EVOLUTION AND REVERSIBILITY OF RENAL FUNCTION AFTER SWITCH FROM TDF TO TAF REGIMENS

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Roberta Gagliardini[1] Patrizia Lorenzini[1], Alessandro Cozzi-Lepri[2], Nicola Gianotti[3], Loredana Sarmati[4], Stefano Rusconi[5], Emanuela Messina[3], Amedeo Capetti[5], Annalisa Saracino[6], Giordano Madeddu[7], Antonella D'Arminio Monforte[8], Andrea Antinori[1], for the Icona Foundation Study Group

[1] Lazzaro Spallanzani National Institute for Infectious Diseases IRCCS, Rome, Italy; [2]University College London, London, UK; [3]San Raffaele Scientific Institute, Milan, Italy; [4]University of Rome Tor Vergata, Rome, Italy; [5]ASST Fatebenefratelli, Milan, Italy; [6]University of Bari, Bari, Italy; [7]University of Sassari, Sassari, Italy; [8]University of Milan, Milan, Italy

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BACKGROUND

- Tenofovir alafenamide (TAF), a pro-drug of tenofovir disoproxil fumarate (TDF) is associated to higher intracellular concentration of tenofovir diphosphate and 91% lower serum concentration of tenofovir, compared to TDF, with less renal and bone toxicity.
- Switching TDF to TAF in randomized clinical trials has shown:
  - Variable eGFR improvement;
  - Marginal benefit in safety with unboosted regimes, according to a recent meta-analysis[1].
- Reversibility of renal function when TDF is discontinued is matter of debate:
  ~37-60% reversibility in observational studies[2-4].

STUDY DESIGN AND METHODS

STUDY POPULATION

- It is a retrospective analysis of prospectively collected data from the Icona Foundation Cohort, an observational cohort, set up in 1997, including HIV-1-infected subjects, naïve from ART at the time of enrolment, involving 51 centers in Italy.
- HIV+ subjects from the Icona Foundation Cohort switching from TDF to TAF maintaining the same third drug (and the same booster, if present), with at least two evaluations before switch and one after switch, were included in the analysis. Regimens including atazanavir were excluded due to its detrimental effect on renal function.
- Renal function was evaluated by eGFR (estimated glomerular filtration rate), through CKD-EPI formula. Due to the strong relationship between increasing age and declining kidney function, we considered age in CKD-EPI formula both as an updating value and as a constant for each patient, using age at switch from TDF to TAF (sensitivity analysis).

STUDY OBJECTIVES

- **Primary objective**:
  - Evaluate reversibility of renal function after switch from TDF to TAF in boosted and unboosted regimens;
- **Secondary objectives:**
  - Compare variation in renal function at 3-12 months after switch from TDF to TAF in boosted and unboosted regimens;
  - Analyze predictors of eGFR recovery after switch from TDF to TAF.

ENDPOINTS

- Proportion of patients with recovery of eGFR after switch to TAF to the eGFR before TDF introduction (recovery was defined as the first of 2 consecutive eGFRs within 5% of the eGFR at the time of TDF initiation);
- Change in eGFR at 3-12 months (the later measurement) after switch from TDF to TAF;
- Proportion of patients with ≥25% eGFR improvement after switch to TAF;
- Proportion of patients with a change of eGFR category in CKD (Chronic Kidney Disease, from 60-89 mL/min/1.73 m² to ≥90).

STATISTICAL ANALYSIS

- T-test for paired samples was used to analyze eGFR changes;
- Poisson regression analysis was used to analyze predictors of eGFR reversibility;
- Kaplan-Meier curves were used to analyze the estimated probability of regaining eGFR.

RESULTS

PATIENTS BASELINE CHARACTERISTICS

1726 patients switching from TDF/FTC to TAF/FTC were evaluated: 1009 were receiving an unboosted regimens, 717 a boosted one (Figure 1 and Table 1). Median follow-up after switch was 8 months (IQR 6-12).

Figure 1 – Patients disposition

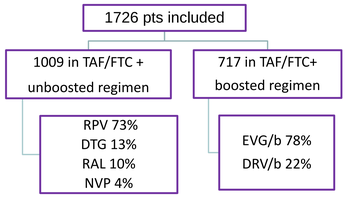
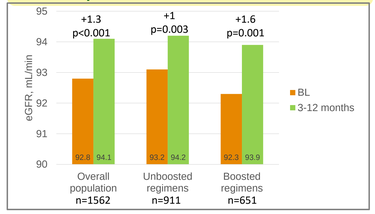


Table 1 – Patients baseline characteristics

	Unboosted (n=1009)	Boosted (n=717)	P value
Female gender	190 (18.8%)	122 (17%)	0.334
Age, years *	44 (36-52)	44 (36-52)	0.733
Mode of HIV transmission			
heterosexual	348 (34.5%)	263 (36.7%)	0.071
IVDU	97 (9.6%)	44 (6.1%)	
homosexual	498 (49.4%)	359 (50.1%)	
other/unknown	66 (6.5%)	51 (7.1%)	
CDC stage C	90 (8.9%)	103 (14.4%)	<0.001
Years of HIV infection *	5.6 (3.2-9.4)	3.6 (2.1-7.9)	<0.001
HCV antibodies			
negative	815 (80.8%)	582 (81.2%)	<0.001
positive	123 (12.4%)	57 (8.0%)	
missing	69 (6.8%)	78 (10.9%)	
HBs antigene			
negative	842 (83.5%)	551 (76.9%)	0.001
positive	59 (5.9%)	46 (6.4%)	
missing	108 (10.7%)	120 (16.7%)	
Nadir CD4, cell/mmc *	332 (214-462)	283 (131-443)	<0.001
CD4 at BL, cell/mmc *	714 (539-922)	630 (434-857)	<0.001
HIV-RNA < 50 cp/mL at BL	855 (84.7%)	610 (85.1%)	0.466
Years of ART *	3.8 (2.3-6.3)	2.7 (1.6-5.3)	<0.001
Years of TDF exposure *	3.5 (2.1-5.6)	2.6 (1.4-4.5)	<0.001
eGFR pre-TDF, mL/min *	108.5 (98-117)	108.1 (98-117)	0.804
eGFR at BL, mL/min *	94.5 (82-106)	93 (81-106)	0.295

Values are expressed as n(%), except for * median (IQR).
Notes: IVDU, Intravenous Drug Use; BL, baseline (switch from TDF to TAF); ART, antiretroviral therapy; eGFR, estimated glomerular filtration rate.

Figure 2– Evolution of eGFR after 3-12 months post switch from TDF to TAF



No differences in mean changes of eGFR between the two groups were observed.

RESULTS

After switching from TDF to TAF:

- a **change of eGFR category** (from 60-89 to ≥90 mL/min/1.73 m²) in CKD was observed in **22.0% of patients** (152/692);
- an **eGFR improvement ≥ 25%** was observed only in **3.2% of patients** (56/1726).

Among those patients with at least an eGFR measurement during TDF therapy inferior to eGFR pre-TDF introduction (n=1392), **23%** (318/1392) **had a recovery of eGFR to pre-TDF values**.

In a multivariate model adjusted for CDC stage and age, being on **a boosted regimen** and **a longer duration of TDF exposure predicted a lower probability of recovery** (Table 2). A sensitivity analysis updating age in eGFR evaluation confirmed similar results (boosted vs unboosted regimen, aIRR 0.72 [95% CI 0.57-0.91], p=0.006).

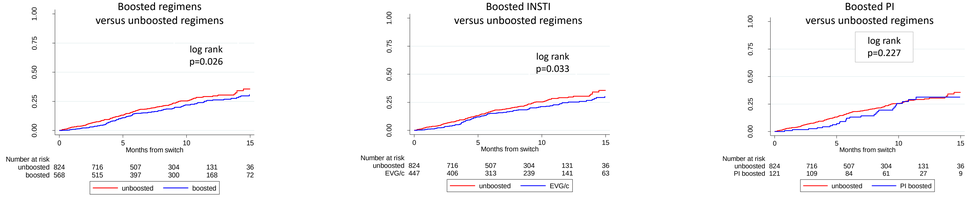
Table 2 – Predictors of eGFR recovery to pre-TDF values

	aIRR	95% CI	P value
CDC stage C	0.83	0.55- 1.25	0.365
Age (+10 years)	0.96	0.87- 1.06	0.427
Years of TDF exposure (+ 1 year)	**0.90**	**0.86- 0.94**	**<0.001**
Boosted vs unboosted regimen	**0.74**	**0.59- 0.92**	**0.008**

Notes: aIRR, adjusted incident rate ratio; CI, confidence intervals.
Variables explored in the model were: gender, age, mode of HIV transmission, ethnicity, years of HIV infection, HCV and HBV coinfection, nadir CD4, current CD4, current CD8, current HIV-RNA, duration of ART exposure, number of previous regimens, smoke habit, hypertension and diabetes.

The estimated probabilities of **recovery of eGFR to pre-TDF values was slightly higher with unboosted regimens**, as shown in Figure 3.

Figure 3 – Estimated probabilities of recovery of eGFR to pre-TDF values



DISCUSSION and CONCLUSIONS

✓ Limitations of the study:
- Short follow up;
- No data about proteinuria or markers of tubular dysfunction;
- Poor representation of boosted PI (due to the design of the study).

✓ Conclusions:
- After switch from TDF to TAF a small but statistically significant improvement in eGFR was observed; the clinical relevance of this improvement remains to be clarified;
- A complete recovery of renal filtrate was demonstrated only in 23% of cases;
- Unboosted regimens seem to be associated with a higher probability of regaining renal filtrate;
- The association of a boosted regimen with TDF was confirmed as to be avoided;
- These data may be useful for defining in which patients to switch to TAF or to maintain TDF without jeopardizing renal function.

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References and notes

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Notes: results presented in this poster refer to data updated with respect to the submitted abstract.

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Contact Information

Roberta Gagliardini, MD, Lazzaro Spallanzani National Institute for Infectious Diseases IRCCS, Rome, Italy, roberta.gagliardini@inmi.it