change was observed over time and eGFR remained stable over the 12 months (**Figure 2**).

Figure 2. Adjusted predicted eGFR over time



Predicted values were calculated by using the following formulas and based on mean age (years) and mean duration of previous TDF usage (years) by sub-group.

Overall
- eGFR = 121.2 + 0.5364 * (months on TAF) – 0.6742 * Age – 1.7212 * (TDF usage)

eGFR at the time of switch < 90 mL/min/1.73m²
- eGFR = 105.4 + 0.9729 * (months on TAF) – 0.6083 * Age – 0.7441 * (TDF usage)

eGFR at the time of switch ≥ 90 mL/min/1.73m²
- eGFR = 104.4 + 0.0223 * (months on TAF) – 0.0884 * Age + 0.2058 * (TDF usage)

eGFR: estimated glomerular filtration rate

Conclusions

This clinical cohort demonstrated an improvement in eGFR in patients switching from E/C/F/TDF to E/C/F/TAF, with a significant increase in estimated glomerular filtration rate and an increase in the percentage of patients with normal renal function from time of switch to month 12.

References

1. European AIDS Clinical Society (EACS) Guidelines Version 9.0 October 2017 www.eacsociety.org/guidelines/eacs-guidelines/eacs-guidelines.html
2. Levey AS, Stevens LA, Schmid CH et al. A new equation to estimate glomerular filtration rate. Ann Intern Med. 2009 May 5;150(9):604-12.