Efficacy and Safety of Switching to E/C/F/TAF in Virologically Suppressed Women

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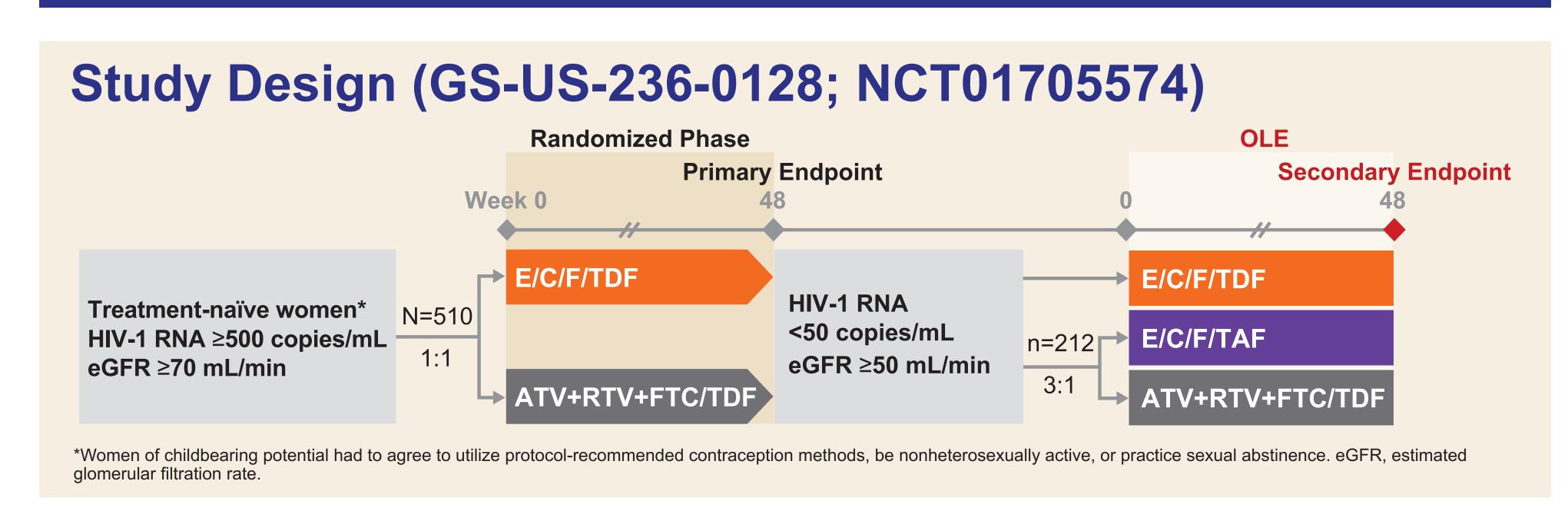
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Introduction

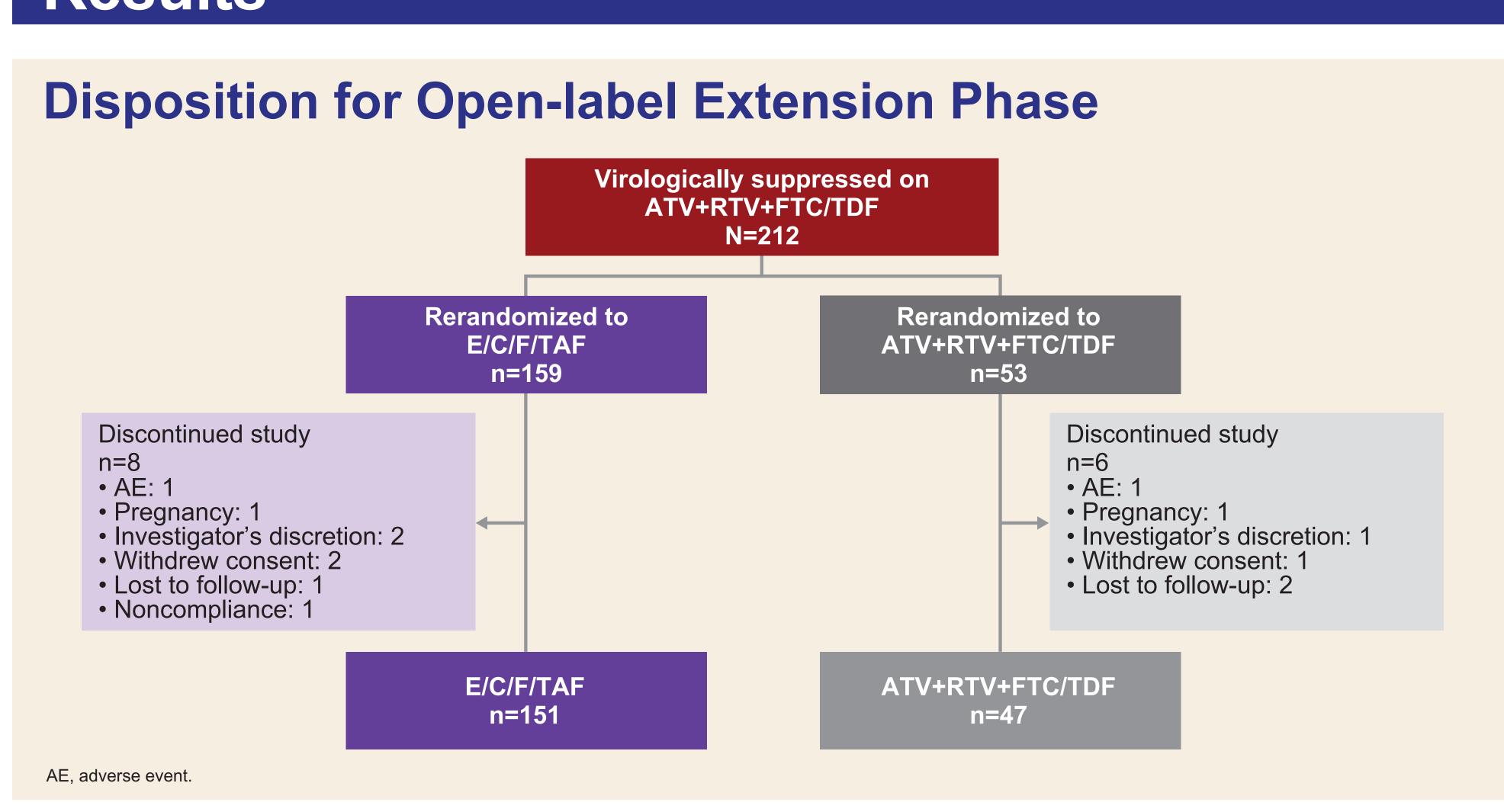
- Worldwide, women comprise 51% of people living with HIV, but remain underrepresented in clinical trials
- ◆ The integrase inhibitor—containing single-tablet regimen (elvitegravir/cobicistat/emtricitabine [FTC]/tenofovir disoproxil fumarate [E/C/F/TDF]) demonstrated superior efficacy to a protease inhibitor regimen (atazanavir [ATV] boosted by ritonavir [RTV] + FTC/TDF) in 575 treatment-naïve women at Week 48¹
- ◆ Tenofovir alafenamide (TAF) has an improved renal and bone safety profile compared with TDF^{2,3}
- ◆ TAF has been coformulated into a single-tablet regimen (E/C/F/TAF) that is recommended as an initial regimen in adults and adolescents^{4,5}
- ◆ Virologically suppressed women in the aforementioned study were given the option to switch to E/C/F/TAF in an open-label extension (OLE) phase, adding to the clinical understanding of the safety and efficacy of E/C/F/TAF in women

Methods



- Phase 3b, randomized, double-blind, active-controlled phase with rerandomized, open-label, active-controlled, extension phase
- ◆ Primary efficacy endpoint in randomized phase met: proportion of participants with HIV-1 RNA <50 copies/mL based on Week 48 FDA snapshot analysis¹
- Secondary endpoints: efficacy, safety, and tolerability at Week 48 in OLE
- ◆ OLE Week 48 analysis (E/C/F/TAF vs ATV+RTV+FTC/TDF) is presented

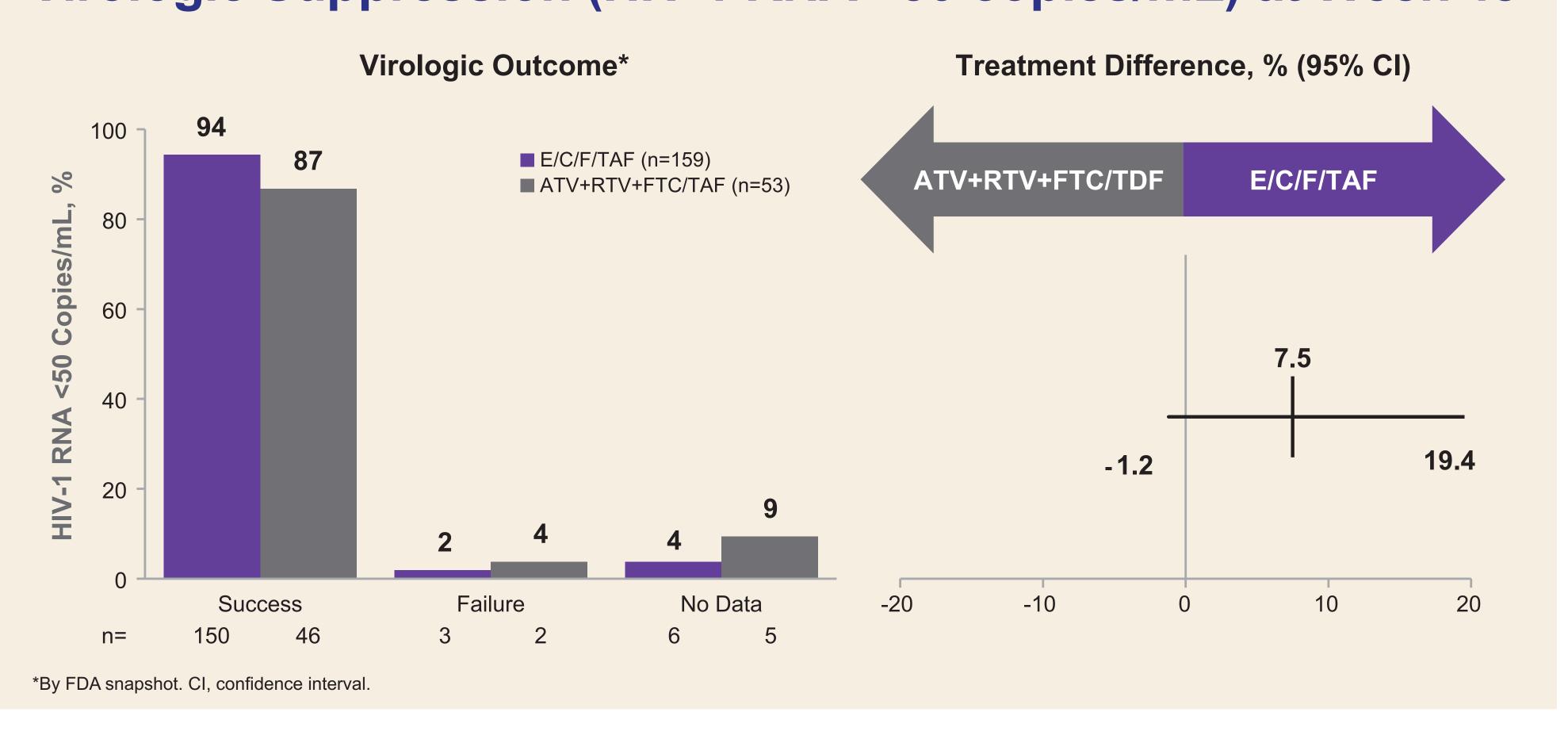
Results



Demographics and Baseline Characteristics

		E/C/F/TAF n=159	ATV+RTV+FTC/TDF n=53
Median age, y (range)		36 (19–63)	36 (21–62)
Race, n (%)	Black	69 (43)	32 (60)
	White	65 (41)	16 (30)
	Asian	12 (8)	3 (6)
Latino/Hispanic, n (%)		15 (9)	3 (6)
Median CD4 count, cells/μL (range)		580 (58–1602)	687 (96–1168)
Median eGFR _{cg} , mL/min (range)		103 (53–260)	101 (35–229)
Proteinuria grade, n (%)*	1	15 (9)	3 (6)
	2	0	1 (2)
HBV surface antigen status, n (%)	Negative	154 (97)	52 (98)
	Positive	5 (3)	0
HCV antibody status, n (%)	Negative	145 (91)	48 (91)
	Positive	14 (9)	4 (8)
o participants had Grade 3 or 4 proteinuria at baseline. C	G. Cockcroft-Gault: HBV. hepatitis B vir	rus: HCV. hepatitis C virus.	

Virologic Suppression (HIV-1 RNA <50 copies/mL) at Week 48



- Greater proportion of participants maintained virologic suppression with E/C/F/TAF vs ATV+RTV+FTC/TDF
- ♦ 85% on E/C/F/TAF vs 72% on ATV+RTV+FTC/TDF had HIV-1 RNA <20 copies/mL (difference 13%; 95% CI 0%, 28%)
- No emergent resistance mutations were detected in either group

Summary of Most Common Adverse Events

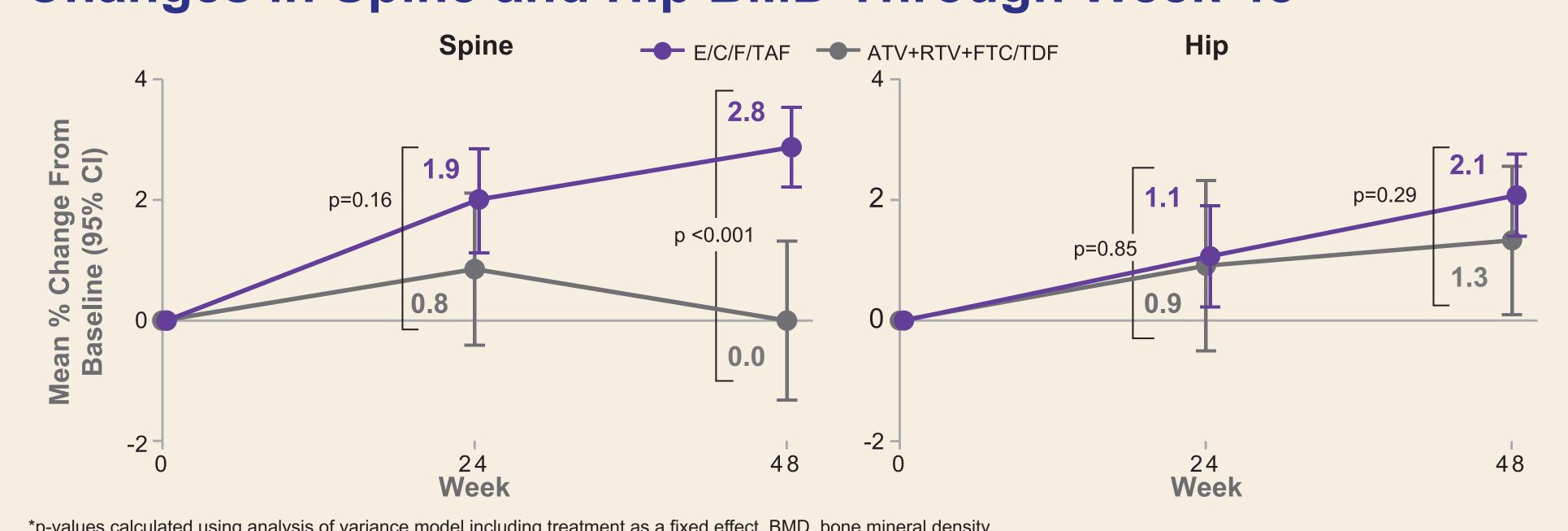
All Grades, n (%)*	E/C/F/TAF n=159	ATV+RTV+FTC/TDF n=53
Any treatment-emergent AE	111 (70)	31 (59)
Upper respiratory tract infection	19 (12)	10 (19)
Headache	15 (9)	3 (6)
Influenza	11 (7)	1 (2)
Back pain	11 (7)	1 (2)
Peripheral neuropathy	9 (6)	7 (13)
Nausea	8 (5)	2 (4)
Vulvovaginal candidiasis	4 (3)	3 (6)
Abdominal pain	3 (2)	3 (6)

 2 AEs leading to study drug discontinuation: confusional state (E/C/F/TAF) and hepatitis (ATV+RTV+FTC/TDF)

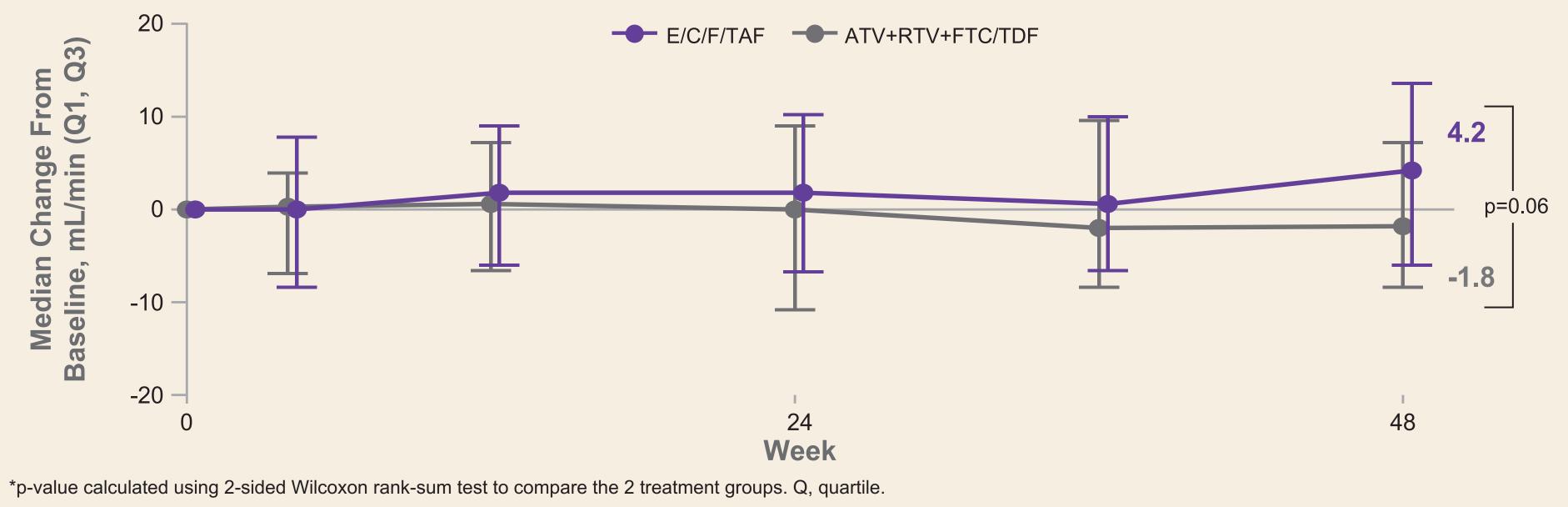
Grade 3 or 4 Laboratory Abnormalities

≥1% in Either Group, n (%)	E/C/F/TAF n=158	ATV+RTV+FTC/TDF n=53
Any Grade 3 or 4 laboratory abnormalities	41 (26)	21 (40)
Hematuria	17 (11)	5 (9)
LDL	13 (8)	1 (2)
Hypercholesterolemia	7 (5)	1 (2)
ALT	3 (2)	0
GGT	3 (2)	1 (2)
Hyperglycemia	3 (2)	1 (2)
Neutropenia	2 (1)	1 (2)
AST	2 (1)	1 (2)
Creatine kinase	2 (1)	0
Amylase	1 (<1)	1 (2)
Glycosuria	1 (<1)	1 (2)
Hyperbilirubinemia	0	15 (28)
Proteinuria	0	1 (2)

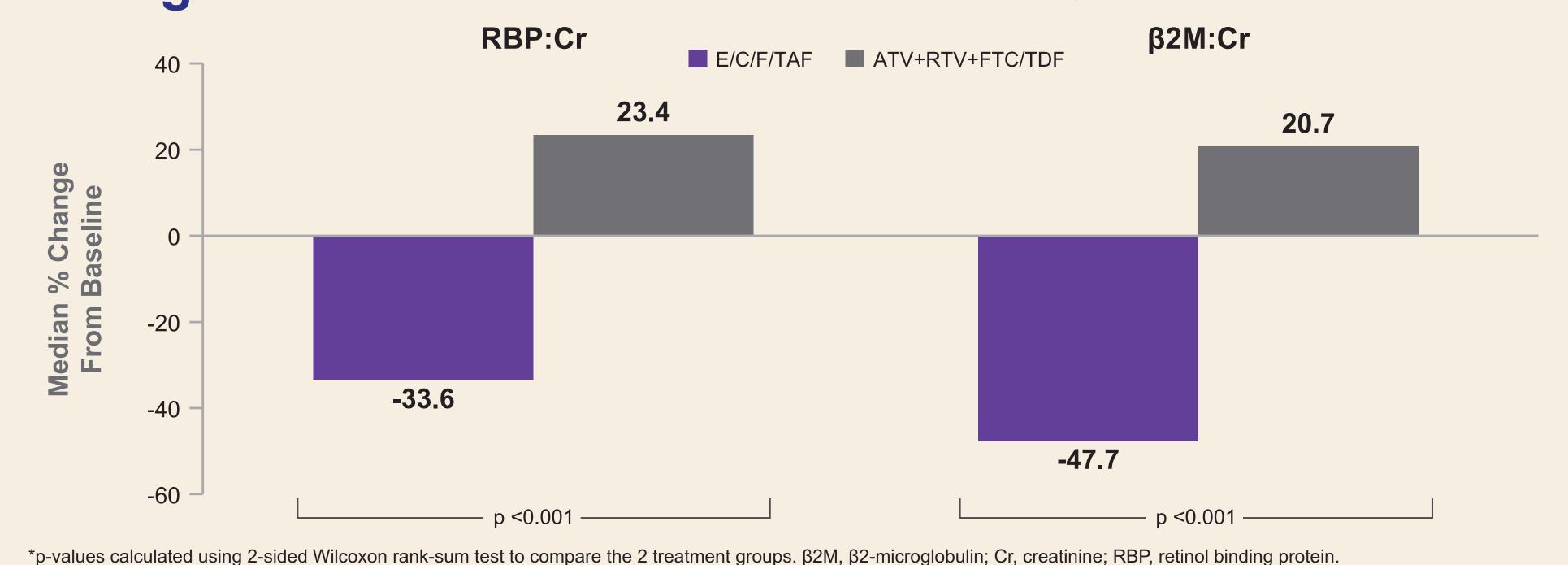
Changes in Spine and Hip BMD Through Week 48*



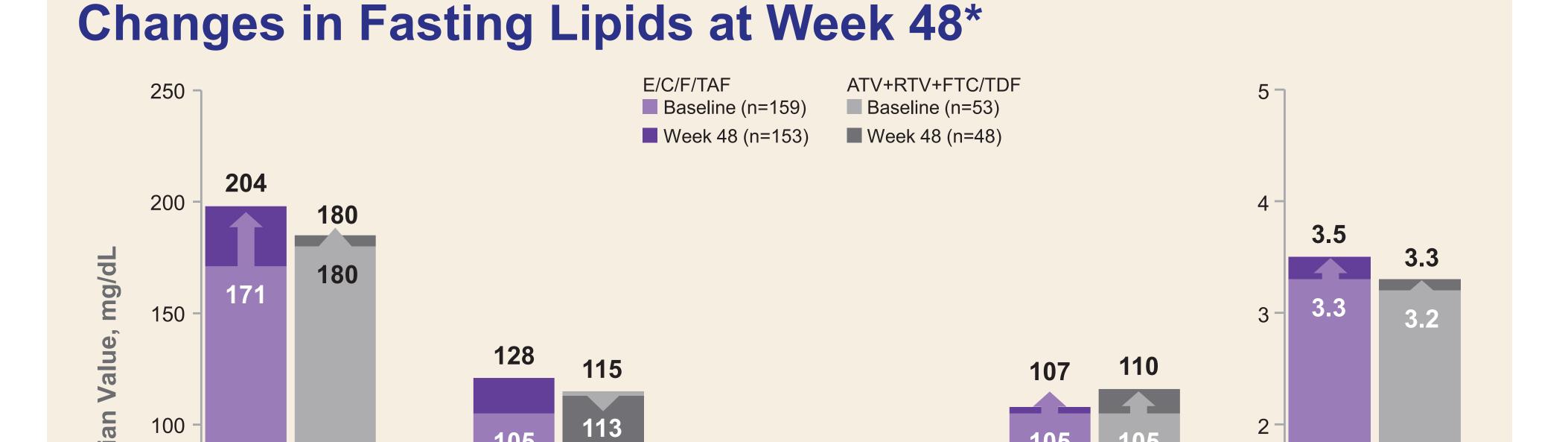
Change in eGFR Through Week 48*



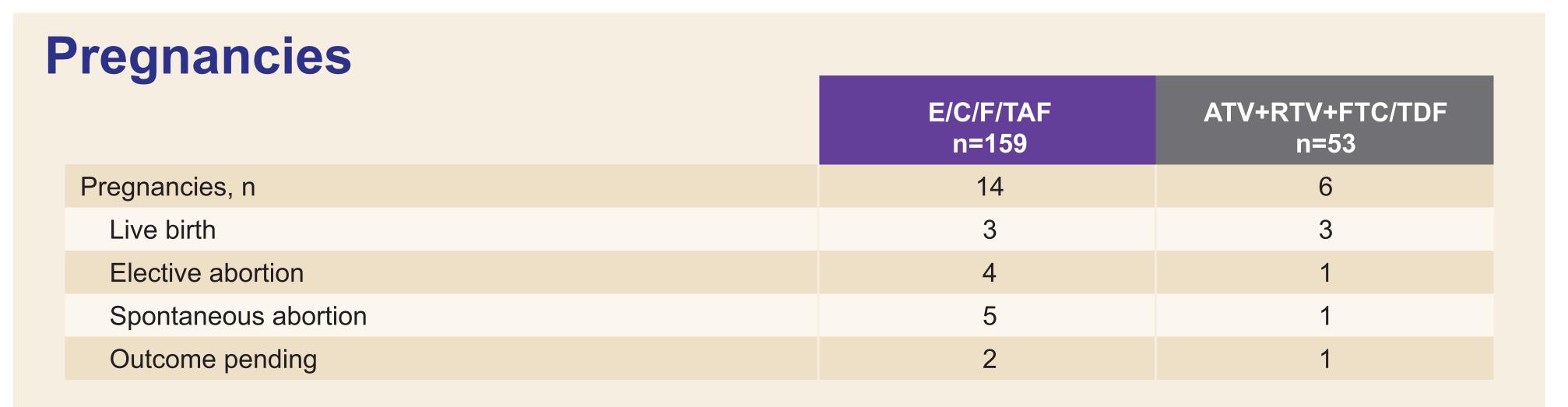
Change in Tubular Proteinuria at Week 48*



No cases of proximal renal tubulopathy were reported in either arm



◆ Rates of initiation of lipid-modifying agents: E/C/F/TAF, 1%; ATV+RTV+ FTC/TDF, 0%



Conclusions

- ◆ Women switching to E/C/F/TAF from a protease inhibitor—based regimen maintained high rates of virologic suppression (94%) through 48 wk
- E/C/F/TAF was generally well tolerated, and safety and discontinuation rates due to AEs were comparable between treatment groups
- E/C/F/TAF compared with ATV+RTV+FTC/TDF demonstrated statistically significant improvements in:
- Spine BMD (p < 0.001)
- Tubular proteinuria (p <0.001)
- No difference in TC/HDL ratio between groups

References

1. Squires K, et al. Lancet HIV 2016;3:e410-20; 2. Mills A, et al. 2015. Lancet Infect Dis 2016;16:43-52; 3. Sax PE, et al. Lancet 2015;385:2606-15; 4. Günthard HE, et al. JAMA 2016;316:191-210; 5. Panel on Antiretroviral Guidelines for Adults and Adolescents. US Dept of Health and Human Services: Washington, DC; Jan 28, 2016: http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf.

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