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Cardiac Events in HIV-infected Patients Who Use Tenofovir-Alafenamide

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BACKGROUND

Although cardiac events were not reported as side effects of Tenofovir-Alafenamide (TAF) in registration trials, we observed some new cardiac events in HIV positive patients who had started TAF. We retrospectively studied all cardiac events in our HIV cohort, with special focus on the use of TAF compared to tenofovir disoproxil fumarate (TDF).

METHODS

- Retrospective cohort study
- Inclusion period: 01-01-2016 - 31-05-2018
- Three mutually exclusive treatment groups:
  - Patients treated with TAF -> *TAF*
  - Patients not treated with TAF but with TDF -> *TDF*
  - Patient not treated with TAF or TDF -> *Non-tenofovir (NT)*

- Exclusion if therapy incompliant and a viral load >200 c/mL
- Cardiac events were defined as myocardial infarction, angina pectoris, cardiomyopathy and arrhythmia
- Cardiac event-free survival calculated with Kaplan-Meier survival analysis
- Hazard ratios for cardiac events were adjusted for previous cardiac history, body mass index (BMI), gender, smoking status and age (by quartile) using Cox proportional hazards analysis.

RESULTS

- A total of 2985 patients included
  - TAF: 1537, TDF: 1170 and NT: 278

- Median follow-up
  - TAF: 2.2 years, TDF: 7.0 years and NT: 9.0 years

Table 1. Number of cardiac events by treatment group

	TAF	TDF	NT
Myocardial infarction	8	23	4
Angina pectoris	13	15	5
Cardiomyopathy	6	3	1
Arrythmia	16	17	1
Total cardiac events	43	58	11

Tenofovir-Alafenamide (TAF) use in HIV treatment was associated with an increased risk of cardiac events, especially in patients with prior cardiac disease and older age

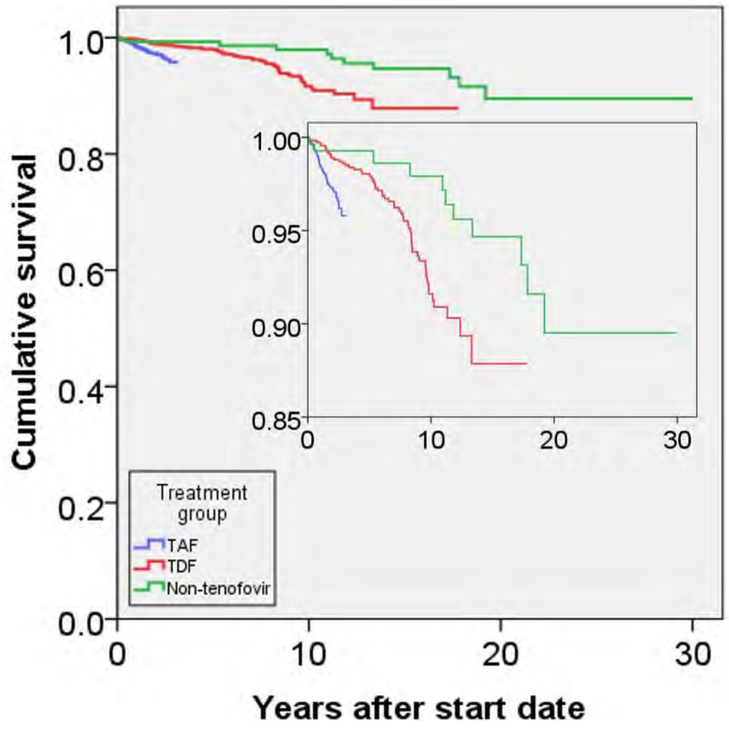


Figure 1. Unadjusted Kaplan-Meier cardiac event-free survival by treatment group. Treatment group was an independent predictor of cardiac events (p< 0.001).

Table 2. Cause specific hazard ratios for cardiac events

	HR(95% CI)	
	Hazard ratio	**p-value**
Cardiac history, Yes = 1	7.04(4.39-11.28)	<0.001*
BMI	1.04(1.00-1.08)	0.035*
Gender, Female = 1	1.02(0.49-2.14)	0.957
Smoking status, Yes = 1	1.61(1.01-2.56)	0.045*
Age at the start of treatment per quartile		
Q1 (0): 2-36 years		
Q2 (1): 37-45 years	2.86(1.22-6.68)	0.015*
Q3 (1): 46-53 years	4.24(1.82-9.90)	0.001*
Q4 (1): 54-86 years	7.75(3.33-18.06)	<0.001*
Treatment group		
TAF (1) vs. Non-tenofovir (0)	3.86(1.51-9.82)	0.005*
TAF (1) vs. TDF (0)	1.94(1.05-3.57)	0.034*
Cardiac events hazard ratio's by cardiac subgroup in TAF vs. TDF		
Arrhythmia	4.14(1.06-16.20)	0.041*
Angina pectoris	1.45(0.530-3.95)	0.47
Cardiomyopathy	4.50(0.37-54.55)	0.237
Myocardial infarction	1.02(0.32-3.21)	0.975

- **Adjusted hazard ratios of cardiac events**
  - TAF vs. NT: 3.86 (95% CI: 1.51-9.82; p=0.005)
  - TAF vs. TDF: 1.94 (95% CI: 1.05-3.57; p=0.034)

CONCLUSIONS

Our real-life cohort showed that the occurrence of cardiac events in TAF was significantly higher compared to TDF and NT. This unexpected finding might be explained by an older population, with more cardiac history compared to the registration trials.

Since follow-up of TAF was short and the rate of cardiac events low, our observations need to be confirmed in larger cohorts, to better advise about the use of TAF in elder patients with a history of cardiac events

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