P019

Tenofovir Alafenamide vs Tenofovir DF in Women: Pooled Analysis of 7 Clinical Trials

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Introduction

- Globally, the majority of people living with HIV (PLH) are cis-women, and the number of women acquiring HIV infection continues to rise[1]
- Research guidelines have long advocated for sex-based assessment of drug efficacy, toxicity, and tolerability profiles, but women continue to be underrepresented in clinical trials assessing efficacy and safety of antiretroviral treatment (ART) among PLH[2,3]
- One of the consequences of this restricted representation is the absence of definitive information about the specific efficacy and safety of ART in women[4-10]
- Tenofovir alafenamide (TAF) has demonstrated an improved renal and bone safety profile relative to tenofovir disoproxil fumarate (TDF) in multiple randomised trials with similar efficacy[11-15]

Objective

- To evaluate the efficacy and safety of TAF vs TDF for ART initiation or switch in cis-women in a pooled analysis of 7 studies (only including cis-women, referred to as women herein), and to compare outcomes to those in men

Methods

Studies Included in Integrated Analysis

779 women from 7 (5 double-blind, 2 open-label) randomised studies*

292-0104	N=867	E/C/F/TAF vs E/C/F/TDF
292-0111	N=866	E/C/F/TAF vs E/C/F/TDF
Treatment Naïve (n=2 studies, 260 women)		

380-1878 OL	N=577	B/F/TAF vs boosted PI-regimens
366-1160	N=875	FTC/RPV/TAF vs EFV/FTC/TDF
366-1216	N=630	FTC/RPV/TAF vs FTC/RPV/TDF
311-1089	N=663	F/TAF + 3rd agent vs F/TDF + 3rd agent
292-0109 OL	N=1436	E/C/F/TAF vs TDF-containing regimens
Virologically Suppressed (n=5 studies, 519 women)		

Outcomes
- Efficacy (Snapshot analysis)
- Safety
  - Overall (most common AEs)
  - Renal
    - AEs, AEs leading to discontinuation, cases of proximal renal tubulopathy (PRT) or Fanconi syndrome
    - eGFR by Cockcroft-Gault (CrCl; mL/min)
    - Glomerular proteinuria (UACR), tubular proteinuria (urine RBP:Cr and β2M:Cr)
  - Bone (BMD)

*Individual studies were not powered to evaluate outcomes by sex. AE, adverse event; B, BIC, bictegravir; BMD, bone mineral density; β2M, β2-microglobulin; C, cobicistat; CrCl, creatinine clearance; E (or EVG), elvitegravir; EFV, efavirenz; eGFR, estimated glomerular filtration rate; F (and FTC), emtricitabine; PI, protease inhibitor; RBP, retinol-binding protein; R, RPV, rilpivirine; SCr, serum creatinine; UACR, urine albumin creatinine ratio.

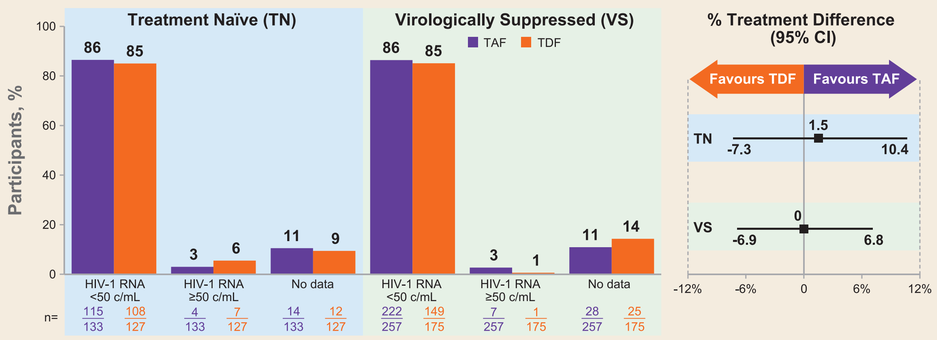
Results

Pooled Baseline Characteristics

		Treatment Naïve		Virologically Suppressed	
		TAF (n=133)	TDF (n=127)	TAF (n=296)	TDF (n=223)
Median age, y (range)		37 (19, 66)	40 (18, 63)	47 (22, 73)	47 (22, 69)
Race/ethnicity, %	Black or African descent	38	32	48	53
	Hispanic/Latina ethnicity	24	27	25	24
Region, %	US	38	42	72	74
	Ex-US	62	58	28	26
Median body mass index, kg/m^2 (IQR)		25 (22, 31)	26 (22, 31)	29 (24, 34)	27 (24, 32)
Median HIV-1 RNA, log$_{10}$ copies/mL (IQR)		4.5 (4, 5)	4.5 (4, 5)	—	—
Median CD4 cell count, cells/μL (IQR)		358 (243, 480)	367 (276, 450)	726 (578, 909)	689 (508, 909)
Median eGFR$_{CG}$, mL/min (IQR)		116 (91, 136)	104 (89, 129)	107 (87, 128)	100 (77, 121)
Medical history, %	Diabetes mellitus	6	10	9	7
	Hypertension	17	19	34	30
	Cardiovascular disease	2	0	4	1
	Hyperlipidemia	7	13	36	25

IQR, interquartile range.

Virologic Outcomes at Week 96 by FDA Snapshot



CI, confidence interval; FDA, Food and Drug Administration.

- Of TN men, 87% on TAF and 85% on TDF achieved HIV-1 RNA <50 c/mL at Week 96; suppression was maintained in 91% of VS men on TDF vs 89% on TAF
- **Efficacy results were similar for TAF vs TDF in both women and men**

Most Common AEs in Treatment-Naïve Women Through Week 144

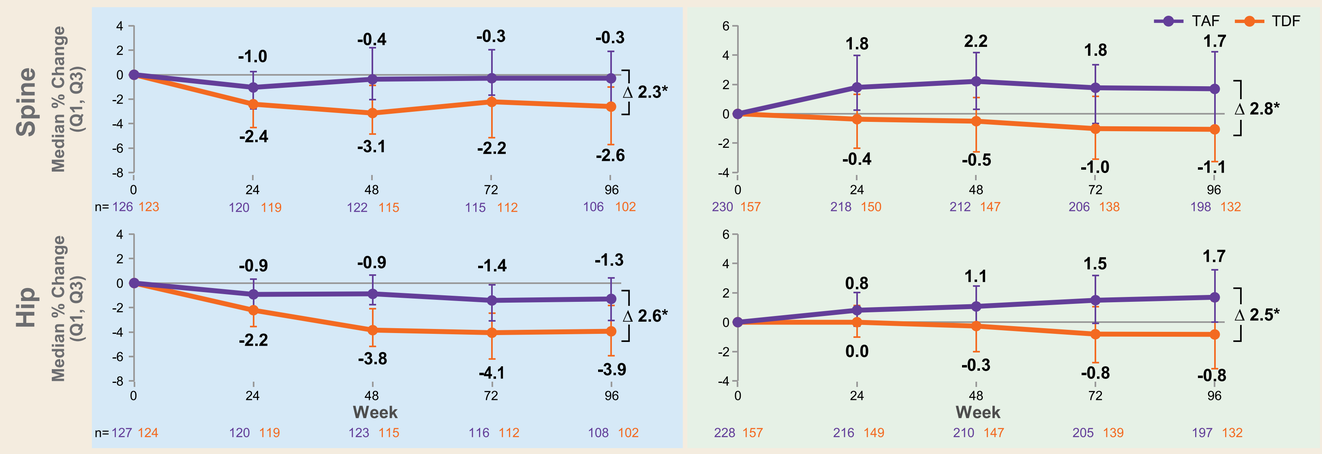
n (%)	TAF (n=133)	TDF (n=127)
Nausea	24 (18)	40 (31)
Nasopharyngitis	30 (23)	32 (25)
Headache	28 (21)	28 (22)
URTI	26 (20)	27 (21)
Diarrhoea	29 (22)	21 (17)
Arthralgia	23 (17)	21 (17)
Urinary tract infection	18 (14)	20 (16)
Dizziness	16 (12)	19 (15)
Back pain	16 (12)	18 (14)
Vaginal disharge	16 (12)	14 (11)
Vomiting	15 (11)	14 (11)
Osteopenia	16 (12)	10 (8)
Abdominal pain	14 (11)	4 (3)

AEs, adverse events; URTI, upper respiratory tract infection.

- Incidence of individual AEs in women was similar for TAF vs TDF and consistent with men
- Discontinuation due to AE/death was 0% on TAF vs 1.6% on TDF in TN women and 1.3% (TAF) vs 2.2% (TDF) in VS women through Week 96
- **TAF was well-tolerated in women with a similar overall safety profile for TAF and TDF, and consistent with data in men**

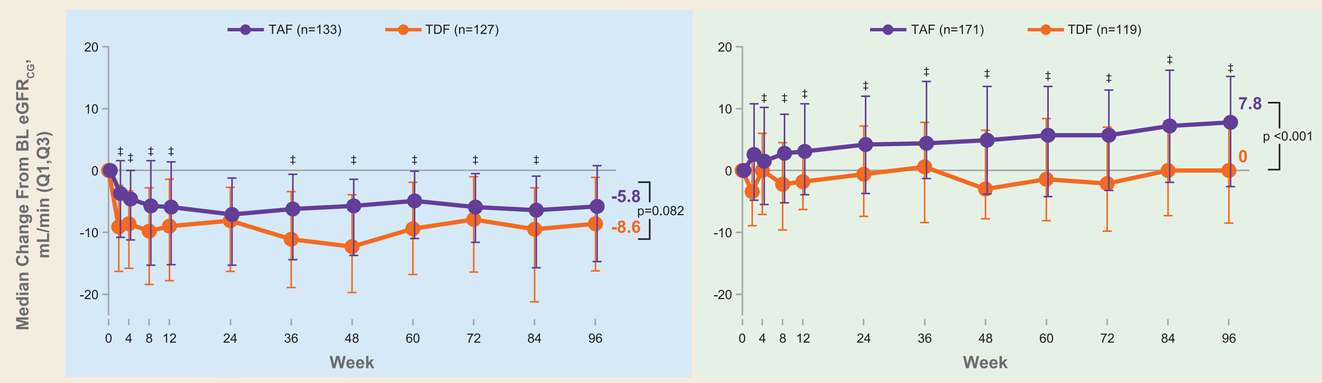
Results (cont'd)

Changes in Bone Mineral Density (BMD) Through Week 96



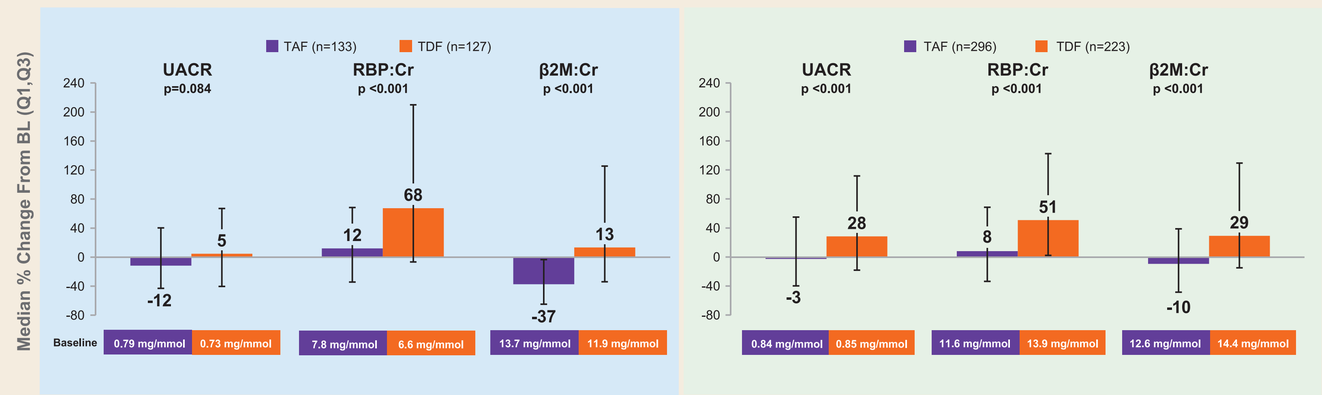
- In TN men, median % change in BMD was -1.0 on TAF and -2.8 on TDF (spine)* and -0.8 on TAF and -3.5 on TDF (hip)* at Week 96
- In VS men, these values were 1.8 for TAF vs 0 for TDF (spine)* and 1.8 for TAF vs -0.5 for TDF (hip)*
- **Women initiating TAF had less BMD decline vs TDF, and women switching to TAF from TDF had improvements in BMD; similar to results in men**

Changes From Baseline in eGFR$_{CG}$ Through Week 96†



- In TN men, median change in eGFR$_{CG}$ was -4.7 mL/min on TAF and -8.0 on TDF‡; in VS men, median eGFR increased by 5.8 mL/min with switch to TAF vs 0.7 staying on TDF‡
- **Women initiating TAF had numerically less eGFR decline vs TDF, and women switching to TAF from TDF had improvements in eGFR, consistent with data in men**

Changes From Baseline in Renal Biomarkers at Week 96



- In TN men, median % change (TAF vs TDF) in UACR was -4 vs 5*; RBP:Cr was 14 vs 75*; β2M:Cr was -30 vs 37*
- In VS men, median % change (TAF vs TDF) in UACR was -6 vs 27*; RBP:Cr was -3 vs 62*; β2M:Cr was -30 vs 55*
- **Women initiating or switching to TAF had less tubular proteinuria (RBP:Cr, β2M:Cr) vs TDF, similar to results in men**

*p <0.001, calculated from analysis of variance model including study and treatment as fixed effects for BMD and by Wilcoxon rank-sum test for renal biomarkers; †VS group excluded women who switched from EFV/FTC/TDF; ‡Significant treatment difference between TAF and TDF (calculated from 2-sided Wilcoxon rank-sum test). Q, quartile; TN, treatment naive; VS, virologically suppressed.

Treatment-Emergent Renal AEs at Week 96

	Treatment Naïve			Virologically Suppressed		
TEAE, %	**TAF (n=133)**	**TDF (n=127)**	**p-value**	**TAF (n=296)**	**TDF (n=223)**	**p-value**
Renal and urinary disorders	5 (4)	10 (8)	0.19	14 (5)	14 (6)	0.44
Dysuria	1 (1)	2 (2)		3 (1)	4 (2)	
Proteinuria	2 (2)	3 (2)		4 (1)	3 (1)	
Haematuria	1 (1)	4 (3)		2 (1)	2 (1)	
Pollakiuria	1 (1)	0		3 (1)	1 (<1)	
Oliguria	0	2 (2)		—	—	
Renal failure	0	1 (1)		—	—	
Acute kidney injury	—	—		0	2 (1)	
Chronic kidney disease	—	—		1 (<1)	1 (<1)	
Chromaturia	—	—		1 (<1)	0	
Leukocyturia	—	—		1 (<1)	0	
Polyuria	—	—		0	1 (<1)	
Sterile pyuria	—	—		0	1 (<1)	
TEAEs leading to drug discontinuation						
Renal and urinary disorders	0	1 (1)	0.31	0	1 (<1)	0.43
Chronic kidney disease	0	0		0	1 (<1)	
Renal failure	0	1 (1)		0	0	

TEAE, treatment-emergent adverse event.

- In women, there were no cases of proximal renal tubulopathy or Fanconi syndrome with TAF vs 1 with TDF*; in men there were 0 cases with TAF vs 9 with TDF

*E/C/F/TDF.

Conclusions

- Cis-women who initiated or switched to TAF had significantly improved BMD and renal tubular biomarkers compared to those on TDF, with similar rates of virologic suppression through Week 96
- Results were similar to those in men
- These pooled data from 7 studies demonstrate a safety advantage for initiating therapy with or switching to TAF compared to TDF in women

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