PE9/50

Safety and Efficacy of Switching From Tenofovir Disoproxil Fumarate to Tenofovir Alafenamide in People With HIV Aged 50 Years and Older

Hans-Jürgen Stellbrink,[1] Frank A. Post,[2] Daniel Podzamczer,[3] Jose Arribas,[4] Eric Cua,[5] Jean-Michel Molina,[6] Chloe Orkin,[7] Jürgen K. Rockstroh,[8] Christoph Carter,[9] Ya-Pei Liu,[9] Lijie Zhong,[9] Moupali Das,[9] Lauren Temme,[9] Laura Waters[10]

[1]ICH Study Center, Hamburg, Germany; [2]King's College Hospital, London, UK; [3]Hospital Universitari de Bellvitge, Barcelona, Spain; [4]Hospital Universitario La Paz, Madrid, Spain; [5]Hôpital L'Archet, Nice, France; [6]Hôpital Saint-Louis, Paris, France; [7]Barts Health NHS Trust, London; [8]Universitätsklinikums Bonn, Germany; [9]Gilead Sciences, Inc., Foster City, California, USA; [10]Mortimer Market Centre, London

Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404
800-445-3235

Introduction

- The Joint United Nations Programme on HIV/AIDS estimates that 5.7 million people aged ≥50 y were living with HIV as of 2016[1]
- In Europe, the increasing number of people living with HIV aged ≥50 y (PWH50+) has been attributed to both improved life expectancy of PWH and an increase in new HIV diagnoses among people aged ≥50 y[2]
- The PWH50+ population has a greater burden of comorbidities and treatment side effects, creating additional challenges for HIV treatment[1]
- Tenofovir alafenamide (TAF) is a prodrug of tenofovir that achieves 90% lower plasma levels of tenofovir compared with tenofovir disoproxil fumarate (TDF)[3]
- TAF has similar antiviral efficacy compared with TDF, and is associated with improved renal safety and less bone mineral density (BMD) decline vs TDF[4-6]

Objectives

- To compare the efficacy and safety of switching from TDF- to TAF-containing antiretroviral regimens in PWH50+

Methods

Included Studies

Trial	Treatment Regimens	Duration	Age ≥/<50 y, n		
			TAF	TDF	Total
292-0109*	E/C/F/TAF vs TDF-containing regimens	96 wk	189/770	104/373	293/1143
311-1089	F/TAF + 3rd agent vs F/TDF + 3rd agent	96 wk	150/183	144/186	294/369
366-1160	R/F/TAF vs EFV/F/TDF	96 wk	205/233	198/239	403/472
366-1216	R/F/TAF vs R/F/TDF	96 wk	119/197	102/212	221/409
380-1878*	B/F/TAF vs boosted PI regimens	48 wk	104/141	88/155	192/296
Total			767/1524	636/1165	1403/2689

*Open-label studies. B, bictegravir; C, cobicistat; E, elvitegravir; EFV, efavirenz; F, emtricitabine; PI, protease inhibitor; R, rilpivirine.

Results

Pre-Switch Antiretroviral Regimens

Participants, n (%)	Age ≥50 y			Age <50 y		
	TAF n=767	TDF n=636	Total n=1403	TAF n=1524	TDF n=1165	Total n=2689
EFV/F/TDF	255 (33)	228 (36)	483 (34)	434 (29)	334 (29)	768 (29)
F/TDF + PI*	243 (32)	183 (29)	426 (30)	559 (37)	409 (35)	968 (36)
R/F/TDF	119 (16)	102 (16)	221 (16)	197 (13)	212 (18)	409 (15)
E/C/F/TDF	65 (8)	34 (5)	99 (7)	241 (16)	119 (10)	360 (13)
F/TDF + NNRTI†	48 (6)	44 (7)	92 (7)	37 (2)	34 (3)	71 (3)
F/TDF + INSTI‡	36 (5)	41 (6)	77 (5)	56 (4)	55 (5)	111 (4)
Other§	1 (<1)	4 (1)	5 (<1)	0	2 (<1)	2 (<1)

*Boosted atazanavir, darunavir, or lopinavir; †EFV, nevirapine, or RPV; ‡Dolutegravir or raltegravir; §Regimens containing TDF + maraviroc or maraviroc + raltegravir. INSTI, integrase strand transfer inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor.

Baseline Demographics

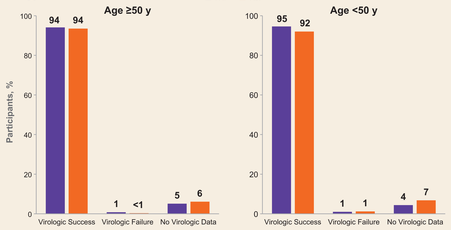
	Age ≥50 y			Age <50 y		
	TAF n=767	TDF n=636	Total n=1403	TAF n=1524	TDF n=1165	Total n=2689
Median age, y (range)	55 (50–78)	54 (50–79)	54 (50–79)	40 (20–49)	40 (19–49)	40 (19–49)
Sex at birth, n (%)						
Male	656 (86)	550 (86)	1206 (86)	1339 (88)	1028 (88)	2367 (88)
Female	111 (14)	86 (14)	197 (14)	185 (12)	137 (12)	322 (12)
Race, n (%)						
Black	159 (21)	129 (20)	288 (21)	326 (21)	274 (24)	600 (22)
Nonblack	606 (79)	507 (80)	1113 (79)	1191 (78)	886 (76)	2077 (77)
Ethnicity, n (%)						
Hispanic/Latinx	118 (15)	91 (14)	209 (15)	354 (23)	241 (21)	595 (22)
Not Hispanic/Latinx	648 (85)	545 (86)	1193 (85)	1167 (77)	921 (79)	2088 (78)

Baseline Medical Characteristics

	Age ≥50 y			Age <50 y		
	TAF n=767	TDF n=636	Total n=1403	TAF n=1524	TDF n=1165	Total n=2689
HIV RNA <50 copies/mL, n (%)	751 (98)	625 (98)	1376 (98)	1500 (98)	1148 (99)	2648 (98)
Median CD4 count/μL (Q1, Q3)	653 (491, 834)	616 (462, 808)	637 (478, 822)	674 (521, 850)	668 (524, 829)	671 (522, 842)
Median $eGFR_{CG}$, mL/min (Q1, Q3)	95 (79, 112)	95 (78, 111)	95 (79, 111)	111 (96, 131)	111 (94, 133)	111 (95, 132)
Median BMI, kg/m^2 (Q1, Q3)	27 (24, 30)	27 (24, 29)	27 (24, 30)	26 (23, 29)	26 (23, 29)	26 (23, 29)
Medical history, n (%)						
Diabetes	46 (8)	47 (9)	93 (8)	24 (3)	18 (2)	42 (3)
Hypertension	222 (38)	208 (39)	430 (39)	135 (18)	144 (18)	279 (18)
Cardiovascular disease	39 (7)	27 (5)	66 (6)	7 (1)	6 (1)	13 (1)
Hyperlipidemia	284 (49)	258 (49)	542 (49)	210 (28)	193 (24)	403 (26)

BMI, body mass index; CD4, cluster of differentiation-4; $eGFR_{CG}$, estimated glomerular filtration rate by Cockcroft-Gault; Q, quartile.

Virologic Efficacy: Week 48, Snapshot Algorithm

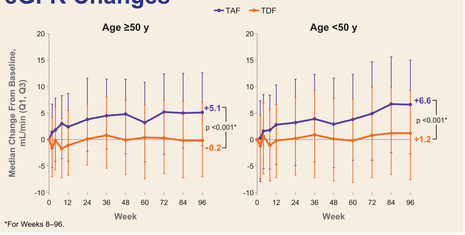


Adverse Events

AE, n (%)	Age ≥50 y		Age <50 y	
	TAF n=767	TDF n=636	TAF n=1524	TDF n=1165
Any AE	672 (88)	549 (86)	1364 (90)	1016 (87)
Grade 3 or 4	91 (12)	74 (12)	125 (8)	97 (8)
Any study drug-related AE	124 (16)	78 (12)	267 (18)	170 (15)
Leading to premature study drug discontinuation	4 (1)	14 (2)	9 (1)	11 (1)
Renal AE	37 (5)	37 (6)	77 (5)	52 (4)
Fanconi syndrome	0	2 (<1)	0	0
Bone AE	36 (5)	44 (7)	85 (6)	70 (6)

AE, adverse event.

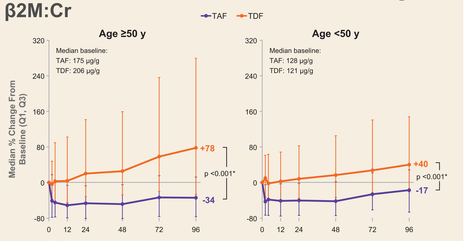
eGFR Changes



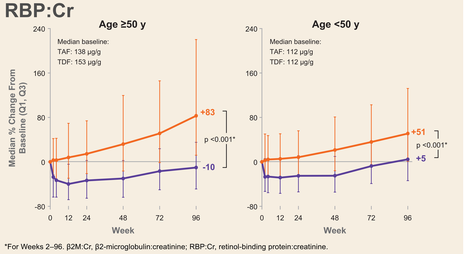
*For Weeks 8–96.

Proximal Tubule Biomarker % Changes

β2M:Cr



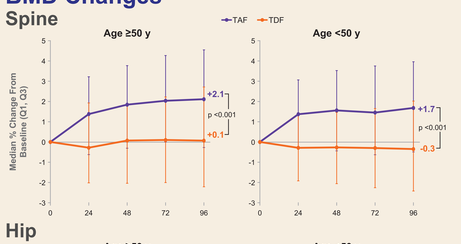
RBP:Cr



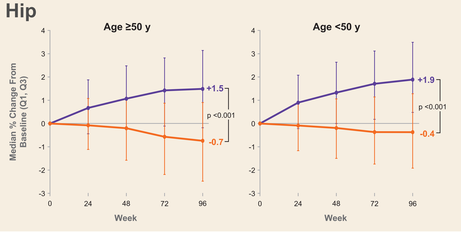
*For Weeks 2–96. β2M:Cr, β2-microglobulin:creatinine; RBP:Cr, retinol-binding protein:creatinine.

BMD Changes

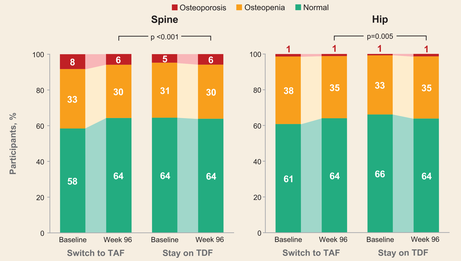
Spine



Hip

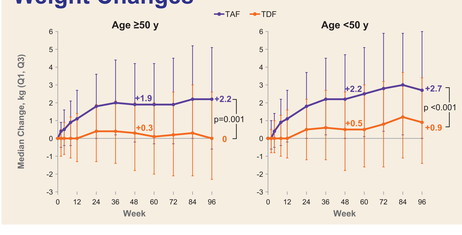


BMD Clinical Status Shifts in PWH50+*



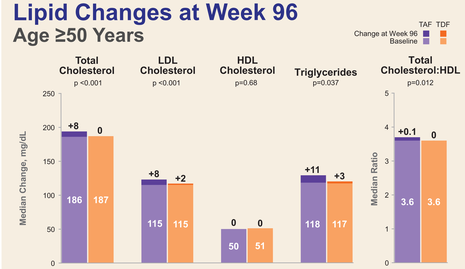
*p-values are from rank analysis of covariance adjusting for baseline clinical status for treatment comparison between TAF and TDF.

Weight Changes

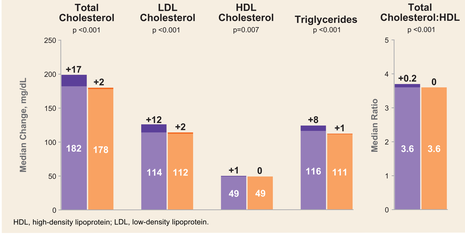


Lipid Changes at Week 96

Age ≥50 Years



Age <50 Years



HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Conclusions

- Among PWH50+ who switched from TDF to TAF:
  - High rates of virologic suppression were maintained
  - Improvements in eGFR and proximal tubular dysfunction were observed
  - Improvements in BMD were observed
  - Small increases in weight and cholesterol were observed, consistent with the removal of TDF-mediated weight and lipid suppression[7,8]
  - The observations in PWH50+ mirrored those in PWH aged <50 y
- Switching to TAF-based antiretroviral therapy preserves renal function and BMD, which is particularly relevant to PWH50+ in whom kidney disease and osteoporosis are of particular concern

References: **1.** Autenrieth CS, et al. PLoS One. 2018;13:e0207005; **2.** Tavoschi L, et al. Lancet HIV. 2017;4:e514-21; **3.** Ruane PJ, et al. J Acquir Immune Defic Syndr 2013;63:449-55; **4.** Arribas J, et al. J Acquir Immune Defic Syndr 2017;75:211-8; **5.** Gupta SK, et al. AIDS 2019;33:1455-65; **6.** Sax P, et al. J Acquir Immune Defic Syndr 2014;67:52-8; **7.** Glidden D, et al. Clin Infect Dis 2018;67:411-9; **8.** Tungsiripat M, et al. AIDS 2010;24:1781-4.

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