Switching to FTC/TAF from FTC/TDF in Virologically Suppressed Patients receiving a Boosted PI or an Unboosted Third Agent

Introduction

Tenofovir alafenamide (TAF) is also an oral prodrug of TFV but is much more stable in plasma. Efficacy and safety of TAF have been mostly evaluated in the context of the coformulation of elvitegravir (E), cobicistat (C), emtricitabine (FTC, F), and TAF (E/C/F/TAF) and have consistently demonstrated the advantages of TAF over TDF for renal and bone safety.

Aim

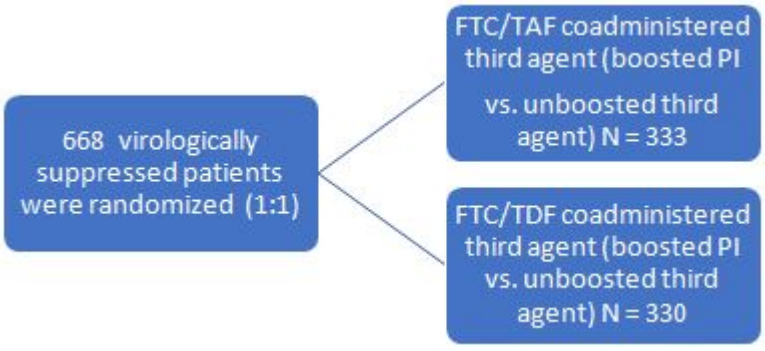
To evaluate the efficacy and safety of switching to FTC/TAF from FTC/TDF by third agent (boosted protease inhibitor [PI] vs unboosted third agent).

Patient Profile

HIV-infected adults (aged ≥18 years) who were virologically suppressed (HIV-1 RNA <50 copies/mL) for at least 6 months on FTC/TDF-containing regimens and had creatinine clearance (CrCl) of >50 mL/min (calculated by the Cockcroft-Gault [CG] equation)

Methods

- Randomized, double-blind, active-controlled phase 3 trial
- 48-week subgroup analysis based on the third agent



- Participants on boosted PIs (atazanavir [ATV] + ritonavir [RTV], darunavir [DRV] + RTV, or lopinavir/RTV [LPV/r])
- Unboosted third agents (efavirenz [EFV], rilpivirine [RPV], nevirapine [NVP], raltegravir [RAL], dolutegravir [DTG], or maraviroc [MVC]) received FTC/TAF 200/25 mg

Assessments

- Laboratory tests included haematological analysis, serum chemistry tests, fasting lipid parameters, CD4 counts, measures of renal function (CrCl, urine protein to creatinine ratio, urine albumin to creatinine ratio, retinol-binding protein to creatinine ratio, and ß2-microglobulin to creatinine ratio and measurement of HIV RNA concentration
- Virological failure was defined as either having virological rebound confirmed within 3–6 weeks or being viremic at the study endpoint or at the time of study drug discontinuation with plasma HIV-1 RNA of 50 copies/mL or higher

Results

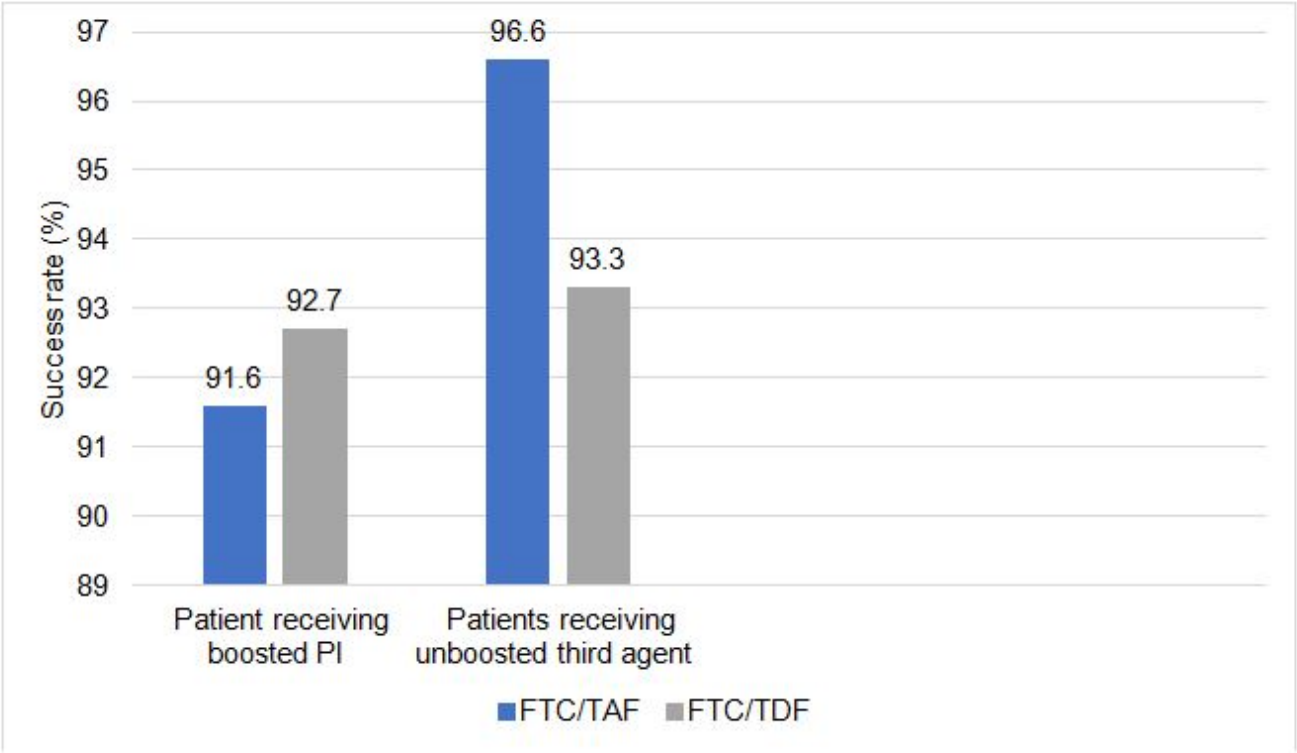
- Baseline characteristics were similar between treatment groups

  - The median (Q1, Q3) age was 49 (22, 79) years
  - 15% were female
  - The median baseline CD4 count was 646 (491, 835) cells/ µL, with approximately three quarters (74.2%) of subjects having a baseline CD4 count ≥500 cells/µL
  - The percentages of participants taking boosted PIs or unboosted third agents were similar between the two treatment groups (boosted PI: FTC/TAF 47%, FTC/TDF 45%; unboosted third agent: FTC/TAF 53%, FTC/TDF 55%).
  - Overall, the median time of FTC/TDF use prior to dosing was 5.1 years.
  - Most subjects (91%) had no proteinuria (Grade 0 by dipstick) on urinalysis, and baseline CrCl was similar between the two treatment groups

Efficacy Analyses

- Virologic success rates at week 48 were similar between treatment groups for those who received a boosted PI and for those who received an unboosted third agent
- Regardless of the third agent (boosted PI or unboosted third agent), FTC/TAF was noninferior to FTC/TDF in maintaining virologic suppression at week 48

Figure 1: Virological success rate at week 48



- Regardless of third agent, mean changes in CD4 cell counts were small and similar between groups
  - boosted PI with FTC/TAF: + 21 cells/ µL, FTC/TDF: + 7 cells/µL;
  - unboosted third agent with FTC/TAF: + 20 cells/µL, FTC/TDF: + 19 cells/µL

Safety Analyses

- Both regimens, regardless of the third agent, were well tolerated through week 48
- At week 48, significant differences in renal biomarkers were observed favouring FTC/TAF over FTC/TDF ($p < 0.05$ for all), with similar improvements in the FTC/ TAF arm in those who received boosted PI vs unboosted third agents.

Table 2: Changes in Renal biomarkers

	Boosted PI		**Unboosted third agent**	
	FTC/TAF (*n* = 155)	**FTC/TDF (*n* = 151)**	**FTC/TAF (*n* = 178)**	**FTC/TDF (*n* = 179)**
Serum creatinine µmol/L				
Baseline	91.1(32.5)	89.3 (17.3)	92.8 (15.0)	91.1 (17.9)
Change at week 48*	−7.1 (29.5)	−2.7 (13.5)	−6.2 (9.2)	−3.5 (8.8)
Urine protein to creatinine ratio (mg/g)				
Baseline, median	57.8 (39.4, 111.7)	66.7 (43.8, 104.2)	60.6 (42.6, 94.1)	59.6 (41.0, 95.1)
% change at week 48*	−11.1 (−38.4, 20.3)	12.8 (−15.7, 57.3)	−16.9 (−39.5, 11.6)	2.1 (−27.0, 40.0)

Urine albumin to creatinine ratio (mg/g				
Baseline	6.3 (4.0, 14.8)	6.4 (4.2, 12.0)	5.8 (4.1, 11.5)	6.1 (4.3, 11.8)
% change at week 48*	−1.8 (−41.6, 43.6)	21.2 (−11.2, 69.2)	−11.6 (−39.7, 25.7)	4.4 (−24.3, 41.1)
Urine β2-microglobulin to creatinine ratio (µg/g)				
Baseline	140.3 (76.7, 444.8)	186.5 (85.4, 604.3)	131.9 (67.1, 508.3)	134.2 (73.2, 349.8)
% change at week 48*	−39.3 (−63.4, 13.4)	36.4 (−22.7, 150.5)	−40.2 (−73.8, 5.5)	14.0 (−26.3 124.0)
Urine retinol-binding protein to creatinine ratio (µg/g)				
Baseline	112.4 (74.0, 256.2)	117.5 (80.8, 253.5)	100.9 (66.7, 183.3)	106.8 (74.8, 182.6)
% change at week 48*	−13.5 (−58.2, 22.9)	24.8 (−19.0, 118.8)	−17.3 (−42.3, 17.2)	11.8 (−19.0, 69.7)

*Values are presented as median (IQR), except for serum creatinine, which is presented as mean (SD). *P values for all between-group differences (FTC/TAF vs FTC/TDF) at week 48 were <0.05, except for total cholesterol to HDL ratio. FTC = emtricitabine; eGFR = estimated glomerular filtration rate*

- BMD increased in the FTC/ TAF group while remaining stable or decreasing in the FTC/TDF group

Table 3: Change in Spine and Hip BMD

	Boosted PI			**Unboosted Third Agent**		
	FTC/TAF (*n* = 155)	**FTC/TDF (*n* = 151**	**P value**	**FTC/TAF (*n* = 178)**	**FTC/TDF (*n* = 179)**	**P-value**
Mean % change in spine BMD	1.544	-0.354	<0.001	1.511	-0.081	<0.001
Mean % change in Hip BMD	1.233	-0.089	<0.001	1.051	-0.205	<0.001

- At week 48, small increases from baseline in fasting lipids were observed in the FTC/TAF group as compared with minimal changes among those who remained on an FTC/ TDF regimen regardless of the third agent

Conclusion

- In virologically suppressed patients, FTC/TAF demonstrated high efficacy in along with renal and

bone safety advantages regardless of the class of coadministered third agent
- FTC/TAF offers safety advantages over FTC/TDF
- The findings suggested that FTC/TAF offers an essential option as an NRTI backbone for use with a spectrum of third agents in the treatment of HIV-infected patients

Reference

HIV Clinical Trials.2017; 18;3:135-140.