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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 rise¹
- 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 women⁴⁻¹⁰
- Tenofovir alafenamide (TAF) has demonstrated an improved renal and bone safety profile relative to tenofovir disoproxil fumarate (TDF) in multiple randomized trials with similar efficacy¹¹⁻¹⁵

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

randomize	n from d studi	/ (5 double-blind, 2 open-labe es*		
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	y Suppr	essed (n=5 studies, 519 women)		

Outcomes

- Efficacy (Snapshot analysis)
- Safety
- Overall (most common AEs)
- AEs, AEs leading to discontinuation, cases of proxima renal tubulopathy or Fanconi syndrome
- eGFR by Cockcroft-Gault (CrCl; mL/min)
- Glomerular proteinuria (UACR), tubular proteinuria
- (urine RBP:Cr and β 2M:Cr)
- Bone (BMD)

ndividual studies were not powered to evaluate outcomes by sex. AE, adverse event; B, BIC, bictegravir; BMD, bone mineral density; β2M, β2-macroglobulin; C, cobicistat; CrCl, creatinine clearance; E (or EVG), elvitegravir; EFV, efavirenz; GR, 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

c, copies; IQR, interquartile range.

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		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 c/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	

Tenofovir Alafenamide vs Tenofovir DF in Women: Pooled Analysis of 7 Clinical Trials Melanie A. Thompson,¹ Indira Brar,² Cynthia Brinson,³ Catherine M. Creticos,⁴ Debbie Hagins,⁵ Ellen Koenig,⁶ Claudia T. Martorell,⁷ Cristina Mussini,⁸ Laura Waters,⁹ Susan Guo,¹⁰ Ya-Pei Liu,¹⁰ Lauren Temme,¹⁰ Devi SenGupta,¹⁰ Moupali Das¹⁰

Virologic Outcomes at Week 96 by FDA Snapshot



 Of treatment naïve men, 87% on TAF and 85% on TDF achieved HIV-1 RNA <50 c/mL at Week 96; suppression was maintained in 91% of virologically suppressed 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)
Diarrhea	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 discharge	16 (12)	14 (11)
Vomiting	15 (11)	14 (11)
Osteopenia	16 (12)	10 (8)
Abdominal pain	14 (11)	4 (3)
URTL upper respiratory tract infection		

Incidence of individual AEs in women was similar for TAF vs TDF and was similar in men, with the exception of nausea which appeared to be lower in women on TAF

Discontinuation due to AE/death was 0% on TAF vs 1.6% on TDF in treatment naïve women and 1.3% (TAF) vs 2.2% (TDF) in virologically suppressed 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



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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[†]

Treatment-Emergent Renal AEs at Week 96

Conclusions

Cis-women who initiated or switched to TAF had significantly improved BMD and renal 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

	Treatment Naïve Virolog			gically Suppressed		
AE, n (%)	TAF (n=133)	TDF (n=127)	p-value	TAF (n=296)	TDF (n=223)	p-value
nal 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)	
Hematuria	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)	
AEs leading to drug discontinuation	n					
nal 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	

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 10 with TDF